

Prophylactic Erythromycin in Acute Upper Gastrointestinal Bleeding: Moving Forward in Improving Endoscopic Efficacy

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In the management of upper gastrointestinal bleeding (UGIB), successful endoscopic hemostasis, together with pharmacotherapy, has been proved to improve clinical outcomes, including rebleeding rates and mortality.^[1] However, effective endoscopic therapy is dependent on adequate visualization of the gastrointestinal mucosa to identify the culprit source of bleeding. Active hemorrhage and large blood clots retained in the stomach can impede visualization and prevent adequate endoscopic evaluation. The inability to sufficiently visualize the gastric fundus in the setting of acute UGIB has been implicated with significant morbidity and bleeding-related mortality.^[2]

Given the importance of effective endoscopic hemostasis, the use of promotility agents to clear the stomach of residual blood pooling and clots before endoscopy has been studied.^[3] Erythromycin, a macrolide antibiotic that also acts a motilin receptor agonist, is known to induce gastric emptying. Early administration of erythromycin before endoscopy in acute UGIB has repeatedly been shown to decrease the need for second-look endoscopy.^[3-5] Other clinical outcomes such as endoscopic visualization, blood transfusions, hospital stay, procedure duration, and mortality have been equivocal.

In this issue, Theivanayagam *et al.*, have performed the most comprehensive meta-analysis to date evaluating the effectiveness of erythromycin in the management of upper gastrointestinal bleeding.^[6] In their analysis, the administration of erythromycin before endoscopy in patients with upper gastrointestinal bleeding led to significant improvements in gastric mucosa visualization (odds ratio, 3.43; $P < 0.01$) when compared with no erythromycin. In addition, the authors showed that erythromycin provides additional benefits, including decreasing the need for a second endoscopy, reducing the number of blood transfusions, and shortening

the length of hospitalization. Among the clinical outcomes measured, the study only failed to show that erythromycin led to shorter endoscopy procedure time. Notably, mortality rates were not addressed. This is probably because many of the individual randomized, controlled studies did not report mortality data, and those that did were often underpowered to detect such a difference.

This meta-analysis contributes to the growing body of evidence that prophylactic erythromycin should be strongly considered in patients with acute UGIB. Erythromycin has potential benefit with regard to endoscopy with no clear detrimental sequelae. The drug is safe and generally well tolerated, with no randomized controlled trials reporting any adverse effects in patients who were given the antibiotic. Furthermore, a cost-effectiveness study found that the strategy of infusing erythromycin before endoscopy in UGIB was cost-effective – as it was both less expensive and resulted in higher quality-adjusted life year – when compared with non pre-medicating regimen.^[7]

So should we routinely administer erythromycin in all patients with UGIB? Probably not. Among patients who present with UGIB, only a small percentage are likely to have a stomach full of blood necessitating gastric emptying before endoscopy. In the five randomized, controlled trials that found a significant improvement in endoscopic visualization with prophylactic erythromycin, only patients presenting with active hematemesis or those who had blood seen on gastric lavage were enrolled.^[8-12] These select patients are the most likely ones to have residual blood pooling in the stomach and would gain the most benefit from erythromycin-induced gastric emptying before endoscopic evaluation. This approach is consistent with the recommendations outlined by the International Consensus group who do not endorse the routine use of promotility agents to increase diagnostic yield of endoscopy.^[1]

Although the evidence for erythromycin is quite convincing, there are still some unsettled questions that remain. The optimal pre-endoscopic protocol for administration of erythromycin in UGIB is unknown. The ideal timing of erythromycin before endoscopy, dosage of erythromycin, duration of infusion, and its use in conjunction with other potential techniques to clear the stomach have not been rigorously examined. Many of the included studies differ with regard to these characteristics – properties that could

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	Quick Response Code:
	Website: www.saudijgastro.com
	DOI: 10.4103/1319-3767.118109

play an important role in erythromycin's impact on clinical outcomes. To date, much of the focus on erythromycin has been its ability to improve endoscopic visualization, a largely subjective measure. However, more meaningful and relevant clinical endpoints may be the frequency of identifying culprit bleeding sources and utilizing hemostasis techniques. These are the truest measures of endoscopic therapy's role in UGIB. Future studies focusing on these parameters are needed.

There may also be other nonpharmacologic tools to help the endoscopist achieve successful endoscopic hemostasis in acute UGIB. For instance, nasogastric lavage has been shown to be effective in improving visualization of the fundus.^[13] When nasogastric lavage was compared with prophylactic erythromycin before endoscopy in UGIB, there were no differences found in any outcome, including satisfactory stomach visualization, need for second endoscopy, number of blood transfusions, or mortality between the two groups.^[14] However, nasogastric tube placement is invasive and is widely considered to be one of the most painful and uncomfortable procedures for patients.^[15] In addition, albeit rare, complications including aspiration, pneumothorax, and gastrointestinal perforation can occur from this procedure.

Newer endoscopic devices may provide adjunctive benefit or may potentially even obviate the need for pre-endoscopic management of acute UGIB. A wide-channel therapeutic endoscope with two working channels is capable of completely evacuating the stomach of blood clots and gastric contents and thereby provide optimal conditions for endoscopic hemostasis.^[16] Another potential device is the BioVac (US Endoscopy, Mentor, OH, USA), a mechanical suction device that can be attached to most standard endoscopes to increase suction power and provide improved irrigation and lavage. In a feasibility study, the use of the BioVac device was able to enhance visualization of the colonic mucosa in several cases of severe lower gastrointestinal bleeding.^[17] One can surmise that such a device could be used analogously to improve visualization of the gastric mucosa in acute UGIB.

Advances in technology and device development may ultimately provide newer and more efficient tools for mucosal visualization in UGIB. In the meantime, erythromycin continues to be a cheap, safe, convenient, and effective strategy to substantially increase our ability to perform early, successful endoscopic hemostasis in UGIB. The judicious use of prophylactic erythromycin in patients presenting with acute UGIB should be encouraged.

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