BJMP

Volume 5 Number 1
March 2012

British Journal of Medical Practitioners

www.bjmp.org
ISSN: 1757-8515

British Journal of Medical Practitioners

Volume 5 Number 1 (March 2012)

http://www.bjmp.org

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British Journal of Medical Practitioners

Volume 5 Number 1 (March 2012)

BJMP March 2012 Volume 5 Number 1

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BJMP 2012;5(1):a510

Editorial

Are opioids effective and necessary for chronic non-malignant pain

Yili Zhou and Bohdan Warycha

In recent years, increasing attention has focused on the treatment of chronic pain with a considerable number of research and publications about it. At the same time, opioid prescription, use, abuse and death related to the inappropriate use of opioids have significantly increased over the last 10 years. Some reports indicated that there were more than 100 'pain clinics' within a one-mile radius in South Florida, between 2009 and 2010, which led to the birth of new opioid prescription laws in Florida and many other states to restrict the use of opioids. In the face of clinical and social turmoil related to opioid use and abuse, a fundamental question facing each clinician is: are opioids effective and necessary for chronic non-malignant pain?

Chronic low back pain (LBP) is the most common pain condition in pain clinics and most family physician offices, which 'requires' chronic use of opioids. Nampiaparampil et al conducted a literature review in 2012[1] and found only one high-quality study on oral opioid therapy for LBP, which showed significant efficacy in pain relief and patient function. Current consensus believes that there is weak evidence demonstrating favourable effectiveness of opioids compared to placebo in chronic LBP.[2]Opioids may be considered in the treatment of chronic LBP if a patient fails other treatment modalities such as non-steroidal anti-inflammatory drugs (NSAIDs), antidepressants, physical therapy or steroid injections. Opioids should be avoided if possible, especially in adolescents who are at high risk of opioid overdose, misuse, and addiction. It has been demonstrated that the majority of the population with degenerative disc disease, including a disc herniation have no back pain. A Magnetic Resonance Imaging (MRI) report or film with a disc herniation should not be an automatic 'passport' for access to narcotics.

Failed back surgery syndrome (FBSS) is often refractory to most treatment modalities and sometimes very debilitating. There are no well-controlled clinical studies to approve or disapprove the use of opioids in FBSS. Clinical experience suggests oral opioids may be beneficial and necessary to many patients suffering from severe back pain due to FBSS. Intraspinal opioids delivered via implanted pumps may be indicated in those individuals who cannot tolerate oral medications. For elderly patients with severe pain due to spinal stenosis, there is no clinical study to approve or disprove the use of opioids. However, due to the fact that NSAIDs may cause serious side effects in gastrointestinal, hepatic and renal systems, opioid therapy may still be a choice in carefully selected patients.

Most studies for pharmacological treatment of neuropathic pain are conducted with diabetic peripheral neuropathy (DPN) patients. Several randomized clinical controlled studies have demonstrated evidence that some opioids, such as morphine sulphate, tramadol,[3] and oxycodone controlled-release,[4] are probably effective in reducing pain and should be considered as a treatment of choice (Level B evidence), even though anti-epileptics such as pregabalin should still be used as the first line medication.[5]

Some studies indicate opioids may be superior to placebo in relieving pain due to acute migraine attacks and Fiorinal with codeine may be effective for tension headache. However there is lack of clinical evidence supporting long-term use of opioids for chronic headaches such as migraine, chronic daily headache, medication overuse headache, or cervicogenic headache. Currently there are large amounts of opioids being prescribed for headaches because of patients' demands. Neuroscience data on the effects of opioids on the brain has raised serious concerns for long-term safety and has provided the basis for the mechanism by which chronic opioid use may induce progression of headache frequency and severity.[6] A recent study found chronic opioid use for migraine associated with more severe headache-related disability, symptomology, comorbidities (depression, anxiety, and cardiovascular disease and events), and greater healthcare resource utilization.[7]

Many patients with fibromyalgia (FM) come into pain clinics to ask for, or even demand, prescriptions for opioids. There is insufficient evidence to support the routine use of opioids in fibromyalgia.[8] Recent studies have suggested that central sensitization may play for role in the aetiology of FM. Three central nervous system (CNS) agents (pregabalin, duloxetine and milnacipran) have been approved by United States Food and Drug Administration (US FDA) for treatment of FM. However, opioids are still commonly prescribed by many

physicians for FM patients by 'tradition', sometimes even with the combination of a benzodiazapine and muscles relaxant - Soma. We have observed negative health and psychosocial status in patients using opioids and labeled with FM. Opioids should be avoided whenever possible in FM patients in face of widespread abuse and lack of clinical evidence.[9]

Adolescents with mild non-malignant chronic pain rarely require long-term opioid therapy.[10] Opioids should be avoided if possible in adolescents, who are at high risk of opioid overdose, misuse, and addiction. Patients with adolescents living at home should store their opioid medication safely.

In conclusion, opioids are effective and necessary in certain cases. However, currently no single drug stands out as the best therapy for managing chronic non-malignant pain, and current opioid treatment is not sufficiently evidence-based. More well-designed clinical studies are needed to confirm the clinical efficacy and necessity for using opioids in the treatment of chronic non-malignant pain. Before more evidence becomes available, and in the face of widespread abuse of opioids in society and possible serious behavioural consequences to individual patients, a careful history and physical examination, assessment of aberrant behavior, controlled substance agreement, routine urine drug tests, checking of state drug monitoring system (if available), trials of other treatment modalities, and continuous monitoring of opioid compliance should be the prerequisites before any opioids are prescribed.

Opioid prescriptions should be given as indicated, not as 'demanded'.

Competing Interests
None declared
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Research Article

BJMP 2012;5(1):a512

Effectiveness of Chlorhexidine oral decontamination in reducing the incidence of ventilator associated pneumonia: A meta-analysis.

E Balamurugan , A Kanimozhi and Govinda Kumari

ABSTRACT

Background and Purpose: Ventilator-associated pneumonia (VAP) is an important nosocomial infection worldwide, which leads to increased length of hospital stay, healthcare costs and mortality. Evidence on oral decontamination with antiseptic in reducing VAP is limited. Hence, a meta-analysis was performed to determine the effect of chlorhexidine oral decontamination in the reduction of VAP in mechanically ventilated patients

Methods: An extensive literaturereview was conducted using the following databases: CINAHL, MEDLINE, Joanna Briggs Institute, Cochrane Library, EMBASE, CENTRAL, and the Google search engine. Retrieved articles were selected based on the methodological quality, inclusion criteria and analysed to find the pooled effect size.

Results: The nine trials included in this meta-analysis revealed a significant reduction in the incidence of VAP among patients who received prophylactic oral decontamination with Chlorhexidine. However no significant effect was found in reducing overall mortality rate among the mechanically ventilated patients.

Conclusion: The safety profile regarding the possible selection and induction of antibiotic resistance and presumed cost benefits of Chlorhexidine make it a highly attractive intervention for the prevention of VAP. This meta-analysis indicated that chlorhexidine can serve as a cost-effective and safe antiseptic in preventing VAP in mechanically ventilated patients.

KEYWORDS : Chlorhexidine; Oral decontamination; Ventilator associated pneumonia; Mechanical ventilation

Introduction

Nosocomial pneumonia in patients receiving mechanical ventilation, also called ventilator-associated pneumonia (VAP), is an important nosocomial infection worldwide which leads to an increased length of hospital stay, healthcare costs, and mortality.[1,2,3,4,5] The incidence of VAP ranges from 9% to 27% with a crude mortality rate that can exceed up to 50%. [6,7,8,9] Aspiration of bacteria from the upper digestive tract is an important proposed mechanism in the pathogenesis of VAP.[9, 10] The normal flora of the oral cavity may include up to 350 different bacterial species, with tendencies for groups of bacteria to colonize different surfaces in the mouth. For example, *Streptococcus mutans, Streptococcus sanguis, Actinomyces viscosus,* and *Bacteroides gingivalis* mainly colonize the teeth; *Streptococcus salivarius* mainly colonizes the dorsal aspect of the tongue; and *Streptococcus mitis* is found on both buccal and tooth surfaces.[11] Because of a number of processes, however, critically ill patients lose a protective substance called*fibronectin* from the tooth surface. Loss of fibronectin reduces the host defence mechanism mediated by reticuloendothelial cells. This reduction in turn results in an environment conducive to attachment of microorganism to buccal and pharyngeal epithelial cells.[12] Addressing the formation of dental plaque and its continued existence by optimizing oral hygiene in critically ill patients is an important strategy for minimizing VAP.[13] Two different interventions aimed at decreasing the oral bacterial load are selective decontamination of the digestive tract involving administration of non absorbable antibiotics by mouth, through a naso-gastric tube, and oral decontamination, which is limited to topical oral application of antibiotics or antiseptics.[14] Though meta-analysis of antibiotics in decontamination of digestive tracts have found positive results[15] , the use of this intervention is, however, limited by concern about the emergence of antibiotic resistant bacteria.[16] One alternative to oral decontamination with antibiotics is to use antiseptics, such as chlorhexidine which act rapidly at multiple target sites and accordingly may be less prone to induce drug resistance.[17] Recently a meta-analysis of four trials on chlorhexidine failed to show a significant reduction in rates of ventilator associated pneumonia[18] but, subsequent randomised controlled trials, however, suggested benefit from this approach.[19] Current guidelines from the Centres for Disease Control and Prevention recommend topical oral chlorhexidine 0.12% during the perioperative period for adults undergoing cardiac surgery (grade II evidence). The routine use of antiseptic oral decontamination for the prevention of ventilator associated pneumonia, however, remains unresolved.[8] Despite the lack of firm evidence favouring this preventive intervention, a recent survey across 59 European intensive care units from five countries showed that 61% of the respondents used oral decontamination with chlorhexidine. As the emphasis on evidence based practice is increasing day by day, integrating recent evidence by meta-analysis could greatly benefit patient care and ensure safer practices. Hence we carried out this meta-analytic review to ascertain the effect of oral decontamination using chlorhexidine in the incidence of ventilator associated pneumonia and mortality in mechanically ventilated adults.[20]

Methods

Table 1: Brief summary of trials

Source	Subjects	Intervention	ComparedWith	Outcome with respect to VAP		Outcome with respect to Mortality	
				C	E	C	E
DeRiso et al., 1996	353- Open Heart surgery patients	Chlorhexidine 0.12% 15 ml preoperatively and twice daily postoperatively until discharge from intensive care unit or death	Placebo	9/180	3/173	10/180	2/173
Fourrier et al., 2000	60- Medical and surgical patients	Chlorhexidine gel 0.2% dental plaque decontamination 3 times daily, compared with bicarbonate solution rinse 4 times daily followed by oropharyngeal suctioning until 28 days discharge form ICU or death	Standard treatment	15/30	5/30	7/30	3/30
Houston et al., 2002	561- cardiac surgery patients	Chlorhexidine 0.12% rinse compared with Listerine preoperatively and twice daily for 10 days postoperatively or until extubation, tracheostomy, death, or diagnosis of pneumonia.	Standard treatment	9/291	4/270	NA	NA
MacNaughton et al., 2004	194 – Medical and surgical patients	Chlorhexidine 0.2% oral rinse twice daily until extubation or death	Placebo	21/101	21/93	29/93	29/101
Fourrier et al., 2005	228 –ICU patients	Chlorhexidine 0.2% gel three times daily during stay in intensive care unit until 28 days	Placebo	12/114	13/114	24/114	31/114
Segers et al.,2005	954 – cardiac surgery patients	Chlorhexidine 0.12%, nasal ointment, and 10 ml oropharynx rinse four times daily on allocation and admission to hospital until extubation or removal of nasogastric tube	Placebo	67/469	35/485	6/469	8/485
Boop et al., 2006	5- cardiac surgery patients as pilot study	0.12% chlorhexidine gluconate oral care twice daily until discharge	Standard treatment	1/3	0/2	NA	NA
Koeman et al., 2006	385 –General ICU patients	2 treatment group: 2%Chlorhexidine, chlorhexidine and colistin, placebo four times daily until diagnosis of ventilator associated pneumonia, death, or extubation	Placebo	23/130	13/127	39/130	49/127
Tontipong et al., 2008	207 –General medical ICU or wards	2% chlorhexidine solution times per day until endotracheal tubes were removed.	Standard treatment	12/105	5/102	37/105	36/102

NA-Not available; C-Control group; E- Experimental group

Articles published from 1990 to May 2011 in English which were indexed in the following databases were searched: CINAHL, MEDLINE, Joanna Briggs Institute, Cochrane Library, EMBASE, CENTRAL, and Google search engine. We also screened previous meta-analyses and the references lists from all the retrieved articles for additional studies. Further searches were carried out in two trial registers (www.clinicaltrials.gov/ and www.controlled-trials.com/) and on web postings from conference proceedings, abstracts, and poster presentations.

Articles retrieved were assessed for inclusion criteria by three independent reviewers from the field of nursing with masters degrees. The inclusion criteria set for this meta-analysis were as follows:

a) VAP definition meeting both clinical and radiological criteria
b) Intubation for more than 48 hours in ICU.

We excluded the studies where clinical pulmonary infection score alone was considered for diagnosing VAP. Thereafter the articles were evaluated for randomisation, allocation concealment, blinding techniques, clarity of inclusion and exclusion criteria, outcome definitions, similarity of baseline characteristics, and completeness of follow-up. We considered randomisation to be true if the allocation sequence was generated using computer programs, random number tables, or random drawing from opaque envelopes. Finally, based on the above characteristics, only 9 trials which fulfilled the inclusion criteria was included for the pooled analysis. A brief summary of the 9 trials were listed in Table 1. The primary outcomes in this meta-analysis were incidence of VAP and mortality rate.

Data analysis

Meta-analysis was performed in this study by using Review Manager 4.2 (Cochrane Collaboration, Oxford) with a random

effect model. The pooled effects estimates for binary variables were expressed as a relative risk with 95% confidence interval. Differences in estimates of intervention between the treatment and control groups for each hypothesis were tested using a two sided z test. We calculated the number of patients needed to treat (NNT, with 95% confidence interval) to prevent one episode of ventilator associated pneumonia during the period of mechanical ventilation. A chi-squared test was used to assess the heterogeneity of the results. A Forest plot graph was drawn using Stats direct software version 2.72 (England: Stats Direct Ltd. 2008). We considered a two tailed P value of less than 0.05 as significant throughout the study.

Results

Effect of Chlorhexidine in reducing the Incidence of VAP

A total of nine trials were included in this meta-analysis[19,21,22,23,24,25,26,27,28]. Pooled analysis of the nine trials with 2819 patients revealed a significant reduction in the incidence of VAP using chlorhexidine (Relative risk 0.60, 0.47 to 0.76; P< 0.01) (Figure 1). In relation to the Number Needed to Treat (NNT), 21 patients would need to receive oral decontamination with Chlorhexidine to prevent one episode of Ventilator associated pneumonia (NNT 21, 14 to 38).

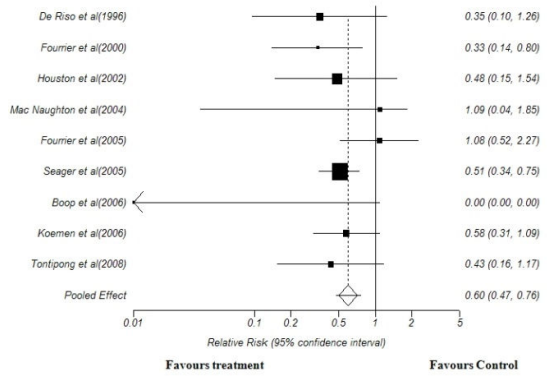

Figure 1: Forest Plot showing the effect of Chlorhexidine oral decontamination in preventing the incidence of ventilator-associated pneumonia. Test for heterogeneity: χ^2 =15.5, df =8, p < 0.01. Test for overall effect: z =4.33, p <0.05.

Effect of Chorhexidine in overall mortality rate

For assessing the outcomes in terms of mortality, only seven out of nine trials were included, since the other two[23,27]did not report the mortality rate. Pooled analysis of the seven trials with 2253 patients revealed no significant effect in reducing the overall mortality rate in patient who received chlorhexidine oral decontamination.(Relative risk 1.02, 0.83 to 1.26; P= 0.781 (Figure 2).

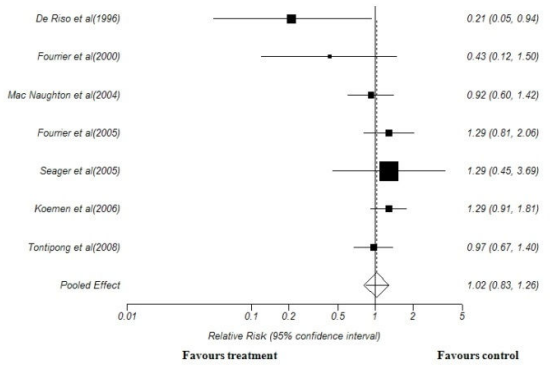

Figure 2: Forest plot showing the effect of Chlorhexidine oral decontamination in reducing overall mortality rate. Test for heterogeneity: χ^2 =0.05, df =6, p = 0.81. Test for overall effect: z =0.27, p = 0.78

Discussion

The effectiveness of oral decontamination to prevent VAP in patients undergoing mechanical ventilation has remained controversial since its introduction, due to partly discordant results of individual trials. In the present meta-analysis nine trials were included to estimate the pooled effect size; the results revealed a significant reduction in the incidence of VAP among patients who were treated with oral chlorhexidine. But, it had no effect in reducing the overall mortality rate among these patients. There is a firm body of evidence that oropharyngeal colonization is pivotal in the pathogenesis of VAP. More than 25 years ago, Johanson et al described associations between increasing severity of illness, higher occurrence of oropharyngeal colonization, and an increased risk of developing VAP .[29,30]Subsequently, cohort and sequential colonization analyses identified oropharyngeal colonization as a important risk factor for VAP.[31,32,33] Our finding confirms the pivotal role of Oro-pharyngeal colonization in the pathogenesis of VAP , since this meta-analysis indicates that oral decontamination may reduce the incidence of VAP. Chlorhexidine was proven to have excellent antibacterial effects, with low antibiotic resistance rates seen in nosocomial pathogens, despite long-term use[34]. Previous meta-analyses examining the effect of prophylaxis using selective decontamination of the digestive tract reported a significant reduction in the incidence of ventilator associated pneumonia[35,36,37]. The most recent meta-analysis indicated that such an intervention combined with prophylactic intravenous antibiotics reduces overall mortality[38]. In comparison our review suggests that oral antiseptic prophylaxis alone can significantly reduce the incidence of ventilator associated pneumonia, but not mortality. A similar result was documented by Ee Yuee Chan et al (2007)[14] who performed a meta-analysis with seven trials with a total of 2144 patients and found a significant result (Odds ratio 0.56, 0.39 to 0.81). Another comparable finding in the present study was, Mortality rate was not influenced by use of Chlorhexidine use, which was in line with the findings of Ee Yuee Chan et al (2007)[14] . Our meta-analysis on Chorhexidine

differs from the findings of Pineda et al, who pooled four trials on chlorhexidine and did not report lower rates of ventilator associated pneumonia (odds ratio 0.42, 0.16-1.06; P=0.07)[18] . Our results also extend those of Chlebicki et al, who did not find a statistically significant benefit using the more conservative random effects model after pooling seven trials on chlorhexidine (relative risk 0.70, 0.47- 1.04; P=0.07), although their results were significant with the fixed effects model[39]. Our meta-analysis included larger data set with a total of 9 trials including recent trials[28] which further adds strength to our analysis.

Limitations

Though our literature search was comprehensive, it is possible that we missed other relevant trials. Electronic and hand searches do not completely reflect the extent of research outcomes. For example, trials reported at conferences are more likely than trials published in journals to contain negative reports. In addition, more positive than negative results tend to be reported in the literature. This failure to publish more studies with negative outcomes is probably more due to authors' lack of inclination to submit such manuscripts than to the unwillingness of editors to accept such manuscripts. Furthermore, many studies not published in English were not included e.g. a study by Zamora Zamora F (2011).[40] These limitations may lead to a risk for systematic reviews to yield a less balanced analysis and may therefore affect the recommendations resulting from the reviews. In addition, the heterogeneity which we found among the trials with respect to populations enrolled, regimens used, outcome definitions, and analysis strategies, may limit the ability to generalize results to specific populations.

Conclusion

The finding that chlorhexidine oral decontamination can reduce the incidence of ventilator associated pneumonia could have important implications for lower healthcare costs and a reduced risk of antibiotic resistance compared with the use of antibiotics. These results should be interpreted in light of the moderate heterogeneity of individual trial results and possible publication bias. It may not be prudent to adopt this practice routinely for all critically ill patients until strong data on the long term risk of selecting antiseptic and antibiotic resistant organisms are available. Nevertheless, Chlorhexidine oral decontamination seems promising. Further studies are clearly needed in testing the effect of Chlorhexidine in specific populations with standard protocols (which includes specific concentration, frequency, and type of agents) to generalize the findings. Studies also may be done to test the effect of different oral antiseptics in reducing VAP, so as to enrich the body of knowledge within this area.

Acknowledgements
The author is grateful to B.B Dixit Library, AIIMS, New Delhi India, for their guidance in retrieving online journals for this meta-analysis.
Competing Interests
None declared
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Research Article

BJMP 2012;5(1):a508

Barriers for Anaesthetists in Performing Nerve Blocks with Ultrasound Guidance

Asif Mahmood, Mohammed Auldin and Asquad Sultan

ABSTRACT

Aim: To review the potential barriers for clinicians in performing nerve blocks with appropriate resolution ultrasound (US) machines as recommended by the National Institute for Health and Clinical Excellence (NICE).

Methods: A paper survey was handed out to anaesthetists of all grades. Information regarding nerve block competencies was gathered along with the availability of ultrasound machines in their area of work, along with any training they may have received in its use.

Results: We gathered responses from 52 anaesthetists. Only 50% of respondents had completed a training course in ultrasound guided nerve blocks. 42% of anaesthetists had their use of an ultrasound for nerve blocks limited by the lack of availability of an ultrasound in their area of work. Of the consultants surveyed, 34% felt competent in performing ultrasound guided interscalene block vs 54% with the landmark technique.

Conclusions: The anaesthetists surveyed demonstrated a range of competencies in the use of ultrasound for the different nerve blocks; this could be due to the lack of training for such blocks, the lack of availability of ultrasound machines or due to competency in performing nerve blocks without ultrasound. This identifies potential deficits in training and the need for appropriate resolution ultrasound machines in the work place.

Background

Nerve blocks have a variety of applications in anaesthesia enabling an extra dimension for patients with regards to their pain control and anaesthetic plan. Anaesthetists can perform nerve blocks by a range of methods including landmark techniques and ultrasound guidance, with both of these techniques having the potential to be used with a nerve stimulator.

Nerve blocks are associated with complications including nerve damage, bleeding, pneumothorax and failure. Ultrasound, if used correctly, may help limit such complications.[1] NICE guidance on the use of ultrasound guidance for procedures, has evolved over the years. Ultrasound guidance is now considered an essential requirement for the placement of central venous lines[2] and is recommended when performing nerve blocks.[3]

Method

This survey aimed to assess the methods used by anaesthetists in performing nerve blocks and audited the use and competencies of clinicians in performing such blocks under ultrasound guidance and landmark techniques. This survey also looked at whether performing nerve blocks under ultrasound guidance was hindered by the lack of availability of appropriate resolution ultrasound machines in the workplace.

A paper survey was completed by anaesthetists of all grades at Kettering general hospital, UK and Birmingham Heartlands Hospital, UK between October and December 2011. The survey consisted of a simple, easy to use, tick box table and a generic area in which participants made further contributions. From this we ascertained the following:

- Grade of clinician.
- Any courses undertaken in ultrasound guided nerve blocks.
- Which nerve blocks the clinicians felt they could perform competently with either method (landmark versus ultrasound guided).
- In the event the anaesthetist could perform a block with or without ultrasound guidance; which method was used if ultrasound equipment was available.
- Was the ability to perform ultrasound guided nerve blocks limited by the availability of an ultrasound machine.

The term "landmark technique" is used when the landmark technique is combined with or without a nerve stimulator and the term "ultrasound technique" when ultrasound guidance is used with or without a nerve stimulator.

Results

We surveyed a total of 52 anaesthetists, subdivided into Consultants 26 (50%), ST/staff grade 17 (33%), CT trainees 9 (17%). Of all grades, only 50% had completed a course in ultrasound guided nerve blocks. 42% of clinicians had encountered situations when they could not use ultrasound guidance for a nerve block because there was no ultrasound machine available at the time of the procedure. The competencies of clinicians with the landmark and ultrasound technique varied depending on the type of nerve block and the grade of clinician (figure 1).

	Consultant (%) n-26		ST/Staff Grade (%) n-17		CT1/2 (%) n-9	
Nerve block	**Competent Landmark**	**Competent US**	**Competent Landmark**	**Competent US**	**Competent Landmark**	**Competent US**
Brachial Plexus						
Interscalene	54	34	58	29	0	0
Supra/Infra clavicular	31	23	29	18	0	0
Axillary	31	31	47	18	0	0
Elbow	12	19	29	12	0	0
Lumbar Plexus	73	0	65	12	11	0
Sciatic						
Anterior	39	8	64	12	0	0
Posterior	42	27	76	18	0	0
Femoral	100	69	100	76	36	11
Epidural	100	19	100	18	36	0
Spinal	100	12	100	18	56	0
Abdominal						
TAP	38	85	29	65	33	11
Rectus Sheath	19	35	18	47	0	11

Figure 1. This table illustrates competencies for different nerve blocks with the landmark technique and ultrasound technique for different grades of anaesthetists

Various routinely performed blocks were surveyed and this revealed a good comparison of the use of ultrasound and landmark technique. For the Interscalene block, the consultants and middle grades combined were competent in performing this block, with the landmark technique 56% and the ultrasound technique 33%. For the Lumbar plexus block, 0% of the consultants surveyed felt competent in performing this block with the ultrasound technique compared to 73% with the landmark technique. The majority of clinicians felt competent in performing the TAP block with the ultrasound technique, 65% versus 35%, for the landmark technique.

Discussion

The findings of this survey and audit have a range of implications for anaesthetists in the workplace:

1) Junior grades of doctors do not feel competent in performing nerve blocks. This may lead to a reliance on senior doctors during on calls to assist in performing blocks such as femoral and TAP blocks. Specific training geared towards junior doctors to make them proficient in such blocks would enable them to provide an anaesthetic plan with more autonomy.

2) A large percentage of consultant grade clinicians felt competent in performing nerve blocks with the landmark technique but not in performing the same blocks with ultrasound guidance. This has implications for training because consultants are the training leads for junior grades of anaesthetists. If consultants do not feel competent in the use of ultrasound guidance for nerve blocks, this could lead to a self perpetuating cycle.

3) Only 50% of clinicians in this survey had completed a course for ultrasound guided nerve blocks, this coupled with the finding that clinicians did not feel comfortable in performing nerve blocks with ultrasound, indicates the possible need for local training accessible to clinicians to improve their everyday practice.

4) It has been shown that ultrasonic guidance improves the success rate of interscalene blocks.[4] The practice amongst clinicians in this survey reveals that the majority of anaesthetists (middle and consultant grades) are competent with the landmark technique 56% compared to the ultrasound technique 36%. This also highlights a training deficit which if addressed would enable clinicians to offer a more successful method of performing the interscalene block.

5) This survey highlighted the lack of availability of appropriate ultrasound machines in different departments, leading to some clinicians utilising the landmark technique, when ultrasound guidance was the preference. This has the potential of a patient receiving a nerve block technique which may have been riskier and less efficient. This highlights a potential need for investment and accessibility of appropriate resolution ultrasound machines in the different work places of a hospital environment.

The main limitation of this project was the small number of clinicians in the respective hospitals the survey was performed in. However, we feel the results reflect the practice of clinicians across most anaesthetic departments. The recommendations highlight a training need for anaesthetic trainees in the use of ultrasound guided nerve blocks. This survey could form the basis of a much larger survey of clinicians across the UK to provide a more insightful review of the competencies and preferences of anaesthetic trainees in performing nerve blocks and the availability of appropriate resolution ultrasound machines.

The difference in the number of clinicians in each category limited comparisons between groups. A larger cohort of participants would enable comparison of nerve block techniques between different grades of clinicians.

This survey included all clinicians regardless of their sub-specialist interest. This may result in a skewing of results, depending on the area of interest of the clinicians surveyed.

This work only highlights the competencies and preferences of clinicians in performing nerve blocks. No extrapolation can be made to complications that arise from the choice of either technique. Studies have shown an improved success rate when performing nerve blocks with ultrasound.[4] However this does not directly apply to a specific clinician who may have substantial experience in their method of choice in performing a nerve block.

Competing Interests

None declared

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Research Article

BJMP 2012;5(1):a504

Are we managing acute knee effusion well?

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ABSTRACT

Background: Non-traumatic knee effusion is a common referral to the on-call Orthopaedic team. The two most common causes of this presentation are septic and crystal arthritis. Crystal-induced arthritis can easily be overlooked or misdiagnosed as septic arthritis resulting in patients having unnecessary antibiotic therapy and surgical procedures.

Objectives: To review our management of patients with hot swollen knees, especially those due to crystal arthritis.

Materials and methods: We performed a retrospective study of patients presenting to the emergency department with acute non-traumatic knee effusion. A total of 180 patients were identified; 60 patients were included in the study.

Results: All joints were aspirated and samples were sent for microscopy, culture and antibiotic sensitivity, and polarized light microscopy. Twenty six patients were admitted and received antibiotic therapy based on clinical suspicion of infection, arthroscopic washout was performed on eight. Four patients showed positive microscopic growth while eight had crystals identified on polarized light microscopy of joint aspirate. Only two (25%) patients with crystal arthropathy received appropriate treatment and a rheumatology referral. Seven patients developed complications during their hospital stay.

Conclusion: Crystal arthritis is a common and serious cause of acute painful knee that can lead to joint damage if not treated properly. We should always remember to follow up the results of polarized light microscopy of joint aspirates. Prompt diagnosis can avoid unnecessary antibiotic therapy and surgical intervention. All patients with confirmed crystal arthritis should receive a rheumatology referral for further management and follow up.

KEYWORDS: Crystal arthritis, gout, hot swollen knee, Pseudogout, polarized light microscopy

Introduction

Acute non-traumatic knee effusion is a common condition presenting to the Orthopaedic department which can be caused by a wide variety of diseases(Table 1). Septic arthritis is the most common and serious etiology. It can involve any joint; the knee is the most frequently affected. Accurate and swift diagnosis of septic arthritis in the acute setting is vital to prevent joint destruction, since cartilage loss occurs within hours of onset[1,2]. Inpatient mortality due to septic arthritis has been reported as between 7-15%, despite improvement in antibiotic therapy[3,4]. Crystal arthritis (Gout/Pseudogout) is the second most common differential diagnosis. It is often under-diagnosed and subsequently patients do not receive rheumatology referral for appropriate treatment and follow-up. In addition, some patients are misdiagnosed and treated as septic arthritis with inappropriate antibiotics. Untreated crystal-induced arthropathy has been shown to cause degenerative joint disease and disability leading to a considerable health economic burden.[6,7]

When the patient is systemically unwell, it is common practice to start empirical antibiotic treatment after joint aspiration for the fear of septic arthritis. This aims to minimize the risk of joint destruction while awaiting gram stain microscopy and microbiological culture results. In a persistent painful swollen knee with negative gram stain and culture, antibiotic therapy can be continued with or without arthroscopic knee washout based on clinical suspicion of infection [8].

We have therefore undertaken a retrospective study to review our management of patients with non-traumatic hot swollen knees and in particular patients with crystal-induced arthritis.

Materials and methods:

We performed a retrospective review of 180 patients presenting consecutively with acute non-traumatic knee effusion referred to the on-call Orthopaedic team in the hospital of study between November 2008 and November 2011. Sixty patients were included in the study (Table 2). There were 43 males and 17 females, with a mean age of 36 years (range, 23- 93 years).

Patient demographics, clinical presentation, co-morbidities, current medications and body temperature were recorded. The results of blood inflammatory markers (WBC, CRP), blood cultures, synovial fluid microscopy, culture and polarized microscopy were also collected. Subsequent treatment (e.g. antibiotics, surgical intervention), complications, and mortality rates were reviewed.

Results:

On presentation, a decreased range of movement was evident in all patients. Associated knee pain was reported by 55 patients (92%), and 24 patients (40%) had fever (temperature ≥ 37.5º). All joints were aspirated prior to starting antibiotics and samples were sent for gram stain microscopy, culture and antibiotic sensitivity, and polarized light microscopy.

Of the 60-patient cohort, 26 were admitted and started on intravenous antibiotics based on clinical suspicion of infection (Table 3). The median duration of inpatient admission was 4 days (range, 2 to 14 days). The median duration of antibiotic

therapy was 6 days (range, 2 to 25 days). Eighteen patients were treated non-operatively by means of antibiotics and anti-inflammatory medications. Arthroscopic washout was performed in the remaining eight knees. In this group of patients, leucocyte count in the joint aspirate ranged from 0-3 leucocyte/mm^3, blood leucocyte count ranged from 4-20 leucocyte/mm^3, while mean CRP was 37.8 mg/l (range, 1-275 mg/l).

Review of laboratory results revealed that four patients had positive microscopic growth on gram stained films. Two samples showed staphylococcus aureus growth and two grew beta haemolytic streptococci. Eight patientshad crystals identified on polarized light microscopy of joint aspirate. Three showed monosodium urate (MSU) crystals while five had calcium pyrophosphate (CPP) crystals. They received antibiotic therapy for a mean duration of 10 days (range, 1-30 days). Two patients were taken to theatre for arthroscopic lavage. Only two patients received rheumatology referral.

Seven patients developed complications during their hospital stay. Four contracted diarrhoea; three of which had negative stool cultures but one was positive for clostridium difficile, developed toxic megacolon and died. One patient with known ischemic heart disease had a myocardial infarction and died. Two further patients acquiredurinary tract infections.

Discussion:

Acute monoarthritisof the knee joint can be a manifestation of infection, crystal deposits, osteoarthritis and a variety of systemic diseases. Arriving at a correct diagnosis is crucial for appropriate treatment [9]. Septic arthritis, the most common etiology, develops as a result of haematogenous seeding, direct introduction, or extension from a contiguous focus of infection. Joint infectionis a medical emergency that can lead to significant morbidity and mortality. Mainstay of treatment comprises appropriate antimicrobial therapy and joint drainage [10,11]. Literature reveals the knee is the most commonly affected joint (55%) followed by shoulder (14%) in the septic joint population[12-13].

The second most common differential diagnosis is crystal-induced monoarthritis. Gout and pseudogout are the two most common pathologies [14]. They are debilitating illnesses in which recurrent episodes of pain and joint inflammation are caused by the formation of crystals within the joint space and deposition of crystals in soft tissue. Gout is caused by monosodium urate (MSU) crystals, while pseudogout is inflammation caused by calcium pyrophosphate (CPP) crystals, sometimes referred to as calcium pyrophosphate disease (CPPD) [15,16]. Misdiagnosis of crystals arthritis or delay in treatment can gradually lead to degenerative joint disease and disability in addition to renal damage and failure [5]. The clinical picture of acute crystal-induced arthritis can sometimes be difficult to differentiate from acute septic arthritis. It is manifested by fever, malaise, raised peripheral WBC, CRP and other acute phase reactants. Synovial fluid aspirate can be turbid secondary to an increase in peripheral polymorphonuclear cells. Diagnosis can be challenging and therefore crystal identification on polarized microscopy is considered the gold standard [17, 18, 19]. Rest, ice and topical analgesia may be helpful but systemic non-steroidal anti-inflammatory medications are the treatment of choice for acute attacks provided there are no contraindications [20].

In this study, all joints were aspirated and samples were sent for microscopy, culture and sensitivity, and polarized microscopy for crystals in-line with the British Society of Rheumatology and British Orthopaedic Association guidelines [8]. Aspiration not only helps diagnosis but in addition reduces the pain caused by joint swelling. Twenty six patients were admitted, on clinical and biochemical suspicion of septic arthritis. They presented with acute phase response manifested by malaise, fever and raised inflammatory markers and were treated with antibiotic therapy and non steroidal anti-inflammatory medications while awaiting the results of microbiology and polarized light microscopy. Four of theses patients developed complications secondary to antibiotic therapy including death due to clostridium difficile infection and subsequent toxic megacolon.

Infection was confirmed to be underlying cause in four patients (6%) who showed positive microscopic growth on gram stained films. They underwent arthroscopic washout and continued antibiotic therapy according to the result of culture and sensitivity of their knee aspirate till their symptoms and blood markers were normal. Arthroscopic washout was required for four patients with negative microscopic growth due to persistant symptoms despite antibiotic treatment, as recommended by the British Society of Rheumatology and the British Orthopaedic Association [8]. Two patients showed calcium pyrophosphate crystals on polarized microscopy and two had no bacterial growth or crystals.

We retrospectively reviewed laboratory results and found that eight patients (13%) were confirmed to have crystal arthritis as crystals (MSU/CPP) were identified in their knee aspirates by means of polarized microscopy. However, only two patients (25%) received this diagnosis whilst in hospital. In both cases, antibiotic therapy was discontinued and they were referred to a rheumatologist for appropriate treatment and follow up. The remaining six patients continued to receive antibiotics and two of them were taken to theatre for arthroscopic lavage on clinical suspicion of infection as symptoms did not improve significantly with medications.

Our study shows that crystal-induced arthritis can easily be overlooked or misdiagnosed as septic arthritis. This results in patients having unnecessary antibiotic therapy, developing serious complications and undergoing surgical procedures, all of which can be avoided. Moreover, they were not referred to a rheumatologist.

Acute knee effusion is a common presentation to the Orthopaedic department and although we seem to be providing a good service for septic arthritis, patients with crystal arthropathy are still slipping through the net. Clinicians should always remember that crystal arthritis is almost as common as septic arthritis and will eventually lead to joint damage if not managed appropriately. It must be excluded as a cause of hot swollen joints by routine analysis of joint aspirate using polarized light microscopy. If crystal arthritis is proved to be the underlying pathology, patients must be treated accordingly and receive a prompt rheumatology referral for further management.

Acknowledgements
This work was performed in Frenchay Hospital, North Bristol NHS Trust, UK.
Competing Interests
None declared
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BJMP 2012;5(1):a502

Research Article

Reminder letters to improve rate of attendance at Community Mental Health Centre

Murali Krishna and Sreedharan Amarjothi

Abstract

Objective: We carried out a naturalistic study to investigate whether reminder letters would improve the rate of attendance in a community-based mental health outpatient clinic.

Methods: We prospectively compared the attendance rates between the experimental and control group over a period of 18 months.

Results: The results from this study confirm that reminder letters within a week before the appointment can improve attendance rates in community mental health clinics for follow up patients.

Conclusion: Non-attendance is an index of severity of mental illness and a predictor of risk. The reasons for non-attendance in mental health clinic are complex. More large, well-designed randomised studies are desirable. We also recommend periodic evaluation of outpatient non-attendance in order to identify high-risk individuals and implement suitable measures to keep such severely mentally ill patients engaged with the services.

Introduction

Non-attendance in outpatient clinics accounts for a significant wastage of health service resources. Psychiatric clinics have high non-attendance rates and failure to attend may be a sign of deteriorating mental health. Those who miss psychiatric follow-up outpatient appointments are more ill with poor social functioning than those who attend (1). They have a greater chance of drop out from clinic contact and subsequent admission (1). Non-attendance and subsequent loss to follow up indicate possible risk of harm to the patient or to others (2).

Prompts to encourage attendance at clinics are often used and may take the form of reminder letters (3), telephone prompting(4) and financial incentives (5). Issuing a copy of the referral letter to the appointee may prompt attendance for the initial appointment (6). Contacting patients by reminder letters prior to their appointments has been effective in improving attendance rates in a number of settings, including psychiatric outpatient clinics and community mental health centres (3).

Studies investigating the efficacy of prompting for improving attendance have generated contrasting findings and non-attendance remains common in clinical practice. We, therefore, carried out a naturalistic, prospective controlled study to investigate whether reminder letters would improve the rate of attendance in a community-based mental health outpatient clinic.

Design and Methods

The study was carried out at the Community Mental Health Centres based in Runcorn and Widnes in Cheshire, UK. The community mental health team (CMHT) provides specialist mental health services for adults of working age. Both CMHTs are similar in demographics, socio-economic need and, have relatively higher non-attendance rates in the clinic. In the week prior to the appointment, clerical staff from community mental health team sent a standard letter to some patients reminding the date and time of the appointment and name of the consulting doctor. They recorded whether patient attended, failed to attend or cancelled the appointment irrespective of whether they had received a reminder letter or not.

We compared the attendance rates between experimental group (those who had received the reminder letters) and the control group (those who had not received the reminder letters) over a period of 18 months. Throughout the study period, the same medical team held the clinics and there had been no major change in the outpatients' clinic setting or administrative and procedural changes influencing outpatients' attendance. Care Planning Approach (CPA) was implemented and in operation even before the introduction of reminding letters at both the sites.

Attendance rates for all the clinics held during the study period were obtained from medical records. For all subjects who failed to attend, age and gender, was obtained from patients' database. Patients whose appointments were cancelled were also included in the study.

Statistics and Data analysis

The data was analysed using SISA - Simple Interactive Statistical Analysis (7). Chi -squared tests were used to investigate the attendance rates between the groups, new patients and follow-ups, with the P value for statistical significance set at 0.05. Odds ratios were calculated to measure the size of the effect. In addition, we examined how age and

gender may have influenced the effect of the text based prompting on attendance.

Results

In the experimental group a total of 114 clinics were booked, with clinic lists totalling 843 patients. Of these, 88 were new referrals and 755 were follow-up appointments. 65 of 114 clinics had full attendance. A total of 228 patients failed to attend the clinic. Of those who failed to attend, 25 patients were new referrals and 203 were follow-up patients. 28 follow up patients and 2 patients newly referred to the team called to cancel their appointments.

In the control group, a total of 71 clinics were booked amounting to a total of 623 patients. Of these, 86 were new referrals and 537 were for follow-up patients. Only 25 out of 71 clinics had full attendance. A total of 211 patients failed to attend. Of those who failed to attend, 32 were new referrals and 179 were follow-up patients. 55 follow up patients and 13 patients newly referred to the team called to cancel their appointments.

Of those who failed to attend in the experimental group, 98 (43%) were women. The mean age of non-attendees was 38 years; with a range of 18-76 yrs .Of those who failed to attend in the control group110 (52%) were women. The mean age of non-attendees was 32 years; with a range of 19-70 yrs.

In our study, failure to attend was not distributed evenly but had seasonal peaks at Christmas and during the summer vacation period.

The outcome from prompting in the experimental group is compared with the control group and displayed in Table 1.

Outcomes	Control group n (%)	Experimental group n (%)	2 (df)	P	OR (CI)
No of clinics with full attendance	25	65	8.32	0.0039	2.44(1.32-4.50
Total No of Pts attended	344	585	15.05	0.0001	1.57(1.25-1.98)
No of new Pts attended	41	61	3.743	0.053	1.9 (0.98-3.67)
No of follow up Pts attended	303	524	11.39	0.0007	1.52(1.19-1.94)
No of Cancellations	68	30	38.63	0	3.85(2.46-6.04)

Table 1. χ^2 = Chi square, df = degree of freedom, OR= Odds Ratio, CI= Confidence Interval

The attendance rate in the experimental group was 71.95% (585/813) as opposed to 56.57% (344/555) in the control group (OR=1.57; p=0.0001).

The attendance rate for new patients in the experimental group was 70.9%(61/88) as opposed to 56.16 %(41/ 86) in the control group (OR=1.9; p=0.053).

The attendance rate for follow up patients in the experimental group was 72.0%(524/727) and 62.8% (303/482) in the control group (0R=1.52; p=0.0007).

In addition, there were significantly more (by 22%) number of clinics with full attendance in the experimental group (OR= 2.44, P=0.003).

The observed difference was not influenced by patient's age or gender.

Discussion

The results from this study confirm previous findings that reminder letters within a week before the appointment can improve attendance rates in community mental health clinics. Our results are similar to those of the Cochrane systematic review, which has suggested that a simple prompt in the days just before the appointment could indeed encourage attendance (8).

Although it has been reported elsewhere(8) that text based prompting increases the rate at which patients keep their initial appointments, our study did not show a similar result for new patients.

It is already demonstrated that new patients and follow-up patients in psychiatric clinics are distinct groups with different diagnostic profiles, degrees of mental illness and with different reasons for non-attendance. Follow-up patients are severely ill, socially impaired and isolated than new patients. (1). Forgetting the appointment and being too unwell are the most common reasons given for non-attendance by follow-up patients, while being unhappy with the referral, clinical error and being too unwell are the most common reasons in the new patient groups (1). In addition, it has also been observed that increased rate at which patients keep their first appointments is more likely related to factors other than simple prompting (4) This explains our finding that prompting was more beneficial for follow-up patients as opposed to new referrals to the Community Mental Health Team.

We also identified several patients with severe mental illness who 'did not attend' for three successive outpatient appointments. Their care plans were reviewed and arrangements made to follow up with their community psychiatric nurses as domiciliary visits at regular intervals. Such measures should reduce duplication of the services and shorten

the waiting times for psychiatric consultation, which are well-recognised factors associated with non-attendance (9).

Non-attendance is an index of severity of mental illness and a predictor of risk (1). In addition to reminder letters, telephone prompts are also known to improve attendance (4). Successful interventions to improve attendance may be labour intensive but they can be automated and, ultimately, prove cost effective (8)

We noticed that there is limited research and lack of quality randomised controlled trials in the area of non-attendance and the effectiveness of intervention to improve attendance in mental health setting. More large, well-designed randomised studies are desirable. We also recommend periodic evaluation of outpatient non-attendance in order to identify high-risk individuals and implement suitable measures to keep such severely mentally ill patients engaged with the services.

There was no randomisation in this study and we relied on medical records. We have not directly compared the characteristics of non-attendees with those patients who did attend the clinics. We did not evaluate other clinical and socio-demographic factors (e.g. travelling distance, financial circumstances, etc) that are known to influence the attendance rates in mental health setting. Hence, there may be limitations in generalising the results beyond similar populations with similar models of service provision.

Acknowledgements
Our sincere thanks to Suzanne Kippax, Informatics, Hollins Park Hospital, Warrington for her help in preparing this manuscript.
Competing Interests
None declared
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Review Article

BJMP 2012;5(1):a506

REM Behavior Disorder (RBD) as an Early Marker for Development of Neurodegenerative Diseases

Umesh Vyas and Rose Franco

ABSTRACT
REM behavior disorder (RBD) is a parasomnia characterized by emergence of purposeful complex motor activity with an enactment of dream related activities. This condition is associated with vivid often violent dreams. In normal adults during REM, diffuse hypotonia of muscles occur and on polysomnography the limb and chin electromyographic (EMG) channels demonstrate a low voltage or even flat signal. In RBD, the EMG demonstrating intermittent loss of electromyographic atoniais one of the criteria for diagnosis. Diagnostic polysomnographyrequire capturing the complex dream behaviors on video and electroencephalography monitoring confirms that the behavior originated out of REM sleep. RBD can be either idiopathic or symptomatic of various underlying conditions and may in fact be a prodromal symptom of neurodegenerative disease. It can present acutely which is almost always induced by medications; or develop gradually over months to years. More than half of those with RBD will eventually exhibit signs and symptoms of a degenerative neurologic disorder. A Polysomnogram (PSG) is necessary to diagnose RBD, showing absence of REM sleep atonia and related abnormal behavior.
KEYWORDS: REM sleep; REM Behavior Disorder; Neurodegenerative diseases; Parkinson's disease; Polysomnogram

Introduction

Normal sleep is divided into Non-REM and REM. REM occurs every 90-120 minutes during adult sleep throughout the night with each period of REM progressing in length such that the REM periods in the early morning hours are the longest and may last from 30-60 minutes. Overall, REM accounts for 20-25% of the sleep time but is weighted toward the second half of the night. During REM sleep with polysomnography monitoring one observes a low voltage mixed frequency amplitude EEG and low voltage EMG in the chin associated with intermittent bursts of rapid eye movements. During the periods of REM breathing becomes irregular, blood pressure rises and the heart rate also increases due to excess adrenergic activity. The brain is highly active during REM and the electrical activity recorded in the brain by EEG during REM sleep is similar to that of wakefulness.

Parasomnias are undesirable, unexpected, abnormal behavioral phenomena that occur during sleep. There are three broad categories in parasomnias. They are

Disorders of Arousal (from Non-REM sleep)
Parasomnias usually associated with REM sleep, and
Other parasomnias which also includes secondary type of parasomnias.

RBD is the only parasomnia which requires polysomnographic testing as part of the essential diagnostic criteria.

Definition of RBD

"RBD is characterized by the intermittent loss of REM sleep electromyographic (EMG) atonia and by the appearance of elaborate motor activity associated with dream mentation" (ICSD-2).[1] These motor phenomena may be complex and highly integrated and often are associated with emotionally charged utterances and physically violent or vigorous activities. RBD was first recognized and described by Schenck CH et al. in 1986.[2] This diagnosis was first incorporated in the International Classification of Sleep Disorders (ICSD) in 1990. (American Academy of Sleep Medicine).

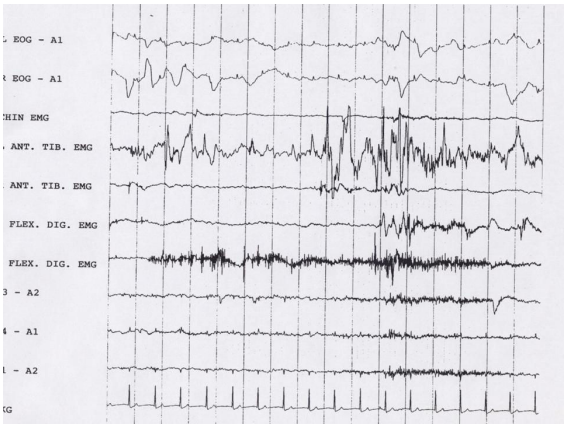

Figure 1

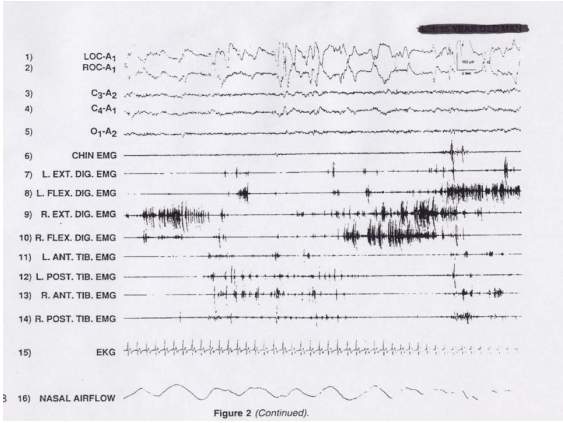

Figure 2

A defining feature of normal REM sleep is active paralysis of all somatic musculature (sparing the diaphragm to permit ventilation). This result in diffuse hypotonia of the skeletal muscles inhibiting the enactment of dreams associated with REM sleep. In RBD there is an intermittent loss of muscle atonia during REM sleep that can be objectively measured with EMG as intense phasic motor activity (figure 1 and 2). This loss of inhibition often precedes the complex motor behaviors during REM sleep. Additionally, RBD patients will report that their dream content is often very violent or vigorous dream enacting behaviors include talking, yelling, punching, kicking, sitting, jumping from bed, arm flailing and grabbing etc. and most often the sufferer will upon waking from the dream immediately report a clear memory of the dream which coincides very well with the high amplitude violent defensive activity witnessed. This complex motor activity may result in a serious injury to the dreamer or bed partner that then prompts the evaluation.

Prevalence

The Prevalence of RBD is about 0.5% in general population.[1, 3] RBD preferentially affect elderly men (in 6th and 7thdecade) with ratio of women to men being 1 to 9.[4] The mean age of disease onset is 60.9 years and at diagnosis is 64.4 years.[5] RBD was reported in an 18 year old female with Juvenile Parkinson disease,[6] so age and gender are not absolute criteria.

In Parkinson disease (PD) the reported prevalence ranges from 13-50%,[7, 14-19] LewyBody Dementia (DLB) 95%,[8] and Multiple System Atrophy (MSA) 90 %.[9] The presence of RBD is a major diagnostic criterion for MSA. RBD has been reported in Juvenile Parkinson disease, and pure autonomic failure[10-12] all neurodegenerative disorders are synucleinopathies.[13]

Physiology

The neurons of locus coeruleus, raphe nuclei, tuberomammillary nucleus, pedunculopontine nucleus, laterodorsal tegmental area and the perifornical area are firing at a high rate, and cause arousal by activating the cerebral cortex. During REM sleep, the aforementioned excitatory areas fall silent with the exception of the pedunculopontine nucleus and laterodorsal tegmental areas. These regions project to the thalamus and activate the cortex during REM sleep. This cortical activation is associated with dreaming in REM. Descending excitatory fibers from the pedunculopontine nucleus and laterodorsal tegmental area innervate the medial medulla, which then sends inhibitory projections to motor neurons producing the skeletal muscle atonia of REM sleep.[20-21]

There are two distinct neural systems which collaborate in the "paralysis" of normal REM sleep, one is mediated through the active inhibition by neurons in the nucleus reticularis magnocellularis in the medulla via the ventrolateral reticulospinal tract synapsing on the spinal motor neurons and the other system suppresses locomotor activity and is located in pontine region.[22]

Pathophysiology

REM sleep contains two types of variables, tonic (occurring throughout the REM period), and phasic (occurring intermittently during a REM period). Tonic elements include desynchronized EEG and somatic muscle atonia (sparing the diaphragm). Phasic elements include rapid eye movements, middle ear muscle activity and extremity twitches. The tonic electromyogram suppression of REM sleep is the result of active inhibition of motor activity originating in the perilocus coeruleus region and terminating in the anterior horn cells via the medullary reticularis magnocellularis nucleus.

In RBD, the observed motor activity may result from either impairment of tonic REM muscle atonia or from increase phasic locomotor drive during REM sleep. One mechanism by which RBD results is the disruption in neurotransmission in the brainstem, particularly at the level of the pedunculopontine nucleus.[23]Pathogenetically, reduced striatal dopaminergic mediation has been found[24-25] in those with RBD. Neuroimaging studies support dopaminergic abnormalities.

Types of RBD

RBD can be categorized based on severity:

1. Mild RBD occurring less than once per month,
2. Moderate RBD occurring more than once per month but less than once per week, associated with physical discomfort to the patient or bed partner, and
3. Severe RBD occurring more than once per week, associated with physical injury to patient or bed partner.

RBD can be categorized based on duration:

1. Acute presenting with one month or less,
2. Subacute with more than one month but less than 6 months,
3. Chronic with 6 months or more of symptoms prior to presentation

Acute RBD: In 55 - 60% of patients with RBD the cause is unknown, but in 40 - 45% the RBD is secondary to another condition. Acute onset RBD is almost always induced or exacerbated by medications (especially Tri-Cyclic Antidepressants, Selective Serotonin Reuptake Inhibitors, Mono-Amine Oxidase Inhibitors, Serotonin Norepinephrine Reuptake Inhibitors,[26] Mirtazapine, Selegiline, and Biperiden) or during withdrawal of alcohol, barbiturates, benzodiazepine or meprobamate. Selegiline may trigger RBD in patients with Parkinson disease. Cholinergic treatment of Alzheimer's disease may trigger RBD.

Chronic RBD: The chronic form of RBD was initially thought to be idiopathic; however long term follow up has shown that many eventually exhibit signs and symptoms of a degenerative neurologic disorder. One recent retrospective study of 44 consecutive patients diagnosed with idiopathic RBD demonstrated that 45% (20 patients) subsequently developed a neurodegenerative disorder, most commonly Parkinson disease (PD) or Lewy body dementia, after a mean of 11.5 years from reported symptoms onset and 5.1 years after RBD diagnosis.[27]

The relationship between RBD and PD is complex and not all persons with RBD develop PD. In one study of 29 men presenting with RBD followed prospectively, the incidence of PD was 38% at 5 years and 65% after 12 years.[7, 28, 29]Contrast this with the prevalence of the condition in multiple system atrophy, where RBD is one of the primary symptoms occurring in 90% of cases.[9] In cases of RBD, it is absolutely necessary not only to exclude any underlying neurodegenerative disease process but also to monitor for the development of one over time in follow up visits.

Clinical manifestations

Sufferers of RBD usually present to the doctor with complaints of sleep related injury or fear of injury as a result of dramatic violent, potentially dangerous motor activity during sleep. 96% of patients reporting harm to themselves or their bed partner. Behaviors during dreaming described include talking, yelling, swearing, grabbing, punching, kicking, jumping or running out of the bed. One clinical clue of the source of the sleep related injury is the timing of the behaviors. Because RBD occurs during REM sleep, it typically appears at least 90 minutes after falling asleep and is most often noted during the second half of the night when REM sleep is more abundant.

One fourth of subjects who develop RBD have prodromal symptoms several years prior to the diagnosis. These symptoms may consist of twitching during REM sleep but may also include other types of simple motor movements and sleep talking or yelling.[30-31] Day time somnolence and fatigue are rare because gross sleep architecture and the sleep-wake cycle remain largely normal.

RBD in other neurological disorders and Narcolepsy:

RBD has also been reported in other neurologic diseases such as Multiple Sclerosis, vascular encephalopathies, ischemic brain stem lesions, brain stem tumors, Guillain-Barre syndrome, mitochondrial encephalopathy, normal pressure hydrocephalus, subdural hemorrhage, and Tourette's syndrome. In most of these there is likely a lesion affecting the primary regulatory centers for REM atonia.

RBD is particularly frequent in Narcolepsy. One study found 36% pts with Narcolepsy had symptoms suggestive of RBD. Unlike idiopathic RBD, women with narcolepsy are as likely to have RBD as men, and the mean age was found to be 41 years.[32] While the mechanism allowing for RBD is not understood in this population, narcolepsy is considered a disorder of REM state disassociation. Cataplexy is paralysis of skeletal muscles in the setting of wakefulness and often is triggered by strong emotions such as humor. In narcoleptics who regularly experienced cataplexy, 68% reported RBD symptoms, compared to 14% of those who never or rarely experienced cataplexy.[32-33] There is evidence of a profound loss of hypocretin in the hypothalamus of the narcoleptics with cataplexy and this may be a link that needs further investigation in the understanding of the mechanism of RBD in Narcolepsy with cataplexy. It is prudent to follow Narcoleptics and questioned about symptoms of RBD and treated accordingly, especially those with cataplexy and other associated symptoms.

Diagnostic criteria for REM Behavior Disorder (ICSD-2: ICD-9 code: 327.42)[1]

A. Presence of REM sleep without Atonia: the EMG finding of excessive amounts of sustained or intermittent elevation of submental EMG tone or excessive phasic submental or (upper or lower) limb EMG twitching (figure 1 and 2).
B. At least one of the following is present:
   i. Sleep related injurious, potentially injurious, or disruptive behaviors by history
   ii. Abnormal REM sleep behaviors documented during polysomnographic monitoring
C. Absence of EEG epileptiform activity during REM sleep unless RBD can be clearly distinguished from any concurrent REM sleep-related seizure disorder.
D. The sleep disturbance is not better explained by another sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder.

Differential diagnosis

Several sleep disorders causing behaviors in sleep can be considered in the differential diagnosis, such as sleep walking (somnambulism), sleep terrors, nocturnal seizures, nightmares, psychogenic dissociative states, post-traumatic stress disorder, nocturnal panic disorder, delirium and malingering. RBD may be triggered by sleep apnea and has been described as triggered by nocturnal gastroesophageal reflux disease.

Evaluation and Diagnosis

- Detailed history of the sleep wake complaints

- Information from a bed partner is most valuable
- Thorough medical, neurological, and psychiatric history and examination
- Screening for alcohol and substance use
- Review of all medications
- PSG (mandatory): The polysomnographic study should be more extensive, with an expanded EEG montage, monitors for movements of all four extremities, continuous technologist observation and continuous video recording with good sound and visual quality to allow capture of any sleep related behaviors
- Multiple Sleep Latency Test (MSLT): Only recommended in the setting of suspected coexisting Narcolepsy
- Brain imaging (CT or MRI) is mandatory if there is suspicion of underlying neurodegenerative disease.

Management

RBD may have legal consequences or can be associated with substantial relationship strain; therefore accurate diagnosis and adequate treatment is important, which includes non-pharmacological and pharmacological management.

Non-pharmacological management: Acute form appears to be self-limited following discontinuation of the offending medication or completion of withdrawal treatment. For chronic forms, protective measures during sleep are warranted to minimize the risks for injury to patient and bed partner. These patients are at fall risk due to physical limitations and use of medications. Protective measure such as removing bed stands, bedposts, low dressers and applying heavy curtains to windows. In extreme cases, placing the mattress on the floor to prevent falls from the bed has been successful.

Pharmacological management: Clonazepam is highly effective in treatment and it is the drug of choice. A very low dose will resolve symptoms in 87 to 90% of patients.[4, 5, 7-34] Recommended treatment is 0.5 mg Clonazepam 30 minutes prior to bed time and for more than 90% of patients this dose remains effective without tachyphylaxis. In the setting of breakthrough symptoms the dose can be slowly titrated up to 2.0 mg. The mechanism of action is not well understood but clonazepam appears to decrease REM sleep phasic activity but has no effect on REM sleep atonia.[35]

Melatonin is also effective and can be used as monotherapy or in conjunction with clonazepam. The suggested dose is 3 to 12 mg at bed time. Pramipexole may also be effective[36-38] and suggested for use when clonazepam is contraindicated or ineffective. It is interesting to note that during holidays from the drug, the RBD can take several weeks to recur. Management of patients with concomitant disorder like narcolepsy, depression, dementia, Parkinson disease and Parkinsonism can be very challenging, because medications such as SSRIs, selegiline and cholinergic medications used to treat these disorders, can cause or exacerbate RBD. RBD associated with Narcolepsy, clonazepam is usually added in management and it is fairly effective.

Follow-up

Because RBD may occur in association with neurodegenerative disorder, it is important to consult a neurologist for every patient with RBD as early as possible, especially to diagnose and provide care plan for neurodegenerative disorder, which includes but not limited to early diagnosis and management, regular follow up, optimization of management to provide better quality of life and address medico-legal issues.

Prognosis

In acute and idiopathic chronic RBD, the prognosis with treatment is excellent. In the secondary chronic form, prognosis parallels that of the underlying neurologic disorder. Treatment of RBD should be continued indefinitely, as violent behaviors and nightmares promptly reoccur with discontinuation of medication in almost all patients.

Conclusions

RBD and neurodegenerative diseases are closely interconnected. RBD often antedates the development of a neurodegenerative disorder; diagnosis of idiopathic RBD portends a risk of greater than 45% for future development of a clinically defined neurodegenerative disease. Once identified, close follow-up of patients with idiopathic RBD could enable early detection of neurodegenerative diseases. Treatment for RBD is available and effective for the vast majority of cases.

Key Points

- Early diagnosis of RBD is of paramount importance
- Polysomnogram is an essential diagnostic element
- Effective treatment is available
- Early treatment is essential in preventing injuries to patient and bed partner
- Apparent idiopathic form may precede development of Neurodegenerative disorder by decades

Competing Interests
None declared
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Review Article

BJMP 2012;5(1):a507

Management of Drooling of saliva

Ganesh Bavikatte , Poh Lin Sit and Ali Hassoon

ABSTRACT
Drooling, also known as ptyalism or sialorrhea can be defined as salivary incontinence or the involuntary spillage of saliva over the lower lip. Drooling could be caused by excessive production of saliva, inability to retain saliva within the mouth, or problems with swallowing. Drooling can lead to functional and clinical consequences for patients, families, and caregivers. Physical and psychosocial complication includes maceration of skin around the mouth, secondary bacterial infection, bad odour, dehydration and social stigmatisation. People with drooling problems are also at increased risk of inhaling saliva, food, or fluids into the lungs especially when body's normal reflex mechanisms, such as gagging and coughing are also impaired. Successful management of sialorrhea can alleviate the associated hygienic problems, improve appearance, enhance self-esteem, and significantly reduce the nursing care time of these sufferers.Chronic drooling can be difficult to manage; this article gives overview of the causes, effects and management of drooling of saliva in general practice.

Saliva is the watery and usually frothy substance produced in and secreted from the three paired major salivary (parotid, submandibular and sublingual) glands and several hundred minor salivary glands, composed mostly of water, but also includes electrolytes, mucus, antibacterial compounds, and various enzymes. Healthy persons are estimated to produce 0.75 to 1.5 liters of saliva per day. At least 90% of the daily salivary production comes from the major salivary glands while the minor salivary glands produce about 10%. On stimulation (olfactory, tactile or gustatory), salivary flow increases five fold, with the parotid glands providing the preponderance of saliva.[1]

Saliva is a major protector of the tissues and organs of the mouth. In its absence both the hard and soft tissues of the oral cavity may be severely damaged, with an increase in ulceration, infections, such as candidiasis, and dental decay. Saliva is composed of serous part (alpha amylase) and a mucus component, which acts as a lubricant. It is saturated with calcium and phosphate and is necessary for maintaining healthy teeth. The bicarbonate content of saliva enables it to buffer and produce the condition necessary for the digestion of plaque which holds acids in contact with the teeth. Moreover, saliva helps with bolus formation and lubricates the throat for the easy passage of food. The organic and inorganic components of salivary secretion have got a protective potential. They act as barrier to irritants and a means of removing cellular and bacterial debris. Saliva contains various components involved in defence against bacterial and viral invasion, including mucins, lipids, secretory immunoglobulins, lysozymes, lactoferrin, salivary peroxidise, and myeloperoxidase. Salivary pH is about 6-7, favouring digestive action of salivary enzyme, alpha amylase, devoted to starch digestion.

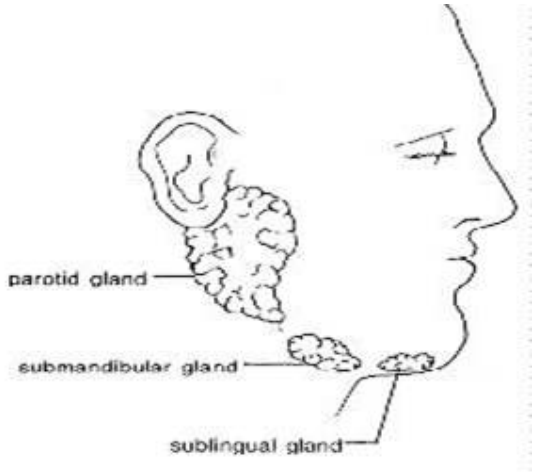


Image -1. (Source of this image- http://www.entdoctor.co.nz)

Salivary glands are innervated by the parasympathetic and sympathetic nervous system. Parasympathetic postganglionic cholinergic nerve fibers supply cells of both the secretory end-piece and ducts and stimulate the rate of salivary secretion, inducing the formation of large amounts of a low-protein, serous saliva. Sympathetic stimulation promotes saliva flow through muscle contractions at salivary ducts. In this regard both parasympathetic and sympathetic stimuli result in an increase in salivary gland secretions. The sympathetic nervous system also affects salivary gland secretions indirectly by innervating the blood vessels that supply the glands.

Drooling (also known as driveling, ptyalism, sialorrhea, or slobbering) is when saliva flows outside the mouth, defined as “saliva beyond the margin of the lip”. This condition is normal in infants but usually stops by 15 to 18 months of age.

Sialorrhea after four years of age generally is considered to be pathologic.

Table 1: Functions of saliva

Digestion and swallowing
Initial process of food digestion
Lubrication of mouth, teeth, tongue and food boluses
Tasting food
Amylase- digestion of starch
Disinfectant and protective role
Effective cleaning agent
Oral homeostasis
Protect teeth decay, dental health and oral odour
Bacteriostatic and bacteriocidal properties
Regulate oral pH
Speaking
Lubricates tongue and oral cavity

The prevalence of drooling of saliva in the chronic neurological patients is high, with impairment of social integration and difficulties to perform oral motor activities during eating and speech, with repercussion in quality of lifeDrooling occurs in about one in two patients affected with motor neuron disease and one in five needs continuous saliva elimination[7], its prevalence is about 70% in Parkinson disease[8], and between 10 to 80% in patients with cerebral palsy[9].

Pathophysiology

Pathophysiology of drooling is multifactorial. It is generally caused by conditions resulting in

Excess production of saliva- due to local or systemic causes (table 2)

Inability to retain saliva within the mouth- poor head control, constant open mouth, poor lip control, disorganized tongue mobility, decreased tactile sensation, macroglossia, dental malocclusion, nasal obstruction.

Problems with swallowing- resulting in excess pooling of saliva in the anterior portion of the oral cavity e.g. lack of awareness of the build-up of saliva in the mouth, infrequent swallowing, and inefficient swallowing.

Drooling is mainly due to neurological disturbance and less frequently to hyper salivation.Under normal circumstances, persons are able to compensate for increased salivation by swallowing. However, sensory dysfunction may decrease a person's ability to recognize drooling and anatomic or motor dysfunction of swallowing may impede the ability to manage increased secretion.

Depending on duration of drooling, it can be classified as *acute* e.g. during infections (epiglottitis, peritonsilar abscess) or*chronic*neurological causes.

Table 2 Aetiology of hypersalivation

Physiological
Pregnancy
Local causes
Oral inflammation- teething
Infection –oral cavity infection, dental caries, tonsillitis, peritonsilar abscess
Systemic
Toxin exposure- pesticides, mercury, capsaicin, snake poisoning
Medication –tranquilizers, anticonvulsants, anticholinesterases, lithium
Neuromuscular –cerebral palsy, Parkinson's disease, motor neuron disease, bulbar/ pseudobulbar palsy, Stroke
Infection- rabies
Gastric- gastroesophageal reflux

Symptoms

Drooling of saliva can affect patient and/or their carers quality of life and it is important to assess the rate and severity of symptoms and its impact on their life.

Table 3 Effect of untreated Drooling of saliva

Physical	Psychological
Perioral chapping (skin cracking)	Isolation
Maceration with secondary infection	Barriers to education (damage to books or electronic devices)
Dehydration	Increased dependency and level/intensity of care
Foul odour	Damage to electronic devices
Aspiration/ pneumonia	Decreased self esteem
Speech disturbance	Difficult social interaction
Interference with feeding	

Assessment

Assessment of the severity of drooling and its impact on quality of life for the patient and their carers help to establish a prognosis and to decide the therapeutic regimen. A variety of subjective and objective methods for assessment of sialorrhoea have been described[3].

History (from patient and carers)

Establish possible cause, severity, complications and possibility of improvement, age and mental status of patient, chronicity of problems, associated neurological conditions, timing, provoking factors, estimation of quantity of saliva – use of bibs, clothing changing required/ day and impact on the day today life (patient/carer)

Physical examination

Evaluate level of alertness, emotional state, hydration status, hunger, head posture

Examination of oral cavity- sores on the lip or chin, dental problems, tongue control, swallowing ability, nasal airway obstruction, decreased intraoral sensitivity, assessment of health status of teeth, gum, oral mucosa, tonsils, anatomical closure of

oral cavity, tongue size and movement, jaw stability. Assessment of swallowing

Assess severity and frequency of drooling (as per table 4)

Investigation

- Lateral neck x ray (in peritonsilar abscess)
- Ultrasound to diagnose local abscess
- Barium swallow to diagnose swallowing difficulties
- Audiogram- to rule out conductive deafness associated with oropharyngeal conditions
- Salivary gland scan- to determine functional status

Table 4 : System for assessment of frequency and severity of drooling

Drooling severity	**Points**
Dry (never drools)	1
Mild (wet lips only)	2
Moderate (wet lips and chins)	3
Severe (clothing becomes damp)	4
Profuse (clothing, hands, tray, object become wet)	5
Frequency	**Points**
Never drools	1
Occasionally drools	2
Frequency drools	3
Constantly drools	4
Other methods of assessing salivary production and drooling 1) 1- 10 visual analogue scale (where 1 is best possible and 10 is worst possible situation) 2) Counting number of standard sized paper handkerchiefs used during the day 3) Measure saliva collected in cups strapped to chin 4) Inserting pieces of gauze with a known weight into oral cavity for a specific period of time and then re-measuring weight and calculating the difference between the dry and wet weights. 5) Salivary gland scintigraphy / technetium scanning 6) Salivary duct canulation 12 and measuring saliva production.	

Management

Drooling of saliva, a challenging condition, is better managed with a multidisciplinary team approach. The team includes primary care physician, speech therapist, occupational therapist, dentist, orthodontist, otolaryngologist, paediatrician and neurologist. After initial assessment, a management plan can be made with the patient. The person/ carer should understand the goal of treating drooling is a reduction in excessive salivary flow, while maintaining a moist and healthy oral cavity. Avoidance of xerostomia (dry mouth) is important. There are two main approaches

1. Non invasive modalities e.g. oral motor therapy, pharmacological therapy
2. Invasive modalities e.g. surgery and radiotherapy

No single approach is totally effective and treatment is usually a combination of these techniques. The first step in management of drooling is correction of reversible causes. Less invasive and reversible methods, namely oral motor therapy and medication are usually implemented before surgery is undertaken[5]

Non invasive modalities

Positioning prior to implementation of any therapy, it is essential to look at the position of the patient. When seated, a person should be fully supported and comfortable. Good posture with proper trunk and head control provides the basis for improving oral control of drooling and swallowing.

Eating and drinking skills- drooling can be exacerbated by poor eating skills. Special attention and developing better techniques in lip closure, tongue movement and swallowing may lead to improvements of some extent. Acidic fruits and alcohol stimulate further saliva production, so avoiding them will help to control drooling[10]

Oral facial facilitation - this technique will help to improve oral motor control, sensory awareness and frequency of swallowing. Scott and staios et al [18] noted improvement in drooling in patients with both hyper and hypo tonic muscles using this technique. This includes different techniques normally undertaken by speech therapist, which improves muscle tone and saliva control. Most studies show short term benefit with little benefit in long run. This technique can be practiced easily, with no side effects and can be ceased if no benefits noted.

a) Icing – effect usually last up to 5-30 minutes. Improves tone, swallow reflex.
b) Brushing- as effect can be seen up to 20- 30 minutes, suggested to undertake before meals.
c) Vibration- improves tone in high tone muscles
d) Manipulation – like tapping, stroking, patting, firm pressure directly to muscles using fingertips known to improve oral awareness.
e) Oral motor sensory exercise - includes lip and tongue exercises.

Speech therapy- speech therapy should be started early to obtain good results. The goal is to improve jaw stability and closure, to increase tongue mobility, strength and positioning, to improve lip closure (especially during swallowing) and to decrease nasal regurgitation during swallowing.

Behaviour therapy- this uses a combination of cueing, overcorrection, and positive and negative reinforcement to help drooling. Suggested behaviours, like swallowing and mouth wiping are encouraged, whereas open mouth and thumb sucking are discouraged. Behavior modification is useful to achieve (1) increased awareness of the mouth and its functions,

(2) increased frequency of swallowing, (3) increased swallowing skills. This can be done by family members and friends. Although there is no randomized controlled trial done, over 17 articles published in last 25 years, show promising results and improved quality of life. No reported side effects make behavioural interventions an initial option compared to surgery, botulinum toxin or pharmaceutical management. Behaviour interventions are useful prior and after medical management such as botulinum toxin or surgery.

Oral prosthetic device- variety of prosthetic devices can be beneficial, e.g. chin cup and dental appliances, to achieve mandibular stability, better lip closure, tongue position and swallowing. Cooperation and comfort of the patient is essential for better results.

Pharmacological methods

Systematic review of anticholinergic drugs, show Benztropine, Glycopyrrolate, and Benzhexol Hydrochloride, as being effective in the treatment of drooling. But these drugs have adverse side-effects and none of the drugs been identified as superior.

Hyoscine - The effect of oral anticholinergic drugs has been limited in the treatment of drooling. Transdermal scopolamine (1.5 mg/2.5 cm2) offers advantages. One single application is considered to render a stable serum concentration for 3 days. Transdermal scopolamine has been shown to be very useful in the management of drooling, particularly in patients with neurological or neuropsychiatric disturbances or severe developmental disordersIt releases scopolamine through the skin into the bloodstream.

Glycopyrrolate studies have shown 70-90% response rates but with a high side effect rate. Approximately 30-35% of patients choose to discontinue due to unacceptable side effects such as excessive dry mouth, urinary retention, decreased sweating, skin flushing, irritability and behavior changes. A study on 38 patients with drooling due to neurological deficits had shown up to a 90% response rateMier et al[21] reported Glycopyrrolate to be effective in the control of excessive sialorrhea in children with developmental disabilities. Approximately 20% of children given glycopyrrolate may experience substantial adverse effects, enough to require discontinuation of medication.

Antimuscarinic drugs, such as benzhexol, have also been used, but limited due to their troublesome side effects.

Antireflux Medication: The role of antireflux medication (Ranitidine & Cisapride) in patients with gastro esophageal reflux due to esophageal dysmotility and lower esophageal tone did not show any benefits in a study [21].

Modafinil - One case study noticed decreased drooling in two clients who were using the drug for other reasons, but no further studies have been done.

Alternate medications: (Papaya and Grape seed extract) – Mentioned in literature as being used to dry secretions but no research in to their efficacy has been conducted.

Botulinum toxin It was in 1822 that a German poet and physician, Justinus Kerner, discovered that patients who suffered from botulism complained of severe dryness of mouth which suggested that the toxin causing botulism could be used to treat hypersalivation. However, it was only in the past few years that botulinum toxin type A (BTx-A) has been used for this purpose. BTx-A binds selectively to cholinergic nerve terminals and rapidly attaches to acceptor molecules at the presynaptic nerve surface. This inhibits release of acetylcholine from vesicles, resulting in reduced function of parasympathetic controlled exocrine glands. The blockade though reversible is temporary as new nerve terminals sprout to create new neural connections. Studies have shown that injection of botulinum toxin to parotid and submandibular glands, successfully subsided the symptoms of drooling [30,31]. Although there is wide variation in recommended dosage, most studies suggest that about 30- 40 units of BTx-A injected into the parotid and submandibular glands are enough for the symptoms to subside The injection is usually given under ultrasound guidance to avoid damage to underlying vasculature/ nerves. The main side effects from this form of treatment are dysphagia, due to diffusion into nearby bulbar muscles, weak mastication, parotid gland infection, damage to the facial nerve/artery and dental caries.

Patients with neurological disorders who received BTX-A injections showed a statistically significant effect from BTX-A at 1 month post injection, compared with control, this significance was maintained at 6 months. Intrasalivary gland BTX-A was shown to have a greater effect than scopolamine.

The effects of BTx-A are time limited and this varies between individuals.

Invasive modalities

Surgery can be performed to remove salivary glands, (most surgical procedures focused on parotid and submandibular glands). ligate or reroute salivary gland ducts, or interrupt parasympathetic nerve supply to glands. Wilke, a Canadian plastic surgeon, was the first to propose and carry out parotid duct relocation to the tonsillar fossae to manage drooling in patients with cerebral palsy. One of the best studied procedures, with a large number of patients and long term follow up data, is submandibular duct relocation [32, 33].

Intraductal laser photocoagulation of the bilateral parotid ducts has been developed as a less invasive means of surgical therapy. Early reports have shown some impressive results[34.]

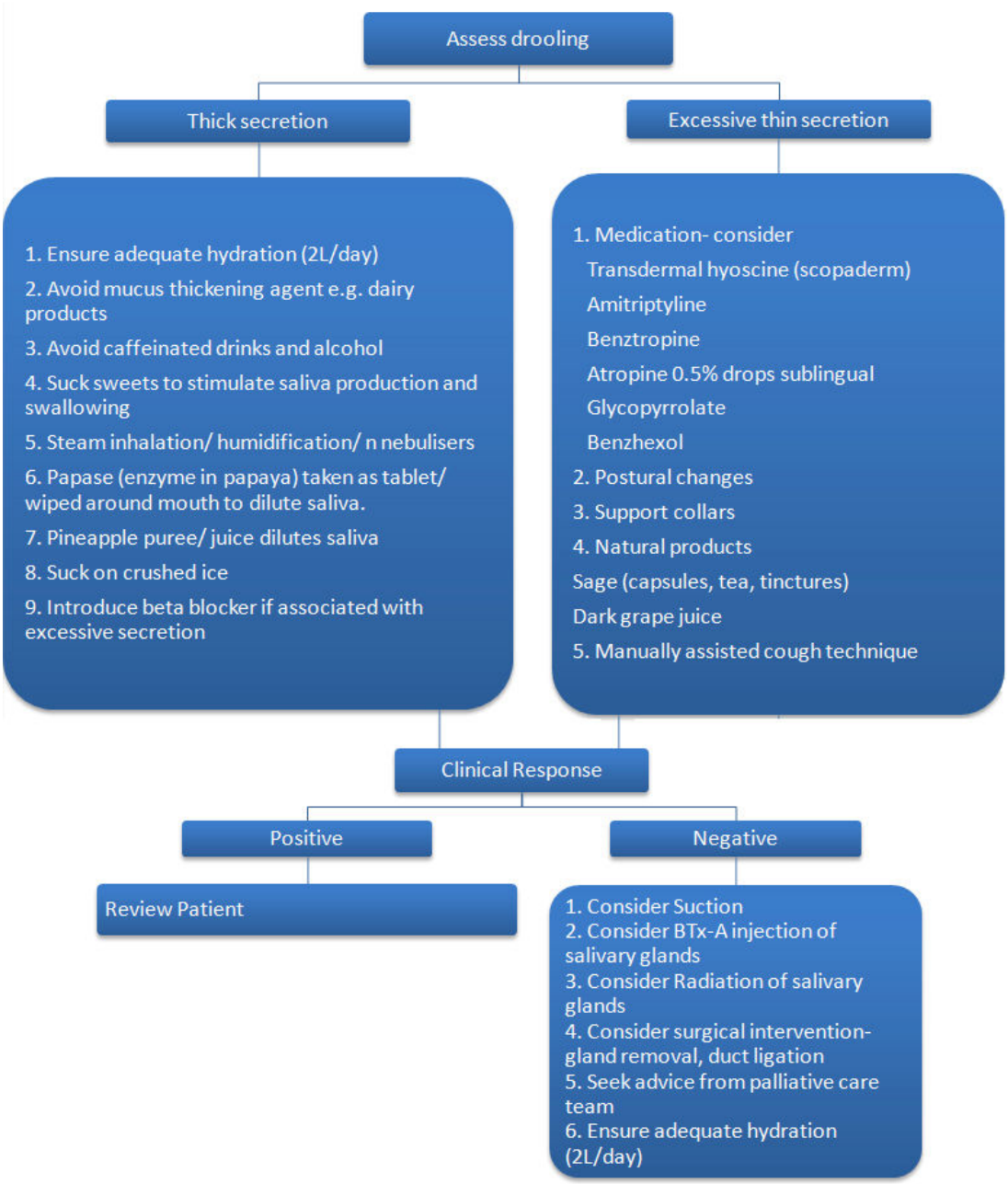
Overall surgery reduced salivary flow and drooling can be significantly improved often with immediate results – 3 studies noted that 80 – 89% of participants had an improvement in

their control of their saliva. Two studies discussed changes in quality of life. One of these found that 80% of those who participated improved across a number of different measures including receiving affection from others and opportunities for communication and interaction. Most evidence regarding surgical outcomes of sialorrhea management is low quality and heterogeneous. Despite this, most patients experience a subjective improvement following surgical treatment [36].

Radiotherapy - to major salivary glands in doses of 6000 rad or more is effective Side effects which include xerostomia, mucositis, dental caries, osteoradionecrosis, may limit its use.

Key messages

- Chronic drooling can pose difficulty in management
- Early involvement of Multidisciplinary team is the key.
- Combination of approach works better
- Always start with noninvasive, reversible, least destructive approach
- Surgical and destructive methods should be reserved as the last resort.



Competing Interests
None declared
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Review Article

BJMP 2012;5(1):a501

Benzodiazepines Revisited

Tauseef Mehdi

Abstract

Up to 1 million people in the UK are currently long-term prescribed benzodiazepine users.[1] Surveys of general practices show that there are over 180 long-term prescribed users per general practice.[2] Despite repeated recommendations to limit benzodiazepines to short-term use (2–4 weeks), doctors in the UK and worldwide are still prescribing them for months or years. Dependence upon prescribed benzodiazepines is now recognised as a major clinical problem and the National Performance Assessment Framework for the NHS makes it a national priority to reduce this within each health board area. Junior doctors who have recently graduated from medical school are commonly placed in rotations where they have to manage patients on benzodiazepine prescriptions. It is necessary for doctors in general to be aware of the essentials of benzodiazepines not only for the adequate management of patients on chronic benzodiazepine prescriptions, but also for responsible prescription of this drug when it is appropriate.

History of benzodiazepines

The advent of benzodiazepines in the late fifties was met with great excitement by the practicing physicians around the world. Their range of actions – sedative/hypnotic, anxiolytic, anticonvulsant and muscle relaxant – combined with low toxicity and alleged lack of dependence potential seemed to make them ideal medications for many common conditions. The drugs were prescribed long term, often for many years, for complaints such as anxiety, depression, insomnia and ordinary life stressors. They began to replace barbiturates; drugs known to be dangerous in overdose, which tended to cause addiction and were associated with troublesome side-effects. Previous compounds including opium, alcohol, chloral and bromides were similarly burdened.

The first benzodiazepine, chlordiazepoxide (*Librium*), was synthesized in 1955 by Leo Sternbach while working at Hoffmann–La Roche on the development of tranquilizers. The compound showed very strong sedative, anticonvulsant and muscle relaxant effects when submitted for a standard battery of animal tests. These impressive clinical findings led to its speedy introduction throughout the world in 1960 under the brand name *Librium*. Following chlordiazepoxide, diazepam was marketed by Hoffmann–La Roche under the brand name *Valium* in 1963.

The benefits of benzodiazepines and the apparent lack of discouraging factors led an alarming rise of benzodiazepine prescriptions. In the late 1970s benzodiazepines became the most commonly prescribed of all drugs in the world.[1] In1980, Tyrer reported that each day about 40 billion doses of benzodiazepine drugs are consumed throughout the world.[3] This figure is staggering by any standards. However, towards the end of the 1970s, awareness begin to grow that benzodiazepines were being unnecessarily over-prescribed and it was noticed that certain patients might become dependent on benzodiazepines after chronic use.[4] In particular, patients found it difficult to stop taking benzodiazepines because of withdrawal reactions and many complained that they had become 'addicted'. Several investigations showed quite unequivocally that benzodiazepines could produce pharmacological dependence in therapeutic dosage.[5-9]

In 1988, the Committee of Safety of Medicines reacted to the concerns by spelling out emphatic guidelines about the use of benzodiazepines drugs. For anxiety and insomnia, benzodiazepines are indicated for short term relief (two to four weeks) only if the condition is severe, disabling and subjecting the individual to extreme distress.[10]

Tolerance and dependence

Tolerance is a phenomenon that develops with many chronically used drugs. The body responds to the continued presence of the drug with a series of adjustments that tend to overcome the drug effects. In the case of benzodiazepines, compensatory changes occur in the GABA and benzodiazepine receptors which become less responsive, so that the inhibitory actions of the GABA and benzodiazepines are decreased. As a result, the original dose of the drug has progressively less effect and a higher dose is required to obtain the original effect.

Dependence is understood to be the inability to control intake of a substance to which one is addicted. It encompasses a range of features initially described in connection with alcohol abuse, now recognised as a syndrome (see box 1) associated with a range of substances.

Dependence has two components: psychological dependence, which is the subjective feeling of loss of control, cravings and preoccupation with obtaining the substance; and physiological dependence, which is the physical consequences of withdrawal and is specific to each drug. For some drugs (e.g. alcohol) both

psychological and physiological dependence occur; for others (e.g. LSD) there are no marked features of physiological dependence.

Box 1: Dependence Syndrome*

Three or more of the following manifestations should have occurred together for at least one month or if persisting for periods of less than one month then they have occurred together repeatedly within a twelve month period.

1. A strong desire or sense of compulsion to take the substance.
2. Impaired capacity to control substance-taking behaviour in terms of onset, termination or level of use, as evidenced by: the substance being often taken in larger amounts or over a longer period than intended, or any unsuccessful effort or persistent desire to cut down or control substance use.
3. A physiological withdrawal state (see F1x.3 and F1x.4) when substance use is reduced or ceased, as evidenced by the characteristic withdrawal syndrome for the substance, or use of the same (or closely related) substance with the intention of relieving or avoiding withdrawal symptoms.
4. Evidence of tolerance to the effects of the substance, such that there is a need for markedly increased amounts of the substance to achieve intoxication or desired effect, or that there is a markedly diminished effect with continued use of the same amount of the substance.
5. Preoccupation with substance use, as manifested by: important alternative pleasures or interests being given up or reduced because of substance use; or a great deal of time being spent in activities necessary to obtain the substance, take the substance, or recover from its effects.
6. Persisting with substance use despite clear evidence of harmful consequences, as evidenced by continued use when the person was actually aware of, or could be expected to have been aware of the nature and extent of harm.

* ICD 10 Classification of Mental and Behaviour disorder, online version 2007.

Withdrawal syndrome and discontinuation syndrome

Any drug consumed regularly and heavily can be associated with withdrawal phenomenon on stopping. Clinically significant withdrawal phenomena occur in dependence to alcohol, benzodiazepines, opiates and are occasionally seen in cannabis, cocaine and amphetamine use. In general, drugs with a short half-life will give rise to more rapid but more transient withdrawal.

Discontinuation syndrome is a common phenomenon and occurs with all classes of antidepressants. It is only experienced when one tries to discontinue its use. The most common symptoms are dizziness, vertigo, gait instability, nausea, fatigue, headaches, anxiety and insomnia. Less commonly shock-like sensations, paraesthesia, visual disturbances, diarrhoea and flu-like symptoms have been reported. Symptoms usually begin 2-5 days after SSRI discontinuation or dose reduction. The duration is variable (one to several weeks) and ranges from mild to moderate intensity in most patients, to extremely distressing in a small number. Tapering antidepressants at the end of treatment, rather than abrupt stoppage, is recommended as standard practice by several authorities and treatment guidelines[11-13].

The terms 'antidepressant withdrawal syndrome' and 'antidepressant discontinuation syndrome' are used interchangeably in the literature. 'Discontinuation' is preferred as it does not imply that antidepressants are addictive or cause a dependence syndrome. The occurrence of withdrawal symptoms does not in itself indicate that a drug causes dependence as defined in ICD 10 (World Health Organisation 1992)[14] and DSM –IV (American Psychiatric Association, 1994)[15].

Understanding how benzodiazepines work and their effects

For the first 15 years after the introduction of benzodiazepines, no clear picture emerged as to how these drugs might exert their psychotropic effects. The great breakthrough in our understanding in the mechanism of action of benzodiazepines came in the mid 1970s when biologists at Hoffman-La Roche demonstrated that benzodiazepines exert their psychotropic effects by potentiating GABA neurotransmission.[16]

GABA, Gamma-Amino butyric acid, is the most important inhibitory neurotransmitter in the mammalian brain representing about 30% of all synapses in the whole brain. GABAergic neurones mediate pre-synaptic inhibition by depressing the release of neurotransmitter at excitatory input synapse, and post-synaptic inhibition by depressing synaptic excitation of the principal neuron. When benzodiazepines react at their receptor site, which is actually situated on the GABA receptor, the combination acts as a booster to the actions of GABA making the neuron more resistant to excitation. Several studies showed that benzodiazepines were able to facilitate both types of inhibition, indicating that the effects of the benzodiazepines were in fact due to an interaction with the GABAergic transmission process[17-19].

Various subtypes of benzodiazepine receptors have slightly different actions. Alpha 1 is responsible for sedative effects. Alpha 2 exerts anxiolytics effects. Alpha 1, Alpha 2 and Alpha 5 are responsible for anticonvulsant effects. As a consequence of the enhancement of GABA's inhibitory activity caused by benzodiazepines, the brain's output of excitatory neurotransmitters including norepinephrine, serotonin, dopamine and acetylcholine is reduced.

The studies on the receptor binding of benzodiazepines and the subsequent changes that occur in the central nervous system have provided us with an adequate explanation for some or all of the actions of benzodiazepines, which are listed in Box 2.

Box 2: Four principle biological properties of benzodiazepines

1. Anxiolytic and behavioural inhibition – The anxiolytic effect is seen in animals as an increase of those behavioural responses that are suppressed experimentally by punishment or which are absent because of innate aversion[20-23].
2. Anticonvulsant – Benzodiazepines are most potent against chemically induced epileptiform activities. At higher doses most, but not all, benzodiazepines also prevent seizures induced by electric shock[24].
3. Sedative/hypnotic – These effects of benzodiazepines are most easily observed as a decrease of spontaneous locomotor activity in rodents placed in an observation chamber. Benzodiazepines will shorten sleep latency (amount of time taken to fall asleep after the lights have been switched off) which can be demonstrated by electroencephalogram[25].
4. Muscle relaxant - Common tests on rodents show that benzodiazepines impair performance at motor performance tasks for example the rodent's ability to balance on a rotating drum. The cat shows marked ataxia at after relatively low doses[25].

What are benzodiazepines used for?

Sleep disorders

The benzodiazepines are used widely in the treatment of sleep disorders and many have been developed and licensed for this purpose. They are mainly known as hypnotic drugs (sleeping pills) because insomnia is the main target use. Certain factors are important in determining the choice of the hypnotic drug. Ideally, the hypnotic should be effective at inducing sleep in the individual, and should enhance objective and subjective elements of sleep. It should have a fast onset with minimal side effects and the absence of withdrawal symptoms.

The early benzodiazepine hypnotics were drugs such as nitrazepam and flurazepam. After their introduction, it was found that they had half-lives of more than a day, and individuals suffered undesirable effects such as sedation, ataxia or amnesia during the day. This was problematic especially for those individuals who needed to drive or operate machinery. Another consequence was of falls with subsequent hip fractures in the elderly population because, due to slower metabolism, they accumulated raised plasma levels of the drug. For these reasons, benzodiazepines with shorter half lives were developed so that plasma levels fall below the functional threshold concentration by the next morning.

The first of the shorter half-life benzodiazepine hypnotics to be introduced were temazepam and triazolam. Temazepam has a half-life of 5 hours and is commonly used in primary, secondary and tertiary settings for insomnia. A possible drawback of very short half-life hypnotics is rebound insomnia. This is a state of worsening sleep which commonly follows discontinuation of a regularly used hypnotic.

An important point to note is that although the subjective efficacies of benzodiazepines are widely reported, the use of polysomnography (a sleep study that involves recording a variety of physiological measures including electroencephalograph, electro-oculogram and electromyogram) has shown that sleep architecture in individuals with insomnia is not normalised by benzodiazepines. The increase in sleep duration can be accounted for by an increase in the time spent in stage 2 of sleep, while the amount of time spent in slow-wave sleep (deep) and REM (rapid eye movement) is actually decreased[26].

Anxiety disorders

It can be argued that the benzodiazepines are probably the most efficacious and best tolerated pharmacological treatments of anxiety. Numerous studies, many of them conducted under stringent double-blind conditions, have consistently shown that benzodiazepines produce significantly more improvement than placebo in both somatic and emotional manifestations of anxiety[27-29].

Before the introduction of benzodiazepines, anxiety disorders were treated either with the barbiturates or related drugs such as meprobomate and glutethimide. These agents were highly likely to be abused and led to a great deal of dependence. Moreover, they were toxic in overdose and fatalities were high in populations using them. The improved efficacy and safety profile of benzodiazepines, aided by intense campaigns to restrict use of barbiturate-type drugs, meant they rapidly became the first choice drugs for anxiety within a few years of them being introduced.

Much clinical practice and opinion suggests that benzodiazepine can be used as first-line treatment for acute anxiety episodes as long as CSM guidelines are adhered to. For more intractable conditions such as established social phobia, generalised anxiety disorder and panic disorder, they should probably be reserved for adjunctive or second-line agents.

In contrast to the treatment of sleep disorders, it is important to achieve a constant level of receptor occupation to maintain anxiolysis throughout the day. So for anxiety, compounds with longer elimination half-lives are preferred, whereas for sleep induction, short half-life drugs are favoured. The principal benzodiazepines used as anxiolytics include diazepam, chlordiazepoxide, clonazepam, lorazepam, alprazolam and oxazepam.

The use of benzodiazepines as first-line agents for anxiety has been on the decline since the 1990s. There are changing cultural and medical attitudes to the prescription of drugs for the treatment of anxiety disorders as a result of growing evidence that psychological approaches are also effective. The risks of dependence and withdrawal difficulties are problematic in a significant number of patients. Another issue is the abuse of benzodiazepines by drug addicts and diversion of legitimate supplies on to the black market. There is competition from other agents (buspirone, tricyclic antidepressants, monoamine oxidase inhibitors and selective serotonin reuptake inhibitors) which have a different side-effect profile and are free from dependence/withdrawal problems.

Seizure Disorders

The anti-convulsant effects of benzodiazepines find their greatest clinical use in the acute control of seizures. Diazepam, clonazepam and lorazepam have all been used in the treatment of status epilepticus.

Status epilepticus is a life-threatening condition in which the brain is in a state of continuous seizure activity which can result in impaired respiration, hypoxic brain damage and brain scarring. It is a medical emergency that requires quick and effective intervention.

Diazepam was reported to be effective for the treatment of status-epilepticus in the mid-1960s [30-32] and is still widely considered to be the drug of choice for the initial control of seizures. Given intravenously, diazepam has a rapid onset of clinical activity achieving cessation of the seizure within 5 minutes of injection in 80% of the patients in one study[33]. Where facilities for resuscitation are not immediately available; diazepam can be administered as a rectal solution.

Although intravenous diazepam is effective for status epilepticus, it is associated with a high risk of thrombophlebitis which is why BNF suggests use of intravenous lorazepam. Lorazepam is also highly active[34]. Its onset of action is rapid but because of its slower rate of tissue distribution, its anticonvulsant activity is prolonged compared to diazepam[35,36].

Gestaut et al (1971) showed that clonazepam was an even more potent anti-convulsant than diazepam in the treatment of status epilepticus[37]. It can be administered via the buccal mucosa (an advantage in children) and can also be given as a suppository.

Benzodiazepines are undoubtedly potent anti-convulsants on acute administration but their use in long-term treatment of epilepsy is limited by the development of tolerance to the anti-convulsant effects and by side-effects such as sedation and psychomotor slowing[38,39]. They are usually considered as an adjunct to standard drugs where these have failed to give acceptable control.

Table 1: Pharmacokinetic profile of common benzodiazepines and their licensed indications

Long-acting	**TMax (hrs)**	**T1/2 (hrs)**	**Licensed indications**[11]
Chlordiazepoxide[42]	2	7-14	Short-term use in anxiety, adjunct to acute alcohol withdrawal
Diazepam[42]	0.5-2	32-47	Short term use in anxiety, adjunct to acute alcohol withdrawal, insomnia, status epilepticus, muscle spasm, peri-operative use.
Clonazepam[43]	2.5	23.5	all forms of epilepsy, myoclonus, status epilepticus
Intermediate-acting			
Temazepam[42]	1	5-8	Insomnia; peri-operative use.
Nitrazepam, Flurazepam*[42]	1-3	16-48	Short-term use for insomnia
Loprazolam, Lormetazepam[42]	1-3	8-10	Short-term use for insomnia
Short-acting$^{\alpha}$			
Lorazepam[42]	1-1.5	10-20	Short term use in anxiety or insomnia; status epilepticus; peri-operative use.
Oxazepam[42]	2.2-3	5-15	Short term use in anxiety
Midazolam[43]	0.6	2.4	Sedation with amnesia, sedation in intensive care, induction of anaesthesia.
Alprazolam[42]	1.2-1.7	10-12	Short term use in Anxiety

T_{max}: time to peak plasma concentration
$T_{1/2}$: half-life
*Nitrazepam and flurazepam have prolonged action and may give rise to residual effects on the following day. Temazepam, Loprazolam and Lormetazepam act for a shorter time and have little or no hangover effect.
$^{\alpha}$ Short-acting compounds preferred in hepatic impairment but carry a greater risk of withdrawal symptoms.

Other uses

Alcohol detoxification – Benzodiazepines have become the standard pharmacological treatment for alcohol withdrawal. In acute alcohol detoxification, long acting benzodiazepines, such as diazepam or chlordiazepoxide are more appropriate than shorter acting agents like lorazepam or temazepam. The two principal reasons for this are 1) former drugs provide stable plasma concentrations over several hours which is necessary to maintain control over central nervous system excitability, and 2)

There is a higher risk of addiction with short-acting drugs in this patient population.

In alcohol dependent patients with hepatic impairment, oxazepam or lorazepam is more suitable as they are not eliminated by hepatic oxidation through the Cytochrome P450 system. Cytochrome p450 (CYPs) is a collective generic term use to describe a superfamily of membrane bound heme-thiolate proteins of critical importance in the oxidative and reductive metabolism of both endogenous and foreign compounds. CYPs are the major enzymes in drug metabolism accounting for 75% of the total metabolism[40]. Many of the CYPs in humans are found in the liver and the gastrointestinal tract. After the acute detoxification is over, many patients enter rehabilitation programmes aimed at maintaining abstinence in the community. There is no evidence that use of benzodiazepines is useful in reducing alcohol craving or facilitating abstinence.

Anaesthesia – The psychotropic effects of benzodiazepines make them appropriate for use as anaesthetic agents or as adjuncts to anaesthesia. Muscle relaxation, sedation and retrograde amnesia are sought after properties in anaesthetic agents. Midazolam is used as a sedative agent in patients undergoing minor invasive practices considered as traumatic, such as dental treatment or endoscopy.[41]

Muscle relaxants – The muscle relaxant properties of benzodiazepines are an indication for their use in some neurological disturbances for symptomatic relief of muscle spasms and spasticity.

Assessment and management of patients with chronic benzodiazepine dependence

Because of the adverse effects, lack of efficacy and socioeconomic costs of continued benzodiazepine use, long-term users have for many years been advised to withdraw if possible or at least to reduce dosage.[10,44] Echoing the CSM advice, the Mental Health National Service Framework (NSF), which was published in 1999, recommended that benzodiazepines should be used for no more than two to four weeks for severe and disabling anxiety. The Mental Health NSF called upon health authorities to implement systems for monitoring and reviewing prescribing of benzodiazepines within local clinical audit programmes. Primary Care Trusts (PCTs) should ensure that this recommendation is still being implemented[45].

In primary care, early detection and intervention are the main principles of assessment. The initial assessment should

- Establish the pattern of benzodiazepine usage: onset, duration, which benzodiazepine/s, dosage history, current regime and any periods of abstinence.
- Check for evidence of benzodiazepine dependence (see box 3).
- If benzodiazepine dependence is present, determine the type of benzodiazepine.
- Detail any history of previous severe withdrawal (including history of seizures).
- Establish the level of motivation to change.

Dependence on benzodiazepines often indicates psychosocial problems in a person. Benzodiazepines are increasingly used in conjunction with other substance of abuse to enhance the effects obtained from opiates, and to alleviate withdrawal symptoms of other drugs of abuse such as cocaine, amphetamines or alcohol. The patient needs to have an individualised and a comprehensive assessment of their physical and mental health needs and any co-morbid use of other drugs and alcohol. Stable psychological health and personal circumstances are desirable features for successful withdrawal from benzodiazepines. Certain patients will be unsuitable for withdrawal, e.g. those patients experiencing a current crisis or having an illness for which the drug is required at the current time. Referral to specialist teams may be appropriate for some, e.g. if the patient is also dependent on other drugs or alcohol, if there is co-existing physical or psychiatric morbidity or if there is a history of drug withdrawal seizures. In some circumstances, it may be more appropriate to wait until other problems are resolved or improved.

Box 3 – Benzodiazepine Withdrawal Symptoms[46]

Psychological symptoms – excitability, sleep disturbances, increased anxiety, panic attacks, agoraphobia, social phobia, perceptual distortions, depersonalisation, derealisation, hallucinations, misperceptions, depression, obsessions, paranoid thoughts, rage, aggression, irritability, poor memory and concentration, intrusive memories and craving (rare).

Physical symptoms – Headache, pain, stiffness, tingling, numbness, altered sensation, weakness, fatigue, influenza-like symptoms, muscles twitches, jerks, tics, "electric shocks", tremor, dizziness, light-headedness, poor balance, visual problems, tinnitus, hypersensitivity to stimuli, gastrointestinal symptoms, appetite change, dry mouth, metallic taste, unusual smell, flushing, sweating, palpitations, over breathing, urinary difficulties, skin rashes, itching, fits (rare).

This list is probably not inclusive. Not all patients get all the symptoms. Different individuals get a different combination of symptoms.

Management of benzodiazepine withdrawal

Withdrawal of the benzodiazepine drug can be managed in primary care if the patients in consideration are willing, committed and compliant. Clinicians should seek opportunities to explore the possibilities of benzodiazepine withdrawal with

patients on long-term prescriptions. Interested patients could benefit from a separate appointment to discuss the risks and benefits of short and long term benzodiazepine treatment[47]. Information about benzodiazepines and withdrawal schedules could be offered in printed form. One simple intervention that has been shown to be effective in reducing benzodiazepine use in long-term users is the sending of a GP letter to targeted patients. The letter discussed the problems associated with long-term benzodiazepine use and invited patients to try and reduce their use and eventually stop[48]. Adequate social support, being able to attend regular reviews and no previous history of complicated drug withdrawal is desirable for successful benzodiazepine withdrawal.

Switching to diazepam: This is recommended for some people commencing a withdrawal schedule. Diazepam is preferred because it possesses a long half-life, thus avoiding sharp fluctuations in plasma level. It is also available in variable strengths and formulations. This facilitates stepwise dose substitution from other benzodiazepines and allows for small incremental reductions in dosage. The National Health Service Clinical Knowledge Summaries recommend switching to diazepam for people using short acting benzodiazepines such as alprazolam and lorazepam, for preparations that do not allow for small reductions in dose (that is alprazolam, flurazepam, loprazolam and lormetazepam) and for some complex patients who may experience difficulty withdrawing directly from temazepam and nitrazepam due to a high degree of dependency[49]. See table 2 for approximate dose conversions of benzodiazepines when switching to diazepam.

Gradual Dosage Reduction: It is generally recommended that the dosage should be tapered gradually in long-term benzodiazepine users such as a 5-10% reduction every 1-2 weeks[1,49]. Abrupt withdrawal, especially from high doses, can precipitate convulsions, acute psychotic or confusional states and panic reactions. As mentioned earlier, benzodiazepines' enhancement of GABA's inhibitory activity reduces the brain's output of excitatory neurotransmitter such as norepinephrine, serotonin, dopamine and acetylcholine. The abrupt withdrawal of benzodiazepines may be accompanied by uncontrolled release of dopamine, serotonin and other neurotransmitters which are linked to hallucinatory experiences similar to those in psychotic disorders[46].

The rate of withdrawal should be tailored to the patient's individual needs and should take into account such factors as lifestyle, personality, environmental stressors, reasons for taking benzodiazepines and the amount of support available. Various authors suggest optimal times of between 6-8 weeks to a few months for the duration of withdrawal, but some patients may take a year or more[11,50]. A personalised approach, empowering the patient by letting them guide their own reduction rate is likely to result in better outcomes.

Table 2: Approximate equivalent doses of benzodiazepines[1]

Benzodiazepine	Approximate equivalent dosage (mg)a
Alprazolam	0.5
Chlordiazepoxide	25
Clonazepam	0.5
Diazepam	10
Flunitrazepam	1
Flurazepam	15-30
Loprazolam	1
Lorazepam	1
Lormetazepam	1
Nitrazepam	10
Oxazepam	20
Temazepam	20

[a] Clinical potency for hypnotic or anxiolytic effects may vary between individuals; equivalent doses are approximate.

Patients may develop numerous symptoms of anxiety despite careful dose reductions. Simple reassurance and encouragement should suffice in most cases however, in a minority who are experiencing significant distress, formal psychological support should be available. Cognitive therapy, behavioural approaches including relaxation techniques and breathing exercises for anxiety management as well as other therapies such as massage and yoga may alleviate difficulties during withdrawal. Psychoeducation around withdrawal symptoms should be offered and a referral to a support organisation or group is helpful.

Resources

- The Ashton Manual, http://www.benzo.org.uk/manual/index.htm.
- NHS Clinical Knowledge Summaries, http://www.cks.nhs.uk/benzodiazepine_and_z_drug_withdrawal.
- The Maudsley Prescribing Guidelines

Summary

Although prescriptions of benzodiazepines have declined substantially since 1988, there is an ongoing challenge within all sectors of the NHS to prevent benzodiazepine dependence. This can be achieved by adhering to official recommendations to limit prescriptions to 2-4 weeks, or for brief courses or occasional usage. All health authorities should have clinical audit programmes reviewing and monitoring prescribing rates for benzodiazepines. Through this, increased awareness of CSM guidelines amongst all health care professionals should aid in more appropriate prescriptions and subsequent monitoring that is required to prevent unnecessary prescriptions. Patients on long-term prescriptions should be offered the opportunity for controlled withdrawal and the relevant psychological and social support.

Competing Interests
None declared
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BJMP 2012;5(1):a511

Case Report

Bradyarrhythmias Associated with the Obstructive Sleep Apnoea Syndrome: A Precursor to Life-threatening Arrhythmias?

Amitasha Mann , Jean Karen Fleischman and Karen Mrejen-Shakin

ABSTRACT

Chronic Obstructive Pulmonary Disease (COPD) is a leading cause of global morbidity that is predicted to become the third most common cause of death worldwide by the year 2020[1]. Obstructive sleep apnoea syndrome (OSAS) is also highly prevalent and is estimated to affect 5% of adults in western countries[2]. The co-existence of both COPD and OSAS in the same patient is termed the Overlap syndrome[3,4]. Overlap patients have more pronounced nocturnal hypoxemia and appear to be at increased risk of death compared with COPD patients matched for Global Initiative for COPD stage without OSA. We present a case of a patient with mild OSA and moderate COPD who was observed on CPAP titration polysomnography to have moderate obstructive sleep apnoea during rapid eye movement (REM) sleep (REM apnoea-hypopnea index (AHI) 28/hr.), with associated Wenckebach second-degree atrioventricular (AV) heart block observed during the nadir of oxygen desaturation associated with obstructive apnoeas. This led to further investigation with a one month event recording which showed progression of a benign Type I Wenckebach second-degree AV heart block to life-threatening Type II AV second-degree heart block and complete AV block with 3.9 seconds of ventricular asystole. Bradyarrhythmias during sleep observed in patients with COPD and OSAS may be a precursor to more life-threatening arrhythmias.

Case Report

A 69 year old male with hypertension, body mass index 24 kg/m^2, neck circumference 16 inches, and moderate COPD, on home oxygen, presented to his pulmonary clinic appointment with worsening complaints of fatigue, leg cramps, and intermittent shortness of breath with chest discomfort. A remote, questionable history of syncope five to ten years ago was elicited. His vital signs were: temperature 98.8^{0}F, blood pressure 119/76 mmHg, pulse 92/min and regular, and respirations 20/min. Physical exam was significant for crowded oropharynx with a Mallampati score of four, distant breath sounds with a prolonged expiratory phase on lung exam with a normal cardiac exam. Laboratory investigation showed normal complete blood counts, haemoglobin 15 g/dL, and normal chemistries. Compared to his previous studies, a pulmonary function study showed stable parameters with a FEV1 1.47 L (69%), FVC/FEV1 ratio 0.44 (62%), and a DLCO/alveolar volume ratio of 2.12 (49%). A room air arterial blood gas revealed pH 7.41, PCO2 44 mmHg, and PO2 61 mmHg, with 92% oxygen saturation. A six minute treadmill exercise test performed to assess the need for supplemental oxygen showed that he required supplemental oxygen at 1L/min via nasal cannula to eliminate hypoxemia during exercise. His chest radiograph was significant for hyperinflation and prominence of interstitial markings. A high resolution computed tomography of the chest demonstrated severe centrilobular and panacinar emphysema only. A baseline electrocardiogram (EKG) showed normal sinus rhythm with an old anterior wall infarct (Figure 1). Echocardiography of the heart revealed a normal left ventricle with an ejection fraction of 65%. Right ventricular systolic function was normal although elevated mean pulmonary arterial pressure of 55 mmHg was noted. A diagnostic polysomnogram performed for evaluation of daytime fatigue and snoring at night revealed mild OSA with an AHI of 6/hr. with sleep time spent with oxygen saturation below 90% (T-90%) of 19%. The EKG showed normal sinus rhythm. A full overnight polysomnogram for continuous positive airway pressure (CPAP) titration performed for treatment of sleep disordered breathing was sub-optimal, however it demonstrated an apnoea–hypopnea index (AHI) of 28 during REM (rapid eye movement) sleep, and a T-90% of 93%. The associated electrocardiogram showed Wenckebach second degree AV heart block during REM sleep usually near the nadir of oxygen desaturation. On a repeat positive airway pressure titration study, therapy with Bilevel pressures (BPAP) of 18/14 cmH_20 corrected the AHI and nocturnal hypoxemia to within normal limits during Non REM (NREM) and REM sleep. His electrocardiogram remained in normal sinus rhythm .A twenty-four hour cardiac holter monitor revealed baseline sinus rhythm and confirmed the presence of second degree AV block of the Wenckebach type. A one month cardiac event recording showed normal sinus rhythm with frequent episodes of second degree AV block. These varied from Type I progressing to Type II with a 2:1 and 3:1 AV block, during sleep. Progression to complete heart block was noted with the longest pause lasting 3.9 seconds during sleep. The patient underwent an electrophysiology study with placement of a dual chamber pacemaker. He was initiated on BIPAP therapy. Subsequently, the patient was seen in clinic with improvements in his

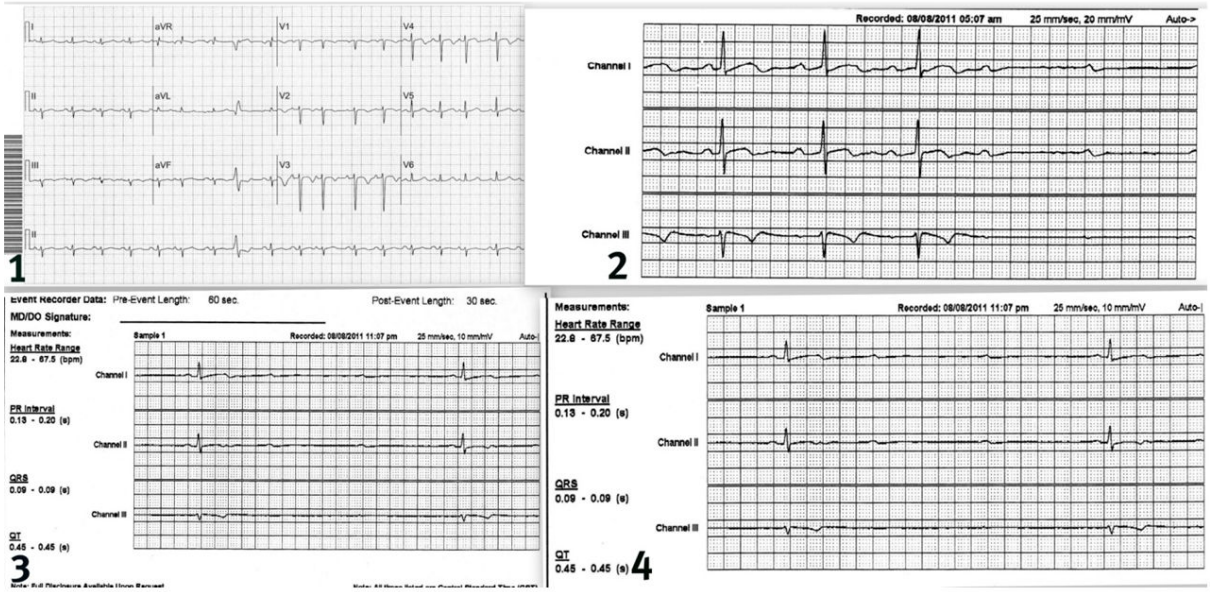

Figure 1- Patient's baseline EKG, normal sinus rhythm. Figure 2 -Progression to Mobitz Type II block 5:07 am. Figure 3 and 4- Sinus pauses, longest interval 11:07 pm 3.9 seconds (Figure 4).

intermittent episodes of shortness of breath, fatigue, and daytime sleepiness.

Discussion

In healthy individuals, especially athletes, bradycardia, Mobitz I AV block, and sinus pauses up to 2 seconds are common during sleep and require no intervention[5]. Cardiac rhythm is controlled primarily by autonomic tone. NREM sleep is accompanied by an increase in parasympathetic, and a decrease in sympathetic, tone. REM sleep is associated with decreased parasympathetic tone and variable sympathetic tone. Bradyarrhythmias in patients with OSA are related to the apnoeic episodes and over 80% are found during REM sleep. During these periods of low oxygen supply, increased vagal activity to the heart resulting in bradyarrhythmias may actually be cardioprotective by decreasing myocardial oxygen demand. This may be important in patients with underlying coronary heart disease.

Some studies have found that Mobitz I AV block may not be benign. Shaw[6] et al studied 147 patients with isolated chronic Mobitz I AV block. They inserted pacemakers in 90 patients, 74 patients were symptomatic and 16 patients received a pacemaker for prophylaxis. Outcome data included five-year survival, deterioration of conduction to higher degree AV block, and new onset of various forms of symptomatic bradycardia. They concluded that survival was higher in the paced groups and that risk factors for poor outcomes in patients with Mobitz I included age greater than 45 years old, symptomatic bradycardia, organic heart disease, and the presence of a bundle branch block on EKG.

The Sleep Heart Health Study[7] found a higher prevalence of first and second-degree heart block among subjects with sleep-disordered breathing (SDB) than in those without (1.8% vs. 0.3% and 2.2 vs. 0.9%, respectively). Gami et al[8]observed thatupon review of 112 Minnesota residents who hadundergone diagnostic polysomnography and subsequentlydied suddenly from a cardiac cause, sudden death occurred between the hours of midnight and 6:00 AM in 46% of those with OSA, as compared with 21% of those without OSA. In a study of twenty-three patients with moderate to severe OSA who were each implanted with an insertable loop recorder, about 50% were observed to have frequent episodes of bradycardia and long pauses (complete heart block or sinus arrest) during sleep[9]. These events showed significant night-to-night intra individual variability and their incidence was under-estimated, only 13%, by conventional short-term EKG Holter recordings.

Physiologic factors predisposing patients with OSA to arrhythmias include alterations in sympathetic and parasympathetic nervous system activity, acidosis, apnoea's, and arousal[2, 10, 11]. Some patients with OSA may have an accentuation of the 'Diving Reflex'. This protective reflex consists of hypoxemia-induced sympathetic augmentation to muscles and vascular beds associated with increased cardiac vagal activity which results in increased brain perfusion, bradycardia and decreased cardiac oxygen demand. In patients with cardiac ischemia, poor lung function (i.e. COPD), or both, it may be difficult to differentiate between these protective OSA-associated Bradyarrhythmias and those which may lead to sudden death. It has been well established that patients with COPD are at higher risk for cardiovascular morbidity[12] and arrythmias[13]. Fletcher[14] and colleagues reported that the effects of oxygen supplementation on AHI, hypercapnea and supraventricular arrhythmias in patients with COPD and OSA were variable. Out of twenty obese men with

COPD studied, in most patients oxygen eliminated the bradycardia observed during obstructive apnoea's and eliminated AV block in two patients. In some patients supplemental oxygen worsened end-apnoea respiratory acidosis however this did not increase ventricular arrhythmias.

CPAP therapy has been demonstrated to significantly reduce sleep–related Bradyarrhythmias, sinus pauses, and the increased risk for cardiac death [9, 15]. Despite this, in certain situations placement of a pacemaker may be required. These include persistent life-threatening arrhythmias present in patients with severe OSAS on CPAP, arrhythmias in patients who are non-compliant with CPAP, and in patients who may have persistent sympathovagal imbalance and hemodynamic fluctuations resulting in daytime bradyarrhythmias[16].

Our case is interesting since it highlights the importance of recognizing the association between OSA, COPD, and life-threatening cardiac arrhythmias. Primary care providers should note the possible association of OSA-associated bradyarrhythmias with life-threatening Type II bradyarrhythmias and pauses. Since bradyarrhythmias related to OSA are relieved by CPAP, one option would be to treat with CPAP and observe for the elimination of these arrhythmias using a 24hour holter or event recorder[17]. Compliance with CPAP is variable and if life-threatening bradycardia is present, placement of a permanent pacemaker may be preferred[18].

Our patient is unusual because most studies showing a correlation with the severity of OSA and magnitude of bradycardia have included overweight patients without COPD[19]. This patient's electrocardiogram revealed a Type II AV block at 5am (Figure 2). This is within the overnight time frame where patients with OSA have been observed to have an increased incidence of sudden death. Figures 3 and 4 show significant sinus pauses. In selected cases where patients have significant co-morbidities (i.e. severe COPD with OSA), in addition to treatment with positive airway pressure, electrophysiological investigation with placement of a permanent pacemaker may be warranted.

Competing Interests
None declared
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Case Report

BJMP 2012;5(1):a509

Retroperitoneal Teratoma in an adult presenting with painful abdominal mass: case history and literature review

Sadaqat Ali Khan, Tariq Mahmood, Muhammad Zeeshan Sarwar, Syed Hamad Rasool, Muhammad Danish Siddique and Zohaib Khan

ABSTRACT
Teratomas are congenital tumors that may contain derivatives of all three germ layers. They usually arise in the gonads and often occur in infancy and childhood. A primary retroperitoneal teratoma is a relatively rare disease in adults. Here we report a case of retroperitoneal teratoma in an adult female. It was benign but its wall was adherent to the aorta. It presented with right hypochondrial pain and examination revealed a mass in the abdomen.

Introduction:

Although one cell type may predominate, teratomas usually comprise of tissue from all three embryonic germ layers[1].Generally arising from the gonads, they may be found in extra-gonadal sites such as sacro-coccygeal region, mediastinum, neck and retroperitoneum.[2] Here we report a case of retroperitoneal teratoma in an adult with successful surgical treatment. Its clinical presentation, diagnosis and treatment are reviewed.

Case Report:

A woman aged 28 years presented with pain in the right hypochondrium of one year duration. There was no associated bowel or urinary symptom. Examination showed minimal fullness in the right hypochondrium. Routine blood tests and urinalysis were within normal limits. A plain abdominal radiograph showed calcification in the right side of the abdomen (Fig. 1). Ultrasonography demonstrated 13.6 x 8.1 cm soft tissue mass in the retro-peritoneum between liver and the right kidney. It was heterogeneous, well circumscribed with sharply defined borders, and had some calcification and cystic areas. CT abdomen revealed a hypo-dense lesion between liver and the right kidney. It had fatty attenuation with internal hyper-dense areas representing calcification. (Fig. 2). Provisional diagnosis of a retroperitoneal teratoma was made and an open exploration was performed with a right sub-costal incision. There was a large cystic mass behind the ascending colon, duodenum and the pancreas. It was located in the retroperitoneal compartment. There were dense, fibrous adhesions of the mass with aorta but entire cystic mass was excised successfully.

Post operatively this tumor mass measuring 5 x 5 cm was excised in vitro and found to be filled with yellowish creamy material containing hair, sebum and bony tissue. Microscopically it was confirmed to be a cystic teratoma with no malignancy. Stratified squamous epithelium with sebaceous and sweat glands, hair shafts, calcification, few bony spicules and bone marrow elements were all demonstrated. (Fig. 3). The post operative course was uneventful and she was well at the 2 months follow up.

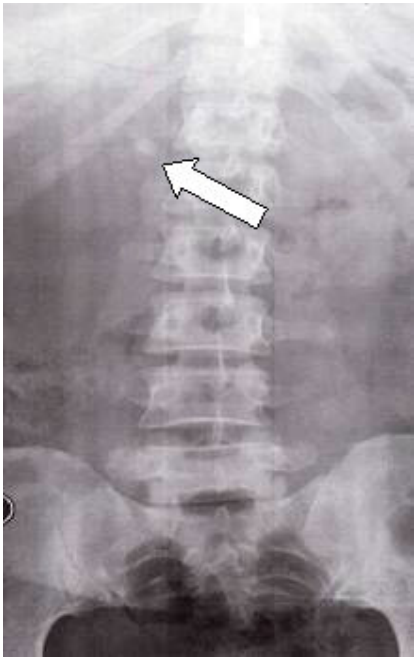

Figure 1. Plain abdominal radiograph showing radio-opaque shadow (arrow heads) in the right upper abdomen.

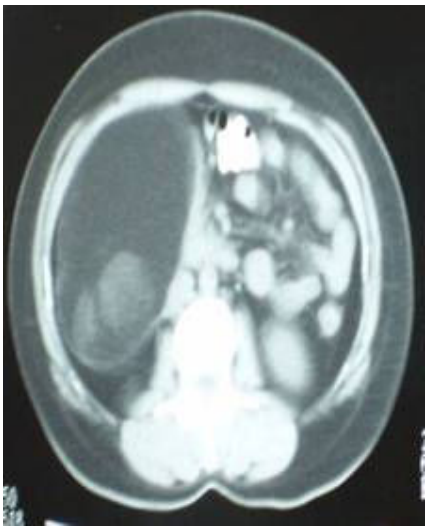

Figure 2: Computed Tomography showing an encapsulated mass that contains multiple tissue elements including fat and areas of calcification.

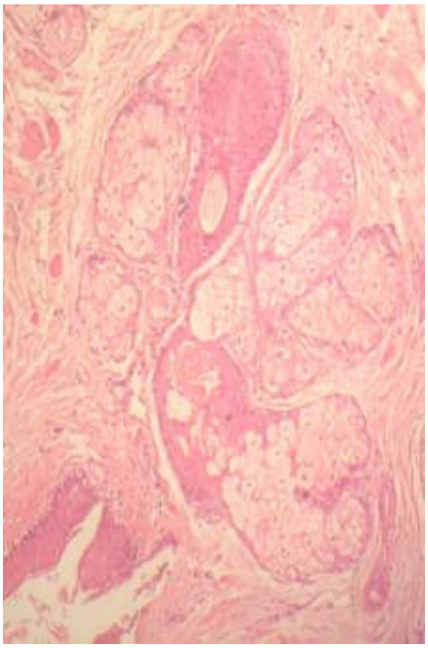

Figure 3: Microscopic examination of the tumor showing squamous epithelium (SE), hair shaft (HS), sebaceous glands (SBG)

Discussion:

Teratomas are congenital tumours arising from pluri-potential embryonic cells and therefore have several recognizable somatic tissues[3], Teratomas are usually localized to the ovaries, testis, anterior mediastinum or the retro-peritoneal area in descending order of frequency.[4] Teratomas constitute less than 10% of all primary retroperitoneal tumours and hence are relatively uncommon[5]. Furthermore, retroperitoneal teratomas occur mainly in children and have been very rarely described in the adults. Half of these cases present in children less than 10 years of age and only a fifth of them present after 30 years of age. Retroperitoneal teratomas are often located near the upper pole of the kidney with preponderance on the left. The case described here is therefore unusual in that it was a primary retroperitoneal teratoma in an adult, on the right side and with adhesions to the aorta.

Retroperitoneal teratomas are seen in females twice as commonly than males. Teratomas are usually benign if they are cystic and contain sebum or mature tissue. They are more likely to be malignant if they are solid and have immature embryonic tissue like fat, cartilage, fibrous and bony elements.[6] In these regards our case is similar to other described cases as our patient is also female and as her teratoma was cystic, it showed lack of malignancy.

Teratomas are usually asymptomatic as the retroperitoneal space is extensive enough to allow for their free growth. When compression of the surrounding structure occurs, patients may get compression symptoms.The diagnosis of a retroperitoneal teratoma cannot be made on clinical grounds alone. Ultrasound and computed tomography are important in its diagnosis and may show the presence of calcification, teeth or fat. Calcification on the rim of tumour or inside the tumour is seen in 53-62% of teratomas and although radiologically three quarters of patients with a benign teratoma may have calcification within it, a quarter of malignant cases may also demonstrate calcification. Computed tomography is better than Ultrasonography in defining the extent and spread of teratoma to the surrounding organs.[7]

The prognosis is excellent for benign retroperitoneal teratoma if complete resection can be accomplished.

Competing Interests
Dr Tariq Mahmood helped only in the scientific writing up of this case based upon material provided by the co-authors. He was not involved in clinical management and therefore cannot verify clinical details of the case.

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Case Report

BJMP 2012;5(1):a505

Unusual presentation of thyrotoxicosis with paraparesis in a young male: A rare case report

Hakim Irfan Showkat, Arif Hussain Sarmast , Rubina Lone , Mehmood Iqbal Qadri and Manzoor Ahmed Wani

ABSTRACT
Thyrotoxic Periodic Paralysis (TPP) is an uncommon disorder seen primarily in Asian males and caused by excessive thyroid hormones. This is an endocrine emergency that can lead to respiratory failure, dysrhythmia, and death. The mainstay of therapy has been potassium replacement. However, recent evidence suggests propranolol is a more effective therapy. We present a case of TPP in a 19-year male with rapidly progressive paraparesis & hypokalemia.

INTRODUCTION:

Even though it is commonly seen in Graves' disease, TPP is not related to the etiology, severity, and duration of thyrotoxicosis. [1]

The pathogenesis of hypokalaemic periodic paralysis in certain populations with thyrotoxicosis is unclear. Transcellular distribution of potassium is maintained by the Na+/K+–ATPase activity in the cell membrane, and it is mainly influenced by the action of insulin and beta-adrenergic catecholamines.[2] Hypokalemia in TPP results from an intracellular shift of potassium and not total body depletion. It has been shown that the Na+/K+–ATPase activity in platelets and muscles is significantly higher in patients with TPP.[3] Hyperthyroidism may result in a hyperadrenergic state, which may lead to the activation of the Na+/K+–ATPase pump and result in cellular uptake of potassium.[2, 4, 5] Thyroid hormones may also directly stimulate Na+/K+– ATPase activity and increase the number and sensitivity of beta receptors.[2, 6] Patients with TPP have been found to have hyperinsulinemia during episodes of paralysis. This may explain the attacks after high-carbohydrate meals.[7]

CASE REPORT:

A 19 year old male patient presented to our emergency room with sudden onset weakness of lower limbs. He was not able to stand or walk. Power of 0/5 in both lower limbs and 3/5 in upper limbs was noticed on examination. Routine investigations revealed to have severe hypokalemia with a serum potassium of 1.6 meq/l (normal range 3.5-5.0 meq/l), a serum phosphorus level of 3.4 mg/dl (normal range 3-4.5 mg/dl) and mild hypomagnesemia with serum magnesium level of 1.5mg/dl (normal range 1.8-3.0 mg/dl). ECG showed hypokalemic changes with prolonged PR interval, increased P-wave amplitude and widened QRS complexes. He was managed on intravenous as well oral potassium and history revealed weight loss, increased appetite and tremors from past 4 months. He had a multinodular goiter and radioactive iodine uptake scan (Iodine 131) showed a toxic nodule (Toxic nodule shows increased iodine uptake while the rest of the gland is suppressed) with no exophthalmos, sensory or cranial nerve deficits. Thyroid function tests revealed thyrotoxicosis with free T4 of 4.3ng/dl (normal range 0.8-1.8ng/dl), T3 of 279 ng/dl (normal range = 60 - 181 ng/dl) and a TSH level of <0.15milliunits/L (normal range = 0.3 - 4 milliunits/L). He was managed on intravenous potassium & propanolol. The patient showed dramatic improvement of his symptoms. The patient was discharged home on carbamazole with the diagnosis of TPP secondary to toxic nodular goiter.

In this case there was a significant family history as one of his elder brother had a sudden death (cause not known) and his mother was primary hypothyroid on levothyroxin replacement therapy.

DISCUSSION :

TPP is seen most commonly in Asian populations, with an incidence of approximately 2% in patients with thyrotoxicosis of any cause.[1,8,9,10] The attacks of paralysis have a well-marked seasonal incidence, usually occurring during the warmer months.[1] Pathogenesis of hypokalaemia has been explained by some authors to be due to an intracellular shift of body potassium, which is catecholamine mediated.[11,12] Shizume and his group studied total exchangeable potassium which revealed that patients with thyrotoxic periodic paralysis were not significantly different from controls when the value was related

to lean body mass.[11] The paralytic symptoms and signs improve as the potassium returns from the intracellular space back into the extracellular space.[13] The diurnal variation in potassium movement where there is nocturnal potassium influx into skeletal muscle would explain the tendency for thyrotoxic periodic paralysis to occur at night.[14] Hypophosphataemia and hypomagnesaemia are also known to occur in association with thyrotoxic periodic paralysis.[14,15,16,17,18] The correction of hypophosphataemia without phosphate administration supports the possibility of intracellular shift of phosphate.[16] Electrocardiographic findings supportive of a diagnosis of TPP rather than sporadic or familial periodic paralysis are sinus tachycardia, elevated QRS voltage and first-degree AV block (sensitivity 97%, specificity 65%).[20] In addition to ST-segment depression, T-wave flattening or inversion and the presence of U waves are typical of hypokalaemia.

The management is to deal with the acute attack as well as treatment of the underlying condition to prevent future attacks. Rapid administration of oral or intravenous potassium chloride can abort an attack and prevent cardiovascular and respiratory complications.[4] A small dose of potassium is the treatment of choice for facilitating recovery and reducing rebound hyperkalaemia due to release of potassium and phosphate from the cells on recovery.[1,2,3] Rebound hyperkalaemia occurred in approximately 40% of patients with TPP, especially if they received >90 mmol of potassium chloride within the first 24 hours.[4] Another mode of treatment is to give propranolol, a nonselective b-blocker, which prevents the intracellular shift of potassium and phosphate by blunting the hyperadrenergic stimulation of Na+/K+–ATPase.[20] Hence, initial therapy for stable TPP should include propranolol.[21,22,23] The definitive therapy for TPP includes treatment of hyperthyroidism with antithyroid medications, surgical thyroidectomy, or radioiodine therapy.

Competing Interests
None Declared
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Clinical Practice

BJMP 2012;5(1):a503

A survey of aseptic technique when performing lumbar puncture: a comparison of medical and anaesthetic trainees

Rajiv Malhotra and Sara Kelly

Abstract

Aim: To compare infection control measures taken by anaesthetic and acute medical trainees when performing lumbar puncture.

Methods: An online anonymous survey was sent to 50 anaesthetic and 50 acute medical trainees currently in training posts. Information on compliance with infection control measures was gathered.

Results: The response rate was 71% (40/50 anaesthetic trainees, 31/50 medical trainees). All anaesthetic trainees complied with the components of aseptic technique. In comparison to this, only 80.6% of medical trainees used sterile gloves, 38.7% used an apron and 77.4% used a dressing pack.

Conclusions: Levels of infection control during lumbar puncture differ between anaesthetic and medical trainees, particularly with the use of equipment as part of an aseptic technique. The difference is likely to be due to a combination of factors including training and the clinical environment.

Introduction

Lumbar punctures are commonly performed by both medical and anaesthetic trainees but in different contexts. Medically performed lumbar punctures are often used to confirm a diagnosis (meningitis, subarachnoid haemorrhage) whilst lumbar puncture performed by anaesthetists are usually a precedent to the injection of local anaesthetics into cerebrospinal fluid for spinal anaesthesia. The similarity relies on the fact that both involve the potential for iatrogenic infection into the subarachnoid space. The incidence of iatrogenic infection is very low in both fields; a recent survey by the Royal College of Anaesthetists[1] reported an incidence of 8/707 000 whilst there were only approximately 75 cases in the literature after 'medical' lumbar puncture.[2] However, the consequences of iatrogenic infection can be devastating. It is likely that appropriate infection control measures taken during lumbar puncture would reduce the risk of bacterial contamination. The purpose of the present study is to compare infection control measures taken by anaesthetic and medical staff when performing lumbar puncture.

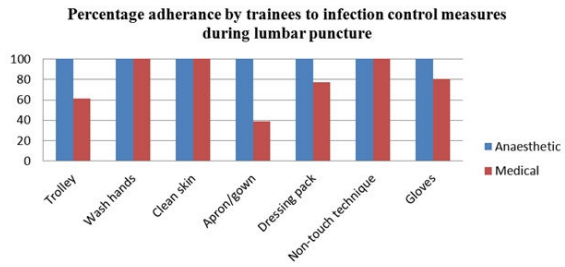
Method

A survey was constructed online (www.surveymonkey.com) and sent by email to 50 anaesthetic and 50 acute medical trainees in January 2011. All participants were on an anaesthetic or medical training programme and all responses were anonymous. The survey asked whether trainees routinely used the following components of an aseptic technique[3] when performing lumbar puncture:

- Sterile trolley
- Decontaminate hands
- Clean patient skin
- Apron/gown
- Dressing pack
- Non-touch technique
- Sterile gloves

No ethical approval was sought as the study was voluntary and anonymous.

Results



The overall response rate was 71% (40/50 anaesthetic trainees and 31/50 medical). All anaesthetic trainees routinely used the components of an aseptic technique when performing lumbar puncture. All medical trainees routinely cleaned the skin, decontaminated their hands and used a non-touch technique but only 80.6% used sterile gloves. 61.3% of medical trainees used a sterile trolley, 38.7% used an apron/gown and 77.4% used a dressing pack.

Discussion

This survey shows that adherence to infection control measures differ between anaesthetic and medical trainees when performing lumbar puncture. The anaesthetic trainees have a

100% compliance rate compared to 80% for the medical trainees for all components of the aseptic technique. Both groups routinely cleaned the patient's skin, decontaminated their hands and used a non-touch technique. However, there were significant differences in the use of other equipment, with fewer medical trainees using sterile gloves, trolleys, aprons and dressing packs.

Although the incidence of iatrogenic infection after lumbar puncture is low, it is important to contribute to this low incidence by adopting an aseptic technique. There may be differences with regards to the risks of iatrogenic infection between anaesthetic and medical trainees. Anaesthetic lumbar punctures involve the injection of a foreign substance (local anaesthesia) into the cerebrospinal fluid and may therefore carry a higher risk. Crucially however, both anaesthetic and medical lumbar punctures involve accessing the subarachnoid space with medical equipment and so the risk is present.

There are many reasons for the differing compliance rates between the two specialties. Firstly, anaesthetic trainees perform lumbar punctures in a dedicated anaesthetic room whilst the presence of 'procedure/treatment rooms' is not universal on medical wards. Secondly, anaesthetic trainees will always have a trained assistant present (usually an operating department practitioner, ODP) who can assist with preparing equipment such as dressing trolleys.

The mechanism of iatrogenic infection during lumbar puncture is not completely clear.[4] The source of microbial contamination could be external (incomplete aseptic technique, infected equipment) or internal (bacteraemia in the patient); the fact that a common cause of iatrogenic meningitis are viridans streptococcus strains[5] (mouth commensals) supports the notion that external factors are relevant and an aseptic technique is important.

It is very likely that improved compliance amongst acute medical trainees would result from a dedicated treatment room on medical wards, but this is likely to involve financial and logistical barriers. The introduction of specific 'lumbar puncture packs', which include all necessary equipment (e.g. cleaning solution, aprons, sterile gloves) may reduce the risk of infection; the introduction of a specific pack containing equipment for central venous line insertion reduced colonisation rates from 31 to 12%.[6] The presence of trained staff members to assist medical trainees when performing lumbar puncture may assist in improved compliance, similar to the role of an ODP for anaesthetic trainees.

The main limitation of this study is that the sample size is small. However, we feel that this study raises important questions as to why there is a difference in infection control measures taken by anaesthetic and medical trainees; it may be that the environment in which the procedure takes place is crucial and further work on the impact of 'procedure rooms' on medical wards is warranted.

Competing Interests
None declared
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