Relation of viscous lidocaine combined with propofol deep sedation during elective upper gastrointestinal endoscopy to discharge

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ABSTRACT

Fusing topical pharyngeal anesthetics (TPAs) to intravenous sedation during esophagogastroduodenoscopy (EGD) has been controversial. This double-blind, randomized, placebo-controlled trial assessed the association of TPA with patient recovery time, post-EGD to discharge. Supplementary aims were to determine the association of TPA with patient and practitioner satisfaction (both measured on a 100-mm visual analog scale), total propofol dose, and side effects. The study included 93 patients (mean age 53.8 years, range 44–67; 37 men and 56 women) undergoing elective EGD at a single academic medical center from September 2015 to October 2016. Urgent or therapeutic EGDs were excluded. Interventions were 7.5 mL 2% lidocaine viscous solution and 7.5 mL placebo solution (3% methylcellulose). There were no statistically significant differences between the lidocaine ($n=46$) and placebo ($n=47$) groups with respect to recovery time (42 ± 17.8 vs 39 ± 15.9 minutes; $P=0.23$), procedure time (6.5 ± 2.7 vs 7 ± 3.6 minutes; $P=0.77$), endoscopist satisfaction (83.2 ± 24.4 vs 77 ± 27.7 , $P=0.23$), patient discomfort (16.6 ± 19.8 vs 24.0 ± 29.7 , $P=0.37$), or total propofol administered (2.3 ± 1.3 vs 2.3 ± 1.0 mg/kg, $P=0.55$). Compared to placebo, topical viscous lidocaine does not appear to delay recovery time or adversely affect sedation-related outcomes.

KEYWORDS Lidocaine; pharyngeal anesthetics; propofol; sedation; upper gastrointestinal endoscopy; viscous xylocaine

Propofol is increasingly utilized for deep sedation during esophagogastroduodenoscopy (EGD) because of its rapid onset of action, relatively rapid recovery time, and improved satisfaction among endoscopists.¹

Topical pharyngeal anesthetics (TPAs) used in conjunction with intravenous sedatives may facilitate endoscopy and improve patient tolerance by diminishing the gag reflex.² The utility of adding TPA to intravenous sedation remains controversial.^{3–5}

TPAs are not intrinsically benign and can result in occasional severe adverse effects, such as methemoglobinemia,^{6,7} anaphylactic reactions,⁸ and aspiration.⁹ This randomized, double-blind, placebo-controlled study examined the effect of viscous lidocaine on time to patient discharge after propofol sedation for EGD. We hypothesized that the use of lidocaine in conjunction with

propofol during elective EGD might delay the time to discharge of patients. As secondary outcomes, we evaluated the effect of viscous lidocaine on endoscopic intubation conditions, patient comfort, total dose of propofol administered, respiratory side effects, acute aspiration events, and gagging events (a clinical measure reflecting the ease of endoscope intubation).¹⁰

METHODS

This double-blind, randomized, placebo-controlled trial was conducted at a single academic medical center from September 2015 to October 2016 (clinicaltrials.gov registry #NCT02507440). Patients provided written informed consent for this study. All study procedures were reviewed and approved by the Mary Imogene Bassett institutional review

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Preliminary data for this study were presented as a poster presentation at the American College of Gastroenterology annual meeting, Las Vegas, NV, October 14–19, 2016.

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board. This research was conducted in accordance with the ethical principles of the Belmont report and requirements of the Code of Federal Regulations (45 CFR 46).

Eligible patients were individuals aged 18 to 75 years scheduled for an elective EGD. Exclusion criteria included intolerance to lidocaine or propofol, impaired swallowing reflex, current pregnancy, dementia, and urgent, emergent, or therapeutic EGDs. Only patients undergoing EGD within the endoscopy suite were included; per institutional protocol, only patients with American Society of Anesthesiologists physical status classification 1 to 3 receive procedures in the endoscopy suite and thus patients with a status of 4 or higher were excluded.

A blinded research nurse (the “observer”) recruited and obtained informed consent on all participants. Subjects were then randomly assigned to the treatment or placebo group in a 1:1 ratio according to a randomization schedule. This schedule was prepared by the study statistician using SAS version 9.3 and was shared with the study pharmacist.

Five minutes prior to intravenous sedation, patients were asked to gargle 7.5 mL of either 2% lidocaine viscous solution or 7.5 mL of placebo for a minimum of 2 minutes (timed by the observer) and then swallow. The placebo solution was made from 3% methylcellulose. Both lidocaine and placebo solutions, prepared by the pharmacist, were cherry flavored and sweetened with a small quantity of saccharin to improve palatability. The characteristics of lidocaine and placebo were indistinguishable by an independent examiner. The solutions were administered via an oral syringe in the posterior pharynx by a certified registered nurse anesthetist.

Sedation was carried out by the administration of intravenous boluses of propofol by the certified registered nurse anesthetist under the supervision of a board-certified anesthesiologist. The propofol administration protocol was a 0.5–1.0 mg/kg bolus dose, repeated as needed to maintain adequate sedation. Sedation was evaluated by lack of response to verbal stimuli. Oxygen saturation was monitored throughout the procedure; any decrease below 90% was considered cause for possible intervention with positive-pressure mask ventilation. Capnography was measured continuously in all patients as an aid to diagnosing apnea or airway obstruction. The EGD was conducted according to standard protocols by board-certified gastroenterologists.

Discharge criteria were standardized using the widely accepted Aldrete postanesthesia scoring system,¹¹ which incorporates aspects of patient activity, respiration, heart rate, consciousness, oxygen saturation, pain, bleeding, and nausea/vomiting. Patients had to achieve an Aldrete score of 8 or higher to be discharged. The Aldrete scoring system was utilized as an objective way to assess discharge readiness while preserving blinding to treatment group.

The primary objective in this study was to compare the time from arrival to the postanesthesia care unit to discharge (“recovery time”) for TPAs combined with propofol sedation versus propofol alone. Secondary endpoints included the gastroenterologist’s satisfaction with endoscope insertion, observed patient discomfort during the procedure, and patient pain ratings. Study endpoints

were collected via questionnaires filled out by the blinded gastroenterologist and the blinded observer and by electronic medical record review by the blinded observer.

Recovery time was collected from the electronic medical record and was calculated as the time of arrival into the postanesthesia care unit until the patient was discharged. The total procedure time was calculated from the time of the first attempt for endoscope insertion by the gastroenterologist to the time of endoscope extubation. Total propofol dosage and demographic information including age, gender, and race were also collected.

After extubation, the gastroenterologist reported satisfaction with the scope insertion based on a standard 100-mm visual analog scale that ranged from 0 (*not at all satisfied*) to 100 (*completely satisfied*). The gastroenterologist was also asked to guess whether lidocaine or placebo had been used during the procedure.

The blinded observer, who witnessed the entire EGD, assessed patient discomfort during the procedure (measured on a similar visual analog scale, ranging from *no observed discomfort* [0] to *extreme observed discomfort* [100]), the number of times the patient gagged, and the number of endoscope insertion attempts by the gastroenterologist. Any adverse events were also recorded. Postprocedure pain scores were collected from the patient upon arrival into the recovery suite and at discharge using the Wong Baker FACES pain scale, which uses facial expressions to self-denote pain ranging from 0 (*no hurt*) to 10 (*hurts the worst*).¹² The follow-up period was limited to the patient’s time in the postanesthesia care unit until discharge.

Sample size was calculated based on a pilot study ($n = 26$ subjects) of elective EGD patients receiving lidocaine pharyngeal anesthetic along with propofol sedation. The mean recovery time for lidocaine-treated patients was estimated to be 52.1 (standard deviation = 19.7) minutes. A difference in recovery time of 10 to 15 minutes between the lidocaine and placebo groups was considered clinically meaningful, based on operating room utilization and the number of patients receiving EGDs per day. Therefore, using a time difference of 12.5 minutes, an alpha of 0.05, and a sample of 50 subjects in each group (100 total) would provide statistical power of 0.88 for the main outcome of recovery time. Secondary endpoints, such as adequacy of sedation, propofol dose, and adverse events, were considered exploratory and therefore no power calculations were performed related to these outcomes.

Differences between treatment groups on categorical variables (gender, race) were tested using chi-square. Due to skew in the distribution of recovery times, comparison between the lidocaine group and the control group was carried out using the Wilcoxon rank sum test. Similarly, because the distributions of several other continuous variables were skewed, differences in values between treatment groups were also tested using the Wilcoxon rank sum test. All statistical analyses were performed using SAS 9.3.

RESULTS

From the initial 93 patients recruited, two subjects who underwent therapeutic procedures during the EGD (break up of adhesions and dilation of Schatzki’s ring) were excluded.

Figure 1. Flow diagram of included and excluded subjects.

One subject was withdrawn after the procedure was aborted due to stomach contents. Three subjects were never given study drug per pharmacist (see [Figure 1](#) for exclusions).

A total of 93 subjects (37 men and 56 women) were included in this analysis. The mean age was 53.8 years (standard deviation 15.1 years). The treatment groups were well balanced, with 46 subjects in the lidocaine group and 47 subjects in the placebo group. Among these 93 included subjects, there were six adverse events: three events in the lidocaine group and three in the placebo group. The minor adverse events were described as vomiting, coughing, desaturation, and hiccups. One case of severe desaturation occurred, causing the procedure to be aborted by the nurse anesthetist (lidocaine group). The subject involved in this case was excluded from the outcomes analysis. A summary of the enrollment process is presented in [Figure 1](#).

There were no meaningful differences in patient characteristics between treatment groups see ([Table 1](#)), indicating the adequacy of subject randomization. Most subjects in both groups were women and predominantly Caucasian. Blinding was also maintained, as demonstrated by the lack of provider accuracy in predicting treatment group.

There was no significant difference between the lidocaine and placebo groups with respect to recovery time ([Figure 2](#)); the median (interquartile range) recovery times in the lidocaine group and placebo group were 39 (32–48) minutes and 37 (30–43) minutes, respectively ($P=0.23$). There were also no statistically significant differences between the lidocaine and placebo groups with respect to procedure time, physician satisfaction, patient discomfort, total amount of propofol administered, or number of gag reflexes ([Table 1](#)). Ninety-eight percent (90

out of 92) of patients had their esophagus intubated with the endoscope by the proceduralist with one attempt; two patients required two attempts. Pain scores of zero were reported by all subjects at the first and last recordings in recovery.

DISCUSSION

Should conscious sedation augmented with topicalization be a standard of care in upper gastrointestinal endoscopy? Some practitioners claim it to be a standard.^{13–15} A recent meta-analysis examining TPA prior to EGD demonstrated both improved ease of endoscope insertion and patient tolerance.¹⁶ Ghallab et al, in a prospective double-blinded study, compared lidocaine gel 15 g as adjunct to propofol sedation versus only propofol sedation.¹⁷ Lidocaine 40 mg was also added to propofol in both groups. It was concluded that lidocaine gel decreased propofol consumption, decreased recovery time, and improved patient comfort. It also improved procedural tolerance with overall decreased cost.¹⁷ Our study, however, failed to find statistically significant differences in recovery time. Whether the intravenous lidocaine was a significant factor is a plausible explanation for the conclusions of Ghallab et al.

Administration of topical lidocaine as an adjunct to intravenous propofol remains controversial.¹⁸ One study noted that the routine use of TPA in patients “adequately” sedated (not clearly defined) with propofol was not supported by the data obtained.¹⁹ The study measured the ease of intubation but did not report time to discharge. A reduction in gag events was reported in the topical lidocaine group as a primary endpoint reflecting ease of endoscope intubation. In addition, it was stated that TPA may be indicated in “selected” patients.

Table 1. Comparisons of patient characteristics and study endpoints, lidocaine versus placebo groups

Variable	Total sample (n = 93)	Lidocaine (n = 46)	Placebo (n = 47)	P value
Male	37 (40%)	20 (44%)	17 (36%)	0.47
Female	56 (60%)	26 (56%)	30 (64%)	
Age (years): mean (SD)	53.8 (15.1)	55.0 (14.2)	52.7 (16.0)	0.57
Median (IQR)	57 (44–67)	57.5 (46–67)	55 (41–66)	
White	91 (98%)	44 (96%)	47 (100%)	0.24
Black	2 (2%)	2 (4%)	0	
Recovery time (min): mean (SD)	40.6 (16.9)	42.3 (17.8)	39.0 (15.9)	0.23
Median (IQR)	38 (31–46)	39 (32–48)	37 (30–43)	
Procedure time (min): mean (SD)	6.7 (3.2)	6.5 (2.7)	7 (3.6)	0.77
Median (IQR)	6 (4–9)	6 (5–8)	6 (4–9)	
Physician satisfaction: mean (SD)	80.2 (26.2)	83.2 (24.4)	77.4 (27.7)	0.23
Median (IQR)	89 (77.5–99)	89 (82–100)	87 (67–98)	
Patient discomfort: mean (SD)	20.4 (25.5)	16.6 (19.8)	24.0 (29.7)	0.37
Median (IQR)	10 (1.8–31)	9 (1.5–28)	12 (2–35.5)	
Propofol administered (mg/kg): mean (SD)	2.3 (1.1)	2.3 (1.3)	2.3 (1.0)	0.55
Median (IQR)	1.9 (1.6–2.7)	1.9 (1.5–2.5)	2.0 (1.6–2.7)	
Times patient gagged during procedure: mean (SD)	1.9 (2.8)	1.6 (2.7)	2.1 (2.9)	0.42
Median (IQR)	0 (0–3)	0 (0–2)	0 (0–4)	
Provider-predicted treatment				0.87
Lidocaine	53 (58%)	27 (60%)	26 (55%)	
Placebo	35 (38%)	16 (36%)	19 (41%)	
Unknown	4 (4%)	2 (4%)	2 (4%)	

IQR indicates interquartile range.

This study implied that amnesia may be more important than ease of intubation, demonstrating the different objectives that various specialties have in patient care during EGD.¹⁹

A recent Australian review concluded that propofol sedation is widely used for EGD in Australia. According to the review, the risk of methemoglobinemia is small and is “possibly” an increased risk of aspiration with pharyngeal spray.²⁰ Our study observed no increased risk of aspiration in the immediate perioperative period in the study group compared to the placebo group. We did not follow up for any delayed evidence of pulmonary aspiration.

Use of intravenous or topical lidocaine as an adjunct to induction agents for general anesthesia is common in anesthesiology. Attenuating the adverse hemodynamic response to orotracheal intubation utilizing intravenous or laryngotracheal-administered lidocaine remains controversial,^{19,21} establishing the controversy between viscous lidocaine and spray lidocaine.

Using gag response as a measure of ease of endoscopic intubation has been documented by several studies.³ A recent Swiss study concluded that lidocaine spray for EGD under sedation revealed no statistical advantage over placebo in measuring ease of endoscopic intubation.³ There was no mention

of time to discharge. The study stated that “routine” use of pharyngeal anesthetics in patients “adequately” sedated with propofol was not indicated and that Swiss endoscopists may prefer to omit topicalization and rely on deep sedation.

One major strength of our study was that all members of the study team were blinded. The fact that the endoscopists could not accurately predict whether viscous lidocaine or placebo was administered is *prima facie* that blinding was successful. Another strength was that viscous lidocaine and placebo were cherry flavored to improve palatability and were indistinguishable based upon independent examination. The viscous lidocaine and placebo were also precisely delivered via a syringe, compared to a medicine cup. In addition, delivery of the drug was noninvasive and did not require a tongue blade or laryngoscope. Furthermore, the EGD was performed by experienced board-certified gastroenterologists.

Our study was limited by the fact that it was based in a single center, we did not perform subgroup analysis, and patients >75 years old who may be prone to complications from TPA were excluded. In addition, as per initial protocol and precedent in the literature, subjects were asked to gargle for 5 minutes by

Figure 2. Median recovery times (in minutes) for lidocaine and placebo groups.

the clock. Unfortunately, some patients could not gargle for 5 minutes and either expectorated some of the drug or swallowed it prematurely. All subjects did gargle for a minimum of 2 minutes. This could have affected the efficacy of viscous lidocaine. Patients were also not followed up after 24 hours for late development of aspiration. Finally, data on potentially confounding factors such as body mass index, obstructive sleep apnea, and exact American Society of Anesthesiologists physical status category were not collected; such factors might affect the efficacy of TPAs.

In conclusion, compared to placebo, topical viscous lidocaine does not delay recovery time, and our exploratory analysis showed no indication of adverse effects on short-term aspiration or other sedation-related outcomes. Use of viscous lidocaine during EGD might be recommended in cases where it is desired to limit the depth of propofol sedation, as in patients with pulmonary hypertension or low cardiac output states. Future studies are needed to assess the ideal clinical circumstances for use of viscous lidocaine during EGD.

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