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Editorial

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Efficacy and safety of dietary supplement use in the primary prevention of chronic disease in the general non-pregnant United States adult population

Nasseer A Masoodi

The use of dietary supplements has grown rapidly over the past several decades, and are now used by more than half of the adult population in the United States (US).[1] In 1994, the Dietary Supplements Health and Education Act (DSHEA) significantly changed the Food and Drug Administration's (FDA) role in regulating supplement labeling. According to the DSHEA dietary supplements may contain products taken by mouth including vitamins, minerals, herbs or other botanicals, amino acids, other dietary substances, or combinations or extracts of any of these 'dietary ingredients.' The DSHEA reaffirmed that dietary supplements are to be regulated as foods and not as drugs. Annual sales of supplements to Americans are now reported at about $23 billion, a substantial share of which is spent on vitamins and minerals.

The purpose of this review is to present the discussion from available research to internists and other clinicians to help guide their decisions behind the efficacy and safety of dietary supplement use in primary prevention of chronic disease in the general non-pregnant adult population.

Profile of a dietary supplement user

In general dietary supplements are used by individuals who practise healthier lifestyles. Its use is higher among women and the children of women who use supplements; in elderly persons; among people with more education, higher income, healthier diets, and lower body mass indices; and among residents of the western US.[2] Individuals with chronic illnesses, or those who are seeking to prevent recurrence of a serious disease (for example, cancer) also tend to be more frequent supplement users.[3] Many dietary supplement users perceive their health as better.

Why use dietary supplements?

The growth in supplement use has accelerated rapidly with marketing spurred by claims that chronic conditions could be prevented or treated by supplement use. The commonly used over-the-counter multivitamin and mineral supplements contain at least 10 vitamins and 10 minerals. On a daily basis consumers receive advertising and promotional material of unproven claims made about dietary supplements or other products and the medical wonders they can achieve. Some of the promotional material makes a consumer feel guilty if he or she is not using one. Many users feel so strongly about the potential health benefits of some of these products that they reported that they would continue to take them even if they were shown to be ineffective in scientifically conducted clinical studies.[4] More than half of American adults take dietary supplements in the belief that they will make them feel better, give them greater energy, improve their health, and prevent and treat disease.

Is there clinical evidence for use of dietary supplements?

Most studies do not provide strong evidence for beneficial health-related effects of supplements taken singly, in pairs, or in combinations of 3 or more.[5] In some studies, or subgroups of the study populations, there is encouraging evidence of health benefits such as increased bone mineral density and decreased fractures in postmenopausal women who use calcium and vitamin D supplements.

Huang et al [5] performed a systematic review to synthesize the published literature on the efficacy of multivitamin and mineral supplements and certain commonly used single vitamin or mineral supplements in the primary prevention of cancer and chronic disease in the general adult population. The authors concluded that the strength of evidence for the efficacy of multivitamin/mineral supplementation in the general adult US population was very low for primary prevention of cancer, cardiovascular disease, and hypertension; and low for cataract and age-related macular degeneration.

The National Institutes of Health (NIH) consensus panel statement[2] on 'multivitamin/mineral supplements and chronic disease prevention' did not find any strong evidence for beneficial health-related effects of supplements taken singly, in pairs, or in combinations of 3 or more. The panel concluded that the present evidence is insufficient to recommend either for or against the use of dietary supplements by the American public to prevent chronic disease. It also concluded that the current level of public assurance of the safety and quality of dietary supplements is inadequate, given the fact that manufacturers of these products are not required to report adverse events and the FDA has no regulatory authority to

require labeling changes or to help inform the public of these issues and concerns.

A recent study published in Archives of Internal Medicine[6] raised some disturbing concerns. In this large prospective study, 38,772 older women in the Iowa Women's Health Study were followed up for a mean time of 19.0 years. The authors found that most of the supplements studied were not associated with a reduced total mortality rate in older women. In contrast, they found that several commonly used dietary vitamin and mineral supplements, including multivitamins, vitamins B6, and folic acid, as well as the minerals iron, magnesium, zinc, and copper, were associated with a higher risk of total mortality. Of particular concern, supplemental iron was strongly and dose dependently associated with increased total mortality risk. The association was consistent across shorter intervals, strengthened with multiple use reports and with increasing age at reported use. Supplemental calcium was consistently inversely related to total mortality rate; however, no clear dose-response relationship was observed. The strengths of this study include the large sample size and longitudinal design. In addition, the use of dietary supplements was queried three times: at baseline in 1986, in 1997, and in 2004. The use of repeated measures enabled evaluation of the consistency of the findings and decreased the risk that the exposure was misclassified.

Summary

The use of dietary supplements has grown rapidly over the past several decades even though clinical deficiency of vitamins or minerals, other than iron, is now uncommon in the US.[2] Fortification of foods has led to the remediation of vitamin and mineral deficits. The cumulative effects of supplementation and fortification have also raised safety concerns about exceeding upper levels besides interactions of dietary supplements with the prescriptions drugs taken by a consumer. There is no evidence-based data about what the optimal compositions and dose of a multivitamin and mineral supplement should be. Though dietary supplements are perceived to be safe, that should not be sufficient reason for using them without a valid medical need. Providers should take into consideration their efficacy and cost-effectiveness. There are also no outcomes data or data about quality adjusted life years gained by using dietary supplements taken singly, in pairs, or in combinations. The current data available on the efficacy and safety of dietary supplements is conflicting. Clinicians considering the use of dietary supplements should be aware of their risks, consider the likelihood of the adverse effects, interaction with prescription medications, safety, efficacy, costs, and possibility of unintended effectsof dietary supplements.

Conclusion

The conclusion from the available data (new and old) is that consumption of dietary supplements for prolonged periods appears not to be safe and is not cost-effective in primary prevention of chronic disease in the general non-pregnant adult US population. Practitioners should evaluate each case individually and take a decision based on available evidence-based data when considering dietary supplements in this population. Given the potential for widespread use of dietary supplements, there is a need for robust study methods in the future.

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Research Article

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Seroprotection after Hepatitis B Vaccination in Expanded Programme on Immunisation

Mohammad Afzal, Khaliq Naveed, Shabbir Hussain, Shaukat Mehmood Qureshi, Asifa Majeed, Zia Farooqi, Alizay Gohar and Abdul Wahab

ABSTRACT

Aim: As part of a global strategy, Pakistan included the Hepatitis B (HB) vaccine in the national Expanded Programme on Immunisation (EPI) in 2004. The aim of this study was to know the status of seroprotection amongst those receiving HB vaccination in the EPI in Pakistan.

Introduction: Hepatitis B vaccination has produced very convincing results in reducing disease burden in the developed world. As per the World Health Organisation (WHO) recommendations, most countries have included HB vaccination in the national EPI schedules. Pakistan included the HB vaccination in the EPI in 2004. There are various factors affecting seroprotection after HB vaccination done in the EPI, for example dosing schedule, maintenance of the cold chain and missing the birth dose, etc. There are no published studies to date regarding seroprotection status and anti-HBs antibodies levels after receiving the HB vaccination in the EPI in Pakistan.

Methods: This study was conducted at the paediatric departments of Military Hospital (MH) and Combined Military Hospital (CMH), Rawalpindi from 1st January 2010 to 31st December 2010. One hundred and ninety-four children ranging from 9 months to 2 years of age, who had received HB vaccination according to the EPI schedule, were included. Blood samples were taken and tested for anti–HBs antibody levels by enzyme-linked immunosorbent assay (ELISA) at the Department of Biochemistry of Army Medical College, Rawalpindi. Anti–HBs antibody titres >10 IU/L was taken as seroprotection level as per WHO and kit manufacturers' standards.

Results: Out of 194 children, 133 (68.6%) had anti–HBs titres > 10 IU/L (seroprotected) while 61 (31.4%) had anti–HBs titres <10 IU/L (non-protected). GMT achieved among seroprotected vaccine recipients was 85.81 IU/L. One hundred and twenty-nine were male children and of them 95 (73.6%) had a protective level and 34 (26.4%) were non- protected. Sixty-five were female children and out of them 38 (58.5%) had a protective level while 27 (41.5%) were non-protected. The difference was significant between males and females (p value= 0.032). One hundred and eighty-four children received the vaccine procured through the public sector, out of which 123 (68.5%) developed anti-HBs levels >10 IU/L (protected) and 61 (23.2%) had anti-HBs titres <10 IU/L (non-protected). However, 10 children received privately procured HB vaccines of whom all developed anti-HB titres >10 IU/L (protected). The difference was significant between the public sector procured and privately procured vaccine (p-value= 0.028).

One hundred and thirty-two children received the HB vaccination at army vaccination centres (MH & CMH). Out of them 96 (72.7%) developed anti-HBs levels >10 IU/L (protected) and 36 (27.3%) had antibody titres <10 IU/L (non protected). Sixty-two children were vaccinated at civil health facilities and at home by vaccination teams. Out of them 38 (58.5%) developed anti-HBs levels >10 IU/L (protected) while 27 (41.5%) had antibody titres <10 IU/L (non protected).

Conclusion: Seroprotection achieved after HB vaccination received in the EPI at 6, 10 and 14 weeks in combination vaccination form was 68.6%. This is low as compared to results reported internationally. Geometric mean titre (GMT) levels achieved in seroprotected vaccine recipients are also low (85.81 IU/L) when compared with international data. There is a need to look into relevant aspects of HB vaccination in the EPI to improve seroprotection in future.

KEYWORDS : Hepatitis B, Hepatitis B vaccine, seroprotection, EPI

Introduction

Hepatitis B (HB) is a major disease and is a serious global public health problem. About 2 billion people (latest figures so far by WHO) are infected with the hepatitis B virus (HBV) all over the world. Interestingly, rates of new infection and acute disease are highest among adults, but chronic infection is more likely to occur in persons infected as infants or young children, which leads to cirrhosis and hepatocellular carcinoma in later life. More than 350 million persons are reported to have chronic infection globally at present[1,2]. These chronically infected people are at high risk of death from cirrhosis and liver cancer. This virus kills about 1 million persons each year. For a newborn infant whose mother is positive for both HB surface antigen (HBsAg) and HB e antigen (HBeAg), the risk of chronic HB Virus (HBV) infection is 70% - 90% by the age of 6 months in the absence of post-exposure immunoprophylaxis[3].

HB vaccination is the only effective measure to prevent HBV infection and its consequences. Since its introduction in 1982, recommendations for HB vaccination have evolved into a comprehensive strategy to eliminate HBV transmission globally[4]. In the United States during 1990–2004, the overall incidence of reported acute HB declined by 75%, from 8.5 to 2.1 per 100,000 population. The most dramatic decline occurred in children and adolescents. Incidence among children aged <12 years and adolescents aged 12-19 years declined by 94% from 1.1 to 0.36 and 6.1 to 2.8 per 100,000 population, respectively[2,5].

Population of countries with intermediate and high endemicity rates are at high risk of acquiring HB infection. Pakistan lies in an intermediate endemic region with a prevalence of 3-4% in the general population[6]. WHO has included the HB vaccine in the Expanded Programme on Immunisation (EPI) globally

since 1997. Pakistan included the HB vaccination in the EPI in 2004. Primary vaccination consists of 3 intramuscular doses of the HB vaccine. Studies show seroprotection rates of 95% with standard immunisation schedule at 0, 1 and 6 months using a single antigen HB vaccine among infants and children[7,8]. Almost similar results have been reported with immunisation schedules giving HB injections (either single antigen or in combination vaccines) at 6, 10 and 14 weeks along with other vaccines in the EPI schedule. But various factors like age, gender, genetic and socioenvironmetal influences, are likely to affect seroprotection rates[9].So there is need to know actual seroprotection rates in our population where different vaccines, EPI procured and privately procured incorporated in different schedules are used. This study has been conducted to know the real status of seroprotection against HB in our children. Results will help in future policy-making, highlighting our shortcomings, comparing our programme with international standards and moreover augment future confidence in vaccination programmes.

Materials and Methods

This study was conducted at vaccinations centres and paediatrics OPDs (Outpatient Departments) of CMH and MH, Rawalpindi, Pakistan. Children reporting for measles vaccination at vaccination centres at 9 months of age were included. Their vaccination cards were examined and ensured that they had received 3 doses of HB vaccine according to the EPI schedule, duly endorsed in their cards. They included mainly children of soldiers but some civilians also who were invited for EPI vaccination at the MH vaccination centre. Children of officers were similarly included from the CMH vaccination centre and vaccination record was ensured by examining their vaccination cards. Some civilians who received private HB vaccination were included from paediatric OPDs . Some children beyond 9 months and less than 2 years of age who reported for non-febrile minor illnesses in the paediatric OPD at CMH and MH, were also included and their vaccination status was confirmed by examining their vaccination cards.

Inclusion Criteria

1) Male and female children >9 months and <2 years of age.
2) Children who had received 3 doses of HBV according to the EPI schedule at 6,10 and 14 weeks.
3) Children who had a complete record of vaccination- duly endorsed in vaccination cards.
4) Childen who did not have history of any chronic illness.

Exclusion Criteria

1) Children who did not have proper vaccination records endorsed in their vaccination cards.
2) Interval between last dose of HBV and sampling was <1 month.
3) Children suffering from acute illness at time of sampling.
4) Children suffering from chronic illness or on immunosuppressive drugs.

Informed consent for blood sample collection was obtained from the parents or guardians. The study and the informed consent form was approved by the institutional ethical review board. Participants were informed about results of HBs antibody screening. After proper antiseptic measures, blood samples (3.5 ml) were obtained by venepuncture. Autodisabled syringes were used. Collected blood samples were taken in vaccutainers and labelled by identification number and name of child. Samples were immediately transported to the Biochemistery Department of Army Medical College. Samples were kept upright for half an hour and then centrifuged for 10 minutes. Supernatant serum was separated and stored at -20 ^{0}C in 1.5 ml eppendorf tubes till the test was performed. Samples were tested using ELISA (DiaSorin S.p.A Italy kit) for detection of anti-HBs antibodies according to manufacturers' instructions. The diagnostic specificity of this kit is 98.21% (95% confidence interval 97.07-99.00%) and diagnostic sensitivity is 99.11% (95% confidence interval 98.18-99.64%) as claimed by the manufacturer. Anti-HBs antibody enumeration was done after all 3 doses of vaccination (at least 1 month after the last dose was received).

As per WHO standards, anti-HBs antibody titres of >10 IU/L is taken as protective and samples showing antibody titres <10 IU/L were considered as non-protected. Samples having antibody titres >10 IU/L were taken as seroprotected against HB infection. All relevant information was entered in a predesigned data sheet and used accordingly at the time of analysis. Items entered included age, gender, place of vaccination, type of vaccination (private or government procured), number of doses and entitlement status (dependent of military personnel or civilian). The study was conducted from 1st January 2010 to 31st Dec 2010.

Statistical Analysis

Data was analysed using SPSS version 15. Descriptive statistics were used to describe the data, i.e. mean and standard deviation (SD) for quantitative variables, while frequency and percentages were used for qualitative. Quantitative variables were compared through independent samples' t-test and qualitative variables were compared through the chi-square test between both the groups. A P-value <0.05 was considered as significant.

The mean age of the children was 13.7 months. The overall frequency of children with titres <10 IU/L was 61 (31.4%) while frequency of children with titres >10 IU/L was 133 (68.6%). Geometric mean titres (GMT) were 85.81 for the seroprotected (>10 IU/L) category.

Results

One hundred and ninety-four children, who had received HB vaccination according to EPI schedule, were tested for anti-HBs

titres. Out of them 61 (31.4%) had anti-HBs titres less than 10 IU/L (non-protective level) while 133 (68.6%) had anti-HBs titres above 10 IU/L (protective level) as shown in Figure 1. The GMT of anti-HBs among the individuals having protective levels (> 10 IU/L) was found to be 85.81 IU/L.

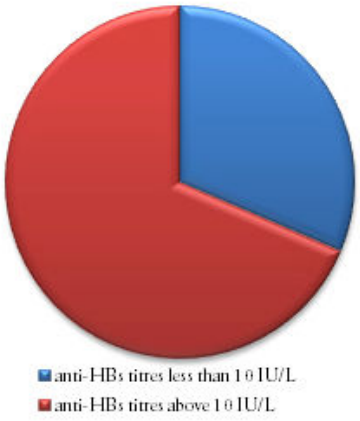

Figure 1

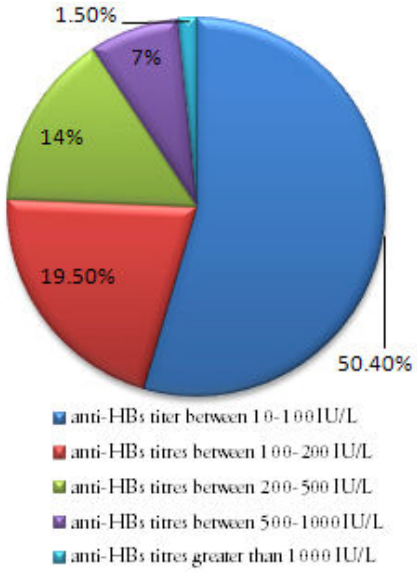

Figure 2

Figure 2 shows that anti-HBs titres between 10–100 IU/L was found in 75 (50.4%) children. Twenty-six (19.5%) individuals had titres between 100–200 IU/L. Twenty (14%) children had titres between 20–500 IU/L, 10 (7%) children had titres between 500–1000 IU/L and only 2 (1.5%) children had anti-HBs titres > 1000 IU/L.

One hundred and eighty-four children received vaccination supplied by government sources (Quinevaxem by Novartis) out of which 61 (33.1%) children had anti-HBs titres <10 IU/L (non- protective) and 123 (66.9%) had anti-HBs titres >10 IU/L (protective level). Only 10 children had received vaccination obtained from a private source (Infanrix Hexa by GSK), out of which all 10 (100%) had anti-HBs titres >10 IU/L (protective level). Comparison between the two groups revealed the difference to be significant (P value= 0.028).

One hundred and thirty-two children received vaccination from army health facilities (CMH and MH) out of which 36 (27.3%) had anti-HBs titres < 10 IU/L while 96 (72.7%) had anti-HBs titres >10 IU/L. Sixty-two children were vaccinated at civilian health facilities (health centres or vaccination teams visiting homes). Out of them 25 (40.3%) had anti-HBs titres <10 IU/L while 37 (59.7%) had anti- HBs titres >10 IU/L. The difference was insignificant (P value= 0.068). Gender analysis revealed that in the study group 129 (68.5%) were male children. Out of them 34 (26.4%) had anti-HBs titres <10 IU/L and 95 (73.6%) had anti-HBs titres >10 IU/L. Sixty-five (31.5%) were female children and out of them 27 (41.5%) had anti-HBs titres <10 IU/L while 38 (58.5%) had anti-HBs titres > 10 IU/L. Statistical analysis revealed the difference between males and females was significant (P value= 0.032).

One hundred and twenty-two (62.9%) children were less than 1 year of age. Out of them 37 (30.3%) had anti-HBs titres <10 IU/L and 85 (69.7%) had anti- HBs titres >10 IU/L. Seventy-two (37.1%) children ranged between 1 to 2 years of age. Out of them 24 (33.3%) had anti-HBs titres <10 IU/L while 48 (66.7%) had anti-HBs titres >10 IU/L. On comparison the difference between the two groups was insignificant (P value= 0.663), as shown in Table 1.

Patient characteristics	Anti-HBs titres (< 10 IU/L) (n = 61)	Anti-HBs titres (> 10 IU/L) (n = 133)	P – values
Age groups			
< 1year (n = 122)	37 (30.0%)	85 (69.7%)	0.63
> 1year (n = 72)	24 (33.3%)	48 (66.7%)	NS
Gender			
Male (n = 129)	34 (26.4%)	95 (73.6%)	
Female (n = 65)	27 (41.5%)	38 (58.5%)	0.032
Hospital			
Army (n = 132)	36 (27.3%)	96 (72.7%)	0.068
Civilian (n = 62)	25 (40.3%)	37 (59.7%)	NS
Vaccine Type			
Government (n = 184)	61 (33.2%)	123 (66.8%)	
Private (n = 10)	0 (0%)	10 (100%)	0.028

Table 1 (NS = Insignificant; * = Significant)

Discussion

HB is a global health problem with variable prevalence in different parts of the world[1]. Various studies carried out in different parts of Pakistan in different groups of population have shown diverse figures regarding prevalence of HB. However, a figure of 3-4% is accepted as general consensus by and large, thus making Pakistan an area of intermediate endemicity for HB[6]. Yet when we extrapolate these figures to

our population, it is estimated that Pakistan hosts about seven million carriers of HB which is about 5% of the worldwide 350 million carriers of HB[10,11].

Age at the time of infection plays the most important role in acquisition of acute or chronic HBV disease. HBV infection acquired in infancy is responsible for a very high risk of chronic liver disease due to HBV in later life[12]. HB is a preventable disease and fortunately vaccination at birth and during infancy can eradicate the disease globally, if vaccination strategy is effectively implemented[13]. This can be claimed as the first anti-cancer vaccine which prevents hepatocellular carcinoma in later life.

In Pakistan, the HB vaccine was included in the EPI in 2004, given along with DPT (Diphtheria, Pertussis, Tetanus) at 6, 10 and 14 weeks of age. The vaccine is provided through government health infrastructure to health facilities. Private HB vaccines supplied as a single antigen or in combination vaccines are also available in the market. The efficacy of these recombinant vaccines is claimed to be more than 95% among children and 90% among normal healthy adults[14]. The immunity of the HB vaccination is directly measured by development of anti-HBs antibodies more than 10 IU/L, which is considered as a protective level[15]. However, it is estimated that 5–15 % of vaccine recipients may not develop this protective level and remain non-responders due to undermentioned reasons.[16] Published studies regarding antibody development in relation to various factors in terms of immunogenicity and seroprotection, show highly varied results. Multiple factors like dose, dosing schedules, sex, storage, site and route of administration, obesity, genetic factors, diabetes mellitus and immunosupression, affect HB antibodies development response[17].

Although the HB vaccine was included in the EPI in 2004 in Pakistan, until now no published data showing seroconversion and seroprotection among vaccine recipients of this programme is available on a national level to our knowledge. Our study has revealed that out of 194 children, only 133 (68.6%) had anti-HBs titres in the protective range (>10 IU/L) while 61 (31.4%) did not develop seroprotection. These results are low as compared to other international studies. A study from Bangladesh among EPI vaccinated children shows a seroprotection rate of 92.2%[13]while studies from Brazil[18] and South Africa[19] have separately reported seroprotection rates of 90.0% and 86.6%, respectively. Studies from Pakistan carried out in adults also show seroprotection rates (anti-HBe titres >10 IU/L) of more than 95% in Karachi University students[14] and 86% in health care workers of Agha Khan University Hospital[20], respectively. However, in these studies the dosing schedule was 0, 1 and 6 months, and participants were adults. These results are consistent with international reports.

The gravity of low seroprotection after HB vaccination is further aggravated when we extrapolate these figures to our overall low vaccination coverage rates of 37.6% to 45% as shown in studies at Peshawar and Karachi respectively[21,22]. One can imagine a significantly high percentage of individuals vulnerable to HBV infection even after receiving HB vaccine in an extensive national EPI programme. Therefore, a large population still remains exposed to risk of HBV infection, and national and global eradication of HBV infection will remain a dream. Failure of seroprotection after receiving the HBV vaccination in the EPI will also be responsible for projecting a sense of false protection among vaccine recipients.

Dosing schedule is an important factor in the development of an antibody response and titre levels. According to the Advisory Committee on Immunization Practices (ACIP) of America, there should be a minimum gap of 8 weeks between the second and third doses and at least 16 weeks between the first and third doses of the HB vaccination[23]. To minimize frequent visits and improve compliance, the dosing schedule has been negotiated in the EPI to 6, 10 and 14 weeks[24]. Although some studies have shown this schedule to be effective, the GMT of anti-HBs antibodies achieved was lower than that achieved by the standard WHO schedule[25]. This may be one explanation of lower rates of seroprotection in our study. The GMT achieved in our study among the children having protective levels of antibodies is 85.81 IU/L which is lower than most other studies. This supports the observation that GMT achieved in this schedule is lower than that produced by the standard WHO schedule. This may result in breakthrough infection of HB in vaccinated individuals in later life due to waning immunity. However, the immune memory hypothesis supports protection of vaccinated individuals in later life in spite of low anti-HBs antibody titres[26]. Yet further studies are required to dispel this risk.

Another shortcoming of this schedule is to miss the dose at birth ('0 dose'). It has been reported that the 0 dose of the HB vaccine alone is 70% - 95% effective as post-exposure prophylaxis in preventing perinatal HBV transmission without giving HB immunoglobulins[27]. This may also be a factor contributing to lower rates of seroprotection in our study as we have not done HBsAg and other relevant tests to rule out HBV infection in these children. Moreover pregnant ladies by and large are not screened for HBV infection in Pakistan routinely in the public sector except in a few big cities like Islamabad, Lahore or Krachi. Therefore, we do not know the HB status of pregnant mothers and the risk of transmission to babies remains high. Different studies have reported much varied figures of HB status in pregnant ladies. A study from Karachi reports 1.57% pregnant ladies are positive for HBsAg while a study from Rahim Yar Khan reports this figure to be up to 20%[28,29]. A study by Waheed et al regarding the transmission of HBV infection from mother to infants reports the risk to be up to 90%[30]. All of these studies support the importance of the birth dose of the HB vaccination and augment the fact that control and eradication of HB with the present EPI schedule is not

possible. Jain from India has reported a study using an alternative schedule of 0, 6 weeks and 9 months. He has reported it to be comparable to the standard WHO schedule of 0, 1, 6 months in regards to seroprotection and GMT levels achieved[31]. This schedule can be synchronised with the EPI schedule, avoiding extra visits and incorporating the birth dose. A similar schedule can also be incorporated in our national EPI.

In our study, seroprotection rates were found to be low in the female gender and the difference was significant. This finding differs with other studies which report lower seroprotection rates in males[32]. Although the number of female children was less, there is no plausible explanation for this observation. The site of inoculation of the HB vaccine is also very important for an adequate immune response. Vaccines given in the buttocks or intradermally produce lower antibody titres than intramuscular injections given in the outer aspect of the thigh in children, due to poor distribution and absorption of the vaccine within the host body. The practice of giving vaccinations in the buttocks by vaccinators is a common observation which they feel convenient for intramuscular injection in children. This may also be one reason for low seroprotection rates in our study, as we picked the children at random who had received vaccination at public health facilities except a small number of private cases.

The effectiveness of the vaccine also depends on the source of procurement and proper maintenance of the cold chain. In this study 100% seroprotection was observed in children who received the HB vaccine procured from a private source. Although the number of private cases was less, this factor of source and the cold chain also needs attention. To address this issue proper training of EPI teams regarding maintenance of temperature, injection techniques, motivation and monitoring can improve outcomes substantially.

The findings of this study are different from published literature because this is a cross-sectional observational study. This reports the actual seroprotection rates after receiving the HB vaccination in the EPI schedule. While most other studies show the results after ensuring control of influencing factors such as type of vaccine, dose, schedule, route of administration, training and monitoring of local EPI teams and health status of vaccine recipients, etc. Therefore, this is an effort to look at a practical scenario and evaluate outcomes which can help in framing future guidelines to achieve the goal of control and eradication of HB infection. Further studies are required at a large scale to determine the effect of HB vaccination at a national level.

Conclusion

The HB vaccination programme has decreased the global burden of HBV infection, but evidence of decreased burden is not uniform amongst world population.Of course figures witness marked decrease in developed world while in developing world statistics show little change. Unfortunately, implementation of this programme is not uniformly effective in all countries, thus resvoirs of infection and the source of continued HBV transmission persists. HBV infection is moderately endemic in Pakistan. The HB vaccine has been included in the national EPI since 2004. The present study shows seroprotection rates of only 68.6% in vaccine recipients, which is low when compared with other studies; 31.4% of vaccine recipients remain unprotected even after vaccination. Moreover GMT achieved in seroprotected vaccine recipients is also low (85.81 IU/L). There can be multiple reasons for these results, such as type of vaccine used, maintenance of the cold chain, route and site of administration, training and monitoring of EPI teams and dosing schedule. In present practice, the very important birth dose is also missing. These observations warrant review of the situation and appropriate measures to be taken to rectify the above mentioned factors, so that desired seroprotection rates after HB vaccination in the EPI can be achieved among vaccine recipients.

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Research Article

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Dexmedetomidine versus ketamine combined with midazolam; a comparison of anxiolytic and sedative premedication in children

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ABSTRACT

Background: Preanaesthetic medication plays an important role in the anaesthetic care of children by allaying anxiety, decreasing vagal stimulation and preventing postoperative psychological sequelae. This study was undertaken to evaluate the efficacy of dexmedetomidine when administered orally as a hypnotic and anxiolytic compared to oral combination ketamine/midazolam as preanaesthetic medication in paediatric patients.

Methods: Sixty-six children aged 2-6 years posted for elective surgical procedures were randomly allocated to one of two groups 'Group D' and 'Group MK'. Group D received oral dexmedetomidine 3 μg/kg and group MK received 0.25 mg/kg oral midazolam (up to a maximum of 15 mg) mixed with 2.5 mg/kg oral ketamine. Drug acceptance was noted. Heart rate, arterial pressure, respiratory rate, sedation score and anxiolysis score were noted before drug administration and every 5 min for up to 30 min after drug administration. Parental separation score at 30 min and mask acceptance score in addition to parental satisfaction were also noted.

Results: premedication with oral MK appeared to be superior to oral dexmedetomidine, in addition to evident haemodynamic stability and higher degree of parental satisfaction (90%), but 97% of children better accepted oral dexmedetomidine. No significant side effects were attributable to either premedication. Emergence from anaesthesia was comparable between groups.

Conclusion: premedication with oral midazolam ketamine appeared to be superior to oral dexmedetomidine, with evident haemodynamic stability and a higher degree of parental satisfaction, although oral dexmedetomidine was more accepted by the children.

KEYWORDS : Dexmedetomidine, Midazolam, Ketamine, Paediatric, Premedication

Introduction

Fear of physicians, injections, operations, the operation theatre and the forced separation from parents make the operative experience more traumatic for young children and can cause nightmares and postoperative behavioural abnormalities. Preanaesthetic medication may decrease the adverse psychological and physiological sequelae of induction of anaesthesia in a distressed child[1]. An important goal of premedication is to have the child arrive in the operating room calm and quiet with intactcardiorespiratoryreflexes. Various drugs have been advocated as premedication to allay anxiety and facilitate the smooth separation of children from parents. The idealpremedicantin children should be readily acceptable and should have a rapid and reliable onset with minimal side effects. Midazolam has sedative and anxiolytic activities, provides anterograde amnesia, and has anticonvulsant properties[2]. Ketamine, on the other hand, provides well-documented anaesthesia and analgesia. It has a wide margin of safety, as the protective reflexes are usually maintainedOral premedication with midazolam and ketamine became widely used inpaediatric anaesthesiato reduce emotional trauma and ensure smooth induction. It provided better premedication than either oral ketamine or midazolam alone[4], but excessive salivation and hallucination were observed[5].

Dexmedetomidine is a highly selective α2-adrenoreceptor agonist drug. Clinical investigations have demonstrated its sedative, analgesic and anxiolytic effects after IV administration to volunteers and postsurgical patients[6]. It has been used to sedate infants and children during mechanical ventilation and also to sedate children undergoing radiological imaging studies[8]In the literature, few articles have used dexmedetomidine orally for the premedication of children. The purpose of this study is to evaluate the efficacy of dexmedetomidine when administered orally as a hypnotic and anxiolytic agent compared to oral combination ketamine/midazolam as preanaesthetic medication in paediatrics.

Methods:

The Hospital Ethics Committee approved the protocol. Written informed consent was obtained from parents prior to inclusion. Sixty six children of ASA physical status I or II, aged between 2 and 6 years and scheduled for elective minor surgery of more than 30 minutes expected duration were enrolled in this prospective, randomized, double-blind study. Exclusion criteria were: a known allergy or hypersensitivity reaction to any of the study drugs, organ dysfunction, cardiac arrhythmia or congenital heart disease, and mental retardation.

Children were randomly allocated to one of the two study groups using computer-generated random numbers. Group D received oral dexmedetomidine 3 μg/kg and group MK received 0.25 mg/kg oral midazolam (up to a maximum of 15 mg) with 2.5 mg/kg oral ketamine. The oral premedication was mixed with 3 ml of apple juice as a carrier to be given thirty minutes before induction of anaesthesia. The oral route was chosen as it is the most acceptable and familiar mode of drug

administration. An independent investigator not involved in the observation or administration of anaesthesia for the children prepared all study drugs. Observers and attending anaesthetists who evaluated the patients for preoperative sedation and emergence from anaesthesia were blinded to the drug administered. Children had premedication in the preoperative holding area in the presence of one parent. All children received EMLA cream unless contraindicated.

After drugs were administrated, the following conditions were observed: 1) response to drug and onset of sedation, 2) response to the family separation circumstance and the entrance to the operating room, 3) response to the venous line (IV) insertion, 4) ease of mask acceptance during induction of anaesthesia. The time to recovery from anaesthesia and to achieve satisfactory Aldrete score were also noted. Onset of sedation was defined as the minimum time interval necessary for the child to become drowsy or asleep.

Sedation statuswas assessed every 5 min for up to 30 min with a five-point scale. A score of three or higher was considered satisfactory. In addition anxiolysis was assessed on a four-point scale. An anxiety score of three or four was considered satisfactory. Cooperation was assessed with a four-point scale. A cooperation score of three or four was considered satisfactory. Taste acceptability was evaluated on a four-point scale. A score of 1–3 was considered satisfactory.

Score	Sedation	Anxiolysis	Cooperation	Taste
1	Alert/active	Poor	Poor	Accepted readily
2	Upset/wary	Fair	Fair	Accepted with grimace
3	Relaxed	Good	Good	Accept with verbalcomplaint
4	Drowsy	Excellent	Excellent	Rejected entirely
5	Asleep			

Heart rate, blood pressure, respiratory rate and arterial oxygen saturation were recorded before premedication, every five minutes for 30 min preoperatively, and then during induction of anaesthesia, every 5 min intra-operatively, every 15 min in recovery room and every 30 min in day-case unit until time of discharge.

The anaesthetic agents administered were standardized.Children were induced with sevoflurane, nitrous oxide in oxygen and fentanyl 1-2 µg/Kg and maintained with the same drugs. The trachea was intubated after administering cisataracurium 0.1 mg/kg.

At the end of the procedure, the neuromuscular blockade was reversed with neostigmine with glycopyrolate and the child was extubated. After that, they were kept in the recovery room (PACU) under observation until discharge. The time to recovery from anaesthesia and to achieve satisfactory Aldrete score were noted. The discharge time was also noted and postprocedure instructions were given. Children were called for checkups the following day, when parents were asked to answer a questionnaire about the surgical experience of the parent and child and side effects experienced, if any.

Statistical analysis was performed using SPSS version 17. All values were reported as mean ± SD and range. Data analysis for numerical data was performed by unpaired Student's t-test to detect the differences between the groups for age, weight, onset of anxiolysis and sedation. Data analysis for categorical data was performed by Fisher's exact test to detect differences for the scores. Other data are reported as mean ± SD or frequency (%). A P value < 0.05 was considered statistically significant. Prior to the study, we chose the null hypothesis (i.e. nosignificantsedation scores between the groups). The number of patients required in each group was determined using power analysis based on previous studies. Assuming that 79% of patients would become drowsy or asleep in the midazolam/ketamine group (15 patients), a sample size of 30 patients per group would have an 80% power of detecting a 20% difference in sedation (from 79% to 99%) at the 0.05 level ofsignificance. We decided to study 66 patients to account for possible dropouts.

Results:

Sixty-six patients were enrolled; four did not receive the study medication and two did not have surgery on the same day, leaving 60 subjects who fulfilled the criteria for the study.Groups were comparable regarding age, sex, weight, ASA physical status, surgical interventions and duration of anaesthesia (Table 1). Operative procedures were evenly distributed and included inguinalherniorrhaphy, hydrocele repair or orchidopexy.

Table 1: Demographic characteristics and duration of anaesthesia:

	Group D	Group MK
No of patients	33	33
No of patients excluded	4	2
Age (years)	4.02±1.98	4.2±1.45
Gender (female/male)	13/16	15/16
ASA (I/II)	25/4	25/6
Weight (Kg)	17.72±4.4	16.56±5.1
Duration of Anaesthesia (min)	35.17±5.9	32.7±8.4

Data are expressed as mean ± SD (range). P > 0.05. No significant difference among groups.
Dex group (D). Midazolam Ketamine group (MK). ASA, American Society of Anesthesiology physical status.

Onset of sedation was significantly faster after premedication with midazolam/ketamine (Fig1), and the level of sedation was significantly better after premedication with

midazolam/ketamine 30 minutes after ingestion of the premedicant.

The anxiolysis score revealed 84 % of children in group MK as being friendly and only 51% of children in group D have similar behaviour (Table 2). The taste of oral dexmedetomidine was judged as significantly better; 13% of children rejected the oral midazolam/ketamine combination (Table 2).

Table 2: Distribution of behaviour and sedation status at time of induction:

	Group D	Group MK	P
Time to onset of sedation (min)	24.52 ± 3.1	18.36 ± 2.6	0.015*
Preoperative sedation score	1.6±0.5	3.1±0.8	0.003*
% asleep at induction	61%	90%	0.024*
Preoperative anxiolysis score	1.4±0.6	2.9±0.7	0.016*
% Face mask acceptance	58%	88%	0.033*
% Venous line insertion acceptance	72%	90%	0.005*
% Satisfactory parental separation	50%	80%	0.04*
% Parental satisfaction	70%	90%	0.036*
% Taste acceptance	97%	87%	0.002*

Data are expressed as mean ± SD (range) or percentage. Dex group (D). Midazolam Ketamine group (MK).
* significant*P <0.05.*

Application of a facemask at induction of anaesthesia was accepted more readily in patients of group MK (Fig 2).Overall, satisfactory cooperation with venous line insertion was found in 90% of children in group MK, while comparatively 72% of children in group D showed satisfactory cooperation with insertion of a venous line (Table 2). Moreover, most of the MK treated children were more calm and sedated than the D-treated group at the time of separation from parents. Parental satisfaction was significantly higher in group MK.

The time interval from end of surgery to spontaneous eye opening in the PACU was significantly less in group D (Fig 1), while the time to discharge from the PACU to ward was similar for groups (Table 3).

Table 3: Time to eye opening and PACU discharge

	Group D	Group MK	P
Time to eye opening (min)	21±4.3	30±6.1	0.032*
Time of PACU discharge (min)	30± 3.9	28.12±5.5	0.316

Data are expressed as median ± SD (range). Dex group (D). Midazolam Ketamine group (MK).
* significant*P < 0.05.*

While no child experienced respiratory complications or arterial oxygendesaturationbefore induction, heart rate and systolic blood pressure were marginally higher after administration of MK. On the other hand, the mean heart rate and systolic blood pressure measurements were 15% lower (than preoperative values) in group D at the same study periods. However, during recovery, haemodynamic responses were similar.

Adverse events were recorded for the three periods. Two children in group MK as well as one in group D experienced nausea but only one patient in group MK vomited before induction. Hallucination was recorded in 10 % of patients in group MK. Excessive salivation occurred in 12% of children receiving the combination of drugs, compared to 7% in D-treated children.

Discussion:

Our study proved that midazolam/ketaminereceiving patients were significantly calmer and more cooperative compared to dexmedetomidine receiving patients during the preoperative period, the insertion of a venous line, during separation from parents and also during the application of a facemask at induction. Several studies have been published demonstrating the advantage of the midazolam/ketamine combination in paediatric premedication[4,9], while others have reported superiority of oral dexmedetomidine premedication to oral midazolam[10,11].

Based on their experience with using oral dexmedetomidineas a preanaesthetic in children, Kamal et al[10] and Zub et al[12] reported that the dose of 3 µg/kg could be safely and effectively applied without haemodynamic side effects.

Midazolam is currently the most commonly usedpaediatric premedication due to easy application, rapid onset, short duration of action and a lack of significant side effects[13]. Meanwhile oral ketamine was used in the 1970s by dentists to facilitate the treatment of mentally handicapped children. In 1982, Cetina found that rectal or oral preanaesthetic ketamine is an excellent analgesic and amnesic agent with no incidence ofdysphoric reactions, possibly related to its high rate of first-pass metabolism[14]. The metabolite norketamine has approximately one-third the potency of ketamine, but reaches higher blood concentration and also causes sedation and analgesia [15]. The use of midazolam and ketamine in combination as a premedicant combines their properties of sedation and analgesia and attenuates drug induced deliriumGhai et al and Funk et al have also reported that a combination of midazolam and ketamine results in better premedication than the individual drugs given alone[4,9].

Like clonidine, dexmedetomidine possesses a high ratio of specificity for the α_2 versus the α_1 receptor (200: 1 for clonidine and 1600: 1 for dexmedetomidine). Through presynaptic activation of the α_2 adrenoceptor, it inhibits the release of norepinephrine and decreases sympathetic tone. There is also an attenuation of the neuroendocrine and haemodynamic responses to anaesthesia and surgery, thereby leading to sedation and analgesia[16]. One of the highest densities of α_2 receptors has

been detected in the locus coeruleus, the predominant noradrenergic nucleus in the brain and an important modulator of vigilance. The hypnotic and sedative effects of α_2-adrenoceptor activation have been attributed to this site in the CNS[16]. This allows psychomotor function to be preserved while letting the patient rest comfortably, so patients are able to return to their baseline level of consciousness when stimulated[17]. Clonidine and dexmedetomidine seems to offer the beneficial properties, but dexmedetomidine has a shorter half-life, which might be more suitable for day surgery. Zuband his colleagues reported that dexmedetomidine may be an effective oral premedicant prior to anaesthesia induction or procedural sedation and it was effective even in patients with neurobehavioural disorders in whom previous attempts at sedation had failedAlso Sakurai et al reported that oral dexmedetomidine could be applied safely and effectively as a preanaesthetic in children[18].

While dexmedetomidine is tasteless and odourless[17] , with 82% bioavailability after extravascular doses in healthy human adults[19], oral midazolam formulations have a bitter taste and were usually prepared by mixing the IV midazolam with a variety of sweet additives. In our study, children judged the taste of oral dexmedetomidine as significantly better than oral midazolam ketamine mixture, although both drugs were given with the same sweet tasting syrup. This observation probably might also reflect the developmental age of these patients and the difficulty of gaining their cooperation in swallowing something that they did not wish to swallow. Recently, new commercially prepared oral midazolam formulations are reported to be more palatable[20], but unfortunately, it is not available yet in our country.

Our data confirmed that onset of sedation and peak sedative effect was significantly slower after oral dexmedetomidine compared to oral midazolam ketamine. These results are consistent with studies by Kamal et al and Schmidt et al who reported slow onset of action of oral dexmedetomidine[21]In addition, Anttila et al reported that, in adults after oral administration, peak plasma concentration is achieved at 2.2 ± 0.5 h after a lag-time of 0.6 ± 0.3 h[19].

In this study, dexmedetomidine premedication with the present study design resulted in slight hypotension and bradycardia, which could be attributed to postsynaptic activation of α_2 adrenoceptors in the central nervous system (CNS) that inhibit sympathetic activity and thus can decrease blood pressure and heart rate[22]. In a finding consistent with our results, Khan et al and Aantaa et al reported that useofdexmedetomidine can beassociatedwithsome cardiovascular side effects including hypotension and bradycardia[24]Conversely, Ray and Tobias did not find significant haemodynamic changes when used dexmedetomidine in providing sedation during electroencephalographic analysis in children with autism and seizure disorders[25].

There were some limitations to this study; the bioavailability of oral dexmedetomidine is based on the adult dataWe need to decide the timing of the oral administration as apremedicantbased on the data in children. Therefore, the bioavailability of oral dexmedetomidine needs to be studied in children. The premedication period was 30 min, however, if a longer premedication period had been allowed, possibly more subjects could have attained satisfactory sedation at separation from parents and at induction of anaesthesia.

Conclusion:

In this study, premedication with oral midazolam/ketamineappeared to be superior to oral dexmedetomidine with evident haemodynamic stability and a higher degree of parental satisfaction demonstrated, although oral dexmedetomidinewas more accepted by the children. No significant side effects were attributable to either premedication. Emergence from anaesthesia was comparable between groups.

Competing Interests
None declared
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Research Article

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Comparison of trauma and elective income in a district general hospital

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ABSTRACT
We aimed to investigate the income of trauma and elective work in our unit and compare inpatient stay and resource allocation. We performed a prospective study of trauma and elective admissions for a one-week period. We calculated the income received using health resource group coding. 48 trauma patients were admitted of which 36 required operative intervention. This generated £134,321 for primary procedures followed by an extra £18,141 for those requiring no surgery. The total income for the week was £171,941. 71 elective patients underwent surgery. The total income generated was £150,318 for this week. This was a typical week in a busy unit. No consultants were on leave. Although the income was higher in the trauma group this was loss making due to the length of stay of those patients with hip fractures. Attempts at profitability should include enhanced rehabilitation services and more realistic tariff for proximal femur fractures.
KEYWORDS : Trauma, Elective, Income, Health Resource Group Codes, Economics, Coding

Introduction:

Payment by results was introduced across the National Health Service (NHS) in 2005. It's aim was to provide a pricing structure (tariff) for the whole country with some allowance for geographical variation[1-2]. The system uses Healthcare Resource Group codes (HRG) in which treatments in similar cost brackets have the same codeA price / tariff is derived from each hospital patient episode and the patient's registered Primary Care Trust (PCT) is billed accordingly.

In order to generate an HRG code data is collected by the hospital clinical coding department including primary diagnosis, comorbidity (which incurs an extra charge if applicable), and complications, surgical procedure, age and duration of stay[4]. Diagnoses (either primary, co morbidities or complications) are coded using ICD-10 codes. Surgical procedure is defined using OPCS-4 codesA piece if software is then utilised to allocate the HRG code. Each HRG code represents a tariff, which is the average cost of a treatment nationwide. Minor regional adjustments are made to reflect the cost of living[2].

Payment by results covers all admissions, attendance in accident & emergency departments and outpatients attendances[5]. The 2004 NHS Improvement plan designated 18 weeks as a target for referral to treatment (RTT)[6]. It is a common misconception that trauma patients do not account for considerable income within the NHS. Trauma is often seen as the poor relation when compared with elective work where a target based culture now prevails. Elective targets must be met or hospital trusts can incur financial penalty. This situation is not apparent for trauma due to the acute nature of service delivery in the majority of cases. The burden of trauma work can block elective admissions and is seen by some as a barrier to target attainment. At least 36% of orthopaedic surgeons in the United Kingdom describe trauma as part of their sub-specialist interestWe aimed to assess the throughput and income generated from one week of trauma workload and compared this with the elective throughput in our unit for the same week. This was performed by means of a prospective study. We are not aware of any published work in this specific area.

Methods:

We followed all acute patients admitted to our trauma unit between 21/02/2008 and 28/02/2008. This represented a "trauma week" which is how the consultant rota is organised in our trust. We then compared this with the throughput in our elective unit for the same calendar period. No surgeons were on leave this week and no theatre sessions were cancelled other than the on call trauma consultant's elective operating sessions. Our trust is a busy district general hospital with over 500 beds and approximately 55,000 emergency attendances per year. The orthopaedic directorate is staffed by ten full time consultants and serves a population of 315,000 patients.

All patient details were recorded prospectively and followed until the end of their inpatient episode. Case notes were then reviewed with the coding department and ICD-10 and OPCS-4 codes were generated. Their length of stay and other required variables were reviewed in order to generate the correct HRG code. Once the analysis was complete income for the trauma and elective groups were calculated.

Results:

Trauma:

48 patients were admitted (22 male) of which 36 required operative intervention. This utilised 14 theatre sessions. Mean age was 53.75 years (range: 7-93, median: 59). Median stay was 4 days with a mean of 13.3. The median and mean trim points

(expected duration of stay before extra charges incurred by PCT) were 14.5 and 26.7 days respectively. Other consultants operated on 6 patients. This was either due to expertise in a specific area or space on an elective list utilised to reduce backlog. The income generated by these cases is included in the trauma total due to them being acute trauma interventions rather than elective cases. These results are summarised in tables 1 and 2.

Table 1: Demographic & Income Data of Trauma and Elective Patients

	Trauma	Elective
Median age (yrs)	59	47
Number of Patients	47	71
No of Males	26	30
Median stay (days)	4	1
Range of stay (days)	1 – 107	1 - 7
Total bed days	637	118
Estimated Bed Costs (£)	203,840	26,550
Mean income per pt (£)	3658.32	2117.15
Total Income (£)	171,941	150,318

Of the 48 patients admitted 12 required no operative intervention. These cases were general 'run of the mill' admissions such as soft tissue infections for intravenous antibiotics, undisplaced fractures where home circumstances obstructed discharge, soft tissue injuries for further investigation and back pain. These will not be discussed further but the income generated (£31,127) does go towards the total. The median stay was 2 days with a mean stay 8.5 days (range: 1 – 47). This reflects the broad comorbidities and social circumstances of this subset.

The group requiring operative intervention included hip fractures (11 patients). Of these, seven required dynamic hip screw fixation but were deemed "complex" due to their comorbidities and therefore attracted the higher tariff rate (£6685). One displaced intracapsular fracture required total hip replacement, attracting a tariff of £7261. One patient required revision from a dynamic hip screw to an intramedullary device and then revision to a total hip arthroplasty. The tariff price was £19,479. The remaining fractured neck of femur patients attracted between £4379 and £6711 dependent on operative procedure. The median stay was 26 days (mean: 14, range 9 – 107). One patient required closed manipulation of a dislocated total hip replacement attracting a tariff price of £1034 and an inpatient stay of one day. In addition one acetabular fracture was sustained requiring open reduction and internal fixation. It attracted a tariff price of £4262 and an inpatient stay of seventeen days.

One patient required open reduction and internal fixation of a patella fracture attracting a tariff of £2405 and was an inpatient for 10 days. Another patient with septic arthritis required two arthroscopic knee washouts, attracting a tariff of £5941 and was an inpatient for 26 days.

Seven ankle fractures were admitted requiring operative intervention, all of these attracted a tariff of £2405 except one, which attracted £4262 due to co morbidity and complexity of injury. The median stay in this group was six days (mean: 4.9, range: 2-7).

Thirteen patients sustained hand and wrist injuries requiring operative intervention. Of these there were two tendon repairs, two abscesses drained and one digital terminalisation. Five wrist fractures required either manipulation and plaster application, closed reduction and Kirschner wiring or open reduction and internal fixation by means of a volar plate. Three fractures of the base of the thumb were manipulated and percutaneously K-wired. These patients attracted a tariff of between £1048 and £3227. Median stay was one day (mean: 1.36, range: 1 – 3). Three of these cases were managed by our hand surgeon on a trauma list.

One patient admitted with cauda equina syndrome required microdiscectomy attracting a tariff of £1271 and was an inpatient for one day. This was performed by one of our spinal surgeons on a trauma list.

Elective:

71 procedures were performed (36 female). This utilised 22 theatre sessions. Mean age was 49.51 years, (11 – 87 median: 47). Mean stay was 2.3 days. The median and mean trimpoints were 2 and 6.35 days respectively. Cases were divided by anatomical region. A table of income for both trauma and elective patients by anatomical region is included (Table 2).

Twelve patients had hip procedures performed. These included hip injections (n=2, tariff £615), sciatic nerve exploration (n=1, tariff £1217), cemented total hip arthroplasty (n=2, tariff £4304), uncemented total hip arthroplasty (n=1, £5305), resurfacing hip arthroplasty (n=5, £4023) and revision hip arthroplasty (n=1, £7185).

Twelve patients had knee procedures performed. These consisted of total knee replacements (n=3, tariff £5613), unicompartmental knee replacements (n=4, £5613), one anterior cruciate ligament reconstruction (£1863), knee arthroscopies (n=2, tariff £1063), one removal of metal work (tariff £1063) and one scar revision (tariff £1091).

Four patients had foot and ankle procedures performed and these all attracted £1217 tariff price. They consisted of one ganglion excision, one hallux valgus correction, one excision of Morton's neuroma and one ankle arthroscopy.

Table 2: Income by Anatomic Region

	Trauma				Elective			
	Length of stay (median) days	No of pts	Total income (£)	Mean income per patient (£)	Length Of Stay (median) days	No of pts	Total income (£)	Mean income per patient (£)
Upper limb	1	18	32,455	1,803	1	9	11,469	1,274
Spine	1	5	10,327	2,065	0	34	44,887	1,320
Hip	26	13	90,891	5,494	4	12	43,660	3,638
Knee	5	5	19,576	3,915	2	12	45,434	3,786
Foot and ankle	6	7	18,692	2,670	1	4	4,868	1,217
Total		**47**	**171,941**	**3658**		**71**	**150,318**	**2117**

Nine patients had upper limb procedures performed. These comprised carpal tunnel decompression (n =1 £1217), radial head excision (n=1 £1217), shoulder stabilisations (n=3 £1217), subacromial decompression (n=1 £1217), acromiclavicular joint excision (n=1 £1063), diagnostic shoulder arthroscopy (n=1 £1217) and arthroscopic cuff repair (n=1 £1887).

34 patients had spinal procedures performed. Inpatient stay ranged from 0 to 5 days with trimpoints of 1 – 13 days. These ranged from nerve root injections (n=23, tariff £522), discography (n=3, tariff £615), microdiscectomy and interspinous distraction (n=2, tariff £3192), decompression, fusions and instrumentation (n= 5, tariff £4252 - £5140), and kyphoplasty (n=1, tariff negotiated: no HRG code. Income £1506). Total income for the spinal group was £44,887.

It can be seen from the data that a wide range of trauma and elective surgery was performed and that the elective group was admittedly younger and had a shorter hospital stay (Table 1). Our unit has the benefit of two spinal surgeons who operate a local and tertiary practice, which changes the demographic of our cohort slightly; other units may not have this factor adjusting their income.

The tariff income for the elective group was £150,318, which was lower than that for the trauma group of £171,941.

Discussion:

This paper is, as far as we are aware the first to compare elective and trauma orthopaedic throughput in a busy district general hospital. It would be bold not to draw attention to our studies limitations. We analysed only one week in the financial year and we accept that seasonal variation may occur. The weather for the week in question involved no snow or ice and was warmer than average for this time of year (5.2°C)[10]. We do not feel that severe weather influenced our admissions. Previous studies have assessed the effect of seasonal variation on admissions rate. One was in a winter sports resort in Switzerland and unsurprisingly showed a positive correlation between season and fracture incidence[11]. Another study based in Tasmania showed no variation in either vitamin D levels or incidence of femoral neck fracture[12]. This goes against the findings of a study based at three latitudes, which showed a high seasonal peak in Scotland, Hong Kong and New ZealandOur locality has a temperate climate with no local winter sports resorts; our experience of seasonal variation is minor.

Miscoding and therefore error in calculations may have occurred; as both the authors and experienced coders reviewed the casenotes the likelihood of this is limited.

Our most important finding was that the mean income per trauma patient (£3658.32) was higher than that for an elective patient (£2045.13) and was statistically significant (p=0.001). The HRG code and income generated represents the money actually received by the hospital from the primary care trust. We openly admit that trauma patients represent a larger burden for the hospital. They have a tendency to be older, have complex co-morbidity and have increased length of stay. They are therefore more costly than elective patients. One study performed in a large university hospital calculated the mean cost for a hip fracture to be £8978.56 (range £3450 - £72,564), this rose to £25,940.44 if there was a superficial wound infection (range £4387 - £93,976) and £34,903 if there was a deep infection (range £9408 - £93,976)[14].

Although actual income from the PCT was higher the trauma group will have been loss making on account of the hip fracture group. Whilst this is hard to quantify it seems likely given the calculations portrayed in the Nottingham study of 3686 patientsInpatient costs for the trauma group ignoring theatre costs amount to approximately £204,000. This exposes a lack of appreciation of this group's requirements in comparison with fit elective hip patients and probably inequality in trauma coding for these patients.

Our study has not tackled implant costs partly due to the fact that inpatient costs have significantly dwarfed these but also due to the fact that we consider these a relatively fixed overhead, costs being determined by local bulk purchase agreements. The

consequence on overall study outcome would be minimal given that trauma implants are several orders of magnitude cheaper than elective joint prostheses.

It became apparent to us during the course of our study that trauma can be under resourced when compared with elective care. The background team currently provided for trauma patients include the on call medical team (Consultant Orthopaedic Surgeon, Specialist Registrar and Senior House officer). In addition there are ward nursing staff, anaesthetist, theatre staff, occupational therapists and physiotherapists. On the elective side there are 4 waiting list clerks, 3 surgical assistants, 3 preoperative clinic sisters as well as reception staff and the background medical team (anaesthetist, consultant orthopaedic surgeon, specialist registrar and senior house officer). In the elective setting the aim is identification and optimisation of comorbidities pre-operatively and discharge planning to ensure throughput and turnover of patients. We admit that pre admission screening is not applicable to trauma but faster throughput could ensure improved efficiency and reduced duration of stay.

Our elective patients have a 30-bed ward with an additional 8-bed day case unit; the trauma ward has 24 inpatient beds. The elective unit has 7 registered nurses and 4 health care assistants; on the trauma ward this figure is 4 and 3 respectively. Our elective patients have 2.5 full time equivalent physiotherapists whilst our trauma patients have 1.5.

This situation is probably not dissimilar to the situation in many units elsewhere in the country. This work has shown that trauma income is higher than that for elective work and from this we can infer that if resources were directed accordingly then length of stay could be reduced and profit could be a possibility. A recent paper using hospital episode statistics (HESS) data has shown that length of stay fell quickly once payment by results was implemented[15]. What was unclear was whether this represented a real change in efficiencies or simply a change in data manipulation by trusts. HESS data has repeatedly been noted to be inaccurate with a range from 10 to 98% dependent on region and disease group.[16-17]. In a 2006 statement by the then Health Minister Mr. A Burnham it was quoted that £88m pounds was being wasted from 390,000 extra unnecessary bed days[18]. This was based on the cost of an elective bed being £225 per day with acute beds being significantly more (approximately £320 in one study)The total stay for 66 elective patients was 118 days whereas that for 48 trauma patients was 637 days. Several outliers hugely increased the figure for trauma. Ten trauma patients represented 464 days of inpatient care. If the inpatient stay was reduced by one day for fractured neck of femur patients alone, this amounts to 500 less days per year and approximately £160,000 per year reduction in overhead costs for the trust.

One study in the USA assessed the use of a caseworker to expedite discharge for elderly patients with hip fractures[19]. The study did not utilise extra physiotherapy and occupational therapy support. Findings were increased theatre, anaesthetic and blood product costs in elderly patients. Increasing age did not correlate with length of stay, cost of stay or income for the hospital. They found that a case manager did reduce the average stay but did not reduce the overall cost. The NHS would do well to note these findings - in many trusts patient flow practitioners are being employed to try and expedite discharge and increase patient turnover. We feel that this money could be channelled into rehabilitation services to effect prompt rehabilitation and discharge.

One final issue is the variation in income between secondary and tertiary centres for certain injuries. One acetabular fracture underwent fixation generating £4262. If this had been referred to a tertiary centre a supplementary specialised service code would have been applicable generating more income (up to 70% in some cases) when intervention was identical. We agree that certain injuries require tertiary treatment by a team with high volume experience and specialised skills. There is an income chasm between the income generated between secondary and tertiary centres for the same injury, which seems perverse.

Overall trauma income was higher than elective income, but still ran at a loss. This was on account of the length of stay of the hip fracture patients and current coding underestimating their true cost to the trust. There is a disparity between rehabilitation services provided for trauma and elective patients, which needs to be addressed to improve efficiency.

Competing Interests
None declared
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Research Article

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Older people with long-term mental illness. A survey in a community rehabilitation service using the Camberwell Assessment of Needs for the Elderly (CANE)

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ABSTRACT

Aims: Following the Royal College of Psychiatrists' recommendations, assessments were carried out by the community rehabilitation team in Newham, East London, using the Camberwell Assessment of Needs for the Elderly (CANE) to assess the needs and quality of service provided to all patients over the age of 65 years.

Results: 49 patients were screened using the CANE. The majority of needs appeared to be met by the current service provision. However, certain needs remained unmet: daytime activity (in 36.7% of patients), lack of company (in 22.4% of patients), help with eyesight and hearing difficulties (in 20.4% of patients) and help with money and budgeting (in 18.4 % of patients) were the most prominent.

Implications: Whereas most psychiatric and practical needs were well met, service planning needs to focus on outreach day activity and befriending services. Mental health services need to closely monitor physical problems which are more specific to older people e.g. eyesight and hearing, and include these in their care plans.

Introduction

The Royal College of Psychiatrists defines the 'graduates' as people who have had enduring or episodic severe mental disorder in adulthood and have reached the age of 65 years. Estimates of the most severely affected range from 11 to 60 per 100 000.[1] This group of people seems to be uniquely disabled by a combination of social, mental health and physical disadvantages and there is a risk of falling between general adult, rehabilitation services and old age psychiatry.[2]

There has been an ongoing debate about identifying the best practice in the management of this group of patients who often have spent most of their lives in the old psychiatric asylums. The recommendations include identifying all graduates within the service followed by a full assessment of the patients' health and social care needs and the implementation of a care plan to meet these needs, to be reviewed at least annually. According to the report, the medical responsibility will rest with a principal in general practice or a consultant psychiatrist, and maintenance of continuous review should be the responsibility of the case manager.[1]

The Recovery and Rehabilitation Team (RRT) in Newham was founded in 1988 to facilitate the discharge of groups of patients from Goodmayes hospital (Essex). Patients discharged to residential care units and other supported schemes usually had spent many years in the institution and the team's remit after relocation into the community was mainly monitoring of mental health by conducting multiprofessional reviews in the care homes, crisis intervention, and the promotion of social networks and leisure activities. Over the following years, the team also received many referrals from Community Mental Health Teams (CMHT) for continuing care of people suffering from long term and severe mental illness. Today, a considerable proportion of these patients have 'graduated' into old age and the current percentage of the total caseload is now nearly 25%.

Our survey was carried out following an independent review by the Health and Social Care Advisory Service (HASCAS) in January 2005 for the rehabilitation services provided in the London Borough of Newham. The recommendations included an assessment of needs for all patients 65 years of age or over, using the Camberwell Assessment of Needs for the Elderly (CANE) .[3]This is a comprehensive needs assessment tool suitable for use in a variety of settings. It has been successfully used for older people in primary care, sheltered accommodation, residential homes, nursing homes, and mental health services for older people. However, it has not been used before to specifically assess the needs of older people who have graduated within the general adult mental health or rehabilitation services. CANE was found to be a valid and reliable tool and easy to use by different professions.[4]

Method:

The RRT database was searched for all patients aged 65 years or over. This yielded 52 names, who were then approached between June and September 2005 for a comprehensive assessment after an explanation about the survey. CMHTs were asked for numbers of graduates in their services, obtained from the respective databases.

The CANE is a structured, 24-item questionnaire covering different areas (see table 2), including social, psychological, mental health and physical needs. It is easily applicable by different professions and requires on average about one hour of assessment time. It measures met and unmet needs and obtains

views from patients, carers, staff and the rater. Assessments were carried out by members of the multi-disciplinary team that consists of a consultant psychiatrist, the team manager, two senior clinical medical officers, two clinical psychologists, two occupational therapists, two social workers, five community psychiatric nurses and four community support workers. All raters had received a one day training provided by Juanita Hoe, one of the contributors in producing the CANE.

The collected data were analysed using Microsoft Excel.

Results

The total number of patients aged 65 years and above under the care of the rehabilitation services was 52 (24.5% of the total caseload of 212 patients). There were a further ten patients under the care of the adult CMHTs in Newham. Attempts were also made to determine the number of the graduates under the care of mental health services for older people, but these were unsuccessful.

Out of the 52 patients, 50 could be assessed using the CANE, two patients declined the assessment and the assessment sheet of one patient could not be traced, giving a total of 49 patients and a response rate of 79% of all known 'graduate' patients under the care of adult mental health services.

Results describing patient characteristics including mean age, gender, type of accommodation and diagnosis, are summarized in Table 1.

Table: 1 Demographic Details

Variable		
Mean Age (years)		72.16
Gender (n(%))		
	Female	16(32.65%)
	Male	33(67.34%)
Type of accommodation (n(%))		
	Residential care	25(51%)
	Supported accommodation	13(26.53%)
	Private accommodation	12(24.48%)
Diagnosis (n(%))		
	Schizophrenia	33(67.34%)
	Schizoaffective Disorder	6(12.24%)
	Bipolar Affective Disorder	5(10.20%)
	Depression	2(4.08%)
	Personality Disorder	1(2.04)
	OCD	1(2.04%)
	Dysthymic Disorder	1(2.04%)

Nearly two-thirds of patients were female, three-quarters of this population were living in supported living or residential care and 90% were suffering from a severe mental illness (two-thirds from schizophrenia).

The met and unmet needs of this population are described in table 2.

Regarding unmet needs, the highest value (nearly 37%) was on daytime activities, which 18/49 people scored. This is followed by company (22.5%), which was a problem for 11 people. Eyesight or hearing also scored strongly (20.5%), followed by money (18.4%) and different problems in areas such as food and self-care, physical health and psychological distress (each 12%). Problems with suicidal behaviour and drug or alcohol abuse were not evident in terms of unmet needs.

Discussion

Our results show that the majority of needs identified by the CANE were adequately met by the current service provision or were only identified as unmet needs by a tiny minority (table 2). Since the vast majority of the patients were living in either residential or supported accommodation (25.51% and 26.53% respectively), items associated with domestic needs and activities appeared to be met to a great extent, e.g. accommodation (44.90% no need, 44.90% met need).

In terms of items related to mental state, the majority of patients seemed to be satisfactorily managed and receiving appropriate treatment. The raised number of patients who suffered from psychological distress could be explained by other psychosocial factors such as lack of daytime activities and lack of company which have been identified as the major unmet needs in our population.

A recent article,[5] named risk of harm, unpredictability of behaviour, poor motivation, lack of insight and low public acceptability as the major reasons for social disability. However, in our review, over one-third of people clearly expressed the wish for more daytime activities, where the named disabilities might prevent a more active and satisfied lifestyle. In the interviews, it transpired that people mostly wished for an outreach service providing social contact, befriending and activities. The majority of people in our population seemed to be rather reluctant to access general facilities, like day centres for the elderly.

As we have assessed most of the patients under the care of adult mental health services, this survey should be able to inform service planning about the needs of this population. The development of an outreach service offering day time activities including a befriending component could be a challenge for the responsible service providers, e.g. social services, adult community mental health services and old age psychiatry.

Table 2: Levels of needs as rated by the rater (n=49)

Item	No Need		Met Need		Unmet Need		Not Known	
	n	(%)	n	(%)	n	(%)	n	(%)
Accommodation	22	44.90%	22	44.90%	2	4.08%	3	6.12%
Household skills	5	10.20%	41	83.67%	3	6.12%	0	0.00%
Food	9	18.37%	34	69.39%	6	12.24%	0	0.00%
Self-care	12	24.49%	31	63.27%	6	12.24%	0	0.00%
Caring for other	47	95.92%	2	4.08%	0	0.00%	0	0.00%
Daytime activities	16	32.65%	14	28.57%	18	36.73%	1	2.04%
Memory	34	69.39%	4	8.16%	5	10.20%	6	12.24%
Eyesight/hearing	24	48.98%	14	28.57%	10	20.41%	1	2.04%
Mobility	26	53.06%	18	36.73%	5	10.20%	0	0.00%
Continence	28	57.14%	16	32.65%	3	6.12%	2	4.08%
Physical health	14	28.57%	29	59.18%	6	12.24%	0	0.00%
Drugs	17	34.69%	30	61.22%	2	4.08%	0	0.00%
Psychotic symptoms	18	36.73%	28	57.14%	3	6.12%	0	0.00%
Psychological distress	29	59.18%	14	28.57%	6	12.24%	0	0.00%
Information	28	57.14%	11	22.45%	6	12.24%	4	8.16%
Safety(deliberate self harm)	44	89.80%	4	8.16%	0	0.00%	1	2.04%
Safety(accidental self-harm)	35	71.43%	11	22.45%	2	4.08%	2	4.08%
Safety(abuse or neglect)	35	71.43%	10	20.41%	4	8.16%	1	2.04%
Behaviour	32	65.31%	12	24.49%	4	8.16%	1	2.04%
Alcohol	47	95.92%	2	4.08%	0	0.00%	0	0.00%
Company	29	59.18%	8	16.33%	11	22.45%	1	2.04%
Intimate relationship	40	81.63%	3	6.12%	4	8.16%	2	4.08%
Money	21	42.86%	19	38.78%	9	18.37%	0	0.00%
Benefits	37	75.51%	3	6.12%	4	8.16%	5	10.20%

The specific physical needs (especially eyesight and hearing) make it necessary for services to monitor these closely and implement this in the care plan in liaison with General Practitioners.

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Similar reviews should be undertaken by community mental health services in other boroughs to highlight the needs of this specific group of patients, as the respective unmet needs might be dependent upon the level of service provision.

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Review Article

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Latest diagnosis and management of diverticulitis

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Abstract
Diverticular disease is extremely common especially amongst the elderly. It mainly presents as sigmoid diverticulitis but there is potential for serious complications. In the acute setting Computed Tomography is the gold standard investigation and helps classify the stage. Evidence to support outpatient treatment of uncomplicated diverticulitis is appearing however hospital admission and treatment with intravenous antibiotics is often required and is highly effective. The decision to proceed with elective surgery is judged on an individual basis with a long-term conservative approach suitable for most. For elective surgery there is evidence to advocate a laparoscopic approach. In Hinchey stage III or IV disease, laparotomy followed by either a Hartmann's procedure or ideally, a resection followed by primary anastomosis may be required. Radiologically guided drainage of an abscess is an established alternative and laparoscopic lavage is another less invasive option that has emerged. Following successful acute medical management, colonoscopy is usually performed several weeks after resolution to rule out other colonic pathology.
Keywords: Diverticulitis, Diagnosis, Management, Surgery

Introduction

A colonic diverticulum is defined as a sac-like protrusion of mucosa through the muscular component of the colonic wall[1]. The terms "diverticulosis" and "diverticular disease" are used to express the presence of diverticula without associated inflammation. While the term "diverticulitis" indicates there is inflammation of a diverticulum or diverticula, which is commonly accompanied by either microscopic or macroscopic perforation[2].

In the developed world, diverticular disease of the colon is widespread and in those aged over 65 years of age it is present in greater than 65%[3]. The incidence increases dramatically with time and while only 5% of the western population are affected in the fifth decade this rises steeply to over 50% by the eight decade and 60% in the ninth [4].

Although diverticulosis is extremely common, complications requiring surgery only occur in 1% of patients overall [5] and 10% of those admitted to hospital as an emergency for treatment[6]. Despite this, there is a substantial healthcare burden inflicted by diverticular disease and within the United States alone it accounts for 312,000 hospital admissions, 1.5 million days of inpatient treatment and a total estimated cost of 2.6 billion dollars per annum [7].

The aetiology of the diverticulosis is poorly understood but it is probably a multi-factorial process involving dietary habits (specifically low fibre intake) as well as changes in colonic pressure, motility and wall structure that are associated with ageing[8]. The pathogenesis of diverticulitis is also uncertain, however stasis or obstruction in a narrow necked diverticulum leading to overgrowth of pathogens and local tissue ischemia is thought likely [2].

This review will discuss the common presentations, investigations and current treatment strategies utilised in the management of acute diverticulitis and its complications as well as providing an up to date synopsis of existing recommendations for follow up and prevention.

Symptoms and Signs

In Western nations, diverticula are most commonly situated in the left colon[9] and 99% of patients will have some element of sigmoid involvement[10]. Therefore patients commonly present with sigmoid diverticulitis that typically displays features of left iliac fossa pain and fever with raised inflammatory markers (see below). Physical exam will disclose left lower quadrant peritonism for simple disease, but in complicated cases physical examination findings may reveal a palpable abdominal mass, evidence of fistulas or obstruction, or widespread peritonitis[11].

In cases of complicated diverticulosis, a stricture may lead to obstructive symptoms with complaints of nausea, vomiting and distension being present. If a fistula has developed, a history of recurrent urinary tract infection, pneumaturia and faecaluria may also be elicited[12]. In a female with a previous history of hysterectomy suspicion will be further raised as colovesical and colovaginal fistulas are rare in females with their uterus in place. If a patient reports passing stools per vagina, insertion of a vaginal speculum and inspection may confirm this latter diagnosis[12].

Differential diagnosis

The differential diagnosis for diverticulitis and its complications is extensive and includes irritable bowel syndrome, inflammatory bowel disease, ischaemic or infective colitis, pelvic inflammatory disease and malignancy. It is obviously most

imperative to exclude the latter differential [4], particularly in the case of a stricture that is impassable on colonoscopy, as many of these specimens following resection (32% in one series[13]) will transpire to be adenocarcinoma[4]. It should also be noted that sigmoid diverticulitis may also masquerade as acute appendicitis if the colon is long and redundant or otherwise situated within the abdomen or pelvis such that the inflamed segment lies in the suprapubic region, right iliac fossa or McBurney's point[2].

Complications

Although diverticulosis is present in nearly two thirds of the elderly population, the vast majority of patients will remain entirely asymptomatic. Even so, an estimated 20% of those affected will manifest symptomatology, mainly as diverticulitis, but potentially with further complications of perforation, abscesses, fistulas, and obstruction, as well as bleeding per rectum[6].

The European Association for Endoscopic Surgeons (EAES) developed a classification scheme based upon the severity of diverticulitis, which broadly classifies patients into either simple symptomatic or complicated disease (Table 1)[14]. Where an abscess or perforation develops the Hinchey classification is used as a staging tool and can provide prognostic information on the likely outcome (Table 2)[15].

Table 1 - European Association for Endoscopic Surgeons classification system for diverticulitis [14]

Grade of disease	**Clinical explanation of grade**	**Clinical state of the patient**
I	Symptomatic uncomplicated disease	Pyrexia, abdominal pain, CT findings consistent with diverticulitis
II	Recurrent symptomatic disease	Recurrence of Grade I
III	Complicated disease	Bleeding, abscess formation, phlegmon, colonic perforation, purulent and faecal peritonitis, stricturing, fistula and obstruction

Table 2 – Hinchey classification of perforated diverticulitis [15]

Hinchey stage	**Features of disease**	**Risk of death[71]**
Stage I*	Diverticulitis with a pericolic abscess	5%
Stage II**	Diverticulitis with a distant abscess (this may be retroperitoneal or pelvic)	5%
Stage III	Purulent peritonitis	13%
Stage IV	Faecal peritonitis	43%

*Stage I has been divided into Ia Phlegmon and Ib confined pericolic abscess in later modifications[38, 72]

** Stage II has been divided into IIa abscesses amenable to percutaneous drainage and IIb complex abscess with or without fistula in later modifications[14, 73]

Perforation is probably the most feared complication and the annual prevalence of perforated diverticulitis within a northern European population is currently thought to stand at 3.8 per 100,000 of the population, which is a figure that is increasing[16]. Despite this only 1-2% of patients who attend for urgent assessment and treatment will have a gross perforation[2] but for 80% this will be their first presentation so a high index of suspicion is still required[17].

Blood investigations

In clinical practice, inflammatory markers, commonly the White Blood Cell (WBC) count and C-Reactive Protein (CRP) level, are frequently employed to assist in diagnosing diverticulitis and its complications. In a recent retrospective study, a White Blood Cell (WBC) count >10,000/µL was present in 62% of patients with Computed Tomography (CT) confirmed diverticulitis and the presence of leukocytosis was significantly more common in patients with diverticulitis and associated perforation than without (86% v 65%, p=0.01)[18].

CRP has also been shown to be of considerable benefit in the diagnosis of acute left sided colonic diverticulitis [19]. A recently established diagnostic nomogram with a reported accuracy of 86% that was developed to improve the clinical diagnosis of diverticulitis includes an elevated CRP >50mg/l as well other variables including age, previous episodes, aggravation of pain on movement, absence of vomiting and localization of symptoms and tenderness in the left iliac fossa[19].

In addition, it has been demonstrated that in acute sigmoid diverticulitis a CRP below 50mg/l is unlikely to correlate with an associated perforation (negative predictive value 79%) while a CRP above 200mg/l is an indicator that the patient may have a perforation (positive predictive value 69%)[20]. In this latter study, CRP also had the highest diagnostic accuracy in diagnosing perforation in acute sigmoid diverticulitis across a range of parameters assessed that included WBC count as well as less commonly used tests like bilirubin and alkaline phosphatase[20].

Imaging investigations

In the acute phase of diverticulitis the extent of the extramural component of inflammation is more important than the degree of the intramural inflammation and as such CT associated with the use of intravenous and oral contrast and, in ideal conditions, rectal contrast is the gold standard means of investigation[21].

CT can accurately identify extra-luminal complications such as an abscess, phlegmon, adjacent organ involvement, or fistula, as well as recognising other alternative diagnoses such as appendicitis, pelvic inflammatory disease, tubo-ovarian abscess or inflammatory bowel disease[22].

The two most frequent signs of diverticulitis on CT are bowel wall thickening (96%) and fat stranding (95%) (Figure 1) with less common but highly specific signs including fascial thickening (50%), free fluid (45%), and the presence of inflamed diverticula (43%) [23]. Specifically, abscess formation (Figure 2a and b) and extracolonic air or contrast (Figure 3a and b) are findings that are known to predict severity as summarised in the CT classification system developed by Ambrosetti *et al* [24].

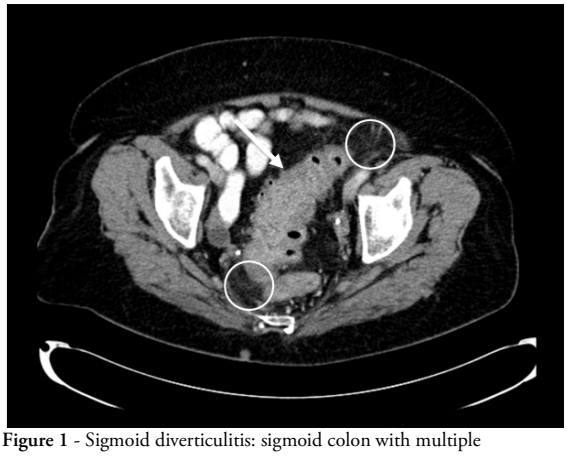

Figure 1 - Sigmoid diverticulitis: sigmoid colon with multiple diverticula, significant mural thickening (arrow) and pericolic fat stranding (circles)

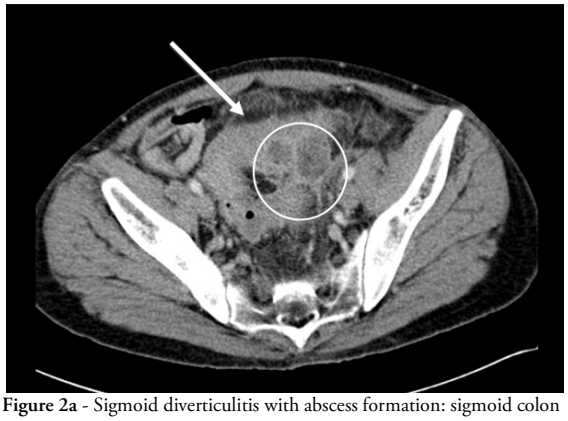

Figure 2a - Sigmoid diverticulitis with abscess formation: sigmoid colon displaying diverticulosis mural thickening, and pericolic fat stranding (arrow). Adjacent low attenuation, septated collection (circle) representing abscess formation.

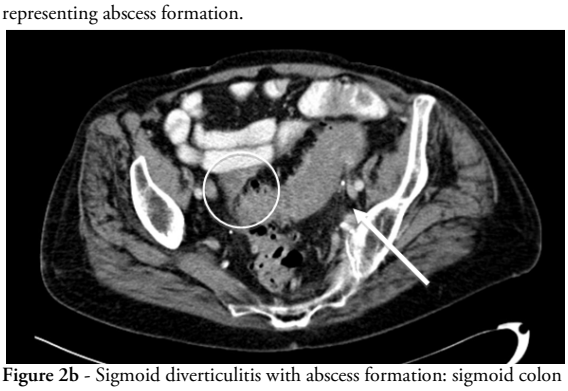

Figure 2b - Sigmoid diverticulitis with abscess formation: sigmoid colon displaying mural thickening, diverticulosis and pericolic fat stranding (arrow). Adjacent low attenuation, septated collection (circle)

representing abscess formation, with adhesion noted to adjacent small bowel loops.

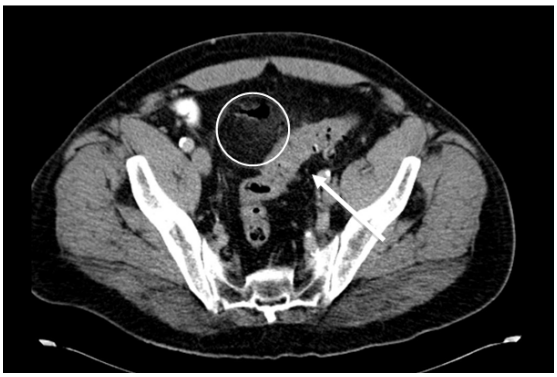

Figure 3a - Perforated sigmoid diverticulitis: sigmoid colon displaying diverticulosis and mural thickening (arrow) with adjacent collection of intra-abdominal free air and adjacent inflammatory fat stranding (circle), representing active diverticulitis with perforation.

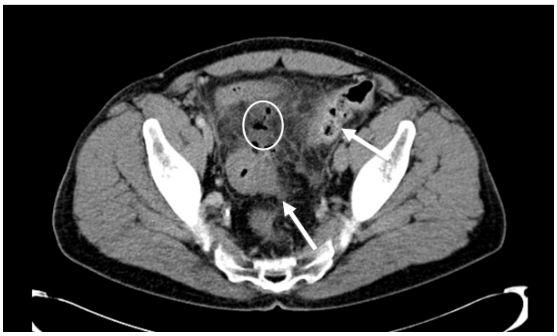

Figure 3b - Perforated sigmoid diverticulitis: sigmoid colon displaying diverticulosis, mural thickening and pericolic inflammatory fat stranding (arrow) with adjacent collection of intra-abdominal free air and adjacent inflammatory fat stranding (circle), again representative of active diverticulitis with perforation.

However despite CT having a reported sensitivity of 97%, specificity of 98%, and global accuracy of 98%[25], a misdiagnosis of diverticulitis in cancer patients is relatively common and occurs in 5% of cases[21]. Therefore investigation of the colonic lumen by endoscopic means or barium enema after the acute attack is mandatory[4] but avoided in the initial stages for fear of perforation and exacerbation of the disease[2].

In expert hands ultrasound is the next best alternative investigation with a reported sensitivity of 94%[26]. It has been supported by a recent systematic review[27] as well as current practice guidance[4] and in critically ill patients it avoids the use of intravenous and intra-luminal contrast[21]. However it is rarely used in practice as it is operator dependent[21] and for it to be accurately utilised it requires a highly skilled/trained individual to be available at all times[28].

The other practical alternative to CT is a hydro-soluble contrast enema, however this investigation is significantly inferior both in terms of sensitivity (98 v 92%, $p<0.01$) and evaluation of the severity of inflammation (26 v 9%, $p<0.02$)[29]. While Magnetic resonance imaging (MRI) has a good

sensitivity of 94% and a specificity of 87%[30], in the acute setting it may be impractical both in terms of examination time and patient co-operation[21]. Finally, laparoscopy can also be helpful for diagnostic purposes but again in practical terms, with the increasing availability of cross-sectional imaging, it is rarely required for this purpose[4].

Outpatient treatment

Evidence for successful and economical outpatient treatment of uncomplicated diverticulitis is beginning to emerge. In a prospective study of 70 patients classified on the basis of an ultrasound examination as having mild-to-moderate acute colonic diverticulitis (as defined by either limited inflammation within a diverticulum extending up to an abscess < 2 cm in diameter), 68 patients were successfully treated with oral antibiotics with an initial liquid diet and this led to a cost saving on inpatient treatment of 80%[31].

In a further retrospective analysis, among a cohort of patients who were referred for outpatient treatment it was found that such treatment was effective for 94% of patients, with women and those with free fluid on CT scan appearing to be at higher risk for treatment failure[32].

In reality the prospect of outpatient treatment in uncomplicated cases of acute diverticulitis is determined largely by access to the necessary investigative tools for accurate diagnosis and staging of disease, the general fitness of the patient, their ability to maintain adequate oral intake, the possibility of further outpatient review, patient compliance with medications, satisfactory social support and ability to plan for endoscopic follow up[21].

In broad terms, if symptoms are not severe and the patient has no significant co-morbidities and is compliant with medical treatment, then a course of broad spectrum antibiotics can be administered orally on an outpatient basis and the patient followed up at subsequent outpatient clinics. However if the patient is systemically unwell, elderly, has significant co-morbidities or there are any other concerns it is safer to arrange for a hospital admission and treatment with intravenous antibiotics[12].

Conservative inpatient treatment

Simple diverticulitis requiring hospital admission is usually treated by rehydration, symptomatic relief and intravenous antibiotics. Most patients with uncomplicated disease respond well to medical treatment and generally experience significant improvement in their abdominal pain, temperature and inflammatory markers within two days of initiation of antibiotic treatment[33]. If this is not the case or there is clinical concern a repeat CT is advocated and operative intervention or percutaneous drainage considered (see below)[2].

It should be noted at this stage while the use of broad spectrum antibiotics in acute uncomplicated diverticulitis is supported by guidelines[34] there is no actual evidence mandating the routine use of antibiotics in mild uncomplicated diverticulitis[35] and in some European countries it is not routine[36].

High-quality evidence regarding the most effective type of antibiotic is also lacking[35]. However anaerobic bacteria (usually bacteroides, clostridium, fusobacterium and peptostreptococcus) are the most commonly cultured organisms with gram-negative aerobes, especially *Escherichia coli*, and facultative gram-positives, such as streptococci, often grown as well[37]. Therefore coverage against both Gram-negative and anaerobic bacteria is widely advocated[2 21 38].

If combination antibiotics are selected, Metronidazole provides excellent anaerobic cover with less risk of *clostridium difficle* infection than alternatives[4]. However use of single agent may be more cost effective[39]. Local protocols are likely to influence selection but the patient may be safely switched from intravenous to oral therapy when they can tolerate a diet and oral medicines[22] as intravenous antibiotics are not felt to be vastly superior[40]. Seven to ten days of antibiotic therapy is an acceptable treatment period[22] however evidence is emerging to support shorter courses[41].

Elective surgery

In a recent position statement from the Association of Coloproctology of Great Britain and Ireland (ASCPGBI) it was concluded that the majority of patients, whether young or old, presenting with acute diverticulitis could be managed with a conservative, medical approach in the longer term. Previous blanket recommendations for elective resection e.g. following two acute episodes of diverticulitis[14] were challenged in this statement and it was proposed that the decision on elective resection should be made on an individual basis[4]. The traditional practice of waiting for a period of 4-6 weeks after a diverticulitis attack before performing an elective operation was not disputed[12].

Surgery in the elective setting can be by either an open or laparoscopic technique with a recent randomised trial identifying a 27% reduction in major morbidity[42] along with less pain, improved quality of life and shorter hospitalization at the cost of a longer operating time with the laparoscopic approach[43]. In expert centres conversion rates as low as 2.8% and median hospitals stays of 4 days can be achieved[44] and individual case reports of resections using single laparoscopic port access have also emerged[45]. However if a laparoscopic resection is considered, it is currently recommended that patients should be treated after full recovery from the acute episode of inflammation as there is evidence to suggest lower complication and conversion rates can be achieved[4].

The principles for both approaches are the same. A colorectal anastomosis is a predictor of lower recurrence rates after elective

sigmoid resection for uncomplicated diverticulitis[46]. Therefore it is recommended that the distal resection margin is taken onto the rectum as opposed to the distal sigmoid and the splenic flexure is fully mobilised to facilitate this[4], however in the case of a long redundant left colon this may not be necessary[12]. The proximal resection margin is less clear but should be made onto soft compliant bowel[4 34]. Often it is possible to identify the ureters intra-operatively however, there may be cases of complicated diverticulitis in which the extent and degree of inflammatory changes warrant the use of pre-operatively placed ureteric stents to help aid their identification and avoid injury[12].

Emergency surgery for complicated diverticulitis

The indications for emergency operative intervention in acute diverticulitis include the presence of generalised peritonitis, uncontained visceral perforation, gross uncontrollable sepsis, a large undrainable or inaccessible abscess, bowel obstruction and lack of improvement or clinical deterioration with initial medical management [2].

Historically, perforated diverticulitis was treated with a three-stage procedure consisting of faecal diversion with a stoma, resection of the diseased segment of bowel, followed by takedown of the stoma and restoration of intestinal continuity. This then shifted to performing a Hartmann's procedure which includes a primary resection of the diseased segment and end colostomy followed by subsequent colostomy reversal at a second operation[11]. In this case reconstruction generally involves a second laparotomy because although laparoscopic reconstruction is effective, it is infrequently performed[47-48]. As a result reversal is often permanently deferred.

In selected cases the ideal therapeutic option in colonic perforation is a one-stage procedure with resection followed by primary anastomosis, which adds the benefits of being a definitive treatment with the avoidance of the morbidity and mortality associated with a stoma and its reversal[49]. A protective ileostomy after resection and primary anastomosis is viewed as a valid additional step in patients at high risk of an anastomotic leak (immunosuppression, American Society of Anaesthesiologists (ASA) grade IV, faecal peritonitis)[21] but a Hartmann's procedure may also be selected.

Particularly in cases where there is a stricture causing obstruction and significant faecal loading, a resection in conjunction with on-table colonic lavage and primary anastomosis may be used. This technique has also been described as facilitating a primary anastomosis in the case of a perforation[50]. However in certain patients with obstruction depending on the viability of the proximal colon a subtotal colectomy with ileorectal anastomosis may be required[12] and because small-bowel obstruction may also occur, especially in the presence of a large diverticular abscess, this may also warrant further treatment[2].

The use of endoscopic colonic stenting as a treatment of acute obstruction of the large bowel secondary to colonic cancer has been well documented in the literature either as a definitive procedure or as a bridge to surgery and can effectively decompresses the obstructed colon in 90% of cases[51]. However the use of stents in benign disease is less well documented , with it used mainly as a bridge to surgery[52] and because is associated with a higher incidence of complications in acute diverticular disease[53] it cannot as yet be recommended.

Laparoscopic surgery in the emergency setting

There have been a number of recent reports of laparoscopic lavage with or without the placement of an intra-abdominal drain for patients with acute diverticulitis and perforation, with the reported advantages including the avoidance of an acute resection and the possibility of a stoma [4]. The evidence that has been produced thus far to support its case is highly promising.

A recent systematic review of laparoscopic lavage for perforated colonic diverticulitis identified two prospective cohort studies, nine retrospective case series and two case reports with 231patients and the vast majority of patients (77%) had Hinchey grade III purulent peritonitis. Laparoscopic peritoneal lavage successfully controlled abdominal and systemic sepsis in 95.7% of patients, mortality was 1.7%, morbidity 10.4% and only four (1.7%) patients received a colostomy[54].

In the largest series in the literature to date, Myers *et al* reported 100 patients with perforated diverticulitis and generalised peritonitis. Eight patients with Hinchey IV disease required conversion to an open procedure, with the overall mortality being 4% and recurrence rates only 2% over a median time period of 36 months[55].

Percutaneous therapy

The appropriate management of diverticular abscesses is a matter of some debate. However according to the American Society of Colon and Rectal Surgeons (ASCRS) radiologically guided percutaneous drainage is usually the most appropriate treatment for patients with a large diverticular abscess as it avoids the need for emergency surgery and possibility of a colostomy[34].

When the abscess diameter is over 5 cm, percutaneous CT guided drainage, in combination with antibiotics, is the standard treatment and offers rapid improvement in symptoms in over 90% of cases, albeit with a high recurrence rate in more severe cases[38] and higher likelihood of surgery being needed in those involving the pelvis[56].

In practical terms diverticular abscesses less than 3 cm in diameter usually cannot be successfully drained, as the diameter of the pigtail of most drainage catheters will be a similar dimension[28]. Also for smaller abscesses[21], especially those less than 2cm resolution usually occurs with the use intravenous

antibiotics alone[34]. However if a drain is sited it is advisable that before it is removed, resolution of the abscess should be confirmed and a potential bowel fistula excluded by a further contrast study[28].

Finally, diverticular disease of the colon is also a relatively common cause of acute lower gastrointestinal bleeding and is in fact the diagnosis in 23% of cases[57]. This usually settles with conservative management but if the bleeding is profuse angiography and endovascular intervention may be helpful, with surgery very rarely required for this indication[4].

Follow up

Following successful medical management of an acute episode of diverticulitis, colonoscopy, flexible sigmoidoscopy or barium enema should be performed several weeks after the resolution of symptoms to confirm the diagnosis and rule out other colonic pathology such as malignancy, inflammatory bowel disease, or ischemia[22].

Following surgery there is reported to be a high incidence of the order of 25% for recurrent symptoms, which is put down to the diagnostic overlap that exists with irritable bowel syndrome[58]. However any suspicion of recurrent diverticulitis following surgical resection should be confirmed by CT scan after which antibiotic treatment should be initiated, as for a case of primary uncomplicated disease[12]. If this is excluded the high incidence (17.6%) of symptomatic anastomotic stenosis after elective laparoscopic sigmoidectomy should be borne in mind with the possibility of endoscopic dilatation considered if applicable[59].

Summary points

- CT scan is the gold standard means of investigation for acute diverticulitis and helps classify the stage of disease.
- Evidence to support outpatient treatment of uncomplicated diverticulitis is beginning to appear, however hospital admission and treatment with broad spectrum intravenous antibiotics is often required and is highly effective.
- The decision to proceed with elective surgery is judged on an individual basis and there is evidence gathering to advocate a laparoscopic approach.
- In Hinchey stage III or IV disease, emergency laparotomy followed by either a Hartmann's procedure or ideally in selected patients a resection followed by primary anastomosis may be required.
- In certain cases percutaneous radiologically guided drainage of abscesses is an established alternative to open surgery with laparoscopic lavage another less invasive and highly promising option.

Lifestyle modifications and prevention

Following treatment weight loss, rationalisation of certain medications and exercise are recommended as obesity is significantly associated with an increased incidence of both diverticular bleeding and diverticulitis[60], as are non-steroidal anti-inflammatory drugs and paracetamol[61], with physical activity significantly associated with a reduction in the risk of complications[62].

Whilst dietary fibre, particularly cellulose[63], is recommended[22] the evidence that supports these recommendations is not particularly strong[64]. However foodstuffs such as nuts, seeds, popcorn and corn that are usually discouraged have no evidence to support the theory that they may lead to increased complications[65].

Small studies without control groups suggest that probiotics may have a positive effect on the recurrence of symptomatic diverticular disease[66-67]. Long term administration of the non-absorbable antibiotic Rifaxamin has also been used with reported success[68] as has the anti-inflammatory mesalazine[69]. However none of these medications have a strong evidence base and as a result are not in routine use[70].

Competing Interests
None declared
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Case Report

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Massive Hepatic Necrosis due to Hepatic Abscesses after Transplantation

Seif Fadi , Gholam Pierre and Montenegro Hugo

ABSTRACT

Delayed hepatic artery thrombosis (HAT) is a rare complication of orthotopic liver transplantion (OLT) that may present with biliary sepsis or remain asymptomatic. Sonography is extremely sensitive for the detection of HAT in symptomatic patients during the immediate postoperative period. Magnetic resonance angiography (MRA) is a useful adjunct in patients with indeterminate ultrasound exams, those who have renal insufficiency or an allergy to iodinated contrast.

In the absence of hepatic failure, conservative treatment appears to be effective for patients with HAT. Whole-graft orthotopic liver transplantation (OLT), Roux-en-Y biliary reconstruction, cold ischaemia and operative times, the use of blood and plasma, and the use of aortic conduits in arterial reconstruction are all risk factors associated with HAT.

We present a patient with a case of delayed HAT three years after liver transplantation who presented with mild symptoms and was later found to have a massive hepatic abscess and significant necrosiswith positive cultures forClostridium perfringens. There was evidence of complete occlusion of the hepatic artery 2 cm from its origin.

Introduction:

The clinical features of early HAT are well defined, yet the features of delayed HAT are less clear. Delayed HAT is a rare complication of OLT that may present with biliary sepsis or remain asymptomatic. Sonography is extremely sensitive for the detection of HAT in symptomatic patients during the immediate postoperative period. However, the sensitivity of ultrasonography diminishes as the interval between transplantation and diagnosis of HAT increases due to collateral arterial flow. MRA is a useful adjunct in patients with indeterminate ultrasound exams and in those who have renal insufficiency or an allergy to iodinated contrast.

In the absence of hepatic failure, conservative treatment appears to be effective for patients with HAT but retransplantation may be necessary as a definitive treatment.

Case Presentation:

A 52 year old male with a history of whole graft OLT for primary sclerosing cholangitis presented with two days of fever, nausea, and mild abdominal discomfort.

One week prior to presentation, he was seen in the liver clinic for regular follow-up. At that time, he was totally asymptomatic and his laboratory workup including liver function tests were within normal range.

He has undergone OLT three years prior. At the time of transplant he required transfusion of 120 units of packed red blood cells, 60 units of fresh frozen plasma and 100 units of platelets due to extensive intraoperative bleeding secondary to chronic changes of pancreatitis and severe portal hypertension, but had an otherwise uneventful postoperative recovery.

On physical examination the temperature was 39C, heart rate was 125 beats per minute, respiratory rate was 22 bpm. Initial laboratory workup revealed a white blood cell count of 25,000/mm^3, AST of 6230 U/L, ALT of 2450 U/L, total bilirubin of 11 mg/dL , BUN 55 mg/dL and Creatinine of 4.5 mg/dL. Lactate level was 5 mmol/L. Doppler ultrasonography revealed an extensive intrahepatic gas (Image 1A). Computed tomography of the abdomen and pelvis revealed extensive area of hepatic necrosis with abscess formation measuring 19x14 cm with extension of gas into the peripheral portal vein branches (Image 1B,C). Upon admission to the hospital, the patient required endotracheal intubation, mechanical ventilator support and aggressive~~ly~~ fluid resuscitation. He was started on broad-spectrum antibiotics and a percutaneous drain was placed that drained dark, foul smelling fluid. Cultures from the blood and the drain grew *Clostridium perfringens*.

Magnetic resonance imaging (MRI), MRA revealed occlusion of the hepatic artery 2 cm from its origin and also evidence of collaterals (Image 2A,B).

Following drain placement, the patient's clinical condition markedly improved with significant reduction of liver function test values. Retransplantation was considered but delayed in the setting of infection and significant clinical and laboratory testing improvement.

The patient was transferred to the medical floor in stable condition, and the drain was then removed.

A week later the patient developed low grade fever~~s~~ and tachycardia. One day later he began to experience mild abdominal discomfort and high grade fevers. Repeat CT of the abdomen revealed worsening hepatic necrosis and formation of

new abscesses. His clinical condition decompensated quickly thereafter requiring endotracheal intubation, mechanical ventilation and aggressive resuscitation. Percutaneous drain was placed and again, drained pus-like, foul-smelling material. His overall condition deteriorated, and he eventually expired a few days later.

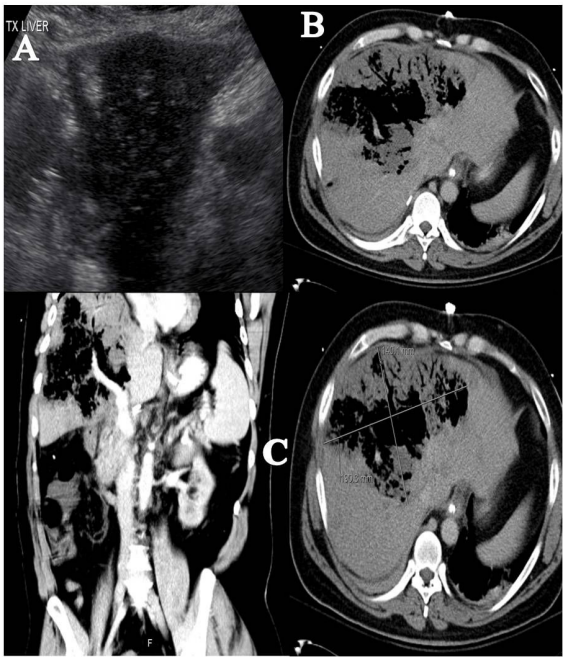

Image 1: (Pannel A) Doppler ultrasonography reveal extensive intrahepatic gas. (Pannel B&C) Computed tomography of the abdomen and pelvis reveal an extensive area of hepatic necrosis with abscess formation measuring 19x14 cm with extension of gas into the peripheral portal vein branches.

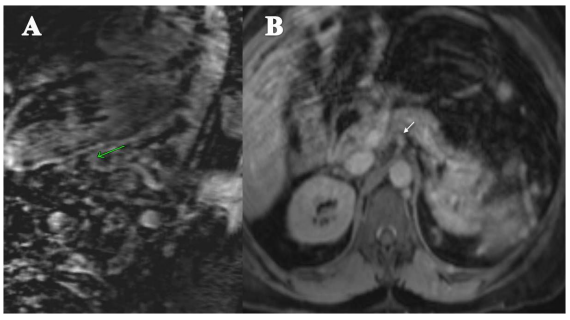

Image 2: MRI & MRA reveal occlusion of the hepatic artery 2 cm from its origin and also evidence of collaterals.

Discussion:

Delayed (more than 4 weeks after transplantation) HAT is a rare complication of OLT with an estimated incidence of at around 2.8%[1].

Risk factors associated with development of HAT include Roux-en-Y biliary reconstruction, cold ischaemia and operative time, the use of greater than 6 units of blood, the use of greater than 15 units of plasma, and the use of aortic conduits on arterial reconstruction during transplant surgery[2].

Collateralization is more likely to develop after Live Donor Liver Transplantation (LDLT) than after whole-graft cadaveric OLT[3]. Therefore, the latter is also associated with increased risk of late HAT.

Although the clinical features of early HAT are well described, the features of delayed HAT are less clearly defined[1]: the patient may present with manifestations of biliary sepsis or may remain asymptomatic for years. Right upper quadrant pain has been reported to occur in both immediate and delayed HAT. The clinical presentations may include recurrent episodes of cholangitis, cholangitis with a stricture, cholangitis and intrahepatic abscesses, and bile leaks[1]. Doppler ultrasonography has been extremely sensitive for the detection of HAT in symptomatic patients during the immediate postoperative period but becomes less sensitive as the interval between transplantation and diagnosis of HAT increases because of collateral arterial flow[4].

3D gadolinium-enhanced MRA provides excellent visualization of arterial and venous anatomy with a fairly high technical success rate. MRA is a useful adjunct in patients with indeterminate ultrasonography examination in patients who have renal insufficiency or who have allergy to iodinated contrast [5].

Antiplatelet prophylaxis can effectively reduce the incidence of late HAT after liver transplantation, particularly in those patients at risk for this complication[6]. Vivarelli et al reported an overall incidence of late HAT of 1.67%, with a median time of presentation of 500 days; late HAT was reported in 0.4% of patients who were maintained on antiplatelet prophylaxis compared to 2.2% in those who did not receive prophylaxis[6]. The option of performing thrombolysis remains controversial. Whether thrombolysis is a definitive therapy or mainly a necessary step in the proper diagnosis of the exact etiology of HAT depends mostly on the particular liver center and needs further analysis[7]. Definitive endoluminal success cannot be achieved without resolving associated and possible instigating underlying arterial anatomical defects. Reestablishing flow to the graft can unmask underlying lesions as well as assess surrounding vasculature thus providing anatomical information for a more elective, better plan and definitive surgical revision[7]. Whether surgical revascularization compared to retransplantation is a viable option or only a bridging measure to delay the second transplantation has been a longstanding controversy in the treatment of HAT.

Biliary or vascular reconstruction do not increase graft survival and ongoing severe sepsis at the time of re-graft results in poor survival[7]. However, although uncommon, delayed HAT is a major indication for re-transplantation[7]. In the absence of

hepatic failure, conservative treatment appears to be effective for patients with hepatic artery thrombosis.

*C. perfringens*is an anaerobic, gram-positive rod frequently isolated from the biliary tree and gastrointestinal tract. Inoculation of Clostridium spores into necrotic tissue is associated with formation of hepatic abscess[8].

Necrotizing infections of the transplanted liver are rare. There have been around 20 cases of gas gangrene or necrotizing infections of the liver reported in the literature. Around 60% of these infections were caused by clostridial species with *C. perfringens* accounting for most of them. Around 80% of patients infected with *Clostridium* died, frequently within hours of becoming ill[9,10]. Those who survived underwent prompt retransplantation and the infection had not resulted in shock or other systemic changes that significantly decreased the likelihood of successful retransplantation[8].

Because the liver has contact with the gastrointestinal tract via the portal venous system, intestinal tract bacteria may enter the liver via translocation across the intestinal mucosa into the portal venous system. Clostridial species can also be found in the bile of healthy individuals undergoing cholecystectomy[9,10].

The donor liver can also be the source of bacteria. Donors may have conditions that favor the growth of bacteria in bile or the translocation of bacteria into the portal venous blood. These conditions include trauma to the gastrointestinal tract, prolonged intensive care unit admissions, periods of hypotension, use of inotropic agents, and other conditions that increase the risk of potential infection [8,9,10]. *C. perfringens* sepsis in OLT recipients has been uniformly fatal without emergent retransplantation. Survival from *C. perfringens* sepsis managed without exploratory laparotomy or emergency treatment has been extremely rarely reported[8]. In those patients who survived, and in whom the infection has not resulted in shock or multiple organ failure, retransplantation may be successful[8].

Although our patient survived his intensive care course, his recovery was tenuous as he quickly developed additional hepatic abscesses that led to his eventual demise. Post-mortem examination in our patient revealed intra-hepatic presence of *Clostridium perfringens*.

He was managed conservatively since he markedly improved both clinically and by liver function tests. Because of this, retransplantation was delayed. He was also already on antiplatelet prophylaxis.

Conclusion:

We report an interesting case of Clostridium perfringens hepatic abscess due to late HAT following OLT. Although the patient initially improved with non-surgical treatment, he eventually died. In similar cases, besides aggressive work-up and medical management retransplantation may be necessary for a better long term outcome.

Competing Interests
None declared
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Viewpoint

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Care Programme Approach: first you have to prove you are ill

Francis J Dunne

The Care Programme Approach (CPA) was introduced in England in 1993 to co-ordinate the care of patients with mental health disorders.[1] Its aim was to ensure that there was a full assessment of the patient's needs, that a care co-ordinator would see that the care was delivered, regular checks would be carried out to review progress, there would be collaboration between health and social services, and that patients (or the term used to 'demedicalise' them in psychosocial Newspeak[2] namely, 'service users') and carers (they also use the service) would have a greater say in the written management plan. Targets were set.

What has happened since? Prior to this I recall that most psychiatrists carried out full assessment needs, regular checks reviewed progress (outpatients), social services were involved when necessary, and patients and their families were nearly always involved in the discussion of after-care, when appropriate. Despite the condescending manner in which patients and carers were treated by the hierarchy, i.e. they would not understand the difference between social services management and other after-care, it was always quite clear to doctors that patients had no difficulty with the concepts of medical intervention (investigations, diagnosis, treatment), psychological therapies, and social help (housing, work, family, finances).

Rather than simplifying the process we now have two tiers of CPA, namely, standard and enhanced. Where the patient has 'complex needs' or is a 'complicated case' then you are in the enhanced bracket. For the rest – back to the General Practitioner (GP)! Not enough resources apparently. Not ill enough more likely. Remember – you have to have a severe and enduring mental health disorder – nothing else counts. Nowadays the GP is expected to be a specialist in mental health and run a risk assessment on every 'psychiatric' patient. The GP is frowned upon by the 'experts in living' should he/she for example, dare refer a mild or moderately (yes - those descriptions again!) ill patient to the Mental Health Services. Because there is no bottomless pit of money, the scenario was changed in 2008 so that those receiving only standard CPA were no longer entitled to it. However, not to appear callous and indifferent to the plight of those suffering from 'less severe' mental health problems, the usual lip service was paid to patients, assuring them that they should be respected and supported, and that their carers be also recognised as having 'needs'. All the buzz words were put in place again – integrated care pathways, working together, reviews about the reviews, good practice, better training, and so forth. Now there is the Supervised Community Treatment Order, (whether you like it or not) and those subject to the new 'order' will be entitled to the 'new' CPA. Wonderful in theory.

So what happens to a patient who is not on CPA? We are informed that such patients should still be open to secondary mental health services, should continue to receive clinical support, that reviews should take place regularly, and a social assessment should be available under the new guidance to local authorities FACS (Fair Access to Care Services), readily available on the Internet. The truth of the matter is that only those patients on enhanced CPA will receive immediate support, the rest will have to jump through the usual hurdles to prove they have a severe, enduring mental illness (enduring is not enough) in order to gain access to NHS 'support' facilities. Some patients are seen as more deserving than others, for example, those admitted to hospital under the Mental Health Act (voluntary admission may count against you), current or potential risk (theoretically, any patient with a mental health disorder, which seems to defeat the purpose of the exercise) or the presence of a dual diagnosis (depression with alcoholism, or is it the other way round?). Anyway, if in doubt, the patient is entitled to a formal reassessment CPA and may be admitted to the 'new' CPA list. If all fails, the patient (remember, one with severe, enduring mental health symptoms) may make a complaint to the local authority or even hire a lawyer.

What is the true state of affairs? To begin with, many patients have enduring mental health problems which are not severe, are not life-threatening, and despite the hardship and drudgery endured, manage to trundle through work, relationships, and family life. Years of talking therapies or psychotropic medication, indeed both, may have only taken the edge off their symptoms. Often symptoms resurge and require alterations or adjustments in medication; sometimes a different psychological approach needs to be considered. Such patients are best left to the fountain of all wisdom, the GP, so it seems. Rather akin to telling the GP to treat for example, a 'minor' cardiac problem (say, palpitations) because the 'specialist unit' only deals with

severe arrhythmias, severe pain, severe disability, 'severe everything'. It is unfair to expect GPs to make informed decisions concerning psychotropic medication (no more than they should about adjusting chemotherapy drugs) and most would be familiar only with specific therapies such as Cognitive Behavioural Therapy (CBT) or Anger Management, where appropriate. The type of patients described here comprise the majority of those seen in outpatients, yet there is now a growing trend to discharge such patients back to the GP, because he/she is not 'care co-ordinated' on enhanced CPA. The burden is on the GP. It does not seem to have registered with politicians or management (doctors included) that chronic schizophrenia is not the same as chronic gastro-oesophageal reflux.

The trend now is for the setting up of Community Clinics (the patient does not necessarily get to see a doctor) where 'all the other psychiatric problems' are dealt with. The traditional psychiatric outpatient department is to be abolished, unless of course, GPs do something about this torrid state of affairs now. It could only happen in Psychiatry which seems to me a specialty doomed to oblivion. Family doctors are becoming increasingly irritated by a system or discipline (Psychiatry especially) which seems to ignore their concerns and is more preoccupied with targets (nothing has changed) and outcomes (back to the GP). Even referrals from GPs, who want a medical opinion, are filtered in order to weed out those not worthy to enter the hallowed walls of the Mental Health Institution. Those patients who 'know the system' or who are vociferous and make complaints ('I know my rights') get to be seen by the Great and Good. Lesser mortals, usually those with serious mental illnesses, do not make any undue demands and are therefore often forgotten or fall by the wayside. A patient with bipolar disorder on lithium is discharged back to a GP who is unsure whether or not the medication needs 'fine tuning' at times, should be discontinued, or reinstated were compliance is a problem in one heading for a relapse. As a corollary of that, I am sure most hospital doctors would not know what the acronym ABVD means in the chemotherapy treatment of Hodgkin's disease. Adjusting psychotropic medication is not quite the same as adjusting an antihypertension regime. Unfortunately, if the patient needs to be referred back into the system the whole Kafkaesque scenario begins again.

A medical colleague once bemoaned to me that psychiatrists are totally out of touch with Medicine. Alas, it seems they are also now out of touch with their medical colleagues.

Competing Interests
None declared
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Medicine in Pictures

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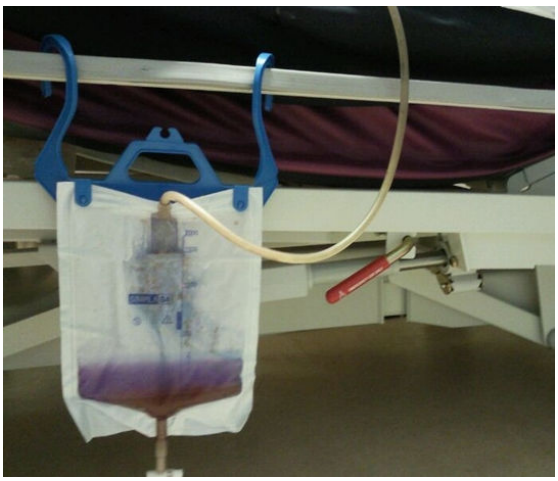
Medicine in Pictures: Purple Urine Bag Syndrome

Capt Gary Chow , Katerina Achilleos and Col Hem Goshai

An 86-year-old lady was admitted from her residential home with acute on chronic confusion, new symptoms of expressive and receptive dysphasia, dysphagia, vacant episodes and urinary incontinence. She had a previous significant history of haemorrhagic stroke with residual right sided weakness, atrial fibrillation, hypertension, and moderate dementia. Following a CT head, this lady was started on acyclovir for encephalitis. She failed to respond to treatment, and developed constipation. With careful consideration of her poor prognosis and quality of life, this lady was placed on the End of Life Pathway. She was catheterised for comfort. Nine days after initial insertion of the urinary catheter, purple urine was noted in the catheter bag with yellow urine in the tubing leading to the bag. Urine dipstick showed Blood ++, Protein ++, Leuc +, Nit –ve, Glu -ve, Ketone +, pH 8.0. Urine microscopy showed: WCC 454, RBC 279, epithelial cells 52, no casts. Urine culture revealed heavy mixed growth with multiple organisms.



Question:

What is the diagnosis?

Answers:

1. Porphyria
2. Propofol infusion syndrome
3. Purple urine bag syndrome
4. Blue diaper syndrome

Differential diagnoses:

Discoloration of urine can be caused by trauma if blood stained, urinary tract infections, ingestion of dye (methylene blue), medications (amitriptyline, indomethacin, triamterene, flutamide, and phenol).

Explanation:

Porphyria usually presents with severe pain with neuropsychological symptoms or photosensitivity, and urine discoloration is likely to occur from initial onset of disease.

Propofol is an anaesthetic agent, excreted in the urine as phenol derivatives which can cause a green urine discolouration[1]. This medication is unlicensed for End of Life Pathway. Propofol infusion syndrome is associated with prolonged high dose infusion, but is not always accompanied by urine discoloration.

Blue diaper syndrome is an inherited metabolic disorder of tryptophan with presentation at infancy[2-3].

Correct answer

Purple urine bag syndrome (PUBS)

Purple urine bag syndrome (PUBS)

PUBS is an uncommon condition with purple discoloration of the urine catheter system. This phenomenon is due to the presence of indigo and indirubin in the collected urine. PUBS was first published in 1978[4]. Some academics would argue that PUBS was reported even earlier historically as an observation in Sir Henry Halford's bulletin in 1811[5-6]. Two recent literature reviews suggested the prevalence of PUBS is as high as 9.8% in institutionalized patients with long-term urinary catheterisation[8-9, 12].

A triad of key factors are suggested as cause of PUBS:

1. High level of tryptophan in the gut due to diet intake or bowel stasis
2. Long term catheterisation[8]
3. Urinary tract infection (uti) with bacteria possessing indoxyl phosphatase and sulphatase enzymes, commonly*providencia stuarttiand rettgeri, pseudomonas*

auruginosa, proteus mirabilis, escherichia coli, klebsiella pneumoniae,morganella, citrobacter species, group b *streptococci* and *enterococci*[8, 13].

It is understood that bowel stasis causes accumulation of tryptophan, which leads to an increase in urinary indoxyl sulphate (UIS). In the presence of indoxyl phosphatase and sulphatase enzyme activities, whilst collected in the catheter system, UIS is degraded to form a mixture of indigo and dissolved indirubin in the plastic[11], coating the catheter system with a purple appearance. Intensity of discoloration is deeper the longer the urine is in contact with the catheter plastic[7, 10-12]. The urine does not appear purple prior to entering the catheter.

Recent literature[7-8] also suggested female gender, alkaline urine, bed bound debilitated patient population, PVC material[7] and institutionalization are further predisposing factors of PUBS.

Management of PUBS requires catheter change and treatment of underlying UTI.

Good catheter hygiene and shorter duration of catheterisation can reduce PUBS[1].

Competing Interests
None declared
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