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Original Article

Hypoalbuminemia is a predictor of mortality and rebleeding in peptic ulcer bleeding under proton pump inhibitor use

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KEYWORDS
Hypoalbuminemia;
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Background/purpose: Peptic ulcer bleeding remains a deadly disease, and a simple indicator of long-term outcomes is crucial. This study validated whether hypoalbuminemia and its related factors in patients with peptic ulcer bleeding can indicate long-term mortality and rebleeding under proton pump inhibitor use.
Methods: The prospective cohort study enrolled 426 patients with peptic ulcer bleeding who had high risk stigmata at endoscopy and had received endoscopic hemostasis. They were divided into 79 patients in the hypoalbuminemia group (Hypo-AG, serum albumin <28 g/L), 135 in the marginal hypoalbuminemia group (Margin-AG, serum albumin 28–34.9 g/L), and 212 in the normal albuminemia group (Normal-AG, serum albumin ≥35 g/L). Each subject received 72-h of intravenous infusion and then the oral form of proton pump inhibitors and were monitored for 84 days to assess all-cause mortality and recurrent bleeding.
Results: The primary outcome of all-cause mortality rates were increased in a stepwise fashion in a trend from Normal-AG, Margin-AG, to Hypo-AG (0–28th day: 1.9%, 2.2%, 12.8%, $p < 0.001$; 29th–84th day: 2.5%, 8.0%, 10.6%, $p < 0.01$). The secondary outcome of recurrent bleeding rates were also increased in the same fashion (0–28th day: 6.4%, 15.4%, 24.6%, $p < 0.001$; 29th–84th day: 0%, 3.0%, 4.2%, $p = 0.01$). Abnormal albuminemia was <30 g/L related to

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hemoglobin levels <70 g/L, nosocomial bleeding, cirrhosis, age ≥70 years, shock, and ulcer size ≥1.0 cm independently ($p < 0.05$).
Conclusion: Hypoalbuminemia in patients with peptic ulcer bleeding can be an alarm indicator of all-cause mortality and recurrent bleeding in a long-term follow-up situation under proton pump inhibitor use (NCT01591083).

Introduction

Peptic ulcer bleeding is the most common gastrointestinal emergency and is a deadly disease. In addition to rebleeding, comorbidity is also a risk factor leading to mortality.[1–4] With advances in endoscopic hemostasis and high potency acid suppression agents, the prognosis of peptic ulcer bleeding has been altered in the past couple of decades.[5–7] However, the mortality rate still remains in a range of approximately 2%–6%.[4,7,8] Therefore, the use of validated prognostic scales to risk stratify patients with peptic ulcer bleeding has been advocated.[9] There are many scores intended to predict outcomes of peptic ulcer bleeding.[4,10–12] However, it is crucial to find an easy to obtain score like a simple blood test. The AIMS65 score includes the serum albumin level, and it has been shown to be an important predictor of short-term intra-hospital mortality in upper gastrointestinal bleeding.[12,13] However, this score is based on analysis of data from both variceal and non-variceal upper gastrointestinal bleeding. There is no doubt that the serum albumin level,[14] which is associated with cirrhosis, is one of the parameters that can be used to predict mortality after variceal bleeding. Nevertheless, it is of importance to validate whether a low serum albumin level by itself can be a simple indicator of rebleeding and mortality due to peptic ulcer bleeding. Moreover, the reason why a low serum albumin level can be a predictor has not been well explored as yet.

In this study, a large-scale comparison of mortality rates in a long-term follow-up between patients with different serum albumin levels was prospectively conducted. It was presumed that our data will be helpful with regard to identifying patients at risk of mortality and rebleeding and answering why hypoalbuminemia can be a predictor in cases of peptic ulcer bleeding under contemporary treatment strategies.

Patients and methods

Patients and study design

This prospective observational cohort study was conducted in the inpatient wards of National Cheng Kung University Hospital, a tertiary healthcare center in Tainan City, Taiwan. The research and ethics committee of the hospital approved the study design (ER-100-008 and trial registration identifier: NCT01591083, ClincalTrials.*gov*). All participants were enrolled after giving written informed consent. A schematic flow chart of the study protocol is shown in Fig. 1. The work described has been carried out in accordance with declaration of Helsinki.

Eligible participants included patients ≥20 years who had undergone gastroscopy due to bleeding peptic ulcers with major stigmata of a recent hemorrhage including Forrest class Ia, Ib, IIa, and IIb. [15] All of the participants were given one or a combination of endoscopic therapies, including a local injection of diluted epinephrine 1:10000, a bipolar heated probe, argon plasma coagulation, band ligation, or hemoclip therapy until cessation of active bleeding or achievement of co-aptive coagulation.[16,17]

Patients were excluded if they had tumors, Dieulafoy lesions, esophageal ulcers, esophageal varices or mechanical factor-related bleeding (e.g., gastrostomy tube induction), hypersensitivity to esomeprazole or pantoprazole, or had previously participated in the study.

Patients were enrolled after successful endoscopic hemostasis and immediately received an 80 mg loading dose of intravenous esomeprazole (Nexium®, AstraZeneca AB, Södertälje, Sweden). The patients then received three days of continuous high-dose (8 mg/h) intravenous esomeprazole as therapy and then received 40 mg oral esomeprazole once or twice daily for the first 2 weeks. Subsequently, all patients received an oral proton pump inhibitor once daily for at least the following 8 weeks.[5,6] Patients who took clopidogrel received the same dose and duration of intravenous and oral pantoprazole (Pantoloc®, Takeda, Singen, Germany) therapy.[18] Patients who took warfarin or antiplatelet therapy discontinued such medication for three days after primary endoscopy.[9,19]

In Fig. 1, all enrolled patients were divided into the hypoalbuminemia group (Hypo-AG), the marginal hypoalbuminemia group (Margin-AG), and the normal albuminemia group (Normal-AG) based on the serum albumin level on arrival, <28 g/L, 28–34.9 g/L, and ≥35 g/L, respectively.[14] Patients who were lost to follow-up were excluded from the analysis of the primary and secondary outcomes.

The AIMS65 score and co-morbidities were evaluated according to relevant studies.[10,12,20] Nosocomial bleeding was defined as peptic ulcer bleeding that developed more than 24 h after admission. Ulcer size was estimated with biopsy forceps, with fully opened cups being 6 mm in diameter (FB-25K-1, Olympus, Tokyo, Japan).

Outcome measures for all-cause mortality and rebleeding within 84 days

All patients except those who expired regularly returned to out-patient clinics for at least 84 days for a clinical manifestation review and to monitor outcomes in hospital and

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