RE: Early application of haemostatic powder added to standard management for oesophagogastric variceal bleeding: a randomised trial

We read with interest the article by Ibrahim *et al*, which describes a randomised controlled trial (RCT) of early endoscopy with Hemospray within 2 hours of admission versus 'early elective endoscopy' at 12–24 hours for acute variceal bleeding (AVB).[1]

We would like to make comments that relate to the internal and external validities of the study. The article indicates that participants consented and were randomised following admission with suspected AVB on the basis of probable underlying liver cirrhosis and fresh blood on nasogastric lavage. However, the article also described how 19 patients were excluded from the trial at endoscopy before randomisation. As the intervention was to undergo an immediate endoscopy, we cannot understand how this could have been the case. Accordingly, contrary to figure 1 in the article, these 19 patients must have been randomised before exclusion.

This has important implications. To be adherent to standard RCT methodology, the specific reasons for exclusion, the arm from which exclusion occurred and the outcomes for these participants should be clearly described (Consolidated Standards of Reporting Trials statement 2010).[2] Furthermore, these individuals should have been included in an intention-to-treat (ITT) analysis. An ITT analysis constitutes an analysis of results based on the initial random allocation of each participant and not on the treatment they actually receive. When ITT analysis is not applied or is applied incorrectly, it can lead to bias.[3]

Mitchell *et al* have already given comment about the low systolic blood pressure within the composite definition of 'clinical haemostasis'.[4] We would like to draw further attention to the fact that 12/30 (40%) of patients with clinical haemostasis in the standard treatment arm died at or before the 6-week follow-up

and that all of them had evidence of active bleeding at endoscopy.

As highlighted by Mitchell *et al*, this mortality rate is in excess of that reported elsewhere.[4] For example, a large retrospective audit of outcomes in 526 patients presenting with AVB in over 200 UK centres reported a mortality at day 30 of 15%, despite only two-thirds of patients undergoing a therapeutic procedure within 24 hours.[5] Ibrahim *et al* are clear that transjugular intrahepatic portosystemic shunts were not available to child B and C patients in this study, and the use of Sengstaken tubes and intensive care is unreported.[1] This is in contrast with UK practice and may partly explain the differences in mortality.[6] However, Gabo *et al* describe an in-hospital mortality of 9% (although over a shorter time frame) in patients presenting with AVB in Egypt, which suggests other factors may be implicated.[7]

Ibrahim *et al* make an exciting contribution towards describing and testing a simple endoscopic procedure that could improve outcomes for patients admitted with AVB. However, the high mortality in the standard care arm and the lack of an ITT analysis that includes all randomised participants should be considered when interpreting its impact.

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