Is Glucagon Effective for Relieving Acute Esophageal Foreign Bodies and Food Impactions?

TAKE-HOME MESSAGE

Glucagon is not associated with improved treatment success of esophageal foreign body and food impaction compared with placebo but does have a higher rate of adverse events.

METHODS

DATA SOURCES

Meta-analysis authors identified studies from PubMed, the Cumulative Index of Nursing and Allied Health, Latin American and Caribbean Health Sciences Literature, Scopus, the Cochrane Database of Systematic Reviews, and the Cochrane Central Register of Controlled Trials from the date of database creation to March 2018, with no language or age restrictions.[1] Authors also reviewed references of included studies and review articles.

STUDY SELECTION

Inclusion criteria consisted of all retrospective, prospective observational, and randomized controlled trials evaluating glucagon for relief of acute esophageal food impactions and foreign bodies when compared with a comparator group. Authors excluded case reports, case series, and studies in abstract form only. Two reviewers independently screened titles and abstracts. Articles meeting initial screening criteria were reviewed as full-text articles. Authors included studies meeting all eligibility criteria, with discrepancies resolved by consensus or with the inclusion of a third author.

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Editor's Note: This is a clinical synopsis, a regular feature of the *Annals'* Systematic Review Snapshot (SRS) series. The source for this systematic review snapshot is: **Peksa GD, DeMott JM, Slocum GW, et al. Glucagon for relief of acute esophageal foreign bodies and food impactions: a systematic review and meta-analysis. *Pharmacotherapy*. 2019;39:463-472.** https://doi.org/10.1002/phar.2236.

Results

Glucagon for relief of esophageal obstruction or impaction.

Outcome	No. of Studies (No. of Patients)	OR or RD (95% CI)	Evidence Quality (GRADE)	Heterogeneity (I^2), %
Success rate	5 (1,185)	OR 0.90 (0.69 to 1.17)	Low	14
Overall adverse events	3 (213)	RD 0.18 (0.03 to 0.33)	Moderate	62
Vomiting	3 (213)	RD 0.07 (−0.03 to 0.17)	Moderate	59

OR, Odds ratio; *RD*, risk difference; *CI*, confidence interval; *GRADE*, Grading of Recommendations Assessment, Development and Evaluation.

A total of 1,988 studies were identified, and after removal of duplicates, 1,842 abstracts were reviewed, with 14 selected for full-text review. Five studies, comprising 23 study sites and 1,185 patients, were selected for the final analysis.[3-7] Four studies were conducted in the emergency department (ED) setting,[4-7] and 1 was conducted in 4 otolaryngology clinics.[3] Two

DATA EXTRACTION AND SYNTHESIS

Two authors independently extracted data from included studies. The primary outcome was treatment success as defined by the original study (ie, subjective symptom relief or radiographic imaging confirmation). Secondary outcomes included overall rates of adverse events, vomiting, and time to impaction relief. Authors measured dichotomous variables with odds ratios or risk differences and 95% confidence intervals and assessed heterogeneity with the I^2 statistic. A fixed-effects model was used in the absence of significant heterogeneity; otherwise, a random-effects model was used. Authors analyzed adverse events reported per dose received rather than per patient, using the most conservative per-patient estimate. Post hoc sensitivity analysis was completed when studies reported posttreatment endoscopic findings of possible treatment success. Two independent authors evaluated risk of bias with the Cochrane Risk of Bias Tool and used the modified tool for nonrandomized studies. They assessed evidence quality for each outcome with the Grading of Recommendations Assessment, Development and Evaluation approach, with discrepancies resolved through consensus and inclusion of a third author if necessary.[2]

studies were randomized controlled trials with a placebo group,[3,4] whereas 3 were retrospective studies with a control group.[5-7] Mean patient age ranged from 5.1 to 59.5 years, and 63.7% were male patients. Most studies used glucagon at 1 mg, with possible repeated dosing. One study used no simultaneous medications with glucagon,[5] 2 studies administered concomitant nitroglycerin or benzodiazepines to a proportion of patients,[6,7] 1 study provided diazepam to all patients,[3] and 1 study administered 2 to 3 ounces of water to all patients.[4] Four studies reported treatment success with clinical signs and symptoms,[3,5-7] whereas one study used radiographic imaging.[4] Two studies reported esophageal abnormalities by treatment group, and they were similar.[5,7] One study found esophageal abnormalities in 37.2% of patients,[3] whereas another found esophageal ring, stricture, web, or narrowing in 30.9%; erosive esophagitis and stricture in 27.7%; and eosinophilic esophagitis in 11.1%.[6]

Treatment success did not differ between the glucagon group and control group (Table). Overall adverse events occurred more frequently in patients receiving glucagon (15% for glucagon versus 0% for comparators) and most commonly consisted of vomiting and retching. Other adverse events included hypotension and lightheadedness. All studies were at overall low risk of bias. One randomized controlled trial was at moderate risk of bias in regard to blinding.[4] All retrospective studies were at moderate risk of bias for confounding. Based on the Grading of Recommendations Assessment, Development and Evaluation approach, evidence certainty was low for the primary outcome and moderate for secondary outcomes. Sensitivity analysis revealed no difference in the primary outcome.

Commentary

Esophageal foreign body impaction occurs when an object or piece of food becomes lodged in the esophagus. This can result in inability to tolerate oral intake, airway obstruction, and esophageal necrosis and perforation, prompting patients to present to the ED for evaluation and management.[8,9] Although endoscopy is the definitive modality for evaluation and management, medical management is often attempted beforehand.[8,9] Glucagon, typically administered in doses of 0.5 to 1.0 mg, is thought to reduce lower esophageal sphincter resting pressure.[10,11] Studies evaluating glucagon are small and demonstrate conflicting results, and the medication may be associated with adverse events, prompting this review.[11-15]

This systematic review and meta-analysis sought to evaluate the efficacy and safety of glucagon for acute esophageal foreign bodies and impaction.[1] It differs from previous systematic reviews by using a more comprehensive search strategy, including only studies with a comparator group, and being the first to perform a meta-analysis.[12,13] Previous studies have suggested efficacy with glucagon in relieving acute esophageal food impaction but did not include a comparator group.[14,15] Consequently, this present meta-analysis found no difference in treatment success with glucagon when a comparator group was used.[1] The meta-analysis also found increased risk of adverse events, of which the most common was vomiting,[1] which can increase the risk of aspiration and esophageal perforation.[16]

This meta-analysis has several limitations.[1] The included retrospective

studies did not control for concomitant medication administration, and they did not standardize care in the comparator groups. However, these studies were at low risk of bias and of overall good quality. Studies used different definitions of treatment success, including radiographic findings and symptomatic relief. Different types of foreign body impaction (eg, food, objects) were included, but this reflects current practice. Rates of underlying esophageal pathology were not included in all studies. Studies also did not control for time to treatment, which may have affected outcomes, but similar probability of occurrence between groups and the large sample sizes do not make this likely. Only 3 studies reported adverse events, and they were not powered to assess this outcome.

In accordance with the current data, glucagon does not appear to improve the relief of esophageal impaction compared with placebo (30.2% versus 33.0%, respectively) and possesses a higher rate of adverse events (15.0% versus 0%, respectively). Future randomized controlled trials should be conducted that evaluate different glucagon dosing strategies, control for concomitant medication administration, are powered to assess for adverse events, and determine the effects in different populations.

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