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BRIEF ARTICLE

Antibiotic prophylaxis in variceal hemorrhage: Timing, effectiveness and *Clostridium difficile* rates

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Abstract

AIM: To investigate if antibiotics administered within 8 h of endoscopy reduce mortality or increase the incidence of *Clostridium difficile* infection (CDI).

METHODS: A 2-year retrospective analysis of all patients who presented with first variceal hemorrhage was undertaken. The primary outcome measure was 28-d mortality. Secondary outcome measures were 28-d rebleeding rates and 28-d incidence of CDI. All patients were admitted to a tertiary liver unit with a consultant-led, 24-h endoscopy service. Patients received standard care including terlipressin therapy. Data collection included: primary and secondary outcome measures, timing of first administration of intravenous antibiotics, etiology of liver disease, demographics, endoscopy details and complications. A prospective study was undertaken to determine the incidence of CDI in the study population and general medical inpatients admitted for antibiotic therapy of at least 5 d duration. Statistical analysis was undertaken using univariate, non-parametric tests and multivariate logistic regression analysis.

RESULTS: There were 70 first presentations of variceal hemorrhage during the study period. Seventy percent of cases were male and 65.7% were due to chronic alcoholic liver disease. In total, 64/70 (91.4%) patients received antibiotics as prophylaxis during their admission. Specifically, 53/70 (75.7%) received antibiotics either before endoscopy or within 8 h of endoscopy [peri-endoscopy (8 h) group], whereas 17/70 (24.3%) received antibiotics at > 8 h after endoscopy or not at all (non peri-endoscopy group). Overall mortality and rebleeding rates were 13/70 (18.6%) and 14/70 (20%), respectively. The peri-endoscopy (8 h) group was significantly less likely to die compared with the non peri-endoscopy group [13.2% *vs* 35.3%, $P = 0.04$, odds ratio (OR) = 0.28 (0.078-0.997)] and showed a trend towards reduced rebleeding [17.0% *vs* 29.4%, $P = 0.27$, OR = 0.49 (0.14-1.74)]. On univariate analysis, the non peri-endoscopy group [$P = 0.02$, OR = 3.58 (1.00-12.81)], higher model for end-stage liver disease (MELD) score ($P = 0.02$), presence of hepatorenal syndrome [$P < 0.01$, OR = 11.25 (2.24-56.42)] and suffering a clinical episode of sepsis [$P = 0.03$, OR = 4.03 (1.11-14.58)] were significant predictors of death at 28 d. On multivariate logistic regression analysis, lower MELD score [$P = 0.01$, OR = 1.16 (1.04-1.28)] and peri-endoscopy (8 h) group [$P = 0.01$, OR = 0.15 (0.03-0.68)] were independent predictors of survival at 28 d. The CDI incidence (5.7%) was comparable to that in the general medical population (5%).

CONCLUSION: Antibiotics administered up to 8 h following endoscopy were associated with improved survival at 28 d. CDI incidence was comparable to that in other patient groups.

Key words: Variceal hemorrhage; Mortality; Antibiotics; Prophylaxis; *Clostridium difficile*

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INTRODUCTION

In chronic liver disease (CLD), variceal bleeding occurs in 22%-61% of patients with cirrhosis during study follow-up periods of 12-42 mo[1-5]. Seventy percent of bleeding occurs in the 2 years following diagnosis[6]. Historical data suggest a mortality at the time of first and subsequent variceal hemorrhage of 24%-49% and 30%, respectively[7]. Following variceal hemorrhage, higher mortality is associated with increasing severity of CLD as assessed by both the Child-Pugh score (mean survival 37.3 mo with score A versus 11 mo with score C)[8] and Model for End-stage Liver Disease (MELD) score[9]. More recently, American and European data have shown that 6-wk mortality rates have fallen, ranging from 14% to 20%[9-12], and following a UK-wide audit, a 28-d mortality figure of 14% for first and subsequent variceal bleeds has been quoted[13].

A number of factors are associated with poor outcome following variceal hemorrhage[10], including MELD score, transfusion requirement, alcohol as etiology, bilirubin, albumin, hepatic encephalopathy and hepatocellular carcinoma[9,10]. Higher hepatic venous pressure gradient at the time of variceal hemorrhage predicts length of stay, greater transfusion requirement and death[14].

There are several clinical scoring tools available to predict outcome, rebleeding and need for endoscopic intervention following acute gastrointestinal hemorrhage, including the Rockall and Blatchford scores[15,16]. However, scoring tools for predicting outcome following variceal hemorrhage are not commonly used due to difficulty in the identification of predictive variables. A recent publication has shown that severity of liver disease, renal impairment and infection adversely affect outcome following variceal hemorrhage[17].

Bacterial infection is commonly associated with variceal hemorrhage and appears to be an independent risk factor for failure to control bleeding[18] and predicts both early rebleeding and death[19,20]. The routine use of prophylactic broad-spectrum antibiotics has shown a marked improvement in outcome in acute variceal hemorrhage. Routine intravenous ceftriaxone or post-endoscopic norfloxacin reduces rebleeding rates compared to on-demand antibiotics[21,22]. A Cochrane meta-analysis of antibiotic prophylaxis in cirrhotic patients with gastrointestinal bleeding, given either before and after variceal hemorrhage, revealed a 27% reduction in mortality and a reduction in the incidence of bacterial infections by 60%[23].

United States guidelines for antibiotic prophylaxis in cirrhotic patients admitted with upper gastrointestinal hemorrhage have been published by the American Society of Gastrointestinal Endoscopy, and recommend intravenous ceftriaxone on admission as first-line prophylaxis[24].

The British Society of Gastroenterology has recently updated guidelines on the use of antibiotic prophylaxis in gastrointestinal endoscopy. The recommendation is to administer a ureidopenicillin or third-generation cephalosporin to all patients with suspected variceal bleeding, or those with decompensated liver disease who develop gastrointestinal bleeding, prior to endoscopy[25].

In the Cochrane primary studies, antibiotics were given either before or after endoscopy, therefore, the evidence for when antibiotics should be given remains unclear. Of the studies using post-endoscopic antibiotics, the timing of antibiotic administration has rarely been reported. Indeed, the Cochrane review has acknowledged that evidence for the timing of administration of antibiotics is lacking[23].

The use of broad-spectrum antibiotics raises concerns regarding healthcare-associated infections, particularly *Clostridium difficile* (*C. difficile*) infection (CDI). In the United States, the number of hospital admissions due to CDI has steadily risen over the last decade from 2.7 per 1000 admissions in 2000 to 5.1 per 1000 in 2003, with the highest incidence in patients > 65 years (228 per 100 000 patient-years)[26]. A similar picture has been seen in England until recently[27,28], with 80% of cases occurring in the > 65-year-old population[28,29].

A recent study has shown that CDI in cirrhotic patients is associated with a higher mortality compared to cirrhotic patients without CDI[30]. There is currently no literature on the incidence of CDI in cirrhotic patients admitted with acute variceal hemorrhage who are given prophylactic broad-spectrum antibiotics.

The aims of this study were to determine if prophylactic antibiotics, or more accurately peri-endoscopy antibiotics (administered before, during or up to 8 h following endoscopy), were effective in reducing mortality following first variceal hemorrhage, and to assess the rebleeding rates and incidence of CDI infection in this patient population.

MATERIALS AND METHODS

Patient population

This was a retrospective analysis of cases of first variceal hemorrhage who presented to the Southampton Liver Unit, a tertiary referral centre, from December 1, 2006 to December 1, 2008. Seventy cases were identified from the endoscopy computer database using multiple search strategies. Only first presentation variceal hemorrhages were included. All cases of variceal hemorrhage transferred to the Southampton liver unit from other centers were excluded from the analysis.

All patients were admitted to the liver unit after admission and were treated under the care of a consultant hepatologist and received standard care, including the use of intravenous vasoactive drugs, access to interventional radiology and a 24-h on-call therapeutic endoscopy service. A protocol for the dose and duration of the terlipressin prescription was followed in all cases.

Data collection

Data collection included demographics, etiology of CLD, antibiotic therapy (timing of first dose relative to the endoscopy, type of antibiotic prescribed and duration of therapy), endoscopy details, terlipressin use (dose and duration of therapy), rebleeding rates within 28 d, survival at 28 d, incidence of CDI at 28 d, incidence of sepsis, hepatorenal syndrome, spontaneous bacterial peritonitis and ascites. The data were collected from hospital notes and computerized pathology databases. The microbiology database collected CDI cases from the community and therefore cases occurring after discharge form hospital were also included.

All patients who received antibiotics within the a priori time period of before, at the time of, or within the 8 h following endoscopy were included in the first analysis group [peri-endoscopy (8 h) group]. This group was compared to the second patient group, those patients receiving antibiotics > 8 h after endoscopy or not receiving antibiotics (non peri-endoscopy group).

CDI incidence

To compare the incidence of CDI in cirrhotic patients with general medical patients receiving antibiotics, an additional prospective study was undertaken during the variceal study period. Over one calendar month, all general medical patients admitted for antibiotic therapy of at least 5 d duration for non-gastrointestinal reasons were studied on two general medical wards. All patients were < 80 years of age. Patients were excluded if there was a history of prior CDI infection.

Statistics analysis

To compare demographic data between survivors and non-survivors at 28 d, initial assessments for normality of data distribution were undertaken using the Shapiro-Wilk test and Q-Q plot. The data were found to be non-normally distributed (for example MELD score data has a Shapiro-Wilk P value < 0.01 for normality and a sigmoidal curve on Q-Q plot). As a consequence, all further statistical analyses were undertaken using non-parametric tests.

Initially, univariate analysis was performed on ordinal data using the χ^2 test to compare outcome (mortality, rebleeding or CDI, the dependent variable) with each risk factor (antibiotics within 8 h, hepatorenal syndrome and sepsis, the independent variable). Continuous demographic data (age, INR, creatinine, bilirubin, sodium and MELD score) were compared between survivors and non-survivors using the Mann-Whitney U test.

Following univariate analysis, a forward multivariate logistic regression model was fitted with all statistically significant variables on univariate analysis. However, given the sample size and number of events, only two variables were fitted to the model. The first was the initial study variable, the administration of antibiotics within 8 h of endoscopy, and the second was the MELD score assessment of severity of CLD. All statistical analyses were performed using SPSS (version 16) and STATA 11 software.

Table 1 Baseline demographics and clinical characteristics of patients (mean ± SD) *n* (%)

Parameter	Alive (n = 57)	Dead (n = 13)	Total (n = 70)
Sex (M:F)	38:19 (66.7)	11:2 (84.6)	49:21 (70.0)
Age (yr)	52.93 ± 13.07	51.46 ± 10.52	52.66 ± 12.65
Etiology			
ALD	37 (64.9)	9 (69.2)	46 (65.7)
HCV	1 (1.8)	0 (0)	1 (1.4)
MISC	8 (14.0)	3 (23.1)	11 (15.7)
DUAL	6 (10.5)	1 (7.7)	7 (10.0)
NASH	5 (8.8)	0 (0)	5 (7.1)
INR	1.58 ± 0.47	1.78 ± 0.66	1.62 ± 0.52
Creatinine	86.23 ± 33.87	99.38 ± 42.28	88.67 ± 35.95
Bilirubin	86.74 ± 95.89	190.23 ± 158.96	105.96 ± 117.47[a]
Sodium	136.89 ± 5.46	135.23 ± 6.10	136.59 ± 5.62
MELD	14.79 ± 6.76	20.38 ± 7.58	15.83 ± 7.25[a]

[a]P < 0.05. ALD: Alcoholic liver disease; HCV: Hepatitis C viral infection; MISC: Miscellaneous; DUAL: Dual aetiology; NASH: Non-alcoholic steatohepatitis; INR: International normalised ratio; MELD: Model for end-stage liver disease.

RESULTS

Patients

Between December 1, 2006 and December 1, 2008, 70 patients with first presentation variceal hemorrhage were admitted to the liver unit, Southampton General Hospital. Baseline demographics are shown in Table 1. The majority of patients were male (70%), and the most common etiology of cirrhosis was alcohol (65.7%). Patients who died within 28 d of the first variceal hemorrhage had a higher baseline MELD score (P = 0.02), mainly due to a higher admission serum bilirubin level (Table 1, P = 0.01). The other component parameters of the MELD score were similar in both groups.

Sixty-four (91.4%) patients received prophylactic antibiotics during their admission, with median (inter-quartile range; IQR) and mean (SE) times from endoscopy to administration of antibiotics of 3.5 (0-7.0) and 5.9 (1.18) h, respectively. The most common antibiotic prescription was cefuroxime and metronidazole (n = 45), followed by ciprofloxacin alone (n = 8) and cefuroxime alone (n = 7). The remaining patients received meropenem alone, or vancomycin in combination with either metronidazole or gentamicin. The median (IQR) and mean (SE) duration of antibiotic therapy was 5.0 (3.0-7.0) and 5.7 (0.57) d, respectively.

Twenty-one patients received antibiotics before or at the time of endoscopy and a further 32 received antibiotics after but within 8 h of the index endoscopy. Therefore, a total of 53 (75.7%) patients received antibiotics before,

Table 2 Univariate analysis for 28-d outcome following first variceal hemorrhage

Variable	Mortality at 28 d			Rebleeding at 28 d		
	P value	OR	95% CI	*P* value	OR	95% CI
MELD	0.02	-	-	0.20	-	-
Antibiotics within 8 h (peri-endoscopy)	0.04	0.279	0.078-0.997	0.27	0.491	0.138-1.741
Hepatorenal failure	< 0.01	11.25	2.243-56.421	0.71	1.389	0.249-7.755
Sepsis	0.03	4.029	1.113-14.581	0.89	0.902	0.218-3.730

MELD: Model for end-stage liver disease; OR: Odds ratio; CI: Confidence interval.

during or within 8 h of endoscopy, and were included in the peri-endoscopy (8 h) group.

Of the 17 (24.3%) patients in the non peri-endoscopy group, 11 received antibiotics at > 8 h after endoscopy and six did not receive antibiotic prophylaxis.

The vast majority of patients received endoscopic variceal band ligation therapy during the index endoscopy (n = 54) with only four receiving sclerotherapy. Nine patients required a Sengstaken-Blakemore tube. Eight patients received transjugular intrahepatic portosystemic shunting during their admission. None of these factors were significantly associated with mortality, although banding therapy significantly reduced the incidence of rebleeding [P = 0.01, odds ratio (OR) = 0.191, 95% confidence interval (95% CI) = 0.054-0.680], and the requirement for a Sengstaken-Blakemore tube was significantly associated with rebleeding (P < 0.01, OR = 27, 95% CI = 4.66-156.57). Nine patients failed endoscopic therapy and, while there was a trend towards increased mortality in this group, it was not statistically significantly (P = 0.22, OR = 2.55, 95% CI = 0.545-11.928).

Clinical outcomes

At day 28 following first variceal hemorrhage, 13 patients (18.6%) had died. The peri-endoscopy (8 h) group showed a significant survival benefit when compared to the non peri-endoscopy group. Antibiotics given before, during or within 8 h significantly reduced mortality at day 28 (P = 0.04, OR = 0.279, 95% CI = 0.078-0.997) and showed a trend towards reducing 28-d rebleeding (P = 0.27, OR = 0.491, 95% CI = 0.138-1.741).

CDI incidence

Four patients (5.7%) with first variceal hemorrhage developed CDI within 28 d of admission. All episodes of CDI were in patients who survived at least 28 d post-variceal hemorrhage. CDI did not predict death (P = 0.33) or rebleeding (P = 0.80). During the study period, the prospective study of patients under 80 years of age admitted to one of two general medical wards in Southampton General Hospital for at least 5 d of broad-spectrum systemic antibiotics were monitored. Of the 40 cases identified, two (5%) developed CDI.

Predictors of survival following first variceal hemorrhage

Univariate analysis revealed four risk factors that were significantly associated with death at 28 d (Table 2): receiving antibiotics > 8 h after endoscopy (P = 0.04, OR = 3.584, 95% CI = 1.003-12.808); higher MELD score (P = 0.02); presence of hepatorenal syndrome (P < 0.01, OR = 11.25, 95% CI = 2.243-56.421); and an episode of clinical sepsis (P = 0.03, OR = 4.029, 95% CI = 1.113-14.583). A forward multivariate logistic regression model was undertaken for 28-d survival. A lower MELD score (P = 0.01, OR = 1.155, 95% CI = 1.041-1.281) and administration of antibiotics within 8 h (peri-endoscopy group, P = 0.01, OR = 0.149, 95% CI = 0.033-0.681) were found to be independent variables that predicted survival (Table 3).

Table 3 Multivariate logistic regression analysis for 28-d survival following first variceal hemorrhage

Variable	*P* value	OR	95% CI
MELD	0.01	1.155	1.041-1.281
Antibiotics within 8 h (peri-endoscopy)	0.01	0.149	0.033-0.681

MELD: Model for end-stage liver disease; OR: Odds ratio; CI: Confidence interval.

DISCUSSION

Acute gastrointestinal hemorrhage is associated with significant mortality, particularly when comparing variceal to non-variceal hemorrhage[31]. Historical data have reported a mortality of up to 61% following variceal hemorrhage[1-5], although current 4-6-wk mortality rates range from 14% to 20%[9-13]. Despite the advances in vasoactive drugs and endoscopic therapies, a significant contribution to the observed fall in mortality has occurred with the introduction of prophylactic broad-spectrum antibiotic therapy[23]. It has now become standard practice to administer prophylactic antibiotics in acute variceal hemorrhage and in cirrhotic patients with gastrointestinal bleeding of any cause[24,25,31].

The clear survival benefit associated with prophylactic antibiotics in gastrointestinal hemorrhage associated with cirrhosis is not in doubt. Both American and British guidelines recommend the administration of antibiotics prior to endoscopy. While this seems logical, the timings of antibiotic administration in randomized studies are heterogeneous with prophylaxis occurring before and after endoscopy, thus the exact timings are unclear[23].

The term preemptive has been used in the field of gastrointestinal hemorrhage to describe antibiotics given after an event likely to cause bacteremia (whether due to the initial bleed or subsequent endoscopy) but before clinical evidence of sepsis. We hypothesize that there is a window of opportunity for the administration of antibiotics, after which their benefit is diminished or lost. Windows of opportunity for effective use of antibiotics have been observed for other infections and patient groups. Significantly higher survival is associated with administering antibiotics within 8 h of admission for patients admitted with pneumonia[32] and within 6 h for meningitis[33]. In a mouse model of intraperitoneal infection that produced septic shock, survival was > 80% if antibiotics were given within 12 h of insult, but < 15% if given after 15 h[34]. For patients treated for septic shock in an intensive care environment, a sequential decrease in survival was noted for each hour of delay in administering antibiotics for the first 6 h[35].

The potential benefit of antibiotics in cirrhosis is balanced by the risk of adverse effects. The use of broad-spectrum antibiotics is a contributing factor to health-care-associated CDI. A recent study has shown that patients with cirrhosis who are given antibiotics are at a higher risk of developing CDI, and this is associated with a higher mortality compared to cirrhotic patients without CDI[30].

The rates of CDI within the cirrhotic patients in our study were no higher than in non-cirrhotic, general medical patients who receive a minimum 5-d course of broad-spectrum antibiotics for non-gastrointestinal indications. Both groups of patients were treated in the same ward areas and were matched for environmental risks and isolation procedures that are known to affect rates of CDI[28]. Cirrhotic patients were younger than general medical patients. However, elderly medical patients over 80 years of age and at highest risk of CDI were excluded.

This study has shown that, if given before, during or within 8 h of the index endoscopy, peri-endoscopy antibiotics are associated with a significantly improved survival at 28 d, and show a trend towards reducing 28-d rebleeding rate. The present study did not address the precise time for peri-endoscopy antibiotics, which needs to be addressed by prospective studies. This highlights the requirement for care pathways to be modified, in this unit and similar units, if the current guidelines for antibiotic administration before endoscopy are to be widely adopted.

The administration of antibiotics within 8 h importantly reduces rates of mortality and rebleeding independently of liver disease severity, judged by MELD and Child-Pugh score, in agreement with previous studies[8,11,12]. The proportion of patients who received prophylactic antibiotics in our study (91.4%) is comparable to other recently published data[12]. Similarly, the 28-d survival for first variceal hemorrhage (81.4%) is comparable to that in the current literature for all variceal bleeding (80%-84%)[9-12], and reflects the changes in standard care in the treatment of variceal hemorrhage over the past 30 years[12].

Patients with second or subsequent variceal hemorrhage were excluded from this study. Previous hospital admission for variceal hemorrhage, particularly if the admission was recent, would have been exposed to broad-spectrum antibiotics and nosocomial infection, including *C. difficile*, and potentially created heterogeneous groups. Similarly, patients transferred to the liver unit from another institution were likely to have been exposed to antibiotics prior to their transfer, and were excluded for similar reasons.

There are several strengths to this study. All included cases were first variceal hemorrhages. Medical notes were reviewed to identify hospital attendances during the 28 d prior to admission for variceal hemorrhage and involved an antibiotic prescription. Any patient who received antibiotics in this run-in period was excluded from the study. All patients were managed in a tertiary referral center and received the standard medical management for variceal hemorrhage. The medical records, clinical outcome data and rates of CDI were available for all included cases, which allowed accurate assessment of the timing of antibiotics. The use of the microbiology database ensured all cases of CDI that occurred after discharge from hospital would be included.

It is acknowledged that this is a retrospective study rather than a prospective trial, which has inherent limitations. To minimize the effects of confounding factors, we attempted to study a homogenized population, managed by standard protocols in the same environment. Cases of *C. difficile* toxin-positive stools were not assessed for severity, either clinically or endoscopically. However, all cases of CDI were in patients alive at 28 d and CDI did not predict rebleeding or death. All efforts were made to exclude patients who had received antibiotics within 28 d of admission. However, any antibiotic prescription made by a primary care physician during this period would have been unknown to the authors, unless declared by the patient. Finally, the study did not include cases of non-variceal hemorrhage in patients with cirrhosis, therefore, the findings cannot be extended to this group.

In conclusion, following variceal hemorrhage, the use of peri-endoscopy antibiotics (administered before, during or up to 8 h after endoscopy) is associated with a significant increase in survival and a trend towards a reduction in rebleeding at 28 d. Peri-endoscopy antibiotic administration is an independent variable for survival in addition to the severity of liver disease. Despite growing concerns about rising healthcare-associated infections and the use of broad-spectrum antimicrobials in cirrhosis, the rates of CDI are comparable to other patient groups who receive broad-spectrum antibiotic therapy, and should not be a reason to withhold antibiotics.

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COMMENTS

Background

Cirrhosis is a common and serious cause of intestinal hemorrhage. Twenty-two

to sixty-one percent of patients with cirrhosis during follow-up studies develop variceal bleeding, usually within 2 years of diagnosis. Variceal hemorrhage is associated with a mortality of 14%-20%. In addition to advances in endoscopic and pharmacological therapies, the prophylactic use of antibiotic drugs has reduced mortality by 27% and infection, the leading cause of death in these circumstances, by 60%. It is unclear if there is a time point after which the benefit of antibiotics is lost.

Research frontiers

Several studied have investigated the use of prophylactic antibiotic therapy following variceal hemorrhage in patients with cirrhosis after the recognition that infection leading to sepsis was a leading cause of death in these patients. Eleven key studies were included in a Cochrane meta-analysis which concluded that antibiotic treatment reduced mortality by 27% and infection by 60%. It is now routine practice to administer antibiotics following variceal bleeding; the timing of administration is unclear in the literature. The increasing use of broad-spectrum antibiotics is associated with serious side effects and complications including *Clostridium difficile* infection (CDI). Patients with cirrhosis are at increased risk of infection due to suppression of the immune system as a direct result of chronic liver disease. It is currently unknown if patients with cirrhosis receiving antibiotics following variceal hemorrhage are at increased risk for acquiring CDI.

Innovations and breakthroughs

Emergency endoscopy is an important technique for the treatment of active variceal bleeding and also for preventing subsequent future episodes of rebleeding. Endoscopic techniques such as variceal band ligation (in which rubber bands are positioned around the bleeding varix) have been shown to be more effective than older therapies such as ethanolamine injection sclerotherapy, and have become the method of choice in these situations. Similarly, vasoactive drug therapies, particularly terlipressin, have been shown to participate in the cessation of bleeding and reduce mortality by redirecting blood flow away from the splanchnic circulation. Transjugular intrahepatic portosystemic shunting is an invasive procedure performed by an interventional radiologist to reduce the portal venous pressure and arrest acute bleeding by placing a stented shunt through the liver, thus connecting the portal and hepatic veins directly. It is currently used in patients with persistent or recurrent variceal bleeding despite maximal endoscopic and pharmacological intervention. It is not currently widely available and is a second-line treatment option in complicated and persistent variceal hemorrhage.

Applications

The article shows that early antibiotics given within 8 h of endoscopy are associated with reduced mortality. Early administration of antibiotics in this situation should be adopted by units that treat patients with acute variceal bleeding and may need to be incorporated into clinical care pathways in acute admission and acute gastrointestinal bleeding units. Further prospective studies might be necessary to clarify the optimal timing of antibiotic administration following variceal hemorrhage. Patients are at no greater risk of CDI than non-cirrhotic patients who are receiving antibiotics, and concerns regarding healthcare-associated infections should not deter clinicians from prescribing antibiotic therapy in this situation.

Peer review

This is a well-written paper that is limited in impact by observational design and single-center patient population.

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