ORIGINAL ARTICLE

The Risk Factors of Gastrointestinal Bleeding in Acute Ischaemic Stroke

B B Hamidon, MMed, A A Raymond, FRCP

Neurology Unit, Department of Medicine, Faculty of Medicine Universiti Kebangsaan Malaysia (UKM), Jalan Yaacob Latiff, Bandar Tun Razak, 56000, Cheras, Kuala Lumpur

Summary

Gastrointestinal (GI) bleeding is one of the most serious complications after an acute ischaemic stroke and may affect stroke outcome. We identified predictors and the eventual outcome of gastrointestinal bleeding during the in-patient period following the commencement of aspirin. This was a study of patients with acute ischaemic stroke admitted to Universiti Kebangsaan Malaysia Hospital from June 2000 to January 2001. A single observer, using pre-defined diagnostic criteria recorded information on demography, risk factors and GI bleeding that occurred during the inpatient period. One hundred and fifteen patients with acute ischaemic stroke were enrolled in the study. Gastrointestinal bleeding was observed in 6 (5.2%) patients. Using univariate analysis, the independent predictors of gastrointestinal bleeding were age (OR 1.25; 95% CI 1.07 to 1.50), and middle cerebral artery (MCA) territory infarcts (OR 9.47; 95% CI 1.62 to 55.5). Using multivariate analysis, the presence of gastrointestinal bleeding increased mortality (OR 24.97; 95%CI 1.97 to 316.91). Older age, and large MCA infarct predict the development gastrointestinal bleeding. Stroke mortality was independently predicted by gastrointestinal bleeding. Prophylactic treatment in elderly patients with large cerebral infarcts may be an area for further investigation.

Key Words: Gastrointestinal bleeding, Ischaemic stroke, Mortality

Introduction

Patients who have had an acute stroke are at risk of developing a wide range of complications[1,2,3,4]. One of the major complications is gastrointestinal (GI) bleeding. This is compounded by the fact that these patients are given anti-platelet agents. Stroke is also associated with Cushing's ulcer, which was first reported in association with brain tumour[5]. GI bleeding occurs frequently in intensive care unit patients who have intracranial disease. Following head injury, endoscopic evidence of mucosal lesions can appear within 24 hours and 17% of patients with GI bleeding may present clinically with significant bleeding[6]. Mortality in patients with GI bleeding can be as high as 50% and this may contribute significantly to stroke mortality[7]. The purpose of this study was to determine the incidence of GI bleeding in an acute ischaemic stroke cohort receiving aspirin and then to analyse its predictors and impact on mortality.

Materials and Methods

In a single hospital (Hospital UKM-HUKM), a cohort of patients was identified. They consisted of consecutive patients who were either admitted to the general medical ward, high dependency ward or the intensive care unit with a clinical diagnosis of ischaemic stroke (first ever or recurrent within one week of onset of symptoms) or had suffered a stroke during an inpatient stay during the period June 2000 to January 2001. Only

This article was accepted: 29 December 2005

Corresponding Author: Hamidon Bin Basri, Jabatan Perubatan Fakulti Perubatan UKM, Jalan Yaacob Latiff, Bandar Tun Razak, 56000 Cheras, Kuala Lumpur

patients given aspirin were included. Acute stroke was defined as "rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer or leading to death, with no apparent cause other than of vascular origin", according to the World Health Organisation (WHO) criteria[8]. GI bleeding was defined as gross blood or coffee ground substance in nasogastric aspirate or haematemesis or melaena[7,9]. A single observer, using pre-defined diagnostic criteria, recorded the type, and frequency of gastrointestinal bleeding that occurred during the inpatient period. All patients were subjected to a brain CT before being admitted to the wards.

Statistical Analyses: Two separate analyses were conducted. In the first analysis, the presence of GI bleeding was determined to be the dependent variable. Independent variables were Glasgow coma score (GCS), age, sex, diabetes mellitus, hypertension, smoking, and type of cerebral infarcts. Given that the event per variable ratio was less than ten, only a univariate analysis was done. In the second analysis, similar steps were followed except that GI bleeding was now considered an independent variable and mortality was made the dependent variable. Variables (including gastrointestinal bleeding) found to have a significant relationship ($p<0.05$) with presence of mortality (univariate analysis) were included in a multiple logistic regression model. In both univariate and multivariate analyses, odd ratios with 95% confidence intervals (CI) were used to estimate the effects of each factor.

Results

During the eight month study period, 115 ischaemic stroke patients were identified. The mean age was 62.79 years (35 to 88 years), and 53 patients (46.1 %) were male. There were 61 (53%) Chinese patients, 46 Malay (40%) patients, 7 Indian (6.1%) patients, and 1 patient of different ethnicity (0.9%). The types of ischaemic stroke found were middle cerebral artery (MCA) territory (20%), lacunar (60.9%), and other infarcts (19.1%).

Gastrointestinal bleeding was observed in six (5.2%) patients. All patients were subjected to upper gastrointestinal endoscopy. Two patients had gastric ulceration, one had duodenal ulceration and three had erosions and inlammation. All the patients were subjected to a standardised treatment procedure based on a standard critical pathway of gastrointestinal bleeding. The case fatality rate for ischaemic stroke was 11.3%. Four out of the six patients who had gastrointestinal bleeding died during the course of the hospital admission. Two variables (age and MCA infarct) were associated with gastrointestinal bleeding in the univariate analysis (Table I). The age (Figure 1) of the patients was normally distributed (Kolmogorov-Smirnov test) and the mean age difference was analysed between those who developed gastrointestinal bleeding and those without. This showed a higher mean age group for the gastrointestinal bleeding group (Figure 2). There was no significant increase in the risk of gastrointestinal bleeding for the other parameters observed, namely GCS infarcts, past history of diabetes mellitus,

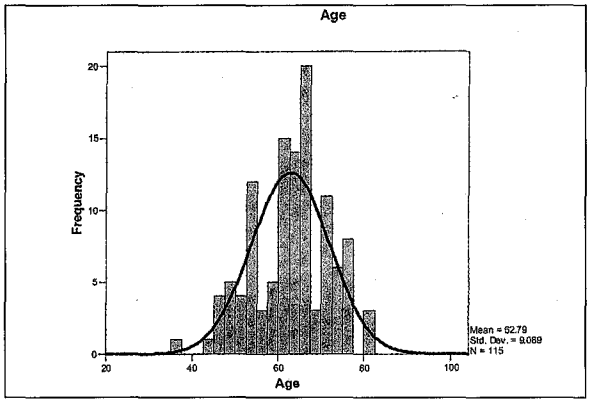

Fig. 1: Age distribution following the normal distribution curve
Mean age 62.79 (SD 9.09)

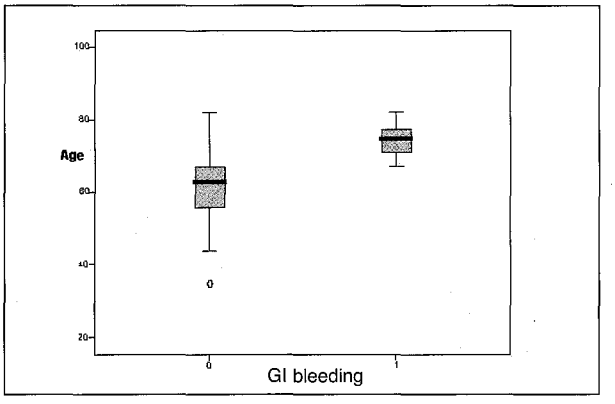

Fig. 2: Box plot showing the mean age difference
0: No GI bleeding; mean age = 62.16 (SD 8.84)
1: GI bleeding; mean age = 74.33 (SD 5.20)

Table I: Univariate analysis of predictors for gastrointestinal bleeding

Parameters	Odds Ratio	Confidence Interval	p Value
Age	1.25	1.07- 1.50	0.004
MCA infarct	9.47	1.62-55.5	0.013
GCS score	1.45	0.73-27.2	0.105
Sex	1.76	0.31-10.01	0.525
Smoking	0.48	0.05- 4.28	0.51
Diabetes mellitus	0.73	0.14- 3.78	0.71

hypertension, sex, and smoking (Table I). Gastrointestinal bleeding following acute stroke independently increased stroke mortality (OR 24.97; 95%CI 1.97 to 316.9)(Table II).

Discussion

Gastrointestinal bleeding occurred in 5.2% of patients. This figure is higher than that reported by Davenport *et al.*[9] (3%) and Dobkin *et al.* (1%)[2]. However, both studies included ischaemic and haemorrhagic strokes. Haemorrhagic strokes tend to have more complications and Misra *et al.*[7] reported a rate as high as 30%. Furthermore, our study looked at a selected group of stroke patients who are at risk of GI bleeding after being given aspirin. Therefore the occurrence is expected to be higher. Previous studies were done retrospectively and the bleeding events may have been under-reported.

Several factors were examined in this study, including age, risk factors for atherosclerosis (diabetes, hypertension, and smoking), admission parameters (blood pressure, blood glucose, and GCS score), and type of infarct. The predictors of gastrointestinal bleeding after an acute ischaemic stroke were middle cerebral artery (MCA) territory infarcts (OR 9.47; 95%CI 1.62 to 55.5), and age (OR 1.25; 95%CI 1.07 to 1.50). MCA territory infarcts are large cerebral infarcts and were found to be a risk factor for gastrointestinal bleeding. In our study, the other territorial infarcts were not analysed due to their small numbers. Large infarcts mean more severe intracranial disease, which may in turn increases the occurrence of Cushing's ulceration and thus the risk of gastrointestinal bleeding is increased. Our study also suggests that gastrointestinal bleeding occurs in an older age group of ischaemic stroke patients. This is not surprising as older patients, particularly those with other associated morbidity have a higher mortality after acute gastrointestinal bleeding. These findings are similar to the study by Davenport *et al*[9]. They also found that large infarcts (total anterior circulation infarct) and older age predict gastrointestinal bleeding using univariate analysis.

The overall mortality rate was 11.3%. This result is similar to that reported in other series[10,11]. It is imperative to identify ischaemic stroke patients who have a high risk of developing gastrointestinal bleeding. Using multiple logistic regression analysis, the presence of gastrointestinal bleeding independently predicts mortality (OR 24.97; 95%CI 1.97 to 316.91). It is probably not practical for prophylactic treatment to be given to all ischaemic stroke patients. However, prophylactic treatment in elderly patients with large cerebral infarcts may be an area for further investigation. Nonetheless, the evidence to support prophylactic treatment of gastrointestinal bleeding in other critically ill patients remains controversial[9].

Conclusion

Gastrointestinal bleeding was found to increase mortality. The independent predictors for the occurrence of gastrointestinal bleeding were MCA territory infarcts, and old age. Therefore, patients who have the aforementioned predictors should be carefully monitored and promptly treated.

Acknowledgements

We would like to thank the Dean of the Medical Faculty Universiti Kebangsaan Malaysia (UKM) for allowing us to publish this paper.

References

1. Dromerick A, Reding M. Medical and neurological complications during inpatient stroke rehabilitation. Stroke 1994; 25: 358-61.
2. Dobkin BH. Neuromedical complications in stroke patients transferred for rehabilitation before and after diagnostic related groups. J Neurol Rehab 1987; 1: 3-7.
3. Bamford J, Dennis M, Sandercock P, Dennis M, Burn J, Warlow C. The frequency, causes, and timing of death within 30 days of a first stroke: the Oxfordshire community project. J Neurol Neurosurg Psychiatry 1990; 53: 824-29.
4. Davenport RJ, Dennis MS, Wellwood I, Warlow CP. Complications after acute stroke. Stroke 1996; 27: 415-20.
5. Cushing H. Peptic ulcers and the interbrain. Surg Gynecol Obstet 1932; 55: 1-34.
6. Kamada T, Fusamoto H, Kawano s. Gastrointestinal bleeding following head injury- a clinical study of 433 cases. J Trauma 1977; 17: 44-47.
7. Misra UK, Kalita J, Pandey S, Mandal SK. Predictors of gastrointestinal bleeding in acute intracerebral haemorrhage. J Neuro Sc 2003; 208: 25-29.
8. Hatano S. Experience from a multicentre stroke register: a preliminary report. Bull World Health Organ. 1976; 54: 541-53.
9. Davenport RJ, Dennis MS, Warlow CP. Gastrointestinal haemorrhage after acute stroke. Stroke 1996; 27: 421-24.
10. Johnston KC, Jiang YL, Li MS, et.al. Medical and neurological complications of ischaemic stroke: Experience from the RANTTAS trial. Stroke 1998; 29: 447-53.
11. Moulin T, Tatu L, Crepin-Leblond T, Chavot D, Berges S, Rumbach T. The Besancon stroke registry: An acute stroke registry of 2500 consecutive patients. Euro Neurol 1997; 38: 10-20.