Review

Lidocaine spray versus viscous lidocaine solution for pharyngeal local anesthesia in upper gastrointestinal endoscopy: Systematic review and meta-analysis

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Objectives: There are two major methods for local anesthesia by lidocaine before upper gastrointestinal endoscopy: simple spray and viscous solution. We aimed to assess the efficacy and safety by meta-analysis between these two methods.

Methods: We searched PubMed, EMBASE, the Cochrane Central Register of Controlled Trials, World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov databases through October 2019 to perform meta-analyses using random-effects models. The primary outcomes were participants’ pain/discomfort, satisfaction, and anaphylactic shock. Three reviewers independently searched for articles, extracted data, and assessed the risk of bias. We evaluated the certainty of evidence based on the Grading of Recommendations, Assessment, Development, and Evaluation approach. This study was registered in PROSPERO (CRD42020155611).

Results: We included seven randomized controlled trials (2667 participants). The participants’ pain/discomfort may be similar between the lidocaine spray and viscous solution [standardized mean difference 0.03, 95% confidence intervals (CI) −0.37 to 0.42; I² = 93%; low certainty of evidence]. The lidocaine spray probably increased participants’ satisfaction compared with the viscous solution (relative risk 1.22; 95% CI, 1.02 to 1.47; I² = 47%; moderate certainty of evidence). No anaphylactic shock occurred in four studies (low certainty of evidence). Four studies had high risks of selection bias.

Conclusion: The use of lidocaine spray for local anesthesia provided better satisfaction scores than the viscous solution, and both methods have the same effect with regards to the control of discomfort and pain. Further studies in large multicenter randomized controlled trials with a pre-registration protocol are needed.

Key words: endoscopy, lidocaine, oral sprays, systematic review, viscosity

INTRODUCTION

UPPER GASTROINTESTINAL (UGI) endoscopy is established as the gold standard for gastric cancer screening, and diagnosis of UGI diseases. 1 UGI endoscopy can reduce gastric cancer mortality. 2 However, intraoral endoscope insertion through the pharynx into the GI tract can cause severe discomfort and pain to the patients due to a strong gag reflex, especially procedures without conscious sedation. 3 More than 7 million UGI endoscopies are performed in the United States annually, 4 and approximately 12% of patients who underwent UGI endoscopy were concerned about the pain resulting from the procedure. 5 Pharyngeal anesthesia before UGI endoscopy contributes to reduce such pains and improves patients’ tolerance. 5,7 One of the most common local anesthesia used before UGI endoscopy is lidocaine, and it is provided in two forms: spray and viscous solution. These two forms have different characteristics: the spray is simple and easy to use but may stimulate the gag reflex. On the other hand, the viscous solution has a bitter taste, irritates the throat during swallowing, and the patient stores the solution in their pharynx for few minutes. 8 It remains unclear which method...
is better prior to endoscopy because no systematic review has been done. Herein, we aimed to investigate the efficacy and safety of lidocaine spray for pharyngeal local anesthesia in UGI endoscopy compared to viscous lidocaine solution.

METHODS

Protocol and registration

We registered our review protocol in PROSPERO (CRD42020155611). We conducted this systematic review according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement (Appendix S1).

Criteria for selecting studies to be included in this review

Type of studies

We included individual randomized controlled trials (RCTs). We excluded cross-over RCTs, cluster-RCTs, quasi-RCTs and non-RCTs. We included studies reported as full text, those published as abstract only, and unpublished data. There was no restriction with regard to publication language.

Type of participants

We included male and female participants who were ≥12 years old and who underwent an observational but not a treatment UGI endoscopy, regardless of the indication (e.g., screening, surveillance, diagnosis). We excluded participants with contraindications for UGI endoscopy and those with clinical evidence of hepatic encephalopathy.

Type of interventions and comparators

We included trials evaluating the effects of using lidocaine spray for pharyngeal local anesthesia in UGI endoscopy compared to viscous lidocaine solution. The intervention used was lidocaine spray to the pharynx or/and tongue by doctors or/and nurses. When the gag reflex was present and strong, we allowed the intervention to use additional lidocaine spray. The maximum dose of lidocaine was 5mg/kg. All participants underwent UGI endoscopy with a regular endoscope, and not with nasal or a magnifying endoscope. The comparator used was viscous lidocaine solution for pharyngeal local anesthesia, which was retained in the mouth without swallowing for approximately 3–5 min. Comparators that used lidocaine gel were included, whereas, candy or lozenge could not be included as comparators.

Types of outcome measures

The primary outcomes were as follows:

1. The mean score of the visual analog scale (VAS)/numeric rating scale (NRS) for participants’ pain/discomfort between the two UGI procedures. The lowest score corresponds to no pain/discomfort while the highest score corresponds to unbearable pain/discomfort; and
2. The proportion of participants who checked the highest satisfaction score; and
3. The proportion of participants who had anaphylactic shock.

The secondary outcomes were as follows:

1. The proportion of participants who showed the best tolerance scores as measured by the endoscopists; and
2. The proportion of participants who showed the easiest insertion scores as measured by the endoscopists; and
3. All adverse events defined by the author.

Search strategy to identify studies

Search resources

We searched the following electronic databases: CENTRAL (the Cochrane Central Register of Controlled Trials), MEDLINE via Ovid (1946 to October 2019), and EMBASE via PROQUEST (1974 to October 2019) (Appendix S2). We also searched the following registries: the World Health Organization International Clinical Trials Platform Search Portal (ICTRP), and ClinicalTrials.gov. We searched the reference lists of guidelines. We handsearched reference lists from trials selected. We considered duplicate published trials only in the final version.

Data collection and analysis

Selection of studies

Three review authors (JW, YI, and AT) independently screened the titles and abstracts of all studies identified by the search, and assessed eligibility based on a full-text review. We resolved disagreements by discussion and consulted the fourth review author (TK).

Data extraction and management

Three review authors (JW, YI, and AT) independently extracted the study characteristics from the included studies.
We extracted the following study characteristics: number of study centers and location, date of study, number of participants, proportion of male, and mean and standard deviation (SD) of age. We resolved discrepancies by a consensus. The fourth review author (YK) adjudicated the discrepancies and obtained a consensus. We attempted to contact the original author by e-mail to obtain further data.

**Assessment of risk of bias in the included studies**

Two review authors (JW and YI) assessed the risk of bias in two of the selected studies based on version 2 of the Cochrane risk-of-bias tool for randomized trials.15 We graded each of the domains in one of three categories (high risk, low risk, some concerns). We resolved any disagreements by discussion and consulted the fourth review author (TK and YK).

**Measures of treatment effect**

We calculated the relative risk (RR) with 95% confidence intervals (CIs) for the following binary outcomes: the highest satisfaction score, proportion of anaphylactic shock, the best tolerance score, and the easiest insertion score. We integrated the mean and SD of continuous variables according to the method described in the Cochrane handbook. 15 We calculated the standardized mean difference (SMD) with the 95% CI of the mean VAS/NRS score corresponding to the pain/discomfort felt by the participants due to the procedure. We summarized all adverse events according to the definition of each study. However, we did not conduct a meta-analysis.

**Dealing with missing data**

We tried to contact the original authors for missing data. When no outcome data were available, we calculated the outcome with the concept of the intention-to-treat (ITT).

**Assessment of heterogeneity**

We first assessed statistical heterogeneity with \( I^2 \) statistic (\( I^2 \) values of 0–40%: may not be important; 30–60%: may represent moderate heterogeneity; 50–90%: may represent substantial heterogeneity; and 75–100%: may represent considerable heterogeneity; or there is a \( P \)-value < 0.1 for the chi-squared test). When heterogeneity was identified (\( I^2 \) statistic >50%), we explored possible sources of heterogeneity using subgroup analysis.

**Assessment of reporting biases**

We searched trial registers (ICTRP and ClinicalTrials.gov) to identify trials that were registered but unpublished. When we included <10 studies in a pooled analysis, we did not perform a funnel plots analysis.

**Data synthesis**

We carried out the analysis using Review manager 5.3 (RevMan 2014; computer program) and use a random-effects model for the meta-analysis.

**Subgroup analysis and investigation of heterogeneity**

We planned the following prespecified subgroup analysis: participants’ gender (male or female), sedation (participants with or without sedation), and diameter of endoscope fiber (<9 or ≥9 mm).

**Sensitivity analysis**

We planned the following prespecified sensitivity analysis: (i) exclusion of studies which used imputed statistics; (ii) missing participants: best-best scenario, best-worst scenario, worst-best scenario; (iii) exclusion of studies which used anesthesia other than lidocaine spray at a total dose of 50 mg and viscous lidocaine solution at a total dose of 100 mg; (iv) exclusion of studies in which endoscopies were not only done by senior endoscopist but also by fellows; (v) exclusion of studies in which the difference in total dose of lidocaine between the spray and viscous groups was ≥70 mg;16 (vi) exclusion of studies which included participants aged 12–14 years.

**RESULTS**

**Search results**

**FIGURE 1 SHOWS** the article selection process. We searched a total of 218 records in October 23, 2019. We finally included seven trials with 2667 participants that compared lidocaine spray with the viscous lidocaine solution in the qualitative synthesis.17–23 Table 1 shows the summary of the characteristics of the included studies. We showed the risk of bias of each study in Figures 2 and 3 and Appendices S3–S7. Overall, four studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.17,18,21,23 We included five of the seven trials in the meta-analyses with primary and secondary outcomes.17,18,21–23
Primary outcomes

Mean score of VAS/NRS for participants’ pain/discomfort

Four studies reported participants’ pain or discomfort. Among them, three studies used a VAS, while one study used the 11-point NRS. There was little or no difference in the mean score of the VAS/NRS for the participants’ pain or discomfort between the lidocaine spray group and the viscous lidocaine solution group (four studies, 2462 participants): SMD 0.03; 95% CI, 0.37 to 0.42; I² = 93%; low certainty of evidence (Fig. 4).17,18,21,23

The proportion of participants who checked the highest satisfaction score

Four studies reported participants who checked the highest satisfaction score. Among them, two studies used a verbal rating scale, while one study used the Group Health Association of America (GHAA-9) questionnaire, and one study did not report a rating method. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution (four studies, 2381 participants): RR, 1.22; 95% CI, 1.02–1.47; I² = 47%; moderate certainty of evidence (Fig. 5).17,21–23

The proportion of anaphylactic shock

In both the lidocaine spray and viscous groups, no anaphylactic shock occurred (three studies, 2332 participants). The certainty of evidence for anaphylactic shock was low.

Secondary outcomes

The proportion of participants who showed the best tolerance score

Two studies reported participants who showed the best tolerance score. The lidocaine spray may result in an increase in the proportion of participants who showed the best tolerance score compared to the viscous lidocaine solution: RR, 1.25; 95% CI, 1.00–1.56; I² = 23%; low certainty of evidence (Fig. 6).17,23

The proportion of participants who showed the easiest insertion score

Two studies reported participants who showed the easiest insertion score. The evidence suggests that the lidocaine
spray results in little or no difference in the proportion of participants who showed the easiest insertion score compared to lidocaine solution: RR, 1.15; 0.76–1.73; I² = 52%; low certainty of evidence (Fig. 7).17,23

All adverse events

Three studies measured adverse events.17,18,21 One study reported no adverse events,18 and two studies reported adverse events (Table 2).17,21

Additional analyses

The prespecified subgroup analyses for the mean score of VAS/NRS for the participants’ pain or discomfort revealed no significant differences among subgroups (Appendices S8 and S9). We could not perform subgroups of the other analyses. All the prespecified sensitivity analyses that could be performed were consistent with the primary findings (Appendices S10–S17) (see details of methods and results in Appendix S18).

DISCUSSION

The results of this review covering seven RCTs and 2667 participants showed that the lidocaine spray probably contributed to a better satisfaction of the participants undergoing UGI endoscopy compared to the viscous lidocaine solution, while there was little or no difference in the participants’ pain and discomfort. This is the first
systematic review evaluating RCTs to determine the efficacy and safety of the lidocaine spray compared to the viscous solution for pharyngeal local anesthesia in UGI endoscopy. The lidocaine spray results in a slight increase in the participants’ satisfaction score compared to the viscous solution. The components of the lidocaine spray and viscous
solution are almost the same. In addition to the main components of lidocaine, both the lidocaine spray and viscous solution contain other ingredients such as ethanol, menthol, and saccharin to improve the solubility and taste. While it is required that the viscous solution be held in the mouth for few minutes, the spray is easy to use directly on the pharynx using a nozzle and patients don’t have to wait. On the other hand, the lidocaine spray and viscous solution had almost the same effect on the participants’ discomfort during endoscopic insertion, and then, the lidocaine spray reduced the participants’ discomfort on local anesthesia procedure compared to the viscous solution.18

The high heterogeneity of the analysis in the mean score of the VAS/NRS for the participants’ pain or discomfort may depend on each participant’s prior experience of both local anesthesia forms: lidocaine spray and viscous solution. One study by Amornyotin et al. showed that the participants’ pain or discomfort with lidocaine spray was less than that of viscous solution, whereas another study by Khodadoostan et al. reported the opposite. Most participants in the study by Khodadoostan et al. may have had no experience of local anesthesia with lidocaine spray. However, Amornyotin et al. reported that most UGI endoscopies were used the two forms of local anesthesia, and then, the participants’ discomfort during endoscopic insertion, and then, the lidocaine spray reduced the participants’ discomfort on local anesthesia procedure compared to the viscous solution.18

We hypothesized that the lidocaine spray may reduce adverse events compared with viscous lidocaine solution, but in fact both groups did not require any specific treatment for adverse events. The main adverse effects were hemodynamic changes, and that was likely to be as a result of stress due to the UGI endoscopy procedures itself. The adverse effects of lidocaine include anaphylactoid reactions and poisoning after increased levels of circulating lidocaine. To avoid poisoning due to an increase in circulating lidocaine concentrations, a total maximum dose of 5 mg/kg lidocaine is recommended. Anaphylactic shock happens very rarely, although it is a life-threatening side effect. Methylparaben, which is added as a preservative and plays a major role in the anaphylactic reaction, is contained in the viscous solution of lidocaine, but not in the lidocaine spray. However, our review showed that neither lidocaine spray nor viscous solution caused anaphylactic shock.

The evaluation of the participants’ satisfaction, pain or discomfort needed to be standardized to allow for appropriate comparisons. The American Society of Gastrointestinal Endoscopy recommended the GHAA-9 questionnaire to evaluate the participants’ satisfaction after UGI endoscopy, while three of the four included studies used authors-defined scales to assess the participants’ satisfaction. Four studies used different scales (VAS, NRS) to assess the participants’ pain or discomfort. A recent systematic review showed that NRS had better compliance compared with VAS for assessment of pain intensity.

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Table 2  Summary of findings

Comparison between the spray and viscous forms for pharyngeal local anesthesia

Patient or population: pharyngeal local anesthesia
Setting: in upper gastrointestinal endoscopy
Intervention: spray
Comparison: viscous

| Outcomes                          | Anticipated absolute effects\(^\d\) (95% CI) | Relative effect (95% CI) | No. of participants (studies) | Certainty of the evidence (GRADE) | Comments                                                                 |
|-----------------------------------|---------------------------------------------|--------------------------|------------------------------|----------------------------------|--------------------------------------------------------------------------|
|                                   | Risk with viscous                          | Risk with spray          |                               |                                  |                                                                          |
| Mean score of the participants’  | SMD 0.03 higher                            | RR 1.22 (1.02–1.47)      | 2462 (4 RCTs)                | LOW                               | The participants’ pain or discomfort was approximately the same between spray and viscous |
| pain or discomfort assessed with: | (0.37 lower–0.42 higher)                   |                          |                              |                                  |                                                                          |
| a visual analog scale or a numeric |                                              |                          |                              |                                  |                                                                          |
| rating scale                      |                                              |                          |                              |                                  |                                                                          |
| Participants’ satisfaction        | 359 per 1000                               | 438 per 1000 (366–528)   | 2381 (4 RCTs)                | MODERATE                         | The spray had a greater number of participants who checked the highest satisfaction category as compared to the viscous |
| Anaphylactic shock                | not pooled                                  | not pooled               | 2332 (3 RCTs)                | LOW                               | Three studies reported no anaphylactic shock                               |
| Participants’ tolerance           | 270 per 1000                               | 338 per 1000 (270–422)   | 1994 (2 RCTs)                | MODERATE                         | Participants demonstrated better tolerance with the spray compared to the viscous in upper gastrointestinal endoscopy |
| Ease of insertion                 | 253 per 1000                               | 291 per 1000 (192–438)   | 1994 (2 RCTs)                | LOW                               | The endoscopists’ ease of intubation                                        |
| Adverse events                    | There were 26.9% adverse events with the    | RR 1.15 (0.76–1.73)      | 2332 (3 RCTs)                | MODERATE                         | Adverse events were tachycardia, hypertension, hypotension, bradycardia, sore throat, nausea/vomiting, and decrease in SpO\(_2\) |
|                                  | spray and 33.4% adverse events with the     |                          |                              |                                  |                                                                          |
|                                  | viscous                                     |                          |                              |                                  |                                                                          |

GRADE Working Group grades of evidence: High certainty: We are very confident that the true effect lies close to that of the estimate of the effect. Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different. Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect. Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of the effect.

\(^\d\)The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

\(^\*\)Downgraded because of high risk of bias due to selection of the reported result.

\(^\d\)Downgraded because of high risk of bias due to selection of the reported result.

\(^\d\)Downgraded because of high risk of bias due to selection of the reported result.

\(^\d\)Downgraded because of inconsistency that there was represent considerable heterogeneity.

\(^\d\)Downgraded because of imprecision due to the small sample size.
Additionally, it would be better if patient anxiety was simultaneously evaluated using a valid questionnaire such as State-Trait Anxiety Index, as anxiety is closely related to patient satisfaction, pain and discomfort.27

This review more clearly showed the advantage of spraying in an analysis of RCTs without additional sedatives. However, in clinical settings such as in Europe and North America, additional drugs such as sedatives and fentanyl are often used for normal observations in addition to the lidocaine spray.30,31 If RCTs increase in the future, it will be useful to conduct subgroup analysis according to the region of origin and the drug used.

The necessity of pharyngeal anesthesia in UGI with sedation is still debatable. A previous systematic review reported that pharyngeal local anesthesia improved patient tolerance during UGI endoscopy under traditional sedation, such as with midazolam or meperidine.6 However, previous RCTs showed that local anesthesia did not affect the total propofol dose, or patient responsiveness.32–34 These differences indicate that depth of sedation with sufficient amnesia may be important. Minimal sedation usually includes intravenous benzodiazepines, and conscious sedation to deep sedation includes high doses of benzodiazepines, or intravenous propofol.35 Propofol exerts excellent hypnotic and sedative effects with a quick onset and short duration of action, making it easier to control the depth of sedation than traditional sedation.36

This review has several limitations. First, four of the seven studies had a high risk of bias in the selection of the reported result because there was no pre-registered protocol or no prespecified outcomes. Secondly, all the included studies were single center trials. We need large multicenter RCTs with low risks of selection bias to verify our findings.

In conclusion, our systematic review and meta-analysis demonstrated that lidocaine spray during UGI endoscopy is probably better than viscous lidocaine solution because of high participant satisfaction. The findings suggested that endoscopists should preferably use lidocaine spray rather than viscous lidocaine solution as pharyngeal anesthesia in UGI endoscopy. Further investigations are needed to assess the efficacy and safety of the lidocaine spray compared to the viscous solution in large multicenter RCT studies with a pre-registered protocol to avoid selection bias.

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CONFLICT OF INTERESTS

AUTHORS DECLARE NO conflicts of interest for this article.

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NONE.

REFERENCES

1 Pimentel-Nunes P, Libánio D, Marcos-Pinto R et al. Management of epithelial precancerous conditions and lesions in the stomach (MAPS II): European Society of Gastrointestinal Endoscopy (ESGE), European Helicobacter and Microbiota Study Group (EHMSG), European Society of Pathology (ESP), and Sociedade Portuguesa de Endoscopia Digestiva (SPED) guideline update 2019. Endoscopy 2019; 51: 365–88.
2 Zhang X, Li M, Chen S et al. Endoscopic screening in Asian Countries is associated with reduced gastric cancer mortality: A meta-analysis and systematic review. Gastroenterology 2018; 155: 347–54.
3 Campo R, Bruurret E, Montserrat A et al. Identification of factors that influence tolerance of upper gastrointestinal endoscopy. Eur J Gastroenterol Hepatol 1999; 11: 201–4.
4 Peery AF, Dellon ES, Lund J et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology 2012; 143: 1179–87.
5 Brandt LJ. Patients’ attitudes and apprehensions about endoscopy: How to calm troubled waters. Am J Gastroenterol 2001; 96: 280–4.
6 Evans LT, Saberi S, Kim HM, Elta GH, Schoenfeld P. Pharyngeal anesthesia during sedated EGDs: Is "the spray" beneficial? A meta-analysis and systematic review. Gastrointest Endosc 2006; 63: 761–6.
7 Hwang SH, Park CS, Kim BG, Cho JH, Kang JM. Topical anesthetic preparations for rigid and flexible endoscopy: A meta-analysis. Eur Arch Otorhinolaryngol 2015; 272: 263–70.
8 Asante MA, Northfield TC. Variation in taste of topical lignocaine anaesthesia for gastroscopy. Aliment Pharmacol Ther 1998; 12: 685–6.
9 Mogensen S, Tredal C, Feldager E et al. New lidocaine lozenge as topical anaesthesia compared to lidocaine viscous oral solution before upper gastrointestinal endoscopy. Local Reg Anesth 2012; 5: 17–22.
10 Chan CK, Fok KL, Poon CM. Flavored anesthetic lozenge versus Xylocaine spray used as topical pharyngeal anesthesia for unsedated esophagogastroduodenoscopy: A randomized placebo-controlled trial. Surg Endosc 2010; 24: 897–901.
11 Liberati A, Altman DG, Tetzlaff J et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 2009; 6: e1000100.
12 ASGE Standards of Practice Committee, Early DS, Lightdale JR et al. Guidelines for sedation and anesthesia in GI endoscopy. Gastrointest Endosc 2018; 87: 327–37.

13 Dumonceau JM, Riphaus A, Schreiber F et al. Non-anestesiologist administration of propofol for gastrointestinal endoscopy: European Society of Gastrointestinal Endoscopy, European Society of Gastroenterology and Endoscopy Nurses and Associates. Guideline-Updated June 2015. Endoscopy 2015; 47: 1175–89.

14 Obara K, Haruma K, Irisawa A et al. Topical viscous lidocaine solution versus lidocaine spray for pharyngeal anesthesia in unsedated upper gastrointestinal endoscopy. Aliment Pharmacol Ther 1996; 10: 975–9.

15 Amornyotin S, Srikureja W, Chalayonnnavin W et al. Topical viscous lidocaine solution versus lidocaine spray for pharyngeal anesthesia in unsedated esophagogastroduodenoscopy. Endoscopy 2009; 41: 581–6.

16 Soweid AM, Yaghi SR, Jamali FR et al. Posterior lingual lidocaine: A novel method to improve tolerance in upper gastrointestinal endoscopy. World J Gastroenterol 2011; 17: 5191–6.

17 Heuss LT, Hanhart A, Dell-Kuster S et al. Propofol sedation alone or in combination with pharyngeal lidocaine anesthesia for routine upper GI endoscopy: A randomized, double-blind, placebo-controlled, non-inferiority trial. Gastrointest Endosc 2011; 74: 1207–14.

18 Sun X, Xu Y, Zhang X et al. Topical pharyngeal anesthesia provides no additional benefit to propofol sedation for esophagogastroduodenoscopy: A randomized controlled double-blinded clinical trial. Sci Rep 2018; 8: 6682.

19 Axon AT. Throat spray, sedation or anaesthetic? Digestion 2010; 82: 77–9.

20 Kilgert B, Rybizki L, Grottke M, Neurath MF, Neumann H. Prospective long-term assessment of sedation-related adverse events and patient satisfaction for upper endoscopy and colonoscopy. Digestion 2014; 90: 42–8.

**SUPPORTING INFORMATION**

ADDITIONAL SUPPORTING INFORMATION may be found in the online version of this article at the publisher’s web site.

**Appendix S1** PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) 2009 checklist.

**Appendix S2** Search strategy.

**Appendix S3** Risk-of-bias graph and table for the highest satisfaction score. Overall, three of the four studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.

**Appendix S4** Risk-of-bias graph and table for anaphylactic shock. Overall, all three studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.

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Appendix S5 Risk-of-bias graph and table for the best tolerance score. Overall, all two studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.

Appendix S6 Risk-of-bias graph and table for the easiest insertion score. Overall, all two studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.

Appendix S7 Risk-of-bias graph and table for adverse events. Overall, all three studies were at a high risk of bias because these studies had high risks of bias in the selection of the reported results.

Appendix S8 Mean score of visual analog scale/numeric rating scale for participants’ pain/discomfort without sedation. The lidocaine spray did not increase mean score of visual analog scale/numeric rating scale for the participants’ pain or discomfort with sedation compared to the lidocaine viscous solution: standard mean difference $-0.12$, $95\%$ confidence interval $-0.38$ to $0.14$.

Appendix S9 Mean score of visual analog scale/numeric rating scale for participants’ pain/discomfort without sedation. The lidocaine spray did not increase mean score of visual analog scale/numeric rating scale for the participants’ pain or discomfort without sedation compared to the lidocaine viscous solution: standard mean difference $0.08$, $95\%$ confidence interval $-0.39$ to $0.55$; $I^2 = 93\%$.

Appendix S10 The proportion of participants who checked the highest satisfaction score in best-best scenario. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution in best-best scenario: risk ratio $1.16$, $95\%$ confidence interval $1.06$ to $1.27$; $I^2 = 0\%$.

Appendix S11 The proportion of participants who checked the highest satisfaction score in best-worst scenario. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution in best-worst scenario: risk ratio $1.22$, $95\%$ confidence interval $1.01$ to $1.48$; $I^2 = 49\%$.

Appendix S12 The proportion of participants who checked the highest satisfaction score in worst-best scenario. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution in worst-best scenario: risk ratio $1.16$, $95\%$ confidence interval $1.06$ to $1.27$; $I^2 = 0\%$.

Appendix S13 Mean score of visual analog scale/numeric rating scale for the participants’ pain or discomfort excluding studies other than lidocaine spray with a total dose of 50 mg and viscous lidocaine solution with a total dose of 100 mg. There was little or no difference in the mean score of the visual analog scale/numeric rating scale for the participants’ pain or discomfort between the lidocaine spray group and the viscous lidocaine solution group excluding studies other than lidocaine spray with a total dose of 50 mg and viscous lidocaine solution with a total dose of 100 mg: standard mean difference $0.12$, $95\%$ confidence interval $-0.92$ to $1.16$; $I^2 = 94\%$.

Appendix S14 The proportion of participants who checked the highest satisfaction score excluding studies other than lidocaine spray with a total dose of 50 mg and viscous lidocaine solution with a total dose of 100 mg. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution excluding studies other than lidocaine spray with a total dose of 50 mg and viscous lidocaine solution with a total dose of 100 mg: risk ratio $1.40$, $95\%$ confidence interval $1.26$ to $1.57$; $I^2 = 0\%$.

Appendix S15 Mean score of visual analog scale/numeric rating scale for the participants’ pain or discomfort excluding studies that the difference in total dose of lidocaine showed 70 mg or more between spray and viscous groups. There was little or no difference in the mean score of the visual analog scale/numeric rating scale for the participants’ pain or discomfort between the lidocaine spray group and the viscous lidocaine solution group excluding studies that the difference in total dose of lidocaine showed 70 mg or more between spray and viscous groups: standard mean difference $0.51$, $95\%$ confidence interval $0.04$ to $1.08$; $I^2 = 94\%$.

Appendix S16 The proportion of participants who checked the highest satisfaction score excluding studies that the difference in total dose of lidocaine showed 70 mg or more between spray and viscous groups. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution excluding studies that the difference in total dose of lidocaine showed 70 mg or more between spray and viscous groups: risk ratio $1.40$, $95\%$ confidence interval $1.26$ to $1.57$; $I^2 = 0\%$.

Appendix S17 The proportion of participants who checked the highest satisfaction score excluding studies including participants aged 12—14 years. The lidocaine spray probably increases the proportion of participants who checked the highest satisfaction score compared to the viscous lidocaine solution excluding studies including participants aged 12—14 years: risk ratio $1.25$, $95\%$ confidence interval $1.04$ to $1.50$; $I^2 = 0\%$.

Appendix S18 The details of the methods and results.