Gastroduodenal

PWE-157 UPPER GASTROINTESTINAL BLEEDING IN HOSPITALISED PATIENTS—PROSPECTIVE CONTROLLED ANALYSIS OF THE ROLE OF ASPIRIN AND OTHER ANTITHROMBOTIC DRUGS

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Introduction Upper gastrointestinal bleeding (UGIB) developing while in hospital is traditionally thought to be due to stress ulceration affecting critically ill patients. The role of potentially damaging drugs is not clear.

Aims Given the increasing use of low-dose aspirin and other antithrombotic drugs—clopidogrel, dipyridamole, and warfarin—for vascular protection, we aimed to clarify their impact on UGIB affecting hospitalised patients.

Methods Between 2008 and 2009, we prospectively assessed the clinical details and outcomes of all inpatient bleeders at our hospital, and compared these with outpatients admitted because of bleeding. For each inpatient we included three outpatients as controls. Patients were excluded if they had a variceal cause. The Charlson comorbidity score and the complete Rockall score for non-variceal upper gastrointestinal bleeding were also calculated. The χ^2 test, Fisher's exact test, Mann–Whitney U test, and logistic regression analyses with ORs and 95% CIs were used as appropriate.

Results Abstract PWE-157 table 1 summarises the main characteristics of patients who bled while in hospital (inpatient bleeders) vs those who were admitted after bleeding (outpatient bleeders). Inpatient bleeders were older and more likely to be males and to have cardiovascular disease. After adjustment for age and sex, the logistic regression analysis still showed that patients who bled as inpatients were significantly more likely to be taking antithrombotic medication, especially non-aspirin agents, than those who were admitted after bleeding, [OR (95% CIs), 2.15 (1.25 to 3.68); p=0.006]. The adjusted odds of death within 30 days of bleeding was almost twice as high in the inpatient group, [OR 1.88 (0.74 to 4.77)]. The endoscopic abnormalities in more than 80% of patients in both groups included erosive oesophagitis, gastric, or duodenal ulcers or erosions.

Abstract PWE-157 Table 1

Covariate	Inpatient bleeders (n=96)	Outpatient bleeders (n=274)	p Value
Age, years, (median, IQR)	77 (67–83)	68 (50–79)	<0.001
Males	44/96 (45.8%)	166/274 (60.6%)	0.016
Cardiovascular disease	50/96 (52.1%)	80/274 (29.2%)	<0.001
Rockall 3+	81/96 (84.4%)	182/273 (66.7%)	0.001
Aspirin	44/96 (45.8%)	86/274 (31.4%)	0.013
Other antithrombotics	35/96 (36.5%)	50/274 (18.2%)	<0.001
Aspirin or other antithrombotics	62/96 (64.6%)	122/274 (44.5%)	0.001
NSAIDs	11/96 (11.5%)	49/273 (17.9%)	0.15
Death at 30 days	9/94 (9.6%)	12/272 (4.4%)	0.074

Conclusion The use of antithrombotic drugs is a significant risk factor for UGIB developing in hospitalised patients. The endoscopic lesions, whether caused by these agents or not, are potentially preventable.

Competing interests None declared.

PWE-158 NON-SELECTIVE NON-STEROIDAL ANTIINFLAMMATORY DRUGS, PROTON PUMP INHIBITORS, AND THE INCIDENCE OF NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING AND *CLOSTRIDIUM DIFFICILE* INFECTION

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Introduction It is not clear what impact the decline of COX-2 selective inhibitors has had on the use of non-selective non-steroidal anti-inflammatory drugs (ns-NSAIDs) or on the incidence of non-variceal upper gastrointestinal bleeding (NV-UGIB). Also, proton pump inhibitors (PPIs), recommended for NSAID-ulcer prophylaxis, have been linked to *Clostridium difficile* infection.

Methods We aimed to measure the incidence [cases per 100 000 population per annum] of NV-UGIB and *C difficile* infection as well as the use of ns-NSAIDs and PPIs in a well-defined population served by a single centre. Data were collected over three calendar years, 2007–2009. Significance was assessed using the χ^2 test for trend.

Results As shown in Abstract PWE-158 table 1, the use of COX-2 selective and newer NSAIDs continues to decline, while that of ns-NSAIDs continues to rise. This has been coupled with a steady rise in the use of PPIs. On the other hand, the incidence of both NV-UGIB and *C difficile* infection has been falling.

Abstract PWE-158 Table 1 The incidence of non-variceal upper gastrointestinal bleeding and *Clostridium difficile* infection, and the annual number of prescriptions [per 100 000 population]

	2007	2008	2009	p Value
Total population	255 330	255 840	255 720	–
COX-2 & Newer-NSAID use	15.0×10^3	14.5×10^3	14.1×10^3	<0.001
Non-selective NSAID use	31.7×10^3	32.4×10^3	33.4×10^3	<0.001
Proton pump inhibitors' use	75.1×10^3	81.8×10^3	86.6×10^3	<0.001
NV-UGIB incidence	134.7	125.1	89.6	<0.001
C difficile incidence	122.3	104.4	72.7	<0.001

Conclusion The incidence of NV-UGIB has been falling despite the increasing use of ns-NSAIDs. This could be, at least in part, due to the rise in PPI use. Also, the incidence of *C difficile* infection has been falling despite more PPIs being used: this might suggest a poor link between these two factors, or might reflect the outcome of other measures being deployed against this infection. While these falls appear promising, both NV-UGIB and *C difficile* infection continue to represent significant clinical challenges.

Competing interests None declared.

PWE-159 THE EFFECT OF NATURAL POLYMORPHISM IN THE PROMOTER OF THE *HELICOBACTER PYLORI* CYTOTOXIN ASSOCIATED GENE, *CAGA*, ON *CAGA* TRANSCRIPTIONAL REGULATION

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Introduction *Helicobacter pylori* persistently colonises the gastric mucosa of almost half the human population. It is the main causative agent of peptic ulcer disease and an important risk factor for

gastric carcinoma. One of its major virulence determinants is cytotoxin associated gene A, *cagA*, and high levels of *cagA* expression are associated with more severe disease. The functional promoter elements of *cagA* in the 436 bp *cagAB* intergenic region have been previously analysed but differences in the promoter region and levels of *cagA* expression between different *H pylori* strains have not been studied in detail. We aimed to analyse the *cagA* promoter region to determine whether naturally occurring polymorphic differences within it contribute to differences in *cagA* expression level.

Methods Biopsy samples were obtained from 17 patients undergoing routine upper GI endoscopy at the Queen's Medical Centre Nottingham, UK. RNA was extracted directly from biopsies and *cagA* expression levels were analysed by real-time qPCR. The *cagAB* intergenic region of all 17 clinical strains were sequenced and aligned using the ClustalW multiple sequence alignment program and ranked in order of *cagA* transcript levels. A potentially relevant natural mutation was then created artificially by site-directed mutagenesis to prove its importance.

Results A potentially important polymorphism was identified within an imperfect inverted repeat where an A was commonly replaced by a T at position -54. Strains possessing T at this position expressed higher *cagA* mRNA levels than those with an A (p=0.016). To test whether this was a direct determinant of *cagA* transcription level, a mutation was engineered at position −54 (T to A) in high transcription strain 83. This resulted in a 30% reduction in *cagA* transcript level when compared to an isogenic control strain without the change (p=0.073). In the complementary experiment, we engineered an A to T mutation in low transcription strain 126 and this led to a 20% increase in the level of *cagA* mRNA compared to its isogenic control (p=0.002).

Conclusion Presence of a T at position −54 within the inverted repeat of the *cagA* promoter region is an important natural determinant of higher levels of *cagA* transcription. We speculate that this may help explain why only some *cagA*$^+$ *H pylori* strains cause disease.

Competing interests None declared.

PWE-160 LIVER RESECTION IN METASTATIC GASTROINTESTINAL STROMAL TUMOURS

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Introduction The benefit, if any and case selection for operation in metastatic GIST has not as yet been evaluated. We report our experience with patients undergoing liver resection for metastatic GIST.

Methods From a prospectively held data base spanning 2000–2011 we identified 12 patients who underwent liver resection and cases notes reviewed. Non-parametric statistics were applied.

Results The M:F ratio was 5:7. The median age at diagnosis of the primary tumour was 55 yr, range 47–71 yr. The site of primary was: Gastric 6, duodenum 1, small intestine 2, colon 2, rectum 1. In three cases liver metastases were present at diagnosis of the primary and these patients underwent synchronous resection of the primary and liver. In the remainder the median disease free interval was 12 m (2–96 m). In nine cases the pattern of metastatic disease was hepatic alone, two cases had in addition peritoneal disease and both had had percutaneous biopsy of the primary tumour. One case had local recurrence. All but one patient received neoadjuvant chemotherapy with imatinib and in two cases 2nd-line treatment with sunitinib and 1 3rd-line with nilotinib. The median duration of systemic therapy before operation was 18 m (10–84) and systemic therapy was stopped after plateau of response or evidence of progression, non-responders were not considered for resection. Liver resections performed: Right extended 1, right 3, left 1, non-anatomic or segmental 7. Additional visceral resection required in 2 (synchronous primary cases excepted). At a median follow-up time of 43 m from liver resection the status is: NED 7, AWD 3, DOC 1, DOD 1. There was no 30-day mortality.

Conclusion The safety of hepatectomy for GIST in the imatinib treated patient is demonstrated. Whether resection of metastatic disease translates into cure, at least in some patients is yet to be proven but it is suggested that the indications for liver resection for metastatic disease might be extended to this disease.

Competing interests None declared.

PWE-161 PLATELET ACTIVATION IN ACUTE UPPER GASTROINTESTINAL BLEEDING

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Introduction Acute upper gastrointestinal bleeding (AUGIB) is a common reason for medical admissions and is associated with significant morbidity and mortality. Studies have previously noted an excess of cardiovascular events in patients who have suffered from AUGIB. Patients who have aspirin withheld for 8 weeks following admission with AUGIB have significantly higher rates of CVS events. The aim of the study was to assess the level of platelet activation, and platelet reactivity, in patients presenting with AUGIB.

Methods Patients admitted to Sandwell and West Birmingham Hospitals NHS Trust with AUGIB were recruited. Dyspeptic patients attending for diagnostic OGD were used as controls. To assess platelet activation citrated whole blood was incubated at room temperature with monoclonal mouse antibodies against constitutively expressed platelet marker CD42a-PerCP, and markers of platelet activation PAC1-FITC, and CD62P-APC. Negative controls were run in parallel. Incubation was terminated after 15 min. Platelet reactivity to an agonist, in this case ADP, was assessed by stimulating blood with ADP for 2 min prior to incubation with antibodies as described above. Samples were analysed using a FACSCalibur flow cytometer. Platelets were identified on the basis of their forward and side scatter properties and the presence of the CD42a platelet-specific marker. CD62P and PAC1 expression were measured by the percentage of platelets expressing these markers. Statistical significance of mean platelet activation was determined by the t-test. The Mann–Whitney U test was utilised for non-normally distributed data. Statistical analysis was performed using SPSS V.18.0 software.

Results A total of 31 patients with AUGIB and 25 controls were recruited. The groups were age and gender matched. The mean age of the AUGIB group is 66.4±18.2 years, and the control group 62.8±6.1 years. There was a significant differences in the level of CD62P positivity between the study groups (18.4±5.8% in AUGIB group and 13.9±3.7% in the control group, p=0.001) and in those staining positive for both CD62P and PAC1 (1.9±1.45% in AUGIB group and 1.2±1.0% in the control group, p=0.027). No differences were seen in PAC1 positivity between the groups (7.1±5.2 vs 5.1±4.2, p=0.127). No differences were seen in the response of platelets to ADP between the study and control groups.

Conclusion Patients presenting with AUGIB have higher levels of platelet activation when compared to controls. Platelet reactivity to