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Original article

Antibiotic use in acute pancreatitis: An audit of current practice in a tertiary centre

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ABSTRACT

Introduction: Intravenous antibiotic prophylaxis is not recommended in acute pancreatitis. According to current international guidelines antibiotics together with further intervention should be considered in the setting of infected necrosis. Appropriate antibiotic therapy particularly avoiding over-prescription is important. This study examines antibiotic use in acute pancreatitis in a tertiary centre using the current IAP/APA guidelines for reference.

Methods: Data were collected on a consecutive series of patients admitted with acute pancreatitis over a 12 month period. Data were dichotomized by patients admitted directly to the centre and tertiary transfers. Information was collected on clinical course with specific reference to antibiotic use, episode severity, intervention and outcome.

Results: 111 consecutive episodes of acute pancreatitis constitute the reported population. 31 (28%) were tertiary transfers. Overall 65 (58.5%) patients received antibiotics. Significantly more tertiary transfer patients received antibiotics. Mean person-days of antibiotic use was 23.9 (sd 29.7) days in the overall study group but there was significantly more use in the tertiary transfer group as compared to patients having their index admission to the centre (40.9 sd 37.1 vs 10.2 sd 8.9; $P < 0.005$). Thirty four (44%) of patients with clinically mild acute pancreatitis received antibiotics.

Conclusions: There is substantial use of antibiotics in acute pancreatitis, in particular in patients with severe disease. Over-use is seen in mild acute pancreatitis. Better consideration must be given to identification of prophylaxis or therapy as indication. In relation to repeated courses of antibiotics in severe disease there must be clear indications for use.

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1. Introduction

Infection of pancreatic necrosis is the most frequent cause of late mortality in severe acute pancreatitis [1–3]. Antibiotic prophylaxis to reduce infective complications in acute pancreatitis was evaluated in a series of randomized trials [4–12]. However meta-

analyses of these trials do not support antibiotic prophylaxis in acute pancreatitis [13–15]. Summarising this evidence, the International Association of Pancreatology/American Pancreatic Association (IAP/APA) produced evidence-based guidelines in 2013 for the management of acute pancreatitis. These state that intravenous antibiotic prophylaxis is not recommended for the prevention of infective complications in acute pancreatitis. The guidelines support antibiotic use in “case of suspected infection of necrotizing pancreatitis” together with consideration for further intervention [16].

Given the dearth of specific, effective interventions in acute pancreatitis, optimal use of antibiotics is important. Under-use may lead to inadequate treatment of infection whereas over-use

Abbreviations: sd, standard deviation; 95% CI, 95% confidence interval; GI, gastrointestinal.

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encourages emergence of resistant bacterial flora and leads to a reduction in available treatments if and when infection does occur. In clinical practice it is likely that the reasons underlying antibiotic use and mis-use in acute pancreatitis are complex and multifactorial. Arguably, the most frequent confounding factor is that making a distinction between infection and the systemic inflammatory response of pancreatitis at the bedside can be difficult. Clinical signs such as fever and tachycardia may be similar and both scenarios are associated with an elevated leukocyte count and C-reactive protein. Further, infection and systemic inflammation can co-exist. Poor compliance with guidelines for antibiotic use in acute pancreatitis is a genuine and important clinical problem seen worldwide [17]. In order to better understand antibiotic use in the contemporary management of acute pancreatitis this study takes the form of an overview of management in a tertiary referral specialist hepato-pancreato-biliary (HPB) centre. The study examined antibiotic use in patients admitted directly to the centre and also in tertiary referral patients initially admitted to other hospitals and transferred during the course of their episode of acute pancreatitis. The current IAP/APA guidelines were used as a reference standard.

2. Methods

2.1. Design and setting

This is a single-centre clinical cohort study based in the regional specialist HPB service of the Manchester Royal Infirmary (MRI) which serves a 3.2 million predominantly urban conurbation of the Greater Manchester and Cheshire Cancer Network.

2.2. Study period

The inclusion period is the 12 months from 1st October 2014 to 1st October 2015.

2.3. Definitions of acute pancreatitis

The diagnosis of acute pancreatitis was confirmed by the presence of (typically) severe epigastric pain accompanied with ≥ 3 -fold elevation in serum amylase or by characteristic findings on contrast-enhanced CT scan. Clinical severity of acute pancreatitis (mild, moderate, severe) was assessed according to the revised Atlanta classification (2012), based on the presence of transient organ failure and local or systemic complications [18]. The diagnosis of infected pancreatic necrosis was based on positive culture of drained peripancreatic fluid or gas containing collection on CT.

2.4. Data collection

Data were collected prospectively from 1st January 2015 (retrospectively for the preceding three months to complete the 12 month study period) by accessing patient notes and using a bespoke case-report form. All data were collected from time of admission to the tertiary care centre including calculation of Acute Physiology and Chronic Health Evaluation (APACHE II) and Marshall Organ Dysfunction scores (MODS). All patients ≥ 18 years old admitted with acute pancreatitis were included in the study. Data were collected on demographic profile, days of in-patient stay and setting (in-patient ward, High Dependency unit with non-invasive ventilation or critical care with ventilatory support) whether the index admission was to this hospital or whether the patient was a tertiary transfer. Re-admitted patients were remained in their originally allocated category (for example an index admission patient who was re-admitted, remained an index admission). Data

were collected on aetiology [biliary, alcohol, endoscopic retrograde cholangiopancreatography(ERCP)-induced, drug-induced, traumatic or idiopathic], admission amylase and C-reactive protein.

2.5. Antibiotic use

Use of antibiotics was recorded together with number of days of treatment (defined as person-days of antibiotic use). During the period of this study there was published guidance for the tertiary centre relating to antibiotic use based on and complying with the IAP/APA guidelines [16]. To further explore the use of antibiotics in this disease, use was categorised as either for acute pancreatitis (for example severe disease or presence of infected necrosis) or for a secondary condition during in-patient stay such as upper respiratory tract infection.

2.6. Use of computed tomography (CT)

Use of CT scan was recorded and Balthazar CT severity score calculated for the purposes of the study [19]. For tertiary transfer patients, the information relating to CT refer to scans undertaken in this centre.

2.7. Radiologic, endoscopic and surgical interventions

Fine needle aspiration of pancreatic necrosis was not routinely employed in this unit during the period of this study. A record was made of other radiologic intervention such as percutaneous catheter drainage and also angiographic radiological intervention such as mesenteric angiographic embolization undertaken during index admission. Endoscopic interventions undertaken during the index admission were recorded. Similarly, surgical interventions were recorded. For the purposes of this study, surgical necrosectomy refers to minimally invasive necrosectomy.

2.8. Analysis plan

Management of patients admitted for acute pancreatitis was summarised descriptively for study variables, including demographics, disease and management variables, in particular number of days of antibiotic treatment and type of antibiotic used. Use of antibiotics was assessed for compliance with the IAP/APA guideline recommendations and contrasted for index and tertiary transferred patients. The influence of level of antibiotic use and adherence to guidelines upon confirmed infection rates, GI complications and length of stay was explored using appropriate general linear models adjusted for recorded patient, disease and management factors and covariates. Thus a p-value of <0.05 was considered to indicate statistical significance for findings meriting further investigation without adjustment for multiple comparisons. Bootstrapped estimation was used for continuous variables, analysis of proportions used Fisher's exact test. Analysis was conducted using SPSS v21 (IBM Corp; IBM SPSS Statistics for Windows, Version 21.0, Armonk, NY, USA).

2.9. Ethics

The study was categorised as an audit by the Central Manchester Hospitals Foundation Trust Research and Development office and was registered with the hospital's audit department (audit number 6513).

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