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Editorial

Femoral Neuropathic Pain After Cardiac Catheterization: An Under-diagnosed but Treatable Condition

YiLi Zhou, Heather Shaw and Sara Webber

Femoral nerve damage, or femoral neuropathy after cardiac catheterization or stent placement could be a very painful [1], but sometimes not well recognized condition. The authors had two cases within the last twelve months.

Case 1

The patient was a 65-year-old female with left leg pain after a femoral stent placed on Aug 1, 2012. Patient reported severe burning pain upon waking up from surgery in her left groin, hip and buttock area, radiating down through the medial side of the left leg. She noted increased pain with standing and walking and had difficulty sleeping due to severe pain. She consulted multiple physicians, including her cardiologist who placed the stent, her family doctor and a neurologist without clear diagnosis and effective treatment. CT of abdomen and left leg were all negative. The patient was told her leg pain was due to degenerative changes in the back. She saw two chiropractors and did five weeks of physical therapy and chiropractic treatment without improvement. She was given a myriad of medications including amitriptyline, hydrocodone, oxycodone, tramadol, and gabapentin to which she experienced serious side effects and had no pain improvement.

Patient presented to our office 4 months after femoral stent placement with a daily VAS pain score of 10. She felt miserable and hopeless. She could only sleep 3 hours a night because of severe pain. On physical examination she was crying and found to have decreased sensation to pinprick throughout the anterior-medial aspect of the left leg in the femoral nerve distribution and diminished patellar reflex on the left leg. Based on history and physical examination, a clinical diagnosis of femoral neuropathy after stent placement was made. The patient was given pregabalin 50 mg BID with an increase to 100 mg BID over 2 weeks. In one-month follow up visit, she indicated improvement in her pain but her pain was still not gone. The dose of pregabalin was increased to 150 mg BID. In two-month follow up visit, the patient was completely pain free. She was also able to sleep on average 7 hours per night and walking normally. The patient is extremely happy with the results of the treatment.

Case 2

Case 2 was a 78 year-old female with right thigh pain, which began four days after a femoral artery cardiac catheterization. She described her pain as burning, throbbing and cramping. The pain started from the right groin area, radiating down to the front thigh and medially to the level of the knee. This pain fluctuated in intensity. It was exacerbated by walking, and was somewhat alleviated by sitting and lying flat on her back. The patient has tried acetaminophen and tramadol without pain relief.

The patient was referred to our pain clinic approximately 5 months after the onset of her pain. She was very depressed and felt hopeless, because she visited many physicians for her leg pain without clear diagnosis and treatment. Her cardiologist told her nothing was wrong at the site where the catheter was inserted. Her family doctor and neurologist could not tell her what the cause of her pain was. On physical examination she was found to have diminished right knee reflex with decreased sensation to pinprick in the pattern of the right femoral nerve enervation including the anterior right thigh and the medial right lower leg. A clinical diagnosis of femoral neuropathy was made, which was further supported by an EMG/NCV study. The compound muscle action potential (CMAP) and sensory nerve action potential (SNAP) were diminished for right femoral nerve and right saphenous nerve respectively.

The patient started on pregabalin 75mg BID. A follow up telephone conversation with the patient after 1 week of treatment with pregabalin revealed significant improvement in the patient's pain. At a follow up visit one month after beginning of the treatment, the patient's pain was completely resolved.

Femoral neuropathic pain after cardiac catheterization or stent is not uncommon. Kent et al followed a group 9585 cardiac catheterizations and reported incidence of 0.21% of peripheral neuropathy, involving the femoral, obturator, or lateral femoral cutaneous nerves [2]. The clinical symptoms of femoral neuropathy after cardiac catheterization include severe pain, numbness in the anterior medial thigh and medial calf, and

occasionally motor deficits [3]. Direct damage to the femoral nerve, hematoma in the iliacus muscle caused by heparin therapy following catheterization or PTCA [4] [5] [6], use of prolonged digital pressure for post-procedural hemostasis[7] and femoral artery pseudoaneurysm [8] all have been implicated in the development of femoral neuropathy and pain after the procedures.

Diagnosis is not difficult. As mentioned above, history of severe pain in the femoral nerve distribution following the cardiac catheterization may suggest the diagnosis. Careful bedside neurologic examination may reveal decreased sensation to pin prick in the anterior medial thigh and medial calf. EMG/NCV test may further confirm the existence of femoral nerve damage. CT or MRI may found retroperitoneal or iliacus hematoma. However it may often be negative, in case there is no hematoma or aneurysm.

Techniques such as minimizing the procedural time, avoiding injury to the vessels and maintaining optimal posture of patient's thigh by limiting abduction and external rotation of hip[7] and avoiding trauma to the iliacus muscle during catheterization can all be utilized to prevent the complications.

Anti-neuropathic pain medications should be used for this condition. Hsin and Hwang[3] reported a case of femoral neuropathic pain after cardiac catheterization, which was successfully treated by a multimodal treatment program including duloxetine. A case of percutaneous approach for femoral nerve stimulation also has been reported to relieve the pain due to femoral nerve damage after cardiac catheterization [9]. In case, a retroperitoneal hematoma or pseudoaneurysm is identified as the cause of the femoral neuropathy, surgical removal of the hematoma or repair of the pseudoaneurysm may be a choice of treatment [8] [10].

Pregabaline, a calcium channel modulator, has been approved by the US FDA for the treatment of multiple neuropathic pain conditions including peripheral diabetic neuropathy, post herpatic neuralgia, central pain due to spinal cord injury[11] and fibromyalgia. Several other studies also reported clinical efficacy of pregabaline for the treatment of other neuropathic pain conditions such as central pain syndrome after stroke [12], neuropathic cancer pain [13] and post-traumatic peripheral neuropathic pain (PTNP)[14]. To the knowledge of the authors, this is the first report of pregabalin for the treatment of neuropathic pain due to femoral nerve damage.

In conclusion, femoral neuropathic pain after cardiac catheterization or stent could be very painful and debilitating. However, this condition is still not well recognized. Both of the two patients in the report had an acute onset of pain after the procedures with pain limited to the femoral nerve distribution. Physical examination findings were typical. However, both of them had consulted many clinicians including the cardiologists, family physicians, neurologists, and chiropractors and physical therapists over the several months period after the onset of their symptoms without being able to reach a diagnosis. Thus an increased attention may be needed to evaluate the possibility of femoral neuropathic pain, if a patient developed severe leg pain after femoral arterial cardiac catheterization, especially when CT or MRI is negative. Treatment with anti-neuropathic pain medication, such as pregabalin may be helpful, even though more studies are needed.

Competing Interests
None Declared
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Research Article

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Risk factors for candida blood stream infection in medical ICU and role of colonization – A retrospective study

Setu Patolia, Eneh Kennedy, Mehjabin Zahir, Swati Patolia, Neerja Gulati, Dharani Narendra, Rakesh Vadde, Saurav Pokharel, Frances M. Schmidt, Danilo Enriquez and Joseph Quist

Abstract

Candida blood stream infection (candidaemia) is one of the most serious hospital acquired infections with high morbidity and mortality rates in the Intensive Care Unit (ICU). A number of risk factors have been identified in a variety of studies. ICU patients are frequently colonised with Candida species. The role of Candida colonisation as a causal factor for candidaemia remains controversial. Our objective for the study was to evaluate the risk factors for candidaemia and to evaluate the role of colonisation to predict candidaemia. We evaluated a total of 1483 patients aged over 18 years who stayed in ICU for more than 7 days. We collected various data about risk factors for candidaemia. A total of 56 patients (3.77%) developed candidaemia. We collected demographic and risk factor data including Candida colonisation of the urinary and respiratory tract. Binary logistic regression with forward likelihood ratio method model was used to analyse these risk factors. In our study, total parenteral nutrition (odds ratio (OR)- 3.274, 95% confidence interval (CI) 1.263-8.486), presence of central venous line (OR- 1.895, CI 1.032-3.478), previous or current antibiotic use (OR 3.268, CI 1.532-6.972), respiratory tract colonisation (OR 2.150, CI 1.078-4.289) and urinary tract colonisation (OR 3.508, CI 1.926-6.388) were significant risk factors for Candida blood stream infection (BSI). Based on the model, we calculated the candidaemia risk score and based on the receiver operative curve analysis, a score more than 2 would be associated with a higher risk of candidaemia. Candida species isolated in the respiratory tract or urine were similar to that found in Candida BSI (Kappa coefficient for agreement of 0.83 and 0.47 respectively). So, it can be concluded that Candida colonisation of the respiratory tract and/or urine is a significant risk factor for Candida BSI along with the other risk factors.

Keywords: Candidemia, Risk factors, Central Venous line, Colonization.

Abbreviations: ICU- intensive care unit,OR- odds ratio,CI- confidence interval,BSI- blood stream infection,HIV- Human immunodeficiency virus,IDSA- Infectious Disease Society of America,COPD- Chronic obstructive pulmonary disease,DM- Diabetes Mellitus,ESRD- End stage renal disease, TPN- Total parenteral nutrition.

Introduction:

Candida species is a leading cause of nosocomial infections and the most common fungal infection in intensive care units. Candida infection ranges from invasive candidal disease to blood stream infections (candidaemia). The incidence of Candida infection has been rising over the past two decades, particularly with the use of immunosuppressive drugs for cancer and HIV[1,2,3] , and most of these infections occur in ICU settings.[4] Candida infection is associated with high mortality and morbidity. Studies have shown that mortality attributable to candidaemia ranges from 5 to 71% depending on the study.[5,6,7]Candidaemia is also associated with longer length of hospital stay and higher cost of care.

Early recognition of Candida BSI has been associated with improved outcome. Candida sepsis should be suspected in a patient who fails to improve and has multiple risk factors for invasive and bloodstream Candida infection. A variety of risk factors identified for candidaemia include previous use of antibiotics, sepsis, immunosupression, total parenteral nutrition, central venous line, surgery, malignancy and neutropaenia. Patients admitted to ICU are frequently colonised with Candida species. The role of colonisation in Candida blood stream infection and invasive candidal disease has always been debated. Few studies support the use of presumptive antifungal treatment in ICU based on colonisation and number of sites colonised by Candida. The NEMIS study has raised doubt about this approach of presumptive treatment. The Infectious Disease Society of America (IDSA) 2009 guidelines identify Candida colonisation as one of the risk factors for invasive candidiasis, but warn about the low positive predictive value of the level of Candida colonisation. [8] We conducted a retrospective cohort study in our medical ICU to identify risk factors for Candida blood stream infections including the role of Candida colonisation.

Hospital and Definitions:

This study was conducted at Interfaith Medical Center, Brooklyn, New York. It is a 280 bed community hospital with 13 medical ICU beds. A case of nosocomial Candida blood stream infection was defined as a growth of Candida Species in a blood culture drawn after 48 hours of admission. Cultures in our hospital are routinely done by the Bactec Method – aerobic and anaerobic cultures. Cultures are usually kept for 5 days at our facility and if yeast growth is identified, then species identification is done. In our ICU it is routine practice to do endotracheal culture and urine culture for all patients who are on mechanical ventilator supports and failing to improve. In

patients who are not mechanically ventilated, it is routine practice to send sputum culture and nasal swabs to identify MRSA colonisation.

Study Design:

This study was a retrospective cohort study. We retrospectively reviewed all patients' charts admitted to our medical ICU from 2000 to 2010 which stayed in the ICU for more than 7 days, irrespective of their diagnosis. Data were collected for demographics – age and sex. Data were also collected for risk factors for candidaemia – co-morbidities (HIV, cancer, COPD, diabetes mellitus, end-stage renal failure (ESRF)), presence or absence of sepsis, current or previous use of antibiotics, presence of central venous lines, steroid use during ICU stay, requirement of vasopressor support and use of total parenteral nutrition (TPN). Culture results for Candida including species identification were obtained for blood, urine and endotracheal aspirates.

Statistical Methods:

Patients were divided in two groups based on presence or absence of Candida BSI. Demographic data and risk factors were analysed using the chi square test to look at the difference between the two groups. Endotracheal aspirates and sputum cultures were combined to create a group with Candida respiratory tract colonisation. Binary logistic regression with forward likelihood ratio method was used to create models. Different models were generated for risk factors. Interactions between antibiotic use, steroid use, vasopressor support and sepsis were analysed in different models. Interactions between urine cultures and endotracheal aspirates/sputum cultures were also analysed by a different model. The model with the lowest Akaike information criterion (AIC) was chosen as the final model. The candidaemia risk score was calculated based on this final model to predict the risk of Candida BSI. Receiver operating curve (ROC) analysis was used to select the best cut-off value for the candidaemia risk score. Candida species in urine and endotracheal aspirates were compared with Candida species in blood culture using the kappa test. Data were analysed using SPSS statistical analysis software version 18.

Study Results:

A total of 1483 patients were included in the study. 56 patients (3.77%) had a blood culture positive for Candida species. Table 1 demonstrates demographic characteristics of the study population. There were no significant differences in the both groups for age, sex, diabetes mellitus, COPD, HIV, cancer and ESRF. As demonstrated in the table, 82.1% of patients in candidaemia groups recently used or were taking antibiotics as compared to 39.6% of patients in groups with no candidaemia. The P value was significant for this difference. Similarly, 71.4% of patients in the group with candidaemia had sepsis as compared to 30.6% in the other group with a P value of 0.000. Use of vasopressor (severe septic shock) was different between two groups – 23.2% and 10.1%, P value of 0.004. Steroid use, central lines and total parenteral nutrition use was higher in the candidaemia group as compared to the group without candidaemia. Similarly the rate of positive Candida cultures in urine and endotracheal aspirates was higher in the candidaemia group as compared to the group without.

Table 1: Demographic characteristic of study population

Characteristic	Candidaemia (total 56) N (% of candidaemia)	No candidaemia (total 1427) N (% of no candidaemia)	Chi Square
Age >65 years	34 (60.7%)	676(47.40%)	0.06
Male sex	27 (48.2%)	694(48.6%)	0.530
Diabetes mellitus	22 (39.3%)	506(35.5%)	0.325
COPD	1(1.8%)	75(5.3%)	0.206
HIV	9 (16.1%)	253(17.7%)	0.458
Cancer	4(7.1%)	99(6.9%)	
ESRF	11(19.6%)	251(17.6%)	0.401
Previous or current antibiotic use	46 (82.1%)	565(39.6%)	0.00
Sepsis	40(71.4%)	436(30.6%)	0.000
Vasopressor support (Septic shock)	13(23.2%)	144(10.1%)	0.004
Steroid use	27(48.2%)	431(30.2%)	0.004
Central line	30(53.6%)	267(18.7%)	0.000
Total parenteral nutrition	7(12.5%)	29(2.0%)	0.000
Candida in endotracheal aspirate/sputum culture	13(23.2%)	112(7.8%)	0.000
Candida in urine culture	34(60.7%)	262(18.4%)	0.000

Table 2 shows that 57.1% of Candida BSI were caused by C. Albicans, 30.4% by C. Glabrata and 12.5% by C. Parapsilosis. This incidence rate of species is similar to that found in other studies. Table 3 shows the two models with the lowest AIC value. The only difference between these two models was antibiotic use- previous or current use of antibiotics compared to current use of antibiotic in sepsis. Table 4 shows that when multifocal site positivity (urine and endotracheal culture) were used in the model, the AIC value increased significantly. This means that when multifocal sites were used in place of individual sites for the model, good amounts of information were lost and this model did not have good predictive value as compared to the model where individual sites are used for prediction of candidaemia. The model with lowest AIC was chosen as the final model. Binary logistic regression analysis with forward conditional analysis showed that only TPN, central venous line, previous or current antibiotic use,

endotracheal aspirate culture positivity for Candida species and urine culture positive for Candida species were included in a statistical significant model. The final model had a P value of 0.000. Odds ratio with 95% confidence intervals and respective P values for all these risk factors are shown in Table 5. Age greater than 65 years, sex, sepsis or septic shock, co-morbidities and steroid use were not significant risk factors for candidaemia.

From this model, the candidaemia risk score calculated would be: Candidaemia risk score = 1.184 for previous or current antibiotic use + 0.639 for presence of central venous line + 1.186 for total parenteral nutrition + 0.760 for positive endotracheal culture for Candida + 1.255 for positive urine culture for Candida.

Table 6 shows the relationship between the Candida strain identified in endotracheal/sputum culture to that in blood culture. Similarly, Table 7 shows the relationship between the Candida strain identified in urine culture and that in blood culture. Strains identified in endotracheal aspirate culture had a very high value for the Kappa test and urine culture had a moderate value for agreement by the Kappa test. Thus, it can be inferred that Candida strain identified in blood culture was very similar to that identified in urine or endotracheal culture.

Table 2: Candida strains responsible for Candida blood stream infection

Species in the blood culture	Number (%)
Candida Albicans	32(57.1%)
Candida Glabrata	17 (30.4%)
Candida Parapsilosis	7 (12.5%)

Table 3: Models with lowest two AIC

Variables	-2 log likelihood	AIC
Previous or current antibiotic use CVP line Total parenteral nutrition Endotracheal culture Urine culture	394.822	406.822
CVP line Total parenteral nutrition Endotracheal culture Urine culture Current antibiotic use in sepsis	395.730	407.73

Table 4: Model with 2 sites positive for Candida

Variables	-2 log likelihood	AIC
Sepsis CVP line Total parenteral nutrition Endotracheal and urine culture	407.920	417.92

Table 5: Odds ratio with 95% confidence interval for risk factors for candidaemia

Effect	Co efficient (•)	Odds ratio	95 % Confidence limit		P value
			Lower	Upper	
TPN	1.186	3.274	1.263	8.486	0.015
CVP line	0.639	1.895	1.032	3.478	0.039
Antibiotic Use	1.184	3.268	1.532	6.972	0.002
Endotracheal/ sputum culture	0.760	2.150	1.078	4.289	0.030
Urine	1.255	3.508	1.926	6.388	0.000

Table 6: Endotracheal aspirate culture in candidaemic patients

Endotracheal/Sputum Culture	Blood Culture		Kappa Test For Agreement
	C. Albicans	C. Glabrata	
C. Albicans	9	0	0.83
C.Glabrata	0	3	
C. Tropicalis	0	1	

Table 7: Urine cultures in candidaemic patients

Urine culture	Blood culture			Kappa Test for the agreement
	C. Albicans	C. Glabrata	C. Tropicalis	
C. Albicans	15	5	1	0.47
C. Glabrata	1	10	0	
C. Krusei	1	1	0	

Discussion

Candida is the most common nosocomial fungal infection in the ICU. Candidaemia accounts for approximately 5-8% of nosocomial BSI in the hospitals in the US.[9,10,11] It accounts for approximately 50-75% of the cases of invasive fungal infection in the ICU[12,13] and its rate varies from 0.2-1.73 per 1000 patient days.[9,14,15] In a study done by Theoklis et al., candidaemia was associated with a mean 10.1 day increase in length of stay and a mean $39,331 increase in hospital charges.[16] A study of 1,765 patients in Europe found that Candida colonisation was associated with increased hospital length of stay and increase in cost of care by 8000 EUR.[17] ICU patients are at increased risk of infection because of their underlying illness requiring ICU care, immunosuppressant use, invasive or surgical procedures and nosocomial transfer of infections. A number of risk factors have been identified in different studies. In a matched case-control trial, previous use of antibiotic therapy, Candida isolated at other sites, haemodialysis and presence of a Hickman catheter were associated with increased risk of candidaemia.[13] Similarly age of more than 65

years, steroid use, leucocytosis and prolonged ICU stays were risk factors for Candida BSI in 130 cases.[18] Surgery, steroids, chemotherapy and neutropaenia with malignancy are the other identified risk factors.[19]

Candida BSI has a very high mortality rate. The attributable mortality varies from 5-71% in different studies.[5,12,16,20] Even with treatment, there is high mortality as demonstrated in a study by Oude Lashof et al where out of 180 patients treated for candidaemia, 33% died during treatment and 55% completed treatment without complications.[21] Risk factors for increased mortality in patients receiving antifungal treatment are delayed Candida antifungal treatment or inadequate dosing.[22] Multivariate analysis of 157 patients with Candida BSI, APACHE II score, prior antibiotic treatment and delay in antifungal treatment were independent risk factors for mortality with odds ratio of 1.24, 4.05 and 2.09, respectively.[23]Delayed treatment is also associated with increased fluconazole resistance as compared to early treatment and preventive treatment.[24] Inadequate antifungal medication dose and retention of central venous catheters were also associated with increased mortality in a study of 245 Candida BSI, with adjusted odds ratios of 9.22 and 6.21, respectively.[25,26]

Candida albicans accounts for 38.8-79.4 % of the cases of Candida BSI. C. Glabrata is responsible for 20-25% of cases of candidaemia and C. tropicalis is responsible for less than 10% of cases of candidaemia in the US.[9,20] ICU patients are frequently colonised with different Candida species. Candida colonisation can be from either endogenous or exogenous sources. Candida colonisation rates vary with the site- tracheal secretion (36%), throat swabs (27%), urine (25%) and stool (11%).[27] Candida colonisation increases with the duration of the stay, use of urinary catheters and use of antibiotics.[28,29,30]

The role of Candida colonisation in Candida BSI is frequently debated. Some studies have suggested that Candida colonisation of one or more anatomical sites are associated with increased risk of candidaemia.[31,32,33,34] Typically, 84-94% of the patients developed candidaemia within a mean time of 5- 8 days after colonisation according to two studies.[35,36] In another study, only 25.5% of colonised patients developed candidaemia.[37] Similarity between strain identified in blood culture and that identified at various colonising sites was observed in one study.[38] Candida colonisation by exogenously acquired species has also been implicated as a cause of candidaemia.[39] In one study, 18-40% of cases of candidaemia were associated with clustering defined as "isolation of 2 or more strain with genotype that had more than 90% genetic relatedness in the same hospital within 90 days." [40] Similar correlations for clusters are also noted for C. tropicalis candiduria[41] and for C. Parapsilopsis.[42] In a prospective study of 29 surgical ICU patients colonised with Candida, the APACHE II score, length of previous antibiotic therapy and intensity of Candida colonisation was associated with a significant risk of candidaemia. The Candida colonisation index calculated by non-blood body sites colonised by Candida over the total number of distinct sites tested for patients, was associated with a 100% positive and negative predictive value of candidaemia.[29] Other studies do not support Candida colonisation as a risk factor for candidaemia. In a case-control study of trauma patients, only total parenteral nutrition was associated with an increased risk of candidaemia. Candida colonisation, steroid use, use of central venous catheters, APACHE II score, mechanical ventilation for more than 3 days, number and duration of antibiotics, haemodialysis, gastrointestinal perforation and number of units of blood transfused in first 24 hours of surgery. were not significant risk factors for candidaemia.[43] NEMIS study found that in a surgical ICU, prior surgery, acute renal failure, total parenteral nutrition and triple lumen catheters were associated with increased risk of candidaemia; the relative risk for each risk factor being 7.3, 4.2, 3.6 and 5.4, respectively. Candida colonisation in urine, stool or both were not associated with increased risk of candidaemia.[15]

The effect of Candida colonisation of the respiratory tract on candidaemia and on mortality and morbidity is unclear. In a retrospective study of 639 patients, Candida respiratory tract colonisation was associated with increased hospital mortality (relative risk of 1.63) and increased length of stay (median increase of 21 days).[30] In a study of 803 patients by Azoulay et al., respiratory tract colonisation was associated with prolonged ICU and hospital stays. These colonised patients were at increased risk of ventilator-associated Pseudomonas pneumonia, with an odds ratio of 2.22.[44] However, in a postmortem study of 25 non-neutropaenic mechanically ventilated patients, 40% of the patients were colonised with Candida, but only 8% had Candida pneumonia.[45,46] Jordi et al. found that out of 37 patients, definite or possible colonisation was found in 89% of patients and only 5% of cases were defined as Candida BSI.[47].The effect of candiduria is also ill defined. Candida colonisation in urine has been implicated as a risk factor in certain studies. In a study done by Bross J et al., central lines, bladder catheters, 2 or more antibiotics, azotaemia, transfer from another hospital, diarrhoea and candiduria were significant risk factors for candidaemia. Candiduria had an odds ratio of 27 for development of candidaemia.[48] Similar findings about candiduria were noted by Alvarez-Lerma et al.[49]

IDSA recommends starting empirical antifungal treatment for high risk neutropaenic patients who fail to improve on antibiotics after 4 days. Recommendation to start empirical antifungal therapy in low-risk neutropaenic patients and non-neutropaenic patients are not made by IDSA because of low risk of candidaemia.[8] However, early detection of Candida BSI is vital because of increased mortality associated with delayed antifungal treatment and failure to remove central venous lines. Early detection of Candida BSI in a colonised patient can be facilitated by using a score based on the risk factors.[50,51]Similarly, b-D glucan assays can be used in patient

colonised with Candida, to determine Candida BSI and need for antifungal treatment.[52] Combined used of such risk factor identification systems and b-D glucan assays will help to detect candidaemia in earlier stages and will decrease mortality. Our study suggests that total parenteral nutrition, previous or current antibiotic use, central lines, candiduria and respiratory tract colonisation are risk factors for Candida BSI. With the help of our candidaemia risk score system, a score of more than 2 is associated with a higher risk of Candida BSI. This risk factor scoring system along with b-D glucan assays can be used to detect Candida BSI in earlier stages.

Conclusion:

Our study suggests that urine or respiratory tract colonisation is associated with an increased risk of Candida BSI, along with total parenteral nutrition, central venous lines and previous or current antibiotic use. We identified a scoring system which can be used along with a b-D glucan assay to detect candidaemia earlier.

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Competing Interests
None
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Research Article

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Switching from traditional to automatic sphygmomanometer increases opportunistic detection of atrial fibrillation in hypertensive patients

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Abstract
Routine pulse palpation is one of the screening method to detect asymptomatic atrial fibrillation (AF) in clinical practice. Recently new automatic sphygmomanometers with embedded algorhytms to detect irregular heart beat and possible AF have been commercialized. Whether the switch from the traditional sphygmomanometer to these devices modifies AF detection in usual care is unknown. 12294 patients of 30 GPs members of the Italian College of General practitioners working in Bologna with recorded diagnosis of Hypertension and BP recording were extracted before and after the adoption and use of an automatic device. 14 other GPs who were using a traditional device (Riva-Rocci or aneroid sphygmomanometer), volunteered to provide the same data extraction from their personal database. Heart rhythm should be evaluated while measuring BP with usual devices. This information may be lost with with a few automatic devices, therefore the use of automatic devices with algorithms which can detect possible AF is an appealing choice. Our data show that switching from the traditional device to an automatic device with algorithm for irregular beat detection increases the identification rate of previously unknown AF in hypertensive population.
Keywords: atrial fibrillation, hypertensive patients
Abbreviations: BP - Blood Pressure, AF - Atrial Fibrillation, CE - European Community

Introduction

Routine pulse palpation is the recommended screening method to detect asymptomatic atrial fibrillation (AF) in clinical practice[1]. Since this is part of the blood pressure (BP) measurement technique when using the Riva Rocci (mercury) device or the aneroid device, most patients are evaluated for rhythm irregularity while checking their BP, and, if pulse isn't palpated, heart rhythm can be evaluated through auscultation of Koroktoff' sounds. According to the European Community law (2007/51 CE; 2007 September 27th), the mercury sphygmomanometers should not be sold any more, therefore aneroid or automatic devices will replace them in a few years. Recently new devices with embedded algorithms to detect irregular heart beat and possible AF have been commercialised. Whether the switch from Riva-Rocci or aneroid sphygmomanometer to this device will affect detection of AF in usual care is unknown. We explored this issue using a retrospective, naturalistic observation of a group of GPs who abandoned the "old" Riva-Rocci or the aneroid sphygmomanometer and adopted this new device.

Methods

In September 2011 the members of the Italian College of General Practitioners based in Bologna (a medium size city in Central Italy) decided to standardize their office BP measurements. They received an unconditional grant for 30 automatic upper arm blood pressure monitors (Microlife- Afib ®) to be used in office by the GP him/herself. This device embeds an algorithm that calculates the irregularity index (standard deviation divided by mean) based on interval times between heartbeats; if the irregularity index is above a certain threshold value, atrial fibrillation is likely to be present and an atrial fibrillation icon is displayed on the screen. The 30 general practitioners who received the device agreed to a later proposal to examine their database to evaluate detection of new AF patients. They all had the same professional software (Millewin®), and used an automatic extraction. All the patients with recorded diagnosis of hypertension were identified, then BP recording and AF diagnosis were extracted before (365 days preceding the use of Microlife) and after (4 months since starting the use of Microlife) the adoption of the automatic devices. The proposal to examine AF detection was made after four months after they received the devices, therefore the GPs weren't aware of this study during the usual professional activity. This study was also neither planned nor known by Microlife. Fourteen other GPs, who were using the traditional device, volunteered to provide the same data extraction from their personal database.

Results

The 30 participants GPs cared for 48,184 individuals, 12,294 (25.5%) of whom had hypertension (mean age 69.9±13.4). The 16 control GPs cared for 23,218 patients, 5,757 (24.8%) with hypertension (mean age 69.7±13.6). The four-monthly AF detection rate for the original group and the control group is reported in table 1. All the new detected AF were then confirmed on ECG. Statistical analysis was made with the chi-square (χ^2) test.

Table 1: Four-monthly AF detection rate in the original GP group and in the control group*

N° GPs and (n° hypertensive patients)	Detected AF % and (n° pts) October 2010- January 2011	Detected AF % and (n° pts) February 2011- May 2011	Detected AF % and (n° pts) June 2011- September 2011	Detected AF % and (n° pts) October 2011-January 2012
30 (12294) - original group	0.37% (46) *	0.3% (39) *	0.37% (45) *	0.63% (77) **
16 (5757) - controls	0.35% (20) ‡	0.45% (26) ‡	0.56% (32) ‡	0.33% (19) ‡‡

*‡ Use of the traditional device: original group vs controls: p NS ($\chi^2 = 3.0421$, df 1)

** Use of the automatic device (other quarters use of traditional device)

**‡‡ Original group: use of the automatic device vs traditional device in AF detection: $p < 0.005$ ($\chi^2 = 9.487$, df 1)

Discussion

Atrial fibrillation can be difficult to diagnose as it is often asymptomatic and intermittent (paroxysmal). The irregularity of heart rhythm can be detected by palpation of the pulse. It may therefore be detected in patients who present with symptoms such as palpitations, dizziness, blackouts and breathlessness, but may also be an incidental finding in asymptomatic patients during routine examination. The diagnosis must be confirmed with an ECG, which should be performed in all patients, whether symptomatic or not, in whom atrial fibrillation is suspected due to the detection of an irregular pulse. Heart rhythm should be evaluated while measuring BP with traditional sphygmomanometers, while this information may be lost with automatic devices, therefore the use of automatic devices with algorithms which can detect possible AF is an appealing choice. The hypothesis that these devices are equal or superior to systematic pulse palpation is currently under investigation by NICE[2]. At the moment the consequences of switching from the classical Riva-Rocci devices to these new ones in usual care isn't known. The AF opportunistic screening in people aged $\geq$ 65 leads to a 1.63% detection rate while usual care has a detection rate of 1.04%, very similar to that observed in our hypertensive population (1.13%)[3]. Our data show that, at least in the short term, switching from the usual device to an automatic device with algorithm for irregular beat detection increases the identification rate of previously unknown AF in the hypertensive population. While waiting for a formal appraisal, GPs who wish or must renounce to their "old" Riva-Rocci can use this device implementing their "usual care" performances.

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Competing Interests
None declared
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Research Article

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Evaluation of the effect of magnesium vs. midazolam as adjunct to epidural bupivacaine in patients undergoing total knee replacement

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ABSTRACT

Background and objectives: Effective pain management is an important component of intraoperative and postsurgical care; it can prevent pain related clinical complications and improve the patient quality of life. This prospective, randomized, double-blind study was designed to evaluate analgesic efficacy of adding magnesium and midazolam to epidural bupivacaine in patients undergoing total knee replacement.

Methods: 120 patients ASA I and II, undergoing total knee replacement surgery were enrolled to receive either bupivacaine 0.5 % or bupivacaine 0.5 % plus magnesium sulphate 50 mg as an initial bolus dose followed by a continuous infusion of 10 mg/h or bupivacaine 0.5 % plus midazolam 0.05 mg/kg as intraoperative epidural analgesia. Postoperatively, all patients were equipped with a patient-controlled epidural analgesia device. Heart rate, mean arterial pressure, oxygen saturation, respiratory rate, pain assessment using a visual analogue scale (VAS),sedation score, patients' first analgesic requirement times and postoperative fentanyl consumption were recorded.

Results: The intraoperative VAS was significantly less in magnesium and midazolam groups. Whereas, in the first postoperative hour, VAS was significantly less in magnesium group. The postoperative rescue analgesia as well as the PCEA fentanyl consumption was significantly reduced in magnesium group.

Conclusion: Co-administration of epidural magnesium provides better intraoperative analgesia as well as analgesic-sparing effect on PCEA consumption without increasing the incidence of side-effects.

KEYWORDS: Epidural analgesia, Magnesium, midazolam

Introduction

The effective relief of pain is of paramount importance to anyone treating patients undergoing surgery. Not only does effective pain relief mean a smoother postoperative course with earlier discharge from hospital, but it may also reduce the onset of chronic pain syndromes[1]. Regional anaesthesia is a safe, inexpensive technique, with the advantage of prolonged postoperative pain relief. Research continues concerning different techniques and drugs that could prolong the duration of regional anaesthesia and postoperative pain relief with minimal side effects[1]. Magnesium is the fourth most plentiful cation in the body. It has antinociceptive effects in animal and human models of pain [2,3]. Previous studies had proved the efficacy of intrathecally administered magnesium in prolonging intrathecal opioid analgesia without increase in its side effectsThese effects have prompted the investigation of epidural magnesium as an adjuvant for postoperative analgesia[4].

Midazolam, a water-soluble benzodiazepine, has proved epidural analgesic effect in patients with postoperative wound painSerum concentrations of midazolam after an epidural administration were smaller than those producing sedative effects in humans[5].

The purpose of this study is to compare the analgesic efficacy of epidural magnesium to that of midazolam when administered with bupavacaine in patients undergoing total knee replacement.

Methods:

After obtaining the approval of the Hospital Research & Ethical Committee and patient's informed consent, 120 ASA I and II patients of both sexes, aged 50-70 years undergoing total knee replacement surgery were enrolled in this randomised, double blinded placebo-controlled study. Those who had renal, hepatic impairment, cardiac disease, spine deformity, neuropathy, coagulopathy or receiving anticoagulants for any cause were excluded from the study.

Prior to surgery, the epidural technique as well as the visual analogue scale (VAS; 0: no pain; 10: worst pain) and the patient-controlled epidural analgesia device (PCEA) were explained to the patients.

The protocol was similar for all patients. Patients received no premedication. Heart rate (HR), mean arterial pressure (MAP) and oxygen saturation (SpO2) were measured. Intravenous access had been established and an infusion of crystalloid commenced.

Before the induction of anaesthesia, an epidural catheter was placed at the L_3-L_4 or L_4-L_5 intervertebral space under local anaesthesia with the use of loss of resistance technique, and

correct position was confirmed by injection of lidocaine 2% (3ml) with epinephrine in concentration 1: 200 000. An epidural catheter was then inserted into the epidural space. The level to be blocked was up to TIn a double blind fashion and using a sealed envelope technique, patients were randomly allocated to one of three equal groups to receive via epidural catheter either 50 mg magnesium sulphate ($MgSO_4$) in 10 ml as an initial bolus dose followed by infusion of 10 mg/h (diluted in 10 ml saline) during the surgery (Mg group) or 10 ml saline followed by infusion of saline 10 ml/h during the surgery (control group) or 0.05 mg/kg of midazolam in 10 ml saline (Midazolam group) followed by infusion of saline 10 ml/h during the surgery. All patients received epidural bupivacaine 0.5 % in a dose of 1ml/segment .

Sensory block was assessed bilaterally by using loss of temperature sensation with an ice cube. Motor block was evaluated using a modified Bromage scale [6] (0: no motor block, 1: inability to raise extended legs, 2: inability to flex knees, 3: inability to flex ankle joints). During the course of operation, epidural bupivacaine 0.5% was given, if required, to achieve a block above T_{10}MAP, HR, SpO2 and respiratory rate (RR) were recorded before and after administration of the epidural medications and every 5 minutes till end of the surgery.

When surgery was complete, all patients received PCEA using a PCEA device (Infusomat® Space, B.Braun Space, Germany) containing fentanyl 2 µg/ml and bupivacaine 0.08% (0.8 mg/ml). The PCEA was programmed to administer a demand bolus dose of fentanyl 5 ml with no background infusion and lockout interval 20 min. The PCEA bolus volume was titrated according to analgesic effect or occurrence of side-effects. Patients' first analgesic requirement times were recorded. The time from the completion of the surgery until the time to first use of rescue medication by PCEA was defined as the time to first requirement for postoperative epidural analgesia. A resting pain score of ≤ 3 was considered as a satisfactory pain relief. If patients had inadequate analgesia, supplementary rescue analgesia with intramuscular pethidine 50 mg was available. MAP, HR, SpO2, RR and pain assessment using VAS were recorded at 30 minutes, and then at 1, 2, 4, 8, 12, and 24 h in the postoperative period. Epidural fentanyl consumption was also recorded at the same time points. Patients were discharged to the ward when all hemodynamic variables were stable with completely resolved motor block, satisfactory pain relief, and absence of nausea and vomiting. Adverse events related with the epidural drugs (sedation, respiratory depression, nausea, vomiting, prolonged motor block) and epidural catheter were recorded throughout the 24 h study period. Sedation was assessed with a five-point Scale: 1: Alert/active, 2: Upset/wary, 3: Relaxed, 4: Drowsy, 5: Asleep. A blinded anaesthesiologist who was unaware of the drug given, performed all assessments.

The results were analyzed using SPSS version 17. The number of subjects enrolled was based on a power calculation of finding a 20% change in HR and MAP. The α-error was assumed to be 0.05 and the type II error was set at 0.20. Numerical data are presented as median and 95% CI. The groups were compared with analysis of variances (ANOVA). The VAS pain scores were analyzed by Mann-Whitney U test. Categorical data were compared using the Chi square test. *P* value of 0.05 was used as the level of significance.

Results:

The three groups were comparable in respect of age, weight, height, sex, ASA status and duration of surgery (Table 1). Patients in all groups were comparable regarding intra or postoperative MAP, HR (Figure 1,2), RR and SpO2 during the observation period with no case of hemodynamic or respiratory instability. No difference in the quality of sensory and motor block before and during the surgery was noted between groups, and none of the patients required supplemental analgesia during surgery.

	Control	**Mg**	**Midazolam**
No of patients	40	40	40
Sex (female/male)	17/23	20/20	19/21
Age (yrs)	59.5 ± 6.1	61.1 ± 4.9	61.9 ± 3
ASA (I/II)	12/28	14/26	11/29
Weight (Kg)	69.7 ± 4.2	66.9 ± 6.7	70.1 ± 5.5
Height (cm)	165.9 ± 8.6	170.2 ± 4.5	167.2 ± 6.9
Duration of surgery (min)	144 ± 21	129 ± 30	130 ± 27
(median and 95% CI or number). No significant difference among groups			

Table 1: Demographic data and duration of surgery.

The intraoperative VAS was significantly less in magnesium and midazolam groups compared to control group after 15 and 30 minutes (Figure 3). Whereas the postoperative VAS was significantly less in the magnesium group in the first postoperative hour compared to other groups (Figure 4).

The time of request for postoperative analgesia was significantly delayed and the number of patients requesting postoperative analgesia was significantly reduced in magnesium group (Figure 5). Moreover, the pethidine rescue analgesia consumption and the total amount of postoperative fentanyl infusion were significantly reduced in magnesium group compared to other groups (Table 2) (Figure 5).

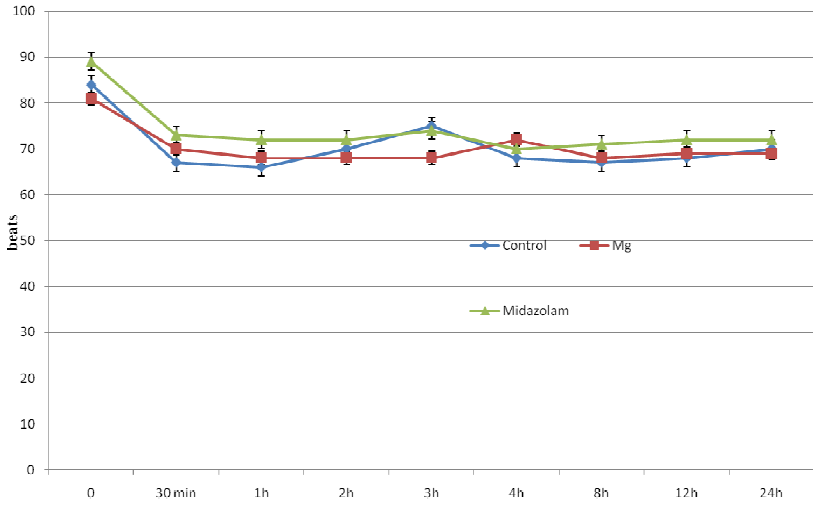

Figure 1: Heart rate changes (HR) of study groups. *Data are* mean±*SD*.

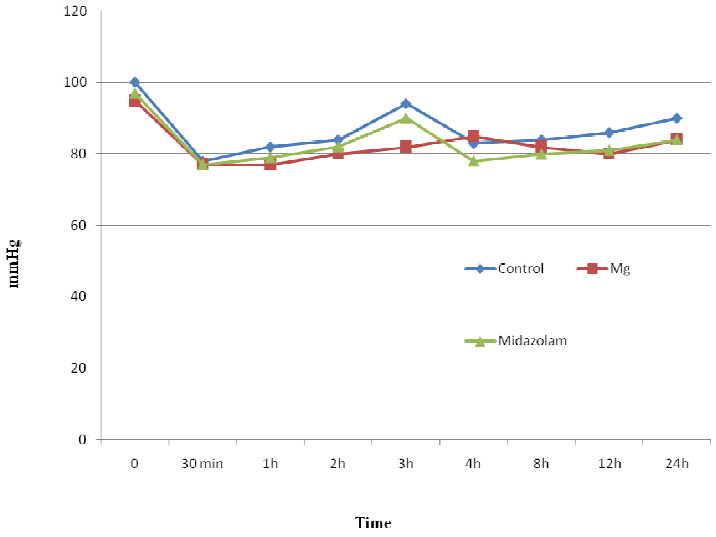

Figure 2: Mean Arterial pressure changes (MAP) of study groups. Data are mean±SD.

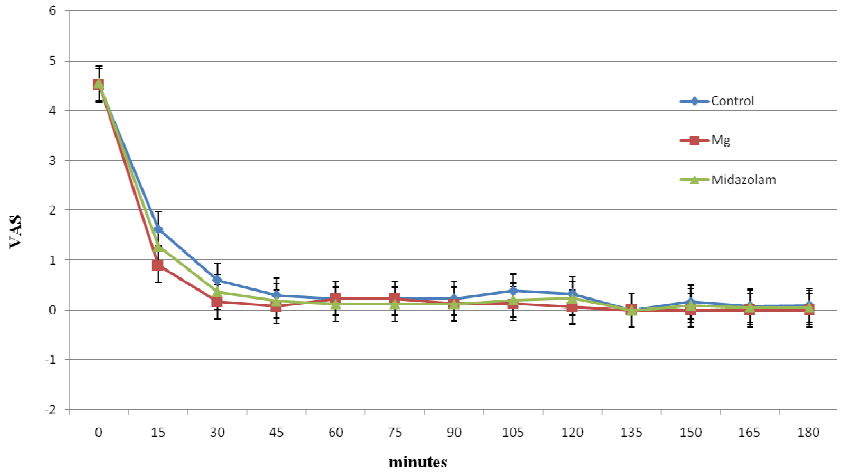

Figure 3: The intra-operative Visual analogue score of study groups. Data are mean±SD.

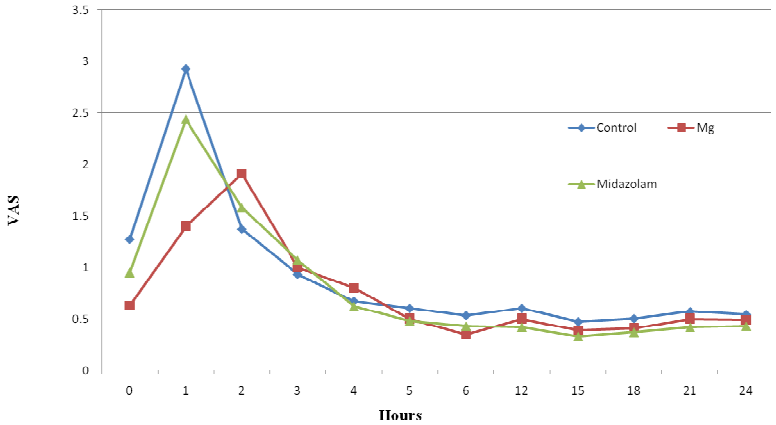

Figure 4: The post-operative Visual analogue score of study groups. Data are mean±SD.

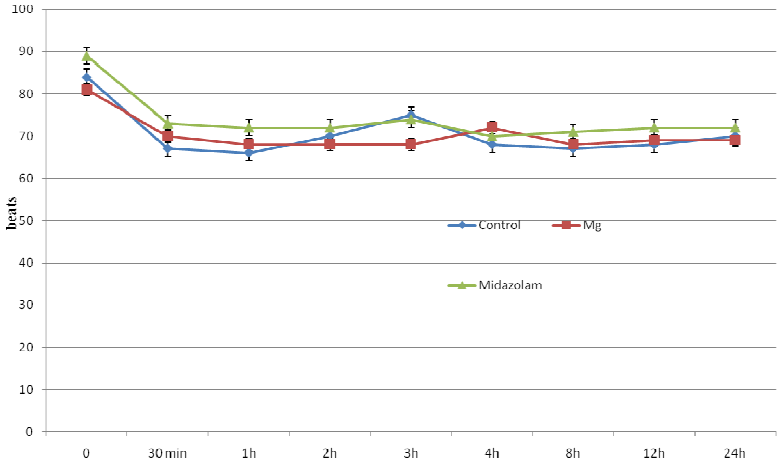

Figure 5: The number of patients and time of requesting analgesia in the first 3 postoperative hours in the study groups. Data are numbers.

	Control	Mg	Midazolam	P
Pethidine (mg)	92.38±10.91	52.56±9.67	70±9.23	0.014*
Total Fentanyl infusion (mcg)/24H	320.67±112.19	219.9±56.86	256.2±53.49	0.00*
Data are expressed as median and 95% CI. * Significant difference (P < 0.05).				

Table 2: Pethidine rescue analgesia and total fentanyl infusion over 24 hours of study groups

	Control	Mg	Midazolam	P
Sedation	0	0	2	0.068
Bradycardia	1	0	0	0.103
Nausea & Vomiting	3	1	2	0.571
Data are expressed as numbers. Significant difference (P < 0.05).				

Table 3: Incidence of sedation, bradycardia and nausea & vomiting in the study groups

No significant differences were recorded regarding the incidence of sedation or any adverse effects between groups (Table 3).

Discussion:

The efficacy of postoperative pain therapy is a major issue in the functional outcome of the surgery[7]. It was evident that epidural analgesia regardless the agent used provides better postoperative analgesia compared with parental analgesiaThe addition of adjuvants to local anaesthetics in epidural analgesia gained widespread popularity as it provides a significant analgesia which allows the reduction of the amount of local anaesthetic and opioid administration for postoperative pain and thus the incidence of side effects[9].

Our study demonstrates a significant intraoperative improvement in VAS in magnesium and midazolam groups, while in the postoperative period magnesium group showed a significant reduction in the number of patients requesting early postoperative analgesia as well as total fentanyl consumption.

The antinociceptive effects of magnesium are primarily based on the regulation of calcium influx into the cell, as a calcium

antagonism and antagonism of N-methyl-D-aspartate (NMDA) receptorTanmoy and colleagues[10] evaluated the effect of adding $MgSO_4$ as adjuvants to epidural Bupivacaine in lower abdominal surgery and reported reduction in time of onset and establishment of epidural block. Whereas, Arcioni and colleagues [11] proved that combined intrathecal and epidural $MgSO_4$supplementation reduce the postoperative analgesic requirements. Farouk et al[12] found that the continuous epidural magnesium started before anesthesia provided preemptive analgesia, and analgesic sparing effect that improved postoperative analgesia. Also, Bilir and colleagues [4] showed that the time to first analgesia requirement was slightly longer with significant reduction in fentanyl consumption after starting epidural $MgSO_4$ infusion postoperatively. Asokumar and colleagues[13] found that addition of $MgSO_4$ prolonged the median duration of analgesia after intrathecal drug administration.

On the other hand, Ko and colleagues[14] found that peri-operative intravenous administration of magnesium sulfate 50 mg/kg does not reduce postoperative analgesic requirements which could be attributed to the finding that the perioperative intravenous administration of $MgSO_4$ did not increase CSF magnesium concentration due to inability to cross blood brain barrier.

Nishiyama et al[17,18,19] reported that epidural midazolam was useful for postoperative pain relief. It was suggested that epidurally administered midazolam exerts its analgesic effects through the □-aminobutyric acid receptors in the spinal cord, particularly in lamina II of the dorsal horn[15] as well as through the opioid receptors. Nishiyama et al[20] showed that intrathecally administered midazolam and bupivacaine had synergistic analgesic effects on acute thermal- or inflammatory-induced pain, with decreased behavioral side effects. While, Kumar et al[21] reported that single-shot caudal coadminstration of bupivacaine with midazolam 50 μg/kg was associated with extended duration of postoperative pain relief in lower abdominal surgery. Whereas, Jaiswal et al[22] concluded that epidural midazolam can be useful and safe adjunct to bupivacaine used for epidural analgesia during labor.

In the present study, there were no significant hemodynamic changes between groups. This is in agreement with many authors who used epidural $MgSO_4$[4,12,23] and midazolam [24] and did not report any hemodynamic or respiratory instability during the observation period.

This study did not record any neurological or epidural drugs related complications postoperatively. Our results are in accord with some of the trials that have previously examined the neurological complications of using epidural $MgSO_4$[,11,12,23]Moreover, Goodman and colleagues [25], found that inadvertent administration of larger doses $MgSO_4$ (8.7 g and 9.6 g) through epidural catheter did not reveal any neurological side effects.

Regarding epidural midazolam, Nishiyama[19] said that epidural administration of midazolam has a wide safety margin for neurotoxicity of the spinal cord due to the small dose used.

Our results did not reveal any significant difference regarding the sedation score. This is in agreement with Bilir et al[4] and El-Kerdawy[23] who did not report any case with drowsiness or respiratory depression when using epidural magnesium.

Whereas, De Beer et al[26] and Nishiyama et al[27] reported that a dose of 50 μg/kg midazolam appears to be the optimum dose for epidural administration, while many patients fell into complete sleep with no response to verbal command and respiratory depression when they used epidural midazolam 0.075 mg/Kg or 0.01 mg/KgMoreover, Nishiyama et al[17,28]reported that when 50 μg/kg epidural midazolam was used, serum midazolam concentration was less than 200 ng/ml which was considered as the lower limit for sedation by intravenous administration.

In conclusion, co-administration of epidural magnesium provides better intraoperative analgesia as well as analgesic-sparing effect on PCEA consumption without increasing the incidence of side-effects compared to bupivacaine alone or with co-administration of epidural midazolam in patients undergoing total knee replacement. The results of the present investigation suggest that magnesium may be one of the useful adjuvants to epidural analgesia.

Competing Interests
None declared
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Review Article

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The Next Pandemic - Tuberculosis: The Oldest Disease of Mankind Rising One More Time

Amer Saleem and Mohammed Azher

Overview Of History

Mycobacterium tuberculosis was first isolated on 24th March 1882 by a German Physician Robert Koch, who received a Nobel Prize for this discovery in 1905 [1]. Tuberculosis is one of the oldest diseases in the history of mankind with evidence of tubercular decay found in some Egyptian mummies from 3000-2400 BC [2]. The study of tuberculosis was also known as phthisiatry from phthisis, the Greek term for tuberculosis. Hippocrates identified phthisis as the most widespread disease of the time which involved the coughing up of blood, fever and was almost always fatal [3]. Avicenna first identified that pulmonary TB was an infectious disease and developed the method of quarantine in order to limit the spread of disease [4 & 5]. The disease was given the name of tuberculosis in 1839 by JL Schonlein [6].

Burden Of Disease

Tuberculosis (TB) is an infectious disease caused by various strains of mycobacteria; of which the commonest cause is Mycobacterium tuberculosis [7]. The disease can affect any part of human body but commonly attacks the lungs. One third of the world's current population has been infected by Mycobacterium tuberculosis and new infections occur at a rate of 1 per second [8]. About 5-10% of these infections leads to active disease which, if left untreated, kills about 50% of its victims. TB affects approximately 8 million people worldwide and about 2 million people die of this disease annually. In the 19th century pandemic tuberculosis killed about 1/4th of the adult population of Europe [9]. Nevertheless, these figures may be only the tip of the iceberg. Tuberculosis is again on the rise and main cause for the resurgence of TB is immunodeficiency as a result of HIV co-infection or, less commonly, immunosuppressive treatment such as chemotherapy or corticosteroids.

Introduction To Mycobacteria

Mycobacteria are aerobic and non-motile bacteria (with the exception of Mycobacterium marinum which is motile within macrophages) which are characteristically alcohol-acid fast [10]. They are present in the environment widely in water and various food sources. They are usually considered to be Gram-positive bacteria, but they do not generally retain the crystal violet stain and are thus called Gram-positive acid-fast bacteria. These acid-fast bacilli (AFB) are straight or slightly curved rods 0.2-0.6 mm wide and 1-10 mm long. Mycobacteria are classified on the basis of growth & their ability to produce pigment.

On the basis of growth:

- Rapid growing: Mycobacteria that forms colonies clearly visible to naked eye within 7 days on sub-cultures
- Slowly growing: Mycobacteria that do not form colonies clearly visible to naked eye within 7 days on sub-culture

On the basis of pigmentation mycobacteria are divided into 3 groups:

- Photochromogens (Group I): Produce non-pigmented colonies in dark and pigmented colonies when exposed to light and re-incubation e.g., M. kansasii, M. marinum etc
- Scotochromogens (Group II): Produce deep yellow to orange colonies when grown in the presence of either light or darkness e.g., M. scrofulaceum, M. xenopi etc
- Non-chromogens (Group III & IV): Non-pigmented in light and dark or only a pale yellow, buff or tan pigment that does not intensify after exposure to light e.g., M. tuberculosis, M. avium-intra-cellulare, M. ulcerans etc

For Clinical Purposes mycobacteria are divided into 3 main classes:

- Mycobacterium tuberculosis complex: These are the mycobacteria which can cause TB and include M. tuberculosis, M. bovis, M. pinnipedii, M. africanum, M. microti and M. canetti.
- Mycobacterium leprae causes leprosy, also known as Hansen's disease.
- Non-tuberculous mycobacteria (NTM) or environmental mycobacteria, atypical mycobacteria and mycobacteria other than tuberculosis (MOTT). These include all other mycobacteria which can cause pulmonary disease resembling tuberculosis, lymphadenitis, skin disease or disseminated disease. These include: Mycobacterium avium complex,

Mycobacterium abscessus, Mycobacterium fortuitum and M. Kansasii which can cause both tuberculosis and leprosy in mammals.

Spread Of Tuberculosis

Today we know that TB is an airborne and highly infectious disease. A person becomes infected when he or she inhales Mycobacterium tuberculosis suspended in air as micro-droplets. Patients suffering from pulmonary TB who have detectable Mycobacterium tuberculosis in their sputum are known as smear positive cases of pulmonary TB. The bacterial load in sputum can be as high as 10,000,000 bacilli/mL. When such smear positive patients of pulmonary TB cough, sneeze or expectorate they produce micro-droplets of phlegm containing Mycobacterium tuberculosis (MTB). The size of these micro-droplets varies from 0.5 to 5mm in diameter. These micro-droplets can remain suspended in air up to 8 hours or even more (depending upon droplet size and environmental conditions including air flow). A single sneeze can produce up to 40,000 of these droplets [11]. MTB cannot invade the mucous membranes of the respiratory tree and must reach the alveoli where it replicates. The size of the MTB-containing micro-droplet must be <1mm to be carried to the end of the bronchial tree otherwise it will be deposited on the walls of bronchial tree and cleared away by mucociliary action. Current knowledge asserts that even less than 10 bacteria may cause pulmonary infection [12 & 13]. A sputum smear positive patient of TB, if left untreated, can cause infection in 10-15 new people each year.

Definition of TB contacts: People exposed to someone with infectious TB, generally including family members, roommates or housemates, close friends, coworkers, classmates, and others. They are a high priority group for latent-TB infection (LTBI) treatment as they are at high risk of being infected with TB.

Definition of close TB contacts: A person who had prolonged, frequent, or intense contact (i.e. >8 hours/day) with a person with sputum positive TB while he or she was infectious. They are more likely to become infected with TB than the contacts those who see the patient less often.

Pathogenesis

Once in the distal end of bronchial tree, MTB is engulfed by a macrophage in order to start replication within this host cell. Depending upon genetic factors, these macrophages can provide a variable environment for the replication of MTB. If this primary infection starts with a single mycobacteria and the initial host response is incapable of halting this process, within weeks or months there will be millions of tubercle bacilli within the body. MTB spreads in sequence from this primary site to the hilar-mediastinal lymph node initially. When seen on the X-ray, this primary focus of pulmonary infection is called a Gohn focus. It is generally located in the upper lobe or the apical segment of the lower lobe [7]. The Gohn focus plus enlarged hilar-mediastinal node is called a Gohn complex. Tubercle bacilli enter the thoracic duct from the hilar-mediastinal lymph nodes, then by passing via the subclavian vein and right atrium, gain access to pulmonary and systemic circulation. As a result MTB can access, and subsequently infect, any organ of the body. Immunocompetent hosts can normally generate an effective immune response within 3-8 weeks, which tackles the primary Gohn focus and can cause involution of the lesions throughout the body. This immune response is a delayed type hypersensitivity reaction to the cell wall protein of bacilli and this is also responsible for positive tuberculin skin test, which appears 4-12 weeks after infection. The primary immune response is not however sufficient to sterilize the tissues and MTB can remain dormant in these foci. Latent foci may persist in the lungs or other organs of the body and are capable of producing disease reactivation which may be pulmonary or extra-pulmonary. In some cases where the initial host response is not capable of causing involution of the primary disease (such as infancy or an immunocompromised state) the infection proliferates and spreads, causing so-called "progressive primary disease".

Mycobacterium bovis is a mycobacterium that causes tuberculosis in cattle but which can also infect humans. It can be transmitted from cattle to human by ingestion of infected milk and very rarely by inhalation of animal aerosol micro-droplets and by eating infected raw meat. The process of pasteurisation kills M. bovis and other bacteria in milk, meaning that infections in human are rare [14].

When To Suspect Tuberculosis

Primary Tuberculosis: Tuberculosis caused by infection with tubercle bacilli and characterized by the formation of a primary complex in the lungs consisting of a small peripheral pulmonary focus and hilar or para-tracheal lymph node involvement; it may cavitate and heal with scarring or progress. It is mainly seen in children but 10% cases of adults suffering from pulmonary TB have primary infection.

Reactivation Tuberculosis: Also known as chronic TB, post-primary disease, recrudescent TB, endogenous reinfection, and adult type progressive TB. It represents 90% of adult cases (in a non-HIV population), and is due to reactivation of dormant AFBs which are seeded at the time of the primary infection. The apical and posterior segments of the upper lobe and superior segment of the lower lobe of the lung are frequently involved.

Clinical Features: Symptoms and signs vary greatly as do radiological signs. A literature review showed that common signs and symptoms seen in TB infection were [15, 16, 17, 18]:

- Cough, which can be either productive or non-productive; it is often initially a dry cough which can later become productive.

- Fever which seen in usually 70% of cases; generally it is low grade but could be as high as 390C, lasting for 14 to 21 days and in 98% cases is resolved completely by 10 weeks.
- Night sweats which is usually seen in 50% of cases
- Weight loss
- Pleural effusion: 50% of the patients with pleuritic chest pain had pleural effusion
- Chest pain: mainly pleuritic with some patients describing retrosternal and inter-scapular dull pain occasionally worsened by swallowing. This pain is believed to be due to enlarged bronchial/ mediastinal lymph nodes
- Dyspnoea can be present in 33% of cases
- Haemoptysis can be seen in 25%of cases
- Fatigue
- Arthralgia
- Pharyngitis

Common radiological findings were as follows:

- Hilar lymphadenopathy: can be seen as early as 1 week after the skin conversion and in almost all of cases within 2 months. It can be associated with right middle lobe collapse
- Pleural effusion: typically within the first 3-4 months but can be seen as late as one year
- Pulmonary infiltrates mainly in the upper zones and peri-hilar areas

How To Investigate [19]

HIV testing should be done in all patients presenting with clinical features of tuberculosis

Active Pulmonary TB

- CXR: Perform an X-ray chest PA view. If the appearance is suggestive of active tuberculosis perform further investigations
- Sputum smear & culture for AFB: send at least 3 sputums for AFB smear and culture including at least one early morning sample. This ideally should be before starting treatment or within 7 days of starting treatment.
- If clinical features and CXR are suggestive of active TB, do not wait for culture and sensitivity results, start the patient on the 4 drug initial treatment. This can be modified according to culture results later on.

Active Non-Respiratory TB

A tissue sample should be taken from the suspected non-respiratory site and sent for histological analysis, AFB smear and culture analysis. Common examples of non-respiratory tuberculosis are tuberculous lymphadenopathy, tuberculous meningitis and disseminated tuberculosis.

Physicians should think about CNS tuberculosis such as TB meningitis if a patient with risk factors (i.e., immigrants from endemic areas, positive history of close contact etc) presents with signs and symptoms such as headache, low grade fever, photophobia and/ or focal neurological signs. Lumbar puncture (LP) after a CT brain to rule out any contra-indication for LP may yield the diagnosis in these scenarios. An MRI brain is also very sensitive for picking up tuberculomas in such cases.

Latent TB

Offer Mantoux testing to the household contacts and close contacts of the person with active TB (aged 5 and older). If the Mantoux is positive or if results are unreliable, as can be the case with BCG-vaccinated persons consider interferon gamma testing (T-spot TB Test). If Mantoux is inconclusive, the patient should be referred to a TB specialist. A similar approach should be used for new entrant TB screening.

QuantiFERON-TB Gold (QFT-G) Test & QuantiFERON-TB Gold in Tube (QFT-GIT) Test

Both of these tests have replaced the QuantiFERON-TB (QFT) Test. It is an interferon gamma release assay (IGRA) and measures a component of cell-mediated immune reactivity to mycobacterium tuberculosis. In QFT-G test a blood sample is mixed with antigens (2 Mycobacterium TB protein) and a control. Mixtures are incubated for 16 to 24 hours and then the amount of interferon gamma is measured. If the patient is infected with mycobacterium TB, white blood cells will release interferon gamma when they come in contact with TB antigens. Clinical features, chest X-ray and sputum/ tissue smear and culture for AFB are needed to differentiate between active and latent TB.

Its advantages over tuberculous skin testing are:

- This test requires a single patient visit to draw a sample
- Results are available within 24 hours
- Results are not dependent on reader
- It is not affected by prior BCG vaccination

Its limitations/ disadvantages include:

- The blood sample must be processed within 12 hours of collection (while white cells are still viable)
- There is limited data for use of QFT-G in immune-compromised patients, children under 17 years of age and persons recently exposed to MTB
- False positive results may occur with Mycobacterium szulgai, kansasii and marinum infection

QFT-GIT is a modification of QFT-G test. It consists of 3 blood collection tubes containing: 1) no antigen, 2) TB antigen, 3) mitogen. These tubes must be transferred to an incubator within 16 hours of blood collection. Interferon gamma detection is then carried out via ELISA. Its specificity varies from 96-99% and sensitivity is as high as 92% in individuals with active disease.

T-Spot TB Test

It is a type of ELISPOT assay, developed by the researchers at the University of Oxford in England. It counts the number of effector T-cells in the blood that produce gamma interferon so gives an overall measurement of antigen load on immune system. As it does not depend upon production of antibody or recoverable pathogen, it can be used to detect latent TB and it is much faster. In one study it was found that its sensitivity is 97.2% [20].

Treatment Of Tuberculosis (Caused By Mycobacterium Tuberculosis)

Active TB will kill 2 of every 3 people affected, if left untreated. Disseminated TB is 100% fatal if untreated. For the treatment of TB, drugs are used in combination and never singly. Patients require regular supervision of their therapy during treatment to monitor compliance and side effects of medications. Treatment of atypical mycobacterial infections should be under the care of specialized units as this needs special care and drug regimens are complicated. Drugs for treatment of TB are divided into 3 categories:

1st Line Drugs: 1stline anti-TB drugs are very effective against TB. There are 5 first line drugs. All have 3 letter and 1 letter standard abbreviations.

- Rifampicin is RMP or R
- Isoniazid is INH or H
- Ethambutol is EMB or E
- Pyrazinamide is PZA or Z
- Streptomycin is STM or S

Using a single drug usually results in treatment failure and drug resistant strains [21]. The frequency of Mycobacterium tuberculosis developing spontaneous mutations conferring resistance to an individual drug is well known: 1 in $10^7$for EMB, 1 in 10^8 for STM & INH, 1 in 10^{10} for RMP [22]. A patient with extensive pulmonary TB usually has 10^{12}bacteria in his body and hence will have about 10^5 EMB-resistant bacteria, 10^4 STM-resistant bacteria, 10^4 INH resistant bacteria and 10^2 RMP resistant bacteria. Drug-resistant tuberculosis occurs when drug-resistant bacilli outgrow drug-susceptible bacilli. Mutations can produce bacilli resistant to any of the anti-tuberculosis drugs, although they occur more frequently for some drugs than others. The average mutation rate in M. tuberculosis for resistance to isoniazid is 2.56×10^{-8}mutations per bacterium per generation; for rifampicin, 2.25×10^{-10}; for ethambutol, 1.0×10^{-7}; and for streptomycin, 2.95×10^{-8}. The mutation rate for resistance to more than one drug is calculated by multiplying the rates for the individual drugs. For example, the mutation rate for resistance to both isoniazid and rifampicin is approximately 2.56×10^{-8} times 2.25×10^{-10}, or 5.76×10^{-18}. The expected ratio of resistant bacilli to susceptible bacilli in an unselected population of M. tuberculosis is about $1:10^6$ each for isoniazid and streptomycin and $1:10^8$ for rifampicin. Mutants resistant to both isoniazid and rifampicin should occur less than once in a population of 10^{14} bacilli. Pulmonary cavities contain about 10^7 to 10^9 bacilli; thus, they are likely to contain a small number of bacilli resistant to each of the anti-tuberculosis drugs but unlikely to contain bacilli resistant to two drugs simultaneously [23].

There are different regimens available for the treatment of TB. The initial 2 months of treatment (usually rifampicin based) is called Initial Phase or Intensive Phase Treatment which later leads to Continuation Phase Treatment. Initial intensive phase treatment is designed to kill actively growing bacteria. Drugs are listed using their single letter abbreviation and a prefix denotes the number of months a treatment has to be given and a subscript denotes intermittent dosage. For example; $2RHEZ/4RH_3$ = 2 months of initial phase treatment with Rifampicin, Isoniazid, Ethambutol, Pyrazinamide and 4 months continuation phase treatment with Rifampicin and Isoniazid given 3 times per week. If there is no subscript, it means the drugs are given daily.

Usual anti-TB regimens are:

- 2RHEZ/4RH3 (in less endemic areas)
- 2RHEZ/4RH (mostly practised, especially in non-endemic areas including UK); standard recommended regimen 24
- 2RHEZ/7RH (in most endemic areas)
- 2RHEZ/10RHE (in cases of disseminated, bone and CNS tuberculosis)

2nd Line Drugs 25 & 26: These are less effective than 1st line drugs, have more toxic side effects and are usually not available in most of the developing countries of the world. There are 6 classes of 2ndline anti-TB drugs:

- Aminoglycosides: e.g., Amikacin (AMK) & Kanamycin (KM)
- Polypeptides: e.g., Capreomycin, Viomycin
- Fluoroquinolones: e.g., Ofloxacin, Ciprofloxacin (CIP), Levofloxacin, Moxifloxacin (MXF)
- Thioamides: e.g., Ethionamide, Prothionamide
- Cycloserine:
- p-Aminosalicylic acid: (PAS or P)

3rd Line Drugs: These are drugs which may be useful, but are not on the WHO list of second line drugs. These are not as effective. 3rdline drugs include:

- Rifabutin (this is an effective drug but is very expensive for developing countries, so it not included in WHO list). Occasionally this can be used for patients who are intolerant to or have bacterial resistance to Rifampicin.
- Macrolides: Clarithromycin (CLR), Azithromycin
- Linezolid: (LZD) not of proven efficacy
- Thioacetazone (T)
- Thioridazine
- Arginine
- Vitamin D
- R207910: efficacy not proven

Indications of Steroids in the treatment of TB

Steroids should be used along with anti-TB drugs in following situations:

- CNS TB (proven benefit)
- TB pericarditis (proven benefit)
- TB involving eye (definitely beneficial)
- TB pleuritis (beneficial – 20-40mg tapered over 4-8 weeks)
- Extremely advanced TB (beneficial)
- TB in children (may be beneficial)
- Miliary TB (beneficial)
- Genitourinary TB (beneficial)
- Laryngeal TB (may be beneficial – scanty evidence)
- TB peritonitis (may be beneficial – scanty evidence)

Important Definitions / Terms [25, 27, 28, 29]

New Case: A patient diagnosed as having TB who has never had anti-TB treatment before or had taken anti-TB treatment for less than 4 weeks.

Sputum Smear Positive Case of Pulmonary TB: A patient who has 2 out of 3 consecutive sputum samples positive for AFB.

Sputum Smear Negative Case of Pulmonary TB: A patient clinically and radiologically suspected to have pulmonary TB but with 3 consecutive sputum samples which are negative for AFB and is also culture negative for AFB.

Culture Positive Case of Pulmonary TB: A patient with 3 consecutive sputum smear samples which are negative for AFB but with at least 1 specimen positive for AFB in culture.

Short Course Therapy for TB: The short course therapy for treatment of TB includes 2RHEZ/4RH and also known as standard regimen. If PZA is not included in the regimen for treating TB, the course should be extended from 6 months to 9 months. If rifampicin is not included in treatment regimen then the length of course should be 18 months in total.

Treatment Failure: A TB patient is said to have treatment failure if they remain smear or culture positive while on treatment at the 5th month or if they were initially smear positive, became negative but then reverted to positive at the end of 5months of treatment. Another scenario is that of a patient who was initially smear negative but then becomes smear positive after 2 months of treatment. Important things to note are:

- Never add a single drug to a failing anti-TB regimen
- Most cases are due to non-compliance
- There is a high chance of Mycobacterium developing resistance to anti-TB drugs

Relapse of TB: A patient is said to have a relapse of TB if they were treated and declared cured but is again smear or culture positive; with the same organism. If the patient gets an infection with a new MTB then they are deemed to be a new case. Because genetic analysis of the infecting MTB is required to determine if re-infection is with the same organism or a new one, it is difficult to accurately diagnose TB relapse.

TB Default Case: A TB patient who completed 1 month of anti-TB treatment, stopped the treatment, and then returns for TB treatment over 2 months after treatment was first initiated. If the patient returns within 2 months of initial treatment, then his/ her initial regimen should be continued.

Re-treatment Regimen: A patient should be a given re-treatment regimen when they relapse or are a TB default case. In highly endemic areas for TB, most authorities prefer an initial intensive phase with 5 drugs for 3 months (2 months RHEZS and 1 month RHEZ).

Chronic Case of TB: A patient is said to be a chronic case of TB, who remains sputum smear positive after 1 re-treatment course. Such patients invariably have drug resistant TB.

Extra-pulmonary TB: TB involving organs other than lungs is called extra-pulmonary TB. For the purpose of treatment and understanding, TB of the central nervous system is excluded from this classification.

Pulmonary TB: Tuberculosis involving lungs is called pulmonary TB.

Respiratory TB: TB involving lungs, pleural cavity, mediastinal lymph nodes or larynx.

CNS Tuberculosis: TB can involve the meninges, brain & spinal cord. It is called TB-meningitis, cerebritis & myelitis respectively. Standard treatment is for 12 months and steroids are mandatory. INH & PZA have 100% penetration into CSF.

Miliary Tuberculosis: This a complication of 1–3% of all TB cases. Tuberculosis involving 2 or more organs/ systems of the body is called disseminated TB or miliary TB. It is also called tuberculosis cutis acuta generalisata and tuberculosis cutis disseminate. It is a form of tuberculosis that is characterized by the wide dissemination and by the tiny size of the TB lesions (1–5 mm). Its name comes from a distinctive pattern seen on a chest X-ray of many tiny spots distributed throughout the lung fields with the appearance similar to millet seeds—thus the term "miliary" tuberculosis. Miliary TB may infect any number of organs, including the lungs, liver, and spleen.

MDR-TB: Multi-drug Resistant TB (MDR-TB) is defined as TB caused by mycobacterium tuberculosis resistant to isoniazid and rifampicin. The diagnosis and appropriate treatment of MDR-TB is still a major challenge.

XDR-TB: Extensively-drug Resistant TB (XDR-TB) is defined as TB caused by mycobacterium tuberculosis resistant to

isoniazid, rifampicin, quinolones and any 1 of 3 injectables: kanamycin, capreomycin or amikacin.

Treatment Categories of TB Patients:

There are four treatment categories of TB patients for details see table 1.

Table 1

Treatment Category	Type of TB Patient
Category I	New sputum smear +ve or Smear –ve pulmonary TB cases with extensive parenchymal involvement New severe extra-pulmonary TB cases
Category II	TB relapse cases TB treatment failure cases
Category III	Non-severe sputum smear –ve pulmonary TB Non-severe extra-pulmonary TB
Category IV	Chronic TB case

Directly Observed Treatment Short-course (DOTS):

In this programme a trained person observes the patient swallowing tablets for preferably the whole course of treatment or at least the initial 2 months of treatment. Daily or thrice weekly dosages are recommended but twice weekly dosages are not recommended because of the risk of omitting (by mistake or by chance) one dose. This would result in once weekly dose and it is not acceptable. WHO recommends the DOTS strategy in an attempt to control tuberculosis. There are 5 main points of action:

- Government commitment to control TB
- Diagnosis based on sputum smear microscopy tests done on patients who actively report TB symptoms
- Direct observation short course chemotherapy treatment
- Definite supply of drugs
- Standardized reporting and recording of cases and treatment outcomes

DOTS-Plus:

WHO extended the DOTS programme in 1998 to include treatment of MDR-TB and this is called DOTS-Plus. It requires the capacity for drug susceptibility testing and provision of 2nd line anti-TB drugs with facilities for identification and drug sensitivities.

Latent TB Infection (LTBI):

A patient is said to have LTBI when he is infected with MTB but does not have any symptoms and signs suggestive of active TB and has a normal chest X-ray. Such patients are non-infectious but 10% of these persons go on to develop active TB in their life at a later stage. They have positive tuberculin skin test and positive Interferon Gamma Release Assay (IGRA) tests (e.g. T-SPOT.TB test, QuantiFERON-TB Gold &QuantiFERON-TB Gold-in tube tests). There are different regimens for treatment of LTBI, commonly used are the following:

- 9H; 9 months INH (gold standard – only practised in USA)
- 6H; 6 months INH
- 3RH; 3 months INH + RMP (recommended in UK)

Common Causes Of Rising Burden Of Tuberculosis

- The following are a few causes of rising burden of TB globally:
- Non-compliance with medication
- Presence of drug resistant strains of mycobacteria
- Faulty regimens
- Un-diagnosed cases
- Under-diagnosed cases
- Lack of newer, more effective anti TB medication.

Role Of Pcr In The Diagnosis Of Tuberculosis

There have been a number of studies regarding the role of PCR in the diagnosis of TB. They show that it has a high sensitivity and specificity but gold standard is still tissue smear and culture for AFB. In certain scenarios PCR of different tissue samples (pulmonary or extra-pulmonary) urine, CSF, sputum and blood can be useful and can also tell us about mycobacterial rifampicin resistance.

Role Of Physicians In Prevention & Control Of Tuberculosis In Relation To Airtravel [30]

- Inform all patients with infectious TB that they must not travel by air on a flight exceeding 8 hours until they have completed at least 2 weeks of adequate therapy.
- Inform all patients with MDR-TB and XDR-TB that they must not travel by air until they are culture-negative.
- Advise patients with TB who undertake unavoidable air travel of less than 8 hours' duration to wear a surgical mask or to otherwise keep the nose and mouth covered when speaking or coughing during the flight. This recommendation should be applied on a case-by-case basis and only with the agreement of the airline(s) involved and the public health authorities at departure and arrival.
- Inform relevant health authorities of the intention of a patient with infectious TB to travel against medical advice.
- Inform relevant health authorities when a patient with infectious TB has a recent history of air travel (travel within 3 months).

Side Effects Of Medications Used For Treatment Of Tuberculosis [31, 32, 33, 34]

Patients who are on treatment for TB should be monitored regularly for any signs of medication toxicity. This may include

blood tests in addition to clinical examination. Common side effects of the routinely used 4 anti-TB medications (INH, rifampicin, Ethambutol & PZA) are as follows:

Hepatotoxicity: INH, PZA and rifampicin are known to cause liver toxicity. Ethambutol is a safer medication in patients with known liver problems. INH is contraindicated in patients with active hepatitis and end stage liver diseases. 20% patients can have an asymptomatic rise in AST concentration in the first 3 months of therapy. Symptoms of liver toxicity include anorexia, nausea, vomiting, dark urine, jaundice, fever, persistent fatigue, abdominal pain especially in the right upper quadrant. Routine base line LFTs are recommended prior to starting treatment. After that they should be repeated at least once a month and more frequently in those who are at risk of developing hepatotoxicity. Patients at increased risk of hepatotoxicity include:

- HIV positive
- Pregnant or post-partum (3 months after delivery)
- History of or at risk of chronic liver disease (daily use of alcohol, IV drug users, hepatitis, liver cirrhosis)
- Patients taking any other medication which have potential hepatotoxic side effects
- The risk of hepatotoxicity increases with age (> 35 years old)

Suspect drug induced liver injury if there is AST/ ALT rise > 3 times base line with symptoms or > 5 times in the absence of symptoms, or disproportionate rise in ALP and total bilirubin. In such a situation:

- Stop hepatotoxic anti-TB medications (INH, rifampicin and PZA) immediately
- Admit the patient to hospital
- Carry out serological tests for Hepatitis A, B, and C (particularly in those who are at risk for hepatitis)
- Look for other causes (hepatotoxic medications, high alcohol consumption)
- In acutely ill smear or culture positive patients start liver friendly medications i.e. Ethambutol Quinolones, and Streptomycin, until the cause for hepatotoxicity is identified.
- Re-challenge: Once LFTs are normal (or < two times the upper normal limit) start with Ethambutol and add INH 1st. If LFTs do not rise after 1 week add Rifampicin. Next add PZA if there is no rise in LFTs after 1 week of adding Rifampicin. If at any point LFTs increase or symptoms recur, stop the last added drug – as this is the culprit drug.

Gastro-intestinal (GI) upset: GI upset is quiet common with anti-TB medications and usually occur in the first few weeks of therapy. Symptoms usually are nausea, vomiting, anorexia, abdominal pain. In such a case recommend good hydration, change the timing of medication (advise to take with a light snack and at bed time) and also check LFTs for possible hepatitis. Aluminium salt containing antacids can reduce bioavailability of INH, so avoid them 1 hour before and 2 hours after INH administration.

Rash: All anti-TB medications can cause a skin rash. Management is based on severity:

- Mild rash or itching: administer anti-histamines 30 minutes prior to anti-TB medications and continue with the therapy. If no improvement, add prednisolone 40mg/day and gradually taper down when the rash clears.
- Petechial rash: Red pinpoint sized dots under the skin due to leakage from capillaries – suspect rifampicin hypersensitivity. Monitor LFTs and full blood count. If platelet count is below normal (base line), stop rifampicin and do not restart it.
- Erythematous rash with fever: and/ or mucous membrane involvement; stop all anti-TB medications immediately and hospitalize the patient. Rule out anaphylaxis (angio-oedema, swollen tongue, throat, stridor, wheezing, flushed face, hypotension) and Stevens-Johnson Syndrome (systemic shedding of mucous membranes and fever). If situation does not permit to stop TB medication then try 3 new drugs i.e. aminoglycoside and 2 oral agents from second line. Once the rash has settled, can re-introduce first line TB medications one by one every 2-3 days, 1st rifampicin, then INH, then PZA and then Ethambutol. While re-introduction, monitor the signs and symptoms of rash, if rash recurs at any point remove the last agent added.

Peripheral neuropathy: signs and symptoms include numbness and tingling in feet and hands, increased sensitivity to touch and stabbing pain. INH can cause peripheral neuropathy. It is more common in malnourished people, diabetes, HIV, renal failure, alcoholism, pregnancy and in breast feeding women. Prevention is the key; prophylaxis is with Pyridoxine (vitamin B6) 10mg/ 100mg INH (normally 25 – 50mg) per week is used in high risk patients.

Optic neuritis: the main agent responsible for this is Ethambutol. It is dose related and gets more intense if treatment is continued. Signs and symptoms are difficulty in reading road signs, decreased red-green colour discrimination, blurring or vision, and colour blindness. These can be unilateral or bilateral. Ethambutol is not recommended in children <5 years of age as visual changes are difficult to monitor. Visual acuity and colour blindness tests are recommended at baseline and also on a monthly basis. Fluctuations of 1 or 2 lines on the Snellen chart is considerable and Ethambutol must be stopped. More than 10% visual loss is considered significant.

Fatigue: INH can cause fatigue and in such situations patients should take the medication at bedtime. If it continues, check LFTs to look for hepatotoxicity.

Flu-like symptoms/joint aches and pains: These are usually seen with Rifampicin and treatment is symptomatic.

Drug-induced lupus: It is seen with INH and blood tests should be done to differentiate it from SLE. It can be managed with steroids while the patient is taking INH.

Competing Interests
None Declared
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Review Article

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Risk of Development of Osteoporosis due to Depression in the Elderly Individuals: Review Article

Umesh Kumar Vyas

Introduction:

Fifteen percent of elderly individuals report clinically significant depression due to variety of reasons. Osteoporosis is a disorder of bone metabolism which can be caused by multiple factors. The elder population has multiple risk factors for development of low Bone Mineral Density (BMD). Data supports that SSRI causes low BMD. There are numerous mediating processes, factors and causes that may contribute to relationship between depression and low BMD, therefore it has been suggested that depression may be an unrecognized risk factor for development of osteoporosis in this patient population.

Low BMD is a common condition among the elder population; prevalence of osteopenia and osteoporosis is expected to increase due to increasing elder population. Low BMD is associated with increased risk for debilitating fractures, particularly hip, vertebrae and distal forearm. There is a growing body of evidence that depression impact the risk for fractures in the older population.

Most studies support that depression is associated with increased risk for both low BMD and fractures. There are many risk factors for low BMD, but some are unalterable. Therefore it is crucial to identify modifiable risk factors to reduce the public health burden of osteopenia, osteoporosis and fractures, and complications associated with them.

Objective:

A literature review was performed to extract evidence and to evaluate risk of Osteoporosis in depression.

Educational Objectives:

At the conclusion of this article, the reviewer will be able to understand,

1. The risk of development of osteoporosis,
2. Need for close monitoring and early assessment of risk,
3. Need for prophylactic treatment to avoid complications due to development of osteoporosis.

Method:

Pubmed.gov was searched by using pre-determined key word.

Key words:

"Depression AND Osteoporosis"

Background:

Osteoporosis was first recognized as a disorder of bone metabolism in 1947 by Albright. It is the most common degenerative disease in developed countries; it is characterized by low bone mineral density (BMD), causing bone fragility and increased fracture incidence. Over past quarter century, it has emerged as a major public health problem in the Western world, prevalence of osteopenia and osteoporosis is expected to increase dramatically in the next 50 years as the population pyramid shift toward old age. In United States alone, app 10 million individuals over age of 50 have osteoporosis. In addition, 33.6 million Americans in this age group have osteopenia (i.e. a decrease in bone mineral density [BMD] that precedes osteoporosis and its potential complications later in life). The estimated annual fracture rate due to an underlying bone disease is 1.5 million. These fractures lead to pain, skeletal mutilation, disability, loss of independence and increased mortality.[1]

Low BMD has been shown to be major risk factor for debilitating bone fractures, particularly of the hip, vertebrae and distal forearm.[2] The established risk factors for osteoporosis include increasing age, female sex, oestrogen deficiency, glucocorticoid therapy and other medications, smoking, alcohol use, inactivity, and low calcium intake.[3] Many prominent risk factors are unalterable, it is therefore crucial to identify modifiable risk factors in order to reduce the public health burden of osteopenia, osteoporosis and the fractures associated with them. In the USA, depression is a common disorder that affects 5 to 9% of women and 1 to 2% men.[4] It ranks second only to hypertension as the most common chronic illness encountered in general medical practice.[5] This disorder carries a considerable risk of death and is associated with a two to three fold increase in all-cause of non-suicide-related death.[6] Fifteen percent of elderly individuals report clinically significant depression.

Definition of Osteopenia and Osteoporosis:

Osteopenia is a condition where bone mineral density is lower than normal, more specifically; it is defined as BMD T-Score between -1.0 and -2.5. It is considered to be precursor to osteoporosis. However, not every person diagnosed with osteopenia will develop osteoporosis. Osteoporosis causes bones to become weak and brittle – so brittle that a fall or even mild stresses like bending over or coughing can cause a fracture.

Osteoporosis-related fractures most commonly occur in the hip, wrist or spine. Bone is a living tissue, which is constantly being absorbed and replaced. Osteoporosis occurs when the creation of new bone does not keep up with the removal of old bone. Osteoporosis affects men and women of all races, but White and Asian women especially those who are past menopause are at highest risk. Medications, dietary supplements and weight-bearing exercise can help strengthen bones.

Literature evidence:

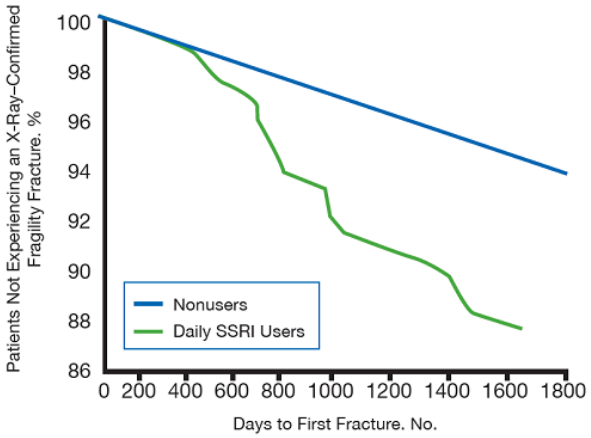
Current evidence supports a bidirectional link between major depressive disorders (MDD), several other mood disorders, and various medical conditions such as osteoporosis and cardiovascular disease.[7] A significant association was found between BMD and depressive symptoms after adjustment for osteoporosis risk factors. In Caucasians, depressive symptoms were associated with both osteoporotic and osteopenic levels of BMD.[8] A meta-analysis reported BMD is lower in depressed than non-depressed subjects. The association between depression and BMD is stronger in women than men, and in premenopausal than postmenopausal women. Only women psychiatrically diagnosed for MDD display significantly low BMD; women diagnosed by self-rating questionnaires do not.[9] Depression is a significant risk factor for fracture in older women.[14] Numerous studies have examined association between antidepressant use (both SSRI and TCA) and fracture risk. The majority have found that use of these medications, regardless of class is associated with increased risk of fracture.[10] Animal studies have also indicated that serotonin may influence bone mass, particularly during stages of bone growth.[11, 12]

Daily SSRI (Table 1) use in adults 50 years and older remained associated with a 2-fold increased risk of clinical fragility after adjustment for potential covariates. Depression and fragility fractures are common in this age group, and the elevated risk attributed to daily SSRI use may have important public health consequences.[15] (Figure 1). SSRI may increase fracture risk because of their effect on bone physiology and on the risk of falling. Functional serotonin receptors and transporters have been localized to bone, while the administration of SSRI decreases bone mass and strength in growing mice. SSRI function by inhibiting the serotonin transporter. Functional serotonin transporters in osteoblasts, osteoclasts and osteocytes raises the possibility that serotonin transporters may play a role in bone metabolism and those medications that affect this transporter system may also affect bone metabolism. Use of SSRI is associated with an increased rate of bone loss at the hip in this cohort of older women; use of a TCA was not similarly associated with increased rates of hip bone loss in our cohort.[16] In men, BMD was lower among those reporting current SSRI use, but not among user of other antidepressants.[17] Meta-analysis proved that MDD is associated with low BMD and should therefore be considered a risk factor for osteoporosis. BMD in subjects with MDD was 4.7% lower at the AP spine, 3.5% lower at the total femur, and 7.3% lower at the femur neck as compared to healthy controls.[18] NIH meta-analysis concluded MDD was associated with lower BMD at the AP spine, femoral neck and total femur. The deficits in BMD in subjects with depression are of clinical significance and likely to increase fracture risk over the lifetime of these subjects.[18]

Table 1: List of SSRI (Selective Serotonin Reuptake Inhibitor) and dosages range:

Generic Name	Brand Name	Dose range
Citalopram	Celexa	10 to 40 mg
Escitalopram	Lexapro	10 to 20 mg
Fluoxetine	Prozac	20 to 80 mg
Fluvoxamine	Luvox	50 to 300 mg
Paroxetine	Paxil	10 to 40 mg
Sertraline	Zoloft	50 to 200 mg

Figure 1: Fracture-free survival by Selective Serotonin Reuptake Inhibitors (SSRI) use



Potential mechanisms of bone loss in depression:

Depression is associated with alterations of the hypothalamic-pituitary-adrenal (HPA) axis at multiple levels, including altered secretion of hypothalamic corticotrophin-releasing hormone (CRH), as indicated by CRH levels in the cerebrospinal fluid, and change in the set point threshold for negative feedback; these changes generally result into hyper-cortisolism.

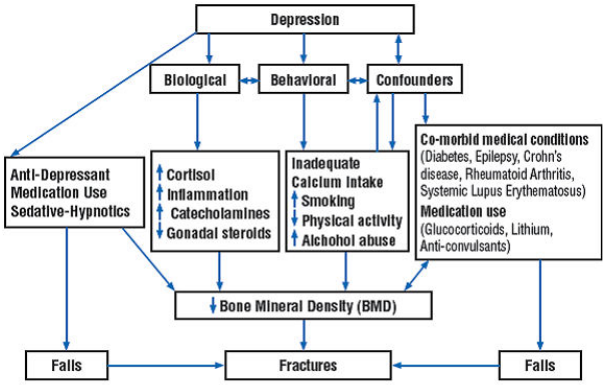
Pro-inflammatory cytokines are increased in depression and IL-6 is a potent activator of the osteoclast. Oestrogen deficiency in women and androgen deficiency in men may affect bone mass and there is at least theoretical evidence for decreased sexual hormones in both genders during the acute phases of depression. Serotonin transporter receptors are present on the osteoblast and use of antidepressants has been associated with more fractures. Commonly accepted life style risk factors for osteoporosis include smoking, inadequate calcium intake, excessive alcohol intake and physical inactivity.

There are three pathophysiologic pathways leading to low BMD.[13] (Figure 2):

1. Inadequate acquisition of bone mass early in life
2. Elevated resorption of bone mass later in life, and
3. Inefficient bone formation during continuous bone remodeling

These pathways are interdependent and the relative importance of each mechanism changes over development and varies by sex.

Figure 2: Pathways linking depression, low bone mneral density and fracture. [13]



Bottom line:

Current available evidence supports that there is increase of development of osteoporosis due to various factors, pathways and medications used in treatment of depression.

Conclusion:

Major depressive disorder is an important but still unrecognized risk factor for osteoporosis. Depression should be considered as an important risk factor for osteoporosis. Depression is associated with low BMD, with a substantially greater BMD decrease in depressed women and in cases of clinical depression. These patients need close monitoring, early assessment of risk and preventive measures to avoid complications. Premenopausal women with major depression should undergo DXA screening. Similar recommendation may be made for postmenopausal women with depression especially in the presence of one or more known risk factors for development of osteoporosis.

Once a diagnosis of osteoporosis is made in subjects with major depression, DXA measurements should be performed with a frequency based on the current WHO algorithm; this model takes into account the presence of other risk factors and age of the subjects.

Clinical Point:

Periodic BMD measurements and anti-osteoporotic prophylactic and curative measures are strongly advocated for these patients.

Competing Interests
None declared
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Case Series

BJMP 2013;6(1):a617

Jeune Syndrome

Ramya H S, Sushanth and Manjunath M N

Abstract
Jeune syndrome or asphyxiating thoracic dystrophy is a rare autosomal recessive skeletal dysplasia characterised by a small chest and short ribs which restrict the growth and expansion of the lungs often causing life threatening complications. The inheritance is autosomal recessive. A locus has been identified on chromosome 15q13 , while recently, mutations were found in the IFT80 gene, encoding an intraflagellar protein. Other symptoms may include shortened bones in the arms and legs, unusually shaped pelvic bones, and extra fingers and/or toes (polydactyly). It is estimated to occur in 1 per 100,000 – 130,000 live births. Children that survive the breathing and lung challenges of infancy, can later develop life-threatening kidney problems. Heart defects and a narrowing of the airway (subglottic stenosis) are also possible. Other, very less common features of Jeune syndrome include liver disease, pancreatic cysts, dental abnormalities, and an eye disease called retinal dystrophy that can lead to the loss of vision. We report a preterm neonate with Jeune syndrome.
Keywords: Jeune Syndrome, Thoracic desease
Abbreviations: SGA - Small for Gestational Age, HMD - Hyaline Membrane Desease, CPAP - Contineous Positive Airway Ptressure, E/T - Endotracheal Tube, ATD - Asphyxiating Thoracic Dystrophy.

Case Report

A 34 week preterm, small for gestational age, third born male neonate to a non consanguinous married couple with father having short extremities was admitted in our NICU prematurely with respiratory distress.

On examination the baby was tachypneic with grunt and lower chest indrawing. The baby was also found to have a narrow thorax, short fingers with postaxial polydactyly in both upper limbs and right lower limb, with syndactyly in right upper and lower limb (figures 1,2,3). The cardiovascular, respiratory, abdominal and neurological examination were unremarkable with no facial dysmorphism. The fundus examination was inconclusive.

The antenatal scan showed all long bones short in configuration. The liver function tests were normal except for mild elevation of alkaline phosphatase. The Ultrasound abdomen showed hepatomegaly and no evidence of any other mass lesions. The urine examination was negative for proteinuria and haematuria. The chest x ray showed short ribs, high position of clavicle and features of hyaline membrane disease (Figure 4).

The baby was put on continuous positive airway pressure and given surfactant through an endotracheal tube twice for two consecutive days, but as the condition deteriorated, with hypercarbia and hypoxia as evident on arterial blood gases, the baby was electively ventilated with minimal settings. The baby improved and hence was extubated. After a few hours of being extubation the baby gradually developed respiratory distress and started to deteriorate. Hence the baby was reintubated. The condition of baby was explained to attenders and as the attenders were not willing to continue the treatment, the baby was discharged from hospital against medical advice and later we were informed that the baby expired within few hours after discharge from the hospital.

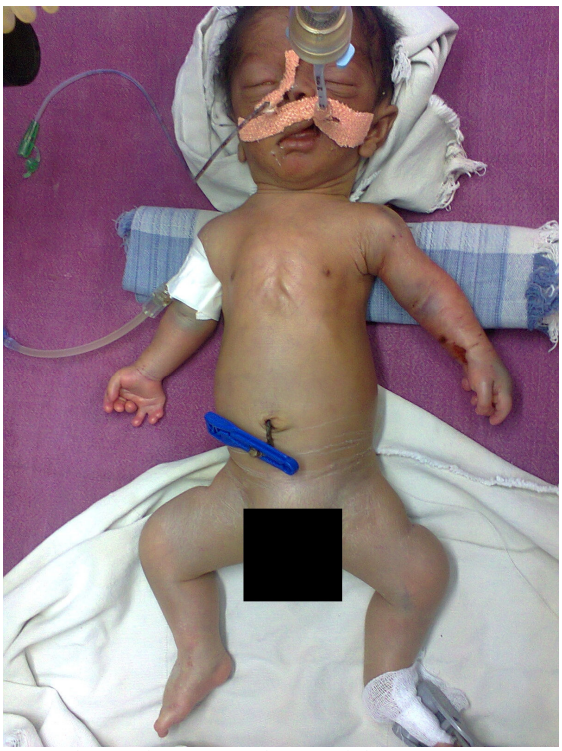
Fig 1 : showing long narrow thorax and short upper extremities

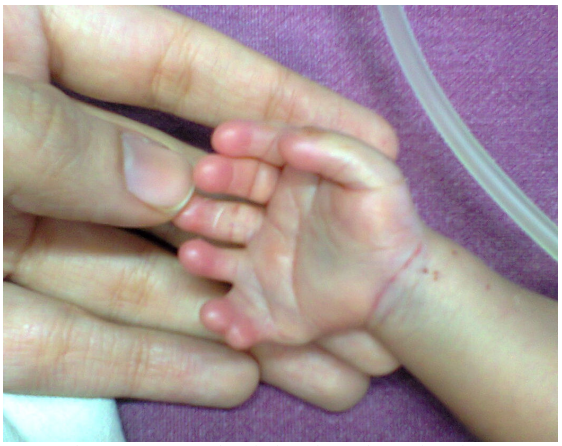

Fig 2 : showing postaxial polydactyly with syndactyly in upper extremity

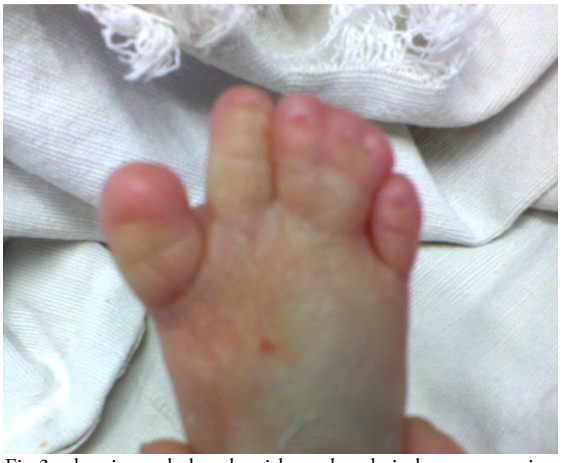

Fig 3 : showing polydactyly with syndactyly in lower extremity

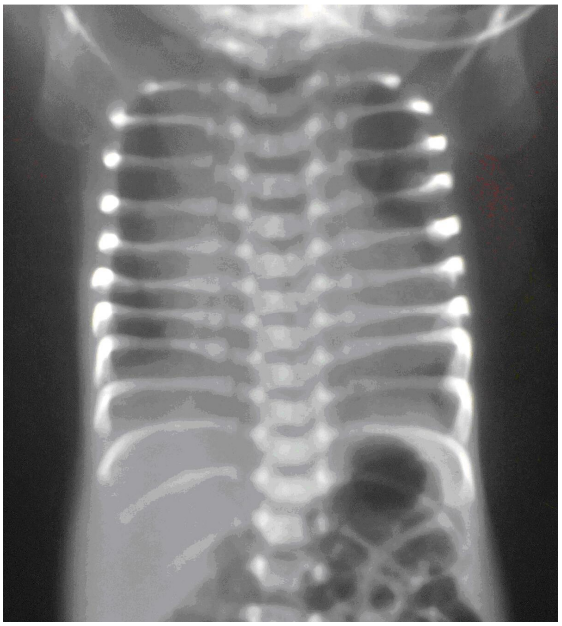

Fig 4 : chest xray showing long narrow thorax and short and horizontally oriented ribs with irregular costochondral junctions and bulbous and irregular anterior ends

Discussion

Jeune syndrome or asphyxiating thoracic dystrophy is a rare autosomal recessive skeletal dysplasia characterised by a small chest and short ribs which restrict the growth and expansion of the lungs[1]. The inheritance is autosomal recessive and a locus has been identified on chromosome 15q13 [2]. Other symptoms may include shortened bones in the arms and legs, unusually shaped pelvic bones, and extra fingers and/or toes (polydactyly)[3] . It is estimated to occur in 1 per 1,00,000 - 1,30,000 (again is this 130,000?) live births[4]. The diagnosis is based on clinical and radiological findings. Our patient fulfills the diagnostic criteria for Jeune syndrome. The most consistent and characteristic findings were the abnormalities of the thoraxand limbs. Jeune syndrome was first described in 1955 by Jeune in two siblings with severely narrow thorax[5]. It is known to be genetically heterogeneous.

Several complications of asphyxiating thoracic dystrophy have been described in the literature. The respiratory problems are the main concern. A large percentage of the children with asphyxiating thoracic dystrophy die as a result of these problems. Percentages up to 80% have been mentioned in literature[6,7]. In our case the baby experienced respiratory distress on day one of life needing ventilator support. The thoracic malformation tends to become less pronounced with age[8]. A possible explanation could be the improved mechanical properties of the chest wall with growth.

Clinically, Jeune syndrome is characterized by a small, narrow chest and variable limb shortness. Associated congenital abnormalities can be postaxial polydactyly of both hands and/or feet (20%). Typical radiographic findings include a narrow, bell-shaped thorax with short, horizontally oriented ribs and irregular costochondral junctions, elevated clavicles, short iliac bones with a typical trident appearance of the acetabula, relatively short and wide long bones of the extremities, and hypoplastic phalanges of both hands and feet with cone-shaped epiphyses[9]. The reported case has long narrow chest, short and horizontally oriented ribs with irregular costochondral junctions and bulbous and irregular anterior ends with post axial polydactyly in both upper extremities and right lower limb with left lower limb being normal.

Jeune syndrome is sometimes compatible with life, although respiratory failure and infections are often fatal during infancy. The severity of thoracic constriction widely varies. For those patients who survive infancy, the thorax tends to revert to normal with improving respiratory function. This suggests that the lungs have a normal growth potential and the respiratory problems are secondary to restricted rib cage deformity [10].

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Competing Interests
None declared
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Clinical Practice

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A comparative review of admissions to an Intellectual Disability Inpatient Service over a 10-year period

Cristal Oxley, Shivanthi Sathanandan, Dina Gazizova, Brian Fitzgerald, Professor Basant K. Puri

ABSTRACT

Aim: To analyse trends in admissions to an intellectual disability unit over a ten year period.

Method: We carried out a retrospective review of medical case notes over two time periods (1999-2001 and 2009-2011). Data collected included patient demographics, reasons for admission, length of stay, delay in discharge and reasons for delay in discharge.

Results: During the initial review there were 60 admissions to the unit, compared to 41 admissions during the later time period. During both periods challenging behaviour followed by psychotic disorder were the most common reasons for admission. Over this ten year period, more than half of the admissions were considered delayed discharges, most commonly due to social reasons (i.e. funding, appropriate placement).

Conclusions: Specialist inpatient assessment and treatment units are a costly necessity. Reducing the average length of stay where possible can reduce the cost of a patient admission. However, this single agenda can lead to problems of pressured early discharge to placements which are unable to sustain the patients. Collaborative approaches together with those involved in community care is crucial to getting the right care at the right financial cost for this relatively small but very complex and vulnerable group of individuals.

INTRODUCTION:

People with intellectual disabilities are a heterogeneous group, who can pose a challenge to services in terms of meeting a wide range of needs. Following the closure of large institutions, the optimum means of service provision for people with intellectual disabilities with additional mental illness and challenging behaviour has been a matter of debate.

Challenging behaviour can be defined as a 'culturally abnormal behaviour of such an intensity, frequency or duration that the physical safety of the person or others is likely to be placed in serious jeopardy, or behaviour which is likely to seriously limit use of, or result in the person being denied access to, ordinary community facilities' – Emerson, 1995[1]. Examples of challenging behaviours include self-injury, aggressive outbursts, destruction of property and socially inappropriate behaviour.

The credit-crunch of recent years has led to an increased use of private sector services delivering care to NHS funded patients. The Winterbourne Scandal unearthed by BBC Panorama in June 2011 (an investigation into the physical abuse and psychological abuse suffered by people with learning disabilities and challenging behaviour at this private hospital in South Gloucestershire), highlighted that whist this maybe an economically viable option, fundamental questions were raised about whether private sector services' safeguards and monitoring protocols were as robust as the NHS in protecting vulnerable patients. It also reawakened longstanding disputes around the way people with complex needs are cared for in residential settings. The discussions centred around 'institutional' versus 'community' care styles; specialist intellectual disabilities services versus generic adult psychiatric services; local versus specialist expertise congregated around a single unit; and also financial questions regarding how best to meet the needs of this population at a time of austerity. Opinions vary widely, and at times are even polarised, as a result of several factors including position within this competitive and complex system, personal and cultural politics and also personal experience. As a result of the government review, subsequent to the Winterbourne investigation, a number of recommendations have been made which will affect the future of care of this vulnerable group of patients. These include, "by June 2013, all current placements will be reviewed, everyone in hospital inappropriately will move to community-based support as quickly as possible, and no later than June 2014… as a consequence, there will be a dramatic reduction in hospital placements for this group of people"[2]

The Department of Health Policy, Valuing People[3], set out 'ambitious and challenging programme of action for improving services', based on four important key principles – civil rights, independence, choice and inclusion. Government Policy as detailed in both Valuing People and the Mansell Report[3, 4] recognises that NHS specialist inpatient services are indeed necessary on a short-term basis for some people with intellectual disabilities and complex mental health needs. Inpatient facilities for people with Intellectual Disability have been described as highly specialised services that are a valuable, but also expensive, component of mental health services[5]. The Enfield Specialist Inpatient unit - the Seacole Centre - is one such service.

The Seacole Centre consists of two inpatient units, with a total of 12 inpatient beds, for people with intellectual disabilities with acute mental illness and/or challenging behaviour. It is located within Chase Farm Hospital in Enfield, Greater London. The Seacole Centre has a multidisciplinary team consisting of nurses, psychologists, psychiatrists, a resident GP, occupational therapists, intensive support team staff, physiotherapists, speech and language therapists, a physical exercise coach and administrative staff. Patients are admitted from a variety of sources, including general psychiatric wards, general medical wards and community intellectual disability teams. Since patients are often referred from other boroughs, in addition to this multidisciplinary team, each patient has their own community and social care team based within their own borough. The use of out-of-area units faces similar challenges to out-of-area placements, use of which has been increasing in the UK, and it is important to explore ways in which service users, out-of-area, can be supported effectively[6].

In 2002, a review of admissions to the unit was completed to describe the management of mental illness and challenging behaviour. Since then there have been several service reconfigurations within the trust, in order to accommodate national, political and financial recommendations. However, despite these changes, it was observed clinically that certain clinical problems including delayed discharges continue to occur. We decided to complete a similar review, to describe current admission trends in further detail, in order to enable us to identify areas of improvement, and also to ascertain the nature and severity of ongoing problems to focus future recommendations.

METHOD:

A retrospective review of the case records of all inpatient admissions to the Seacole Centre was completed over a three-year period – from 1st January 1999 to 31st December 2001.

Data collected included age on admission, gender, borough, diagnosis, psychotropic medication on discharge, date of admission and discharge, length of stay, legal status on admission, delays on discharge, and reason for delay, and living arrangements prior to and after discharge

A successful outcome of admission was discharge from hospital to community care. We used the following definition of the delayed discharge:

"*A delayed transfer occurs when a patient is ready for transfer from a general and acute hospital bed but is still occupying such a bed. A patient is ready for transfer when:*

- *a clinical decision has been made that the patient is ready for transfer*
- *a multi-disciplinary team decision has been made that the patient is ready for transfer*
- *the patient is safe to discharge/transfer.*7"

The review was repeated during a further three-year period between 1st January to 2009 and 31st December 2011.

RESULTS:

Characteristics of 1999-2001 cohort, and comparison with 2009-2011

The basic demographic details can be seen in Table 1.

Table 1 - Demographic details

	1999-2001	**2009-2011**
Number of admissions	60	41
Number of patients	46	40
Average (mean) age/years	29.58	36.16
Age Range / years	14-63	19-72
M:F ratio	1.4:1	3.1:1
Total number of boroughs from which patients admitted	10	7

Trends in Admission Rates

As seen in Tables 1 and 2, there has been a reduction in the total number of admissions between the studies. There has also been a marked reduction in re-admissions. The average length of stay has increased, and although the number of delayed discharges has slightly decreased, it can be seen that this is still a factor in a significant proportion of the admissions.

Table 2 - Trends in admission

	1999-2001	**2009-2011**
Total Number of admissions	60	41
Average (mean) length of stay / days	198.6	244.6
Number of readmissions	16	1
Number of delayed discharges	40 (67%)	24 (59%)

Reason for admission

The trends in reason for admission are shown in Figure 1.

In both time periods, the most frequent reason for admission is challenging behaviour (62%, n=37 between 1999-2001; 63%, n=29, between 2009-2011), followed by psychosis (22%, n=13 between 1999-2001; 11%, n=5, between 2009-2011. Social admissions were the third most common reason for admission in the recent study (0% between 1999-2001; 4%, n=2 between 2009-2011). The range of psychiatric presentations was widest during the original time period.

Patterns on discharge

As shown in Figure 2, most patients in the original study were discharged to either the same residential home or back to the family home, where as in the latter time period patients were

most frequently discharged to either a different residential home or to supported living. Figure 3 summarises this effect, demonstrating the change in discharging the majority of patients to a different place of residence.

Figure 1 – Trends in Reason for Admission, 1999-2001 compared to 2009-2011

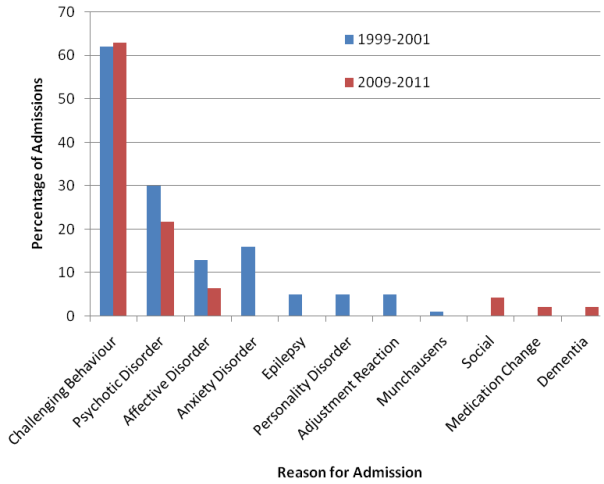


Figure 2 – A graph to show the place of discharge, 1999-2001 compared to 2009-2011

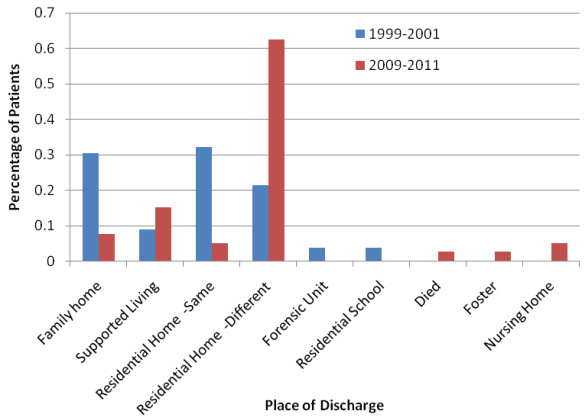
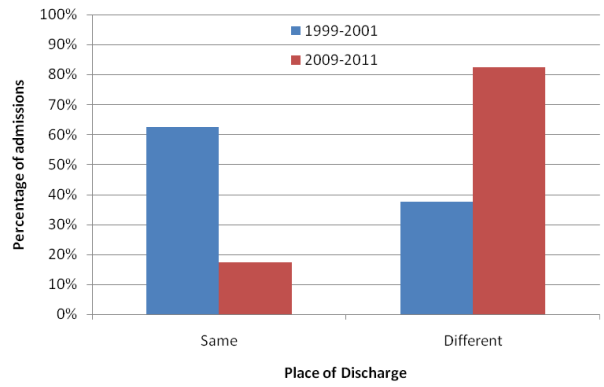


Figure 3 – A Graph to Demonstrate Trends in Place of Discharge – comparing 1999-2001 and 2009-2011



Delayed discharges

The primary cause for delay in both studies was finding appropriate placement, although this was more marked in the recent cohort.

One of the major factors contributing to delayed discharges was lack of identification of suitable placement, which was identified as a major contributing factor to delayed discharges in 69% of cases in 2009-2011 and in 44% in 1999-2001, and apparent delays in the role played by social services (table 2).

DISCUSSION:

Throughout this study spanning 10 years, challenging behaviour followed by psychotic disorder remained the most common cause for admission. Interestingly, by 2008-2011, the third most common cause for admission was related to social reasons (4%). There were no admissions in the original study for this reason. Between 1999 and 2001, there were a wider range of reasons for admission across the mental illness spectrum compared to 10 years on. In previous studies, the largest diagnostic group for all admissions was schizophrenia spectrum disorders[7,8]. However, between 2009-2011, more than a quarter of patients admitted to the Seacole Centre did not have any psychiatric diagnosis on admission. It is important to keep in mind that individuals with intellectual disabilities accessing specialist inpatient services are more likely to present with complex clusters of symptoms and behavioural problems that may span several diagnostic categories.

The most significant improvement from the original review and the re-review is that the number of re-admissions significantly reduced from 24% (14 patients) to 2% (1 patient). Of interest to note is that during 1999-2001 a large proportion of patients were discharged to their original place of accommodation (often the family home) whereas in 2009-2011, it was more common for patients to be discharged to a new place of living, more suited to managing increasing complex needs and behaviours. This may account for some of the reduction in re-admission rates.

The length of stay over the 10-year period has slightly increased from an average of 198.6 days up to 244.6 days, which demonstrate that admissions are considerably longer than in more generic medical settings. The findings are in keeping with a number of other studies regarding patients with intellectual disability who are admitted to a specialist unit and continue as inpatients for significantly longer periods. One study showed a mean length of stay 23.2 weeks for a specialist unit versus 11.1 weeks in generic settings [8]. Another study in South London revealed similar finds of 19.3 weeks compared with generic unit stays of 5.5. weeks[9]. An exploratory national survey of intellectual disability inpatient services in England has shown that 25% of residents had been in the units for more than two years. Only 40% of residents had a discharge plan, and only 20% had both this and the type of placement considered ideal

for them in their home area[10]. Reasons for length of stay are not fully understood in any of these studies. They may include fear of taking risks, lack of local safe or competent amenities, lack of experience or authority amongst those charged with sourcing bespoke services for complex people with challenging needs, and also a potential lack of such resource in terms of time available to see people, read reports, meet with stake holders and find the right services. The results of another retrospective study comparing the generic and specialist models in two districts in the UK by Alexander *et al*[11] suggested that, within the same district, patients do stay longer in the specialist unit, but they are less likely to be discharged to an out of area placement.

There is no evidence to suggest that comprehensive care for people with intellectual disabilities can be provided by community services alone. Likewise, there is also no clear evidence to suggest that a balanced system of mental health care can be provided without acute beds[12]. There is, however, clear evidence that services created by the private sector are used very widely and seen as at time as an economically viable option in the current climate of credit crunches.

The different models of inpatient service provision that have been suggested range from mainstream adult mental health services; alternatively an integrated inpatient scheme whereby people with Intellectual disabilities with additional mental illness or severe challenging behaviour are admitted to adult mental health beds, with provision for extra support from a multidisciplinary learning disabilities team; ranging across to specialist assessment and treatment units[13,14].

Inpatient care is known to consume most of the mental health budget[15] and specialist inpatient units are an expensive component of these services. Cost containment and cost minimisation of inpatient beds within the current economic recession presents a real challenge for those charged with responsibility to provide high-quality, effective, specialist care for adults with intellectual disability. Such cost reduction could be approached in a number of ways, through the reduction of length of stay, optimising drug budgets, reducing rates of re-admissions, and establishment of projects in association with the voluntary and statutory sector to facilitate prompt and safe discharge.

Reducing the average length of stay where possible can reduce the cost, and the resources and budget freed up in this way could be used for other service components[15]. However, this single agenda can lead to problems of pressured early discharge to unsuitable placements. It is known that resource consumption is most intense during the early stages of admission. As such, we observe a position whereby reducing length of stay requires proactive planning throughout the whole process of care, as well as active discharge planning, with a need for clearly defined pathways of care.

A crucial aspect of the patient's transition through inpatient placement to life in the community is efficient and regular communication between the relevant professionals and teams who form part of continuity of on-going care back in the community. This can at times be particularly challenging owing to differences in values and perceptions about patient need and problem, and also varying pressures. Understanding and resolving problems for individuals with complex and severe challenging behaviour or mental illness that requires a period of containment in a specialist service also requires specialist on-going work and risk management to ensure that when the problems are contained and understood, they remain contained and understood on discharge and thereafter so long as the individual remains vulnerable to the point of requiring any care giving. Many people from the general population who develop a serious mental illness requiring hospitalisation, have capacity once well, to make decisions for themselves and articulate a need or otherwise for specific care or intervention. This is rarely completely the case for people with Intellectual disabilities. Collaborative approaches together with those involved in community care is crucial to getting the right care at the right financial cost for this relatively small but very complex and vulnerable group of individuals.

Competing Interests
None
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Viewpoint

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Poor ways of working: dilution of care and responsibility in the specialty of psychiatry

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It seems that psychiatry is gradually losing its allure for future doctors. All around, one can detect an air of pessimism from colleagues about the creeping 'socialisation' of this important field of medicine. There is no longer the breadth of interest in the subject and each sub-branch, for want of a better expression, has its followers and adherents. Proponents of one particular facet of treatment are zealous in the pursuit of their own interests. Psychotherapy is pitched against the neurobiological, rehabilitation and social psychiatry against the pharmacologists, all trying to mark out their own piece of territory, with some yearning for a place in the history books, or at the very least, an acronym. Some psychiatrists do not believe in diagnoses; others ridicule the concept of personality disorder, autistic spectrum disorder, or drug treatment; some believe psychiatric illness is the fault of governments, and there are probably a few who do not believe in psychiatry at all! 'Research' studies are cherry-picked by all sides to illustrate the ineffectiveness of 'alternative' treatments. The full picture or perspective of ill health is blurred and narrowed by a minority who believe they alone know what is right for patients, and psychiatry is 'intellectualised' by others to give it an air of authority and profundity it does not possess. Morale and training are suffering and, if this state of chaos and insanity continues, the discipline itself will implode and cease to be of interest to anyone, save the warring factions in the profession itself.

Once upon a time it was considered that a reasonably broad mixture of community and hospital services would provide benefit for patients with mental illness. Staff involved in their care, who have the rather cumbersome and oxymoronic description of being called 'mental' health professionals, would also widen their experience because of the continuity of care provided. It was hoped patients who clearly did not need to be in hospital (for example, waiting for appropriate accommodation) could be discharged. Clinical need would determine those who required further rehabilitation/treatment in hospital, and would not be swayed by pressures, often financial, to discharge. Now, with the setting up of Home Treatment and other teams the situation has ironically worsened, because there is an implicit opinion in this arrangement that hospital admission, even for the seriously ill or indeed violent patients, is the least desirable option and something to avoid at all cost, even when care in the community is not immediately available or adequate. Care provision for the elderly is a separate concern and is not under discussion here.

In the domain of general adult psychiatry those patients who are in need of care, be it medical or social, are languishing at home, desperate for help, being offered assessment after assessment by disparate teams. There are not enough care professionals to cope with the demand. Home Treatment Teams in particular, are under considerable sustained pressure and stress to ensure further reduction in beds. Rehabilitation beds are being closed. 'It is cheaper to keep patients in the community', we are told. Or, if that does not suit, the liberal stance might be, 'What does hospital admission achieve'? That's fine if the problem is not on your doorstep. Psychiatrists who oversee inpatient care are also pressurised to discharge patients as soon as possible, so the very old notion of 'incarceration' (that worn-out cliché from the antipsychiatry lobby) seems facile, to say the least. On the contrary, doctors now have the added worry of prematurely discharging partially treated ('we need the beds') as well as more vulnerable patients who cannot cope. Most patients who take up psychiatric hospital beds do not want to be in hospital in the first place as they often, rightly or wrongly, do not see themselves as ill. Many hospital beds are now occupied by 'Section patients', and conversely, many very ill patients are left to go it alone because they refuse hospital admission and do not want community team involvement, yet are not 'sectionable'. The inference seems to be, 'If not sectionable or under CPA (Care Programme Approach) it is not our concern.'

Where there are sufficient provisions for outpatient care, some of the damage may be mitigated. Overworked staff including community psychiatric nurses (CPNs), support time recovery workers (STRs) and occupational therapists (OTs) often have the thankless task and enormous responsibility of seeing patients at home, some of whom are threatening and potentially dangerous, others erratic with their outpatient clinics attendance not always through deliberate evasion but often the result of the very condition causing the problem, for example, lack of insight. Other patients do not engage either through hostility or loss of motivation induced by the underlying problem, say, drug and alcohol misuse. Chronic patients are not

ill enough to be on CPA and diagnostic 'conundrums' are left to others to sort out. With the introduction of the New Ways of Working,[1] the traditional outpatient clinics are being abolished and replaced with community clinics ('short-term' outpatients really). Ideally a community clinic should be run by CPNs as they usually understand the medical, psychiatric, psychological, and social needs of patients. In the authors' opinion the clinics should be Consultant-led because despite the tendency to classify everyone as 'clinicians' many staff feel uncomfortable with this role as it implies or infers a degree of clinical responsibility for which they are not qualified. Psychiatric nurses (especially those with a general nursing background) are ideally placed to carry out this function by virtue of their wide experience; also they are aware when to seek medical help when needed. Often they are more informed about patients than the primary physician or indeed the psychiatrist because of more frequent contact, either via liaison with the hospital wards or through home visits in their role as CPNs. Nurses and other staff (for example, social workers) are involved in patients' discharge from hospital (usually determined at pre-discharge meetings) and are therefore an essential link in the continuity of patient care before patients are eventually seen in the 'community clinics'. Requests for domiciliary visits from general practitioners (GPs) to physicians themselves have become a thing of the past, with the exception of those psychiatrists working with Home Treatment Teams and Assertive Outreach Teams. Nowadays it is not uncommon for patients to be waiting months on end (more assessments) before being deemed 'appropriate' to see a Consultant Psychiatrist.

Certainly there are patients who do not need to continue seeing a Consultant Psychiatrist for years on end and should be discharged back to the GP to reduce unnecessary costs and to avoid a dependency culture, in the same way a patient with mild arthritis does not need to see a rheumatologist or a patient with anaemia does not always need the expertise of a haematologist, to use simple analogies. However, sometimes GPs are unwilling to reciprocate or feel out of depth with 'psychiatry' that this is not always possible. The chronicity of many psychiatric disorders perhaps harnesses the belief that new treatments may emerge which only a psychiatrist, with his/her specialized knowledge, can implement and deal with. This type of scenario is seen with many other illnesses in all fields of medicine (chronic psoriasis, rheumatoid arthritis, multiple sclerosis) yet no one is suggesting that GPs solely should be left to manage these conditions. It seems the clinical risk to patient care is not thought through and this no doubt will lead to serious repercussions later. In our estimation, physical and mental illnesses are so often intertwined that their management should be equally shared by physicians and psychiatrists.[2]

Swings and Roundabouts

Such is the pressure by management (under the thumb of civil servants) and 'those in the know', reverentially referred to as 'Commissioners', that health professionals in psychiatry have to defend their clinical judgment and carry out numerous risk assessments (defensive medicine) of patients who are to be discharged from the outpatient clinic back to the GP in any event. Patients may be fortunate enough to receive a few last appointments with the Community Clinic (when they are up and running: some are at the time of writing) before they are shown the door and sent back to the GP, all to save money. Packages of care will not disguise the fact that vulnerable patients are being left to fend for themselves, just as they were in the past when the large institutions closed down without any forward planning as to how and where patients would survive. Yet 'management training' and 'mandatory courses' continue inexorably, often provided by 'expert' outside speakers, costing Trusts considerable amounts of hours lost, let alone the expense, instead of employing more nursing staff to cope with the ever-increasing workload. We are led to believe that reducing 'outpatient numbers' will lead to less pressurised work on staff, which really does not fit. All that will be happening to the extent that 'outpatients' will now be filling to the brim with CPA patients (read 'psychoses') instead of a good case-mix of patients required for general experience and training. It seems to be forgotten that there are patients who feel very unwell and are unable to cope, yet are not suffering from major psychiatric disorders.

The next scenario will be the revolving door 'GP - Access/Assessment Team - possible Consultant Psychiatrist advice and at most two follow-up appointments (if one is really ill) - Community Clinic - discharge to GP system', to replace the premature hospital discharge-readmission system which failed miserably in the past. When the patient relapses (or rather, when the illness remains static) the GP refers back into the system and the whole process begins again. In this way the Trusts receive money by reaching their targets (discharging patients) and are paid a second time when GPs 'purchase' more care. Those patients with 'minor problems' (not in their GP's estimation) will whittle away and remain unhappy. 'They can always see a counsellor' is the unspoken passive riposte. Furthermore, there will be less clinical variety for doctors and students, as their work will amount to prescribing 'powerful drugs' (we are told by the antipsychiatrists), monitoring serum lithium (and other drug) levels or checking blood results and clozapine dosages, because the Talking Therapies will be curing all and sundry. If only. We are reverting to the bad old days of pseudomedicine and pseudoscience.

Academicians and those who sit on government advisory bodies with grandiose names would have us believe there are far more effective ways to support people at home, or if they have no home, a crisis house will do. Meaningless, empty statements such as 'randomised controlled trials' (given the complexity of the issues under study) often with some reference to National Institute for Health and Clinical Excellence (NICE) guidelines, are used to support questionable findings. Despite all the 'new

ways of working' national stress levels are at their highest because of rising unemployment, unexpected redundancies, increasing debt through credit card borrowing, and suicide rates are going up. New ways of Working is not working and any 'ad hoc survey' (note we did not say 'research') will reveal the depth of disillusionment all professionals in the discipline of psychiatry are experiencing, and not just the hallowed psychiatrists. Rudderless multidisciplinary teams are not the answer: teams require management. The term 'leadership' is becoming redundant (one only has to look at successive governments) and is often merely a spur for making money out of meaningless and time-wasting leadership courses which seem to be sprouting everywhere. Among the many qualities 'leadership' embraces are a sense of humour, assertiveness, fairness, creativity, openness, integrity and dedication, all to be found in one individual; presumably! Hierarchical structures may work, contrary to the sweeping statements of some,[3] because people who are experienced in medical, academic and management matters (with perhaps a sense of humour) tend to command respect from team members. It is not enough to be an expert in cognitive behavioural therapy (CBT).

No place like home

How does one establish trust and rapport with patients when there will be less opportunity to do so because their care and progress are determined by market forces? Instead of decreasing outpatient volume or confining this aspect of care to CPA patients only, outpatient departments should cater for the mounting levels of stress in the community (poverty, debts, redundancies, threatened job losses) through increased staffing levels and training/supervision of more social workers, CPNs and occupational health workers. Where possible such staff should attend as many clinics as possible (not just CPAs) to offer a more holistic approach to patient care. If anything, policy makers, clinicians, managers, carers and user groups need to collaborate and clamour for a more integrative mental health service, not fracture the already fragile set-up. Community clinics are seen as a stepping stone to discharging from the mental health services (those who set them up don't like this analogy), which in theory is a good idea. The problem lies in the precipitous nature of transfer from outpatient to community clinics. Some very ill patients with chronic conditions are ironically not a burden to the system, in that they do not need to be seen frequently nor do they not require repeated admissions to hospital, yet if left to their own devices and discharged back to Primary Care would soon find life unmanageable as they rely on the expertise of health professionals to remain reasonably stable. Many patients have physical problems, some partly the result of the very treatments given to alleviate their underlying condition (obesity, hypertension, ECG disturbances, Type 2 diabetes and so forth), and need careful monitoring and supervision which is best provided by CPNs and other staff, in the same way a Health Visitor, Practice Nurse, or Diabetes Nurse Specialist might offer his/her expertise to a GP practice.

There will always be patients who need to be seen in the outpatient department with the emotional security and staff support this provides. We are aware that some 20% of patients miss their mental health appointments but then people miss appointments for other interviews and not always because they are unwell.[4] Some people miss appointments because they feel better. This is surely not a reason for abandoning the outpatient system, which serves the remainder of the patient population quite well. We have experienced an unprecedented expression of worry and disappointment by patients who have been told they are not ill enough to be followed up at the outpatient department. Now mental health professionals are also frustrated, because they perceive their remit is to refer back to the GP as swiftly as possible, without having thoroughly assessed a patient over a period of time. First on the target list will be those patients who have not been seen by a psychiatrist for several months ('We don't see them very often, therefore what is the point?') yet many chronically unwell patients may not want to attend outpatients, or have sufficient insight to realize they need to attend, for reasons outlined above. Will Outreach Teams in every Trust be abandoned to save money? Was it not their role in the first place to help those reluctant to receive treatment? What messages are we giving to patients other than being 'just a number, a hospital statistic''? Those who have had the 'luxury' of a hospital admission usually comprise the very psychotic, and the personality disordered, and of the latter some consider they should not be in hospital anyway. The gains that have been made over the past decade in early intervention and engagement with patients by Assertive Outreach Teams will be lost. Yet, there is a continuing demand from patients and their carers to be seen by doctors.[5]

Here is how the 'new' system works. New Ways of Working, set up some years ago 1 and imposed on us, was meant to be an innovative approach to consultants' contracts by encouraging multidisciplinary teamwork ('When did consultants ever not consult their fellow professionals'?), reviewing the continued necessity for outpatient clinics, advocating more scheduled time for carers (colleagues we have spoken to cannot ever recall not seeing relatives or carers!) and more prominent roles for all team members, encouraging further education and training. Unfortunately we have gone to the other extreme and are being bombarded by all sorts of courses to the extent that much time is lost not seeing patients. Team members may and should undertake postgraduate studies. For doctors, continued professional development is mandatory. We are the only profession that requires revalidation every five years. Nothing can substitute for the medical training doctors undergo and it is a shame that the expertise of psychiatrists is diluted and devalued by their current roles as medication gatekeepers. It is a curious state of affairs or perhaps conveniently forgotten that when Trusts or 'Health Care Reformers' talk nowadays about working in teams and 'shared responsibility', the Consultant-led team concept is dismissed. Where there are Consultants who do not feel up to the role of leading a team, or are uncomfortable

making assertive decisions and would rather take a back-seat thus avoiding the responsibility of being in charge of a team, then a Specialist Registrar nearing the end of training could fill this position. Multidisciplinary means 'several' not 'equal' disciplines of learning, ideally each discipline contributing a part to the whole. The medical member of the team is nowadays confronted with the added indignity of having his/her patients described in management-speak as customers, consumers, clients, service users, in fact any title that does not describe the ill person as a patient. It also reflects a creeping normalisation of 'political correctness' thrust upon us by the social engineers and should be resisted. We want patients to be treated with respect not as 'service users', waiting for the next bus or train. Trusts are now seen to promote a business approach to health care, thereby gaining the approval of their masters, the civil servants and politicians.[6] Lots of tick boxes and targets, with subtle threats of redundancies or talks about 'natural wastage'. Meanwhile, the College sits idly by.

Another concern is the training of future psychiatrists which is slip-shod and bureaucratic (lots of forms and assessments). There is hardly any room to accommodate medical students. Junior doctors who practice psychiatry are not receiving the continuity of supervision which existed years ago. The 'junior doctor' is less visible because of European working time directives, on-call commitments with days off in lieu, study leave, annual leave, and the inevitable sick leave. Passing the Member of the Royal College of Psychiatrists (MRCPsych) exams nowadays does not necessarily equate with clinical experience anymore. Even the nomenclature is confusing - not just to doctors and management ('CT1', 'ST1' and so forth) but also to staff, and reduces the profession to an anomalous set of categories no outsider understands, not to mention the loss of identity it creates in the individual doctor. What was wrong with Senior House Officer (SHO), Registrar, Senior Registrar, and Consultant? Unfortunately, we believe it is now too late to revert this shambles born out of the chaotic modernisation of medical careers. [7]

The future is bleak and many doctors (and indeed nurses) are becoming disenchanted by psychiatry, feeling let down by a Royal College which seems to accommodate every new social trend rather than concentrating on improving the status of a once fascinating field of medicine. Lots of wake-up calls, but no-one is getting out of bed.[8] Strange having a 'trade union' that ignores its members! Could someone inform the College that nowadays most General Adult Psychiatrists are almost reduced to measuring lithium levels, advising on clozapine doses, and attending meetings. No wonder the numbers of potential psychiatrists are falling. How would this dilution of responsibility work in a surgical unit? Would the team members decide how an operation is to be carried out because one of them is trained in resuscitation? Contrary to reports[3] consultants are not happy with the present set-up, though it is unlikely our Royal College hierarchy will do anything about it. Many psychiatrists nowadays have an extensive academic knowledge of medicine, psychology, sociology, and neuropsychiatry, and no longer want to be minor players in the game, or undermined by a system that encourages power without responsibility.

Fragmentation breeds disinterest

What is the answer? The previous system, though not perfect, worked well. This had its shortcomings too (oversized catchments areas, Consultants in charge of many wards, and so forth)7 but the continuity of care was there. Patients discharged from hospital were seen by the same team. GPs could refer directly to Consultants (as is the case in other medical specialties) and patients were then seen in the outpatient clinic. However, often the patient would attend such clinics for years because GPs were reluctant to resume care. Nowadays the training and education of GPs is exemplary and most are more than capable and indeed willing, to continue to provide support for their patients provided there is a back-up plan. The academic training of psychiatrists has never been better but their clinical skills are suspect. Therefore there needs to be an overhaul in the examination system as well. Actors are not patients. Simulated psychiatry is not the same as simulated surgery. Simulation is a technique not a technology, we are told. It is not a substitute for doctors examining real patients in real contexts. The same applies to nurses. All nurses (CPNs) could easily be trained to do ECGs, act as phlebotomists, and arrange routine tests. Many already do. Give back to nurses the skills they enjoy in other fields of medicine. For psychiatrists there are numerous courses one can attend to broaden their medical knowledge. Most GPs take an interest in a holistic approach to their patients (social, psychological, physical). As matters stand GPs now refer to a borough 'Access and Allocation Team' with no one held accountable, and even though requested by the GP, a Consultant Psychiatrist's opinion is not always provided. Responsibility is the province of senior doctors and management and should not be diluted by putting pressure on the Team as a whole whose individual experience varies considerably. Doctors (and nursing staff) should have mandatory training in psychological therapies (cognitive and behaviour therapies specifically). A fixed number of sessions in addition to their usual duties could be part of the job plan for those doctors interested in the psychotherapies per se, or put another way, a holistic approach to patient care, which is what most doctors do in any event. Patients would then have the benefit of medical and psychological input simultaneously (let's call it a cognitive-medical model). Waiting lists would be dramatically reduced at a stroke and Trusts would no longer have the responsibility of finding and employing unqualified (in medicine or psychology) 'talking therapists'. People who are generally physically well and who do not have serious psychosocial problems or psychiatric illnesses could receive treatment elsewhere through their GP, counsellors or other psychotherapists (those with no medical or psychology degrees)

of their own volition. There is no need to clog up the system with 'customers'. We are not a supermarket!

Complaints will inevitably follow when patient dissatisfaction begins to emerge, which is only a matter of time. More serious incidents will be a consequence of too many bed closures and staff shortages. Dilution of responsibility means that no one person seems to be accountable when things go wrong and patients are left stranded (read the Francis Report [9]). Already GPs are frustrated by the lack of informal contact with psychiatrists who are once again seen to be retreating to their ivory towers, having been overwhelmed by lots of courses, lots of training, lots of meetings, lots of empty rhetoric. Too much emphasis nowadays is placed on the sociological/psychological aspects of patients' illness and so serious conditions are missed. GPs should be able to refer directly to their colleagues where there are immediate concerns and not have to wait for triage meetings which delay this process. After all, GPs know their patients best. Community clinics could take the bulk of moderate conditions (which are causing undue stress) and see patients for as long as necessary (not a determined number of appointments) before deciding the GP can resume responsibility. 'Packages of Care' and other outdated expressions should be confined to the dustbin. Patients are not fooled by promises of cardboard boxes with little pink ribbons. Continuity of patient care requires a flexible approach which encompasses easy access to information and a direct pathway to services and medical care when needed.

Knowledge in the making

Psychiatrists should concentrate on more difficult and complicated cases (as was the case in the past) as well as routine moderate conditions, enabling them to use their broad skills more efficiently and effectively. Some psychiatrists see too few patients and this should be changed. Perhaps there is a case for psychiatrists rotating through some specialties say, every five years, for example, between Rehabilitation and General Adult Psychiatry. There are many patients who are not on mood stabilisers or clozapine who require intensive input and combined medical expertise and rotating between posts would offer valuable experience. A more varied approach is thus needed but do we really need all those subspecialties? What ever happened to the general psychiatrist with a special interest? In our view at least one year of neurology training should be mandatory for psychiatrists during their training. No formal examinations, just certificates to prove the courses have been completed; otherwise the system grinds to a halt. Under this system a doctor could still theoretically become a consultant after nine years postgraduate training (three years in foundation training and neurology), and six years Psychiatry (to include neurology, psychology and sociology) which is not unreasonable. Equal emphasis on neuromedical, sociological and psychological factors causing health problems would foster a healthier and friendlier relationship between disciplines which deal with mental illness and primary care providers. As it stands, with the fragmented role of general adult psychiatric services and the emphasis on e-learning and internet training for junior doctors (no hands-on clinical experience) we are facing yet another era of overemphasis on social psychiatry (or rather reverting to ancient belief systems) with its 'neutral' politically correct denigrating sound bites (customers, clients, service users). All will be well if we can just sort out the social problems! The simplistic notion that problems will disappear if we do not smoke, drink, take illicit drugs, keep our weight down, and have a home to go to, is the stuff of social engineering by the 'experts in living,' and alas by doctors who have lost touch with medicine.

Doctors need reminding that psychiatry is that branch of medicine that is concerned with the study, treatment, and prevention of mental illness using medical and psychological therapies as well as paying special attention to social hardship and isolation where present. It is not philosophy or social science. It is to medicine what metaphysics is to philosophy. Psychiatrists need to broaden their horizons and take their heads out of the therapy books to witness the advances in neuroscientific techniques and genetic advancements that have already transformed the nature of medicine. To develop their psychological skills they need to take on board that patients want more than drugs to alleviate distress. Therefore practical techniques such as CBT or DBT (dialectical behaviour therapy) will further heighten their expertise as physicians. Many doctors are already familiar with applying CBT and other therapies. However, doctors should also be aware of the limitations of psychotherapies in general, recognizing and acknowledging that such therapies do not always work either and indeed in some instances may be harmful. Psychiatrists should be part of separate Wellbeing Clinics (perhaps one session per week) to becoming better acquainted and proficient again with physical examinations, investigations, routine procedures (ECGs for example) and interpretation of results (not just screen, but to intervene). This overseeing of the physical health of patients is not always possible in a busy outpatient clinic. Many potentially serious conditions would be revealed and information to the GP or tertiary services made known immediately. Psychiatrists are not 'stuck in a medical model' no more than a physician believes all myocardial infarcts are caused by psychosocial factors or life style. But to ignore the medical advances in molecular biology and neuroscientific diagnostic techniques portrays a profound ignorance of biological psychiatry and is insulting to those scientists who work tirelessly, often without much recognition, to further our understanding of 'brain disorders'. It is all very well to talk about art, philosophy, social sciences and literature as having a great bearing on our interest in psychiatry and congratulate ourselves as 'lateral thinkers' but an understanding of the philosophy of say, Bertrand Russell or indeed the school of Zen Buddhism, will not eliminate mental disorder. Romantic as it might sound in retrospect, Vincent Van Gogh did not enjoy cutting his ear off, nor did Robert

Schumann feel ecstatic when jumping into the Rhine before being carted off to the asylum.

If we do not embrace a holistic view of mental ill-health we risk not only throwing the baby out with the bath water but the bath itself, thereby causing further dissatisfaction and low morale among doctors with an inevitable negative impact on patient care. Psychiatrists are not bemoaning their loss of hegemony - a favourite word and another myth propagated by the antipsychiatry lobby; rather, it is only too obvious to them (as qualified medical doctors) that patients will suffer in the long term by not being referred appropriately to those who have the expertise to recognize and distinguish between human difficulties and illness. There is also a need to re-examine the impact of psychological therapies and not succumb to the popular and naive notion that they are all evidence-based in scientific terms. In the meantime the 'worried well' can indulge themselves with all the peripheral talking therapies and current fads they desire. Likewise, performance management, outcome measures and payment by results have become relentless tick-box exercises creating unnecessary stress among health care professionals (threats of job losses) who 'must meet targets at all costs', all for a slice of the Commissioners' cake. What a way to run a health service! Patients become meaningless statistics in the meantime. No! The wake-up call should be aimed at those who are intent on destroying the good will and values of the very same people they purport to support, through their social engineering and outdated attitudes.

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None declared
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