Original Article

The cricothyroid versus the spray-as-you-go method for topical anesthesia during flexible bronchoscopy: A systematic review and meta-analysis of randomized controlled trials

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ABSTRACT

Background: Lignocaine can be administered during bronchoscopy using either a direct injection through the cricothyroid membrane (the cricothyroid method) or a spray of lignocaine solution through the bronchoscope working channel (the spray-as-you-go method). In this meta-analysis of randomized controlled trials (RCTs), we compared the efficacy of these two methods for topical anesthesia during flexible bronchoscopy. **Methods:** We performed a systematic search to extract the relevant RCTs comparing the two techniques. **Results:** Five RCTs meeting the inclusion criteria (747 subjects) were identified. The cricothyroid method was associated with significantly less cough (standardized mean difference [SMD] = −1.18, 95% confidence interval [CI] [−1.75, −0.62], $P < 0.001$, significant heterogeneity I^2 = 86%, $P < 0.001$). On analysis of secondary outcomes, the cricothyroid method was associated with a greater operator-rated procedure satisfaction (SMD = 1.00, 95% CI [0.74, 1.25], $P < 0.001$), less time for upper airway negotiation (mean difference, MD = −0.99, 95% CI [−1.37, −0.6], $P < 0.001$), and a significantly less cumulative dose of lignocaine administered (MD = −68.12, 95% CI [−130.18, −6.06], $P = 0.03$). The overall procedure duration (MD = 0.08, 95% CI [−0.09, 0.24], $P = 0.36$) and patient discomfort (MD = −0.08, 95% CI [−0.38, 0.22], $P = 0.59$) were not different between the two methods. There was no significant publication bias ($P = 0.94$). **Conclusions:** The cricothyroid method is associated with less cough during flexible bronchoscopy. Other advantages are a greater operator-rated procedure satisfaction at a less cumulative lignocaine dose. These findings highlight the superior performance characteristics of the cricothyroid method for lignocaine administration for flexible bronchoscopy.

KEY WORDS: Airway, bronchoscopy, cough, cricothyroid, lignocaine

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Submitted: 06-Dec-2020 **Revised:** 22-Mar-2021 **Accepted:** 16-Apr-2021 **Published:** 30-Aug-2021

INTRODUCTION

Flexible bronchoscopy is commonly performed for the diagnostic evaluation of various diseases in the respiratory

Access this article online

Quick Response Code:

Website: www.lungindia.com

DOI: 10.4103/lungindia.lungindia_937_20

How to cite this article: Madan K, Iyer H, Arunachalam M, Mittal S, Tiwari P, Hadda V, *et al*. The cricothyroid versus the spray-as-you-go method for topical anesthesia during flexible bronchoscopy: A systematic review and meta-analysis of randomized controlled trials. Lung India 2021;38:416-24.

system. However, the procedure is often reported as unpleasant by the patients. Adequate topical anesthesia and intravenous sedation are the key components of optimizing patient comfort during bronchoscopy.[1] Regardless of the administration of intravenous sedation, adequate topical anesthesia is indispensable and helps to optimize patient comfort and cooperation. This allows smooth conduct of the procedure and overall satisfying conditions for the operator.[2] Lignocaine is the most commonly used drug for topical anesthesia during bronchoscopy.[3] The total dose of lignocaine administered during bronchoscopy needs to be carefully titrated. Serious adverse events (although uncommon) related to lignocaine toxicity have been reported.[4] Therefore, optimization of comfort at a lower dose of lignocaine administered is desirable.

The preferences of individual bronchoscopists are variable with regard to the choice of the method for lignocaine administration. The two described methods for delivering lignocaine to the vocal cords and trachea are either a direct injection through the cricothyroid membrane (the cricothyroid method) or a spray of lignocaine through the bronchoscope working channel, using a syringe (the spray-as-you-go method). The cricothyroid method of lignocaine administration is also known as the recurrent laryngeal nerve block. The available guidelines recommend either of these two methods as acceptable for topical airway anesthesia.[1,5] The broad scope for improvement of patient comfort during bronchoscopy has been previously described.[6] Evidence from recent randomized controlled trials (RCTs) has highlighted the superior anesthesia characteristics with the use of the cricothyroid method during diagnostic flexible bronchoscopy.[7]

In a survey of bronchoscopy practices in India, nearly one-fourth of the respondents reported the use of cricothyroid injection for lignocaine administration during bronchoscopy.[8] The cricothyroid method is often underutilized due to concerns regarding a possible invasive nature of the procedure.[8] The cricothyroid injection is widely used in anesthesia practice also. Bronchoscopists must choose a method, which will deliver the lowest possible dose of lignocaine and also provide adequate comfort leading to favorable conditions for the operator to easily perform airway examination. In this systematic review, we summarize the available evidence regarding the two methods of lignocaine delivery during bronchoscopy. We also perform a meta-analysis on the key reported outcome parameters in the RCTs comparing the cricothyroid with the spray-as-you-go method.

METHODS

We performed this review and meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-analyses statement (2009, PRISMA).[9] As the design for this study was a meta-analysis of RCTs, we did not obtain Institutional Review Board approval. There was no patient-specific intervention; therefore, no informed consents were obtained.

The primary outcome was cough during the bronchoscopy procedure. The secondary outcomes were a comparison of the patient discomfort, operator-rated satisfaction, total lignocaine dose administered, time for upper airway negotiation, and the total bronchoscopy procedure duration between the cricothyroid versus the spray-as-you-go methods.

Search strategy, study selection, and initial review

Two authors (K. M and A. M.) performed a systematic search of the major bibliographic databases: PubMed, EMBASE, Google Scholar, and Cochrane Library to identify the original, peer-reviewed, full-text articles comparing the cricothyroid and spray-as-you go techniques for topical anesthesia in flexible bronchoscopy. The following database-specific Boolean search strategy was used. The literature was searched till September 30, 2020, with no proximal time limits. Free text search terms were "recurrent laryngeal" OR "recurrent laryngeal nerve" OR "recurrent laryngeal nerve block" OR "cricothyroid" OR "transcricoid" OR "transtracheal" AND "bronchoscopy." The studies were imported into reference management software (EndNote). Duplicate citations were discarded. Full texts were downloaded for review. The reference lists of the extracted studies were also reviewed, and the authors also searched their files. The finally selected studies were independently screened by two authors (K. M. and A. M.). The following types of studies were excluded: (a) studies that did not report the utilization of cricothyroid and spray-as-you-go techniques in flexible bronchoscopy, (b) studies describing flexible bronchoscopy without the utilization of cricothyroid and spray-as-you-go techniques or vice versa, (c) studies not in English language, (e) review articles, editorials, abstracts, and letters, and (f) case reports or series. Any disagreement between the authors was resolved after mutual discussion.

Data abstraction

Data from the finally selected studies were abstracted on a data extraction form. The following information was retrieved after a thorough review of the full text – (a) author, (b) year, (c) number of patients, (d) age and sex, (e) comparator groups, (f) study design, (g) topical anesthetic agent, (h) sedation, (i) diagnostic procedures performed, (j) anticholinergic agents used, (k) use of any premedication, (l) use of nebulized lignocaine, (m) use of pharyngeal lignocaine spray, (n) route of scope insertion, (o) nasal anesthesia used, (p) lignocaine concentration used, (q) lignocaine dose, needle gauge used for cricothyroid injection, (s) position during cricothyroid injection, (t) number of operators, (u) bronchoscope diameter, (v) hemodynamic parameters, (w) score for patient discomfort, (x) score for operator satisfaction, (y) cough scores in both groups, and (z) procedure duration. The systematic review methodology is summarized in Figure 1.

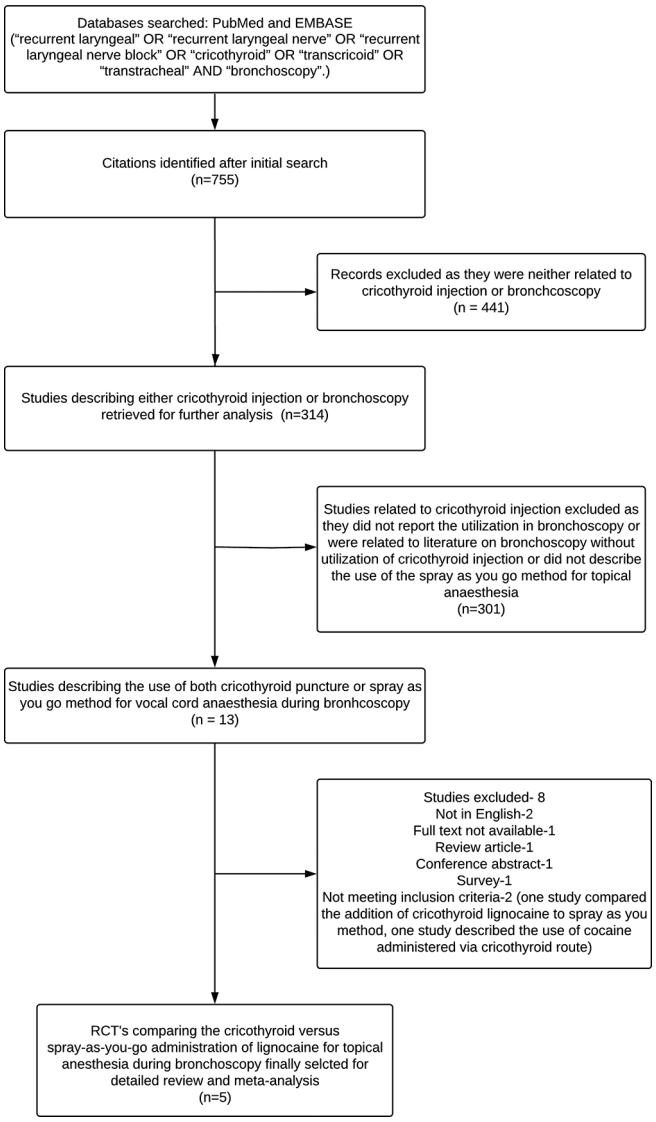

Figure 1: Flow diagram describing the process of systematic review and selection of relevant studies for meta-analysis

Quality assessment

The Cochrane risk of bias tool for randomized trials was used to assess the quality of selected studies.[10] The risk of bias is rated as "low risk," "high risk," or "unclear risk." The domains that are evaluated for bias include random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other potential sources of bias. Two authors (A. M. and K. M.) performed the risk-of-bias assessment independently. Any disagreement was resolved by mutual discussion and a third reviewer (SM).

Statistical analysis and quantitative data synthesis

Statistical analyses were performed using the STATA statistical analysis software (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LLC) and Review Manager (RevMan) (Computer program, Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014). The standard guidelines for conducting and reporting a meta-analysis of RCTs were followed.[9] To perform a meta-analysis of continuous outcome data using mean difference (MD) and standardized mean differences (SMDs), we extracted the mean values of the outcome measurements, the standard deviations of the outcome measurements, and the number of subjects in the cricothyroid and the spray-as-you-go groups of the selected RCTs.

Heterogeneity assessment

The impact of heterogeneity on the pooled estimates of the diagnostic yields and the comparative diagnostic yield was assessed using the I^2 test and Cochran Q statistic.[11] I^2 is a statistical tool to evaluate the impact of unobserved heterogeneity. It describes the percentage of total variation seen across studies that are attributable to heterogeneity rather than chance. An I^2 value of ≥50% indicates significant heterogeneity. For the Cochran Q statistic, $P < 0.1$ is significant for the presence of statistical heterogeneity.

Assessment of publication bias

The Begg's funnel plot (Egger test) was used to assess for publication bias (statistically significant publication bias when $P < 0.1$).[12]

RESULTS

The initial literature search yielded 755 articles. Thirteen studies were selected for initial review and six were excluded for various reasons [Figure 1]. From the seven remaining studies, two were excluded after a detailed review (one study compared additional cricothyroid lignocaine with spray-as-you-go method, while one study used cocaine for topical anesthesia).[6,13] Finally, five RCTs meeting the inclusion criteria were selected for detailed data abstraction and included in the meta-analysis.[7,14-17]

Description of studies and quality assessment

The details of the abstracted characteristics of the five RCTs are summarized in Tables 1 and 2. Overall, in the five RCTs, comparative characteristics of the two methods for topical lignocaine administration were described for 747 patients. The risk of bias for the selected RCTs is summarized in Figure 2.

All the studies were RCTs comparing the two methods of lignocaine administration for bronchoscopy. In one RCT, there were three comparator groups (Isaac *et al.*, a third comparator group of nebulized lignocaine).[14] Bronchoscopy was performed under sedation in three RCTs.[14,16,17] In the study by Madan *et al.*, the use of sedation was optional and all procedures were performed without sedation in the study by Chandra *et al.*[7,15]

Table 1: Study methodology and the patient characteristics in the studies included for review and meta-analysis

Author (year)	Design	Comparator groups	Topical Anesthetic agent	Sedation	Procedures during diagnostic bronchoscopy	Exclusion	Number of patients	Age (years), mean±SD	Anticholinergic or any other premedication	Nebulized lignocaine before the procedure	Pharyngeal lignocaine spray	Route of bronchoscope introduction	Nasal anaesthesia
Webb AR *et al.*, (1990)[16]	RCT	Cricothyroid versus spray as you go	Lignocaine	Yes, alfentanil in all	NA	Contraindications to cricothyroid injection like hemoptysis, stridor, and HIV positive	70 (8 excluded for various reasons) Cricothyroid - 30 Spray as you go - 32	Cricothyroid 62.2±14.2, spray-as-you-go 62.5±15.7	Glycopyrrolate 0.2 mg	No	No	Nasal	5 ml of 2% lignocaine gel
Isaac PA *et al.*, (1990)[14]	RCT	Cricothyroid versus spray as you go versus nebulized lignocaine	Lignocaine	Yes, fentanyl and droperidol in all	NA	NA	98 Cricothyroid - 26 spray as you go - 24	Cricothyroid 58.7±13.1, spray 59.3±12.2	Atropine 0.6 mg was given 60 min before the procedure Others-Lorazepam 1 mg (oral) and amethocaine -lozenge (60 mg)	Not in all, a separate nebulized lignocaine group	Ten sprays of 10% lignocaine only in the spray-as-you-go group	NA	NA
Chandra A *et al.*, (2011)[15]	RCT	Cricothyroid versus spray as you go	Lignocaine	No	Only BAL or Bronchial aspirates	Any contraindication for cricothyroid injection	60 Cricothyroid - 30 spray as you go-30	Cricothyroid 51.7±14.1, spray 48.3±13.3	Atropine 0.6 mg 20 min before procedure	3 ml of 4% lignocaine	No	Nasal	2 ml of 2% lignocaine gel
Lak M *et al.*, (2018)[17]	RCT	Cricothyroid versus spray as you go	Lignocaine	Yes (midazolam, fentanyl, and propofol) in all	NA	Coagulopathy, electrolyte abnormalities, severe anemia, lignocaine, or Propofol hypersensitivity, or bronchoscopy requiring vocal cord assessment	80 cricothyroid - 40 spray as you go - 40	Cricothyroid 63.17±13.2, spray 60.35±11.08	No	No	No	Nasal	2% lignocaine gel
Madan K *et al.*, (2019)[7]	RCT	Cricothyroid versus spray as you go	Lignocaine	Yes optional, not routinely	BAL, TBLB, EBB, TBNA	Contraindications to cricothyroid injection and bronchoscopy (hypoxemia), lignocaine hypersensitivity, bronchoscopy under GA, pregnancy, artificial airway, symptomatic CAO, and active hemoptysis	500 cricothyroid - 248 spray as you go - 247	Cricothyroid 46.74±15.65, Spray 44.04±16.73	No	No	Four sprays of 10% lignocaine	Nasal	5 ml of 2% lignocaine gel

BAL: Bronchoalveolar lavage, CAO: Central airway obstruction, EBB: Endobronchial biopsy, GA: General anesthesia, TBLB: Transbronchial lung biopsy, TBNA: Transbronchial needle aspiration, RCT: Randomized controlled trial, NA: Not available, SD: Standard deviation

Table 2: Procedural details and reported outcomes with the cricothyroid injection and spray-as-you-go method for lignocaine administration

Author	Lignocaine concentration (%)	Baseline lignocaine dose (mg)	Needle gauge for injection (G)/position of patient	Additional bolus lignocaine allowed	Operators	Mean±SD					
						Cough measure	Patient discomfort VAS	Total lignocaine dose (mg)	Operator-rated comfort VAS	Time for upper airway negotiation	Total procedure duration
Webb AR *et al*., (1990)	Cricothyroid: 2 Spray-as-you-go: 4	Cricothyroid: 100 Spray-as-you-go: 240	21 Sitting	Yes, in both groups	NA	Cough during procedure Cricothyroid: 3.56±3.1 Spray: 5.89±4.8 Coughs counted by an assistant with a counting device after passage of the scope across the vocal cords	VAS (patient-rated unpleasantness of bronchoscopy) Cricothyroid: 24.8±23 Spray: 23.7±25	Cricothyroid: 322±25.9 Spray: 451±20.9	NA	Time to complete bronchoscopy after crossing cords Cricothyroid: 9.6 + 5.8 Spray: 9.69 + 4.8	
Isaac PA *et al*., (1990)	Cricothyroid: 4 Spray-as-you-go: 4	Cricothyroid: 160 Spray-as-you-go: 260	NA	Yes (2%), in both groups	Two (one performed all cricothyroid procedures, other performed all spray as you go procedures)	NA	VAS (patient-rated unpleasantness of bronchoscopy) Cricothyroid: 19.3±19.7 Spray: 25.4±22.6	NA	Overall operator-rated quality of topical anesthesia Cricothyroid: 7.5±2.1 Spray: 6.6±2.8	NA	
Chandra A *et al*., (2011)	Cricothyroid: 4 Spray-as-you-go: 4	Cricothyroid: 120 Spray-as-you-go: 160	21 Sitting	Yes, in both groups	Single	Cough during procedure Cricothyroid: 4±0.98 Spray: 4.9±1.24 Cough episodes recorded by an assistant. A bout of coughing counted as a single episode of cough	VAS (patient-rated discomfort of bronchoscopy) Cricothyroid: 0.7±0.7 Spray: 0.73±0.53	Cricothyroid: 314±9.32 Spray: 372.66±24.9	NA	Time to reach carina Cricothyroid: 57.33±12.98 Spray 79.33±22.35	
Lak M *et al*., (2018)	Cricothyroid: 4 Spray-as-you-go: 2	Cricothyroid: 120 Spray-as-you-go: 120	22 NA	No	NA	Cough frequency Cricothyroid: 1.45±1.41 Spray: 4.7±1.45 Technique of cough counting not clearly specified	NA	NA	NA	NA	
Madan K *et al*., (2019)	Cricothyroid: 2 Spray-as-you-go: 2	Cricothyroid: 160 Spray-as-you-go: 180	22 Supine	Yes, in both groups	Multiple	Cough count till reaching carina Cricothyroid: 1.54±1.91 Spray: 5.05±3.81 Cough noted by a dedicated assistant from scope insertion until reaching the carina	NA	Cricothyroid: 305.08±13.4 Spray: 322.18±10.67	Overall operator-rated procedure satisfaction Cricothyroid: 7.86±1.39 Spray: 6.86±1.59	Cricothyroid: 9.65 + 4.44 Spray: 9.24 + 4.67	

NA: Not available, VSA: Visual Analog Scale, SD: Standard deviation

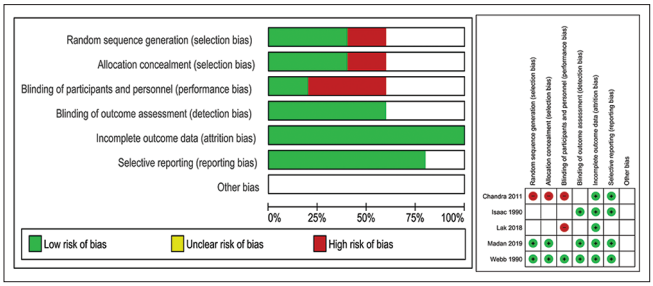

Figure 2: Figure showing the risk of bias assessment of the selected RCTs using the Cochrane tool

Anticholinergic premedication was used in three studies.[14-16] The procedure-related details and key outcomes are summarized in Tables 1 and 2.

Meta-analysis

Primary outcome: Comparison of the cricothyroid versus the spray-as-you-go method on cough during bronchoscopy

Four studies reported the cough outcome comparison between the groups.[7,15-17] The details of method of measurement of cough are described in Table 2. The meta-analysis suggested a significantly less cough favoring the cricothyroid technique (SMD = −1.18, 95% confidence interval [CI] [−1.75, −0.62], $P < 0.001$). There was significant heterogeneity detected across the studies ($P < 0.001$, $I^2 = 86\%$) [Figure 3].

Secondary outcomes

Comparison of the patient discomfort and operator-rated satisfaction between the cricothyroid versus the spray-as-you-go method

Three studies compared the patient discomfort between the methods.[14-16] The meta-analysis did not show a statistically significant difference between the cricothyroid and the spray-as-you-go technique on patient discomfort (SMD = −0.08, 95% CI [−0.38, 0.22], $P = 0.59$). There was no significant heterogeneity detected across the studies ($P = 0.68$, $I^2 = 0\%$) [Figure 4]. Two studies[7,14] reported the operator-rated procedure satisfaction between the two methods. Meta-analysis showed a significantly better operator satisfaction with the cricothyroid method (SMD = 1.00, 95% CI [0.74, 1.25], $P < 0.001$). There was no significant heterogeneity detected across the studies ($P = 0.89$, $I^2 = 0\%$) [Figure 4].

Comparison of the total lignocaine dose administered between the cricothyroid versus the spray-as-you-go method

Three studies reported the total lignocaine dose administered in the two groups.[7,15,16] Meta-analysis showed a significantly lower dose of cumulative lignocaine administered favoring the cricothyroid method (MD = −68.12, 95% CI [−130.18, −6.06], $P = 0.03$). There was significant heterogeneity detected across the studies ($P < 0.001$, $I^2 = 99\%$) [Figure 5].

Comparison of the time for upper airway negotiation and the total bronchoscopy procedure duration between the cricothyroid versus the spray-as-you-go method

Two studies compared the time required for the upper airway negotiation between the two techniques.[15,16] Meta-analysis showed a significantly lower time to negotiate the upper airway favoring the cricothyroid (MD = −0.99, 95% CI [−1.37, −0.62], $P < 0.001$). There was no heterogeneity detected across the studies ($P = 0.35$, $I^2 = 0\%$) [Figure 5]. Two studies reported the total duration of the bronchoscopy procedure between the two techniques.[7,16] Meta-analysis showed no statistically significant difference between the two methods for overall procedure duration.(MD = 0.08, 95% CI [−0.09, 0.24], $P = 0.36$). There was no heterogeneity detected across the studies ($P = 0.69$, $I^2 = 0\%$) [Figure 5].

Publication bias

There was no significant publication bias on the examination of the funnel plot ($P = 0.94$, Egger test) [Figure 6].

Subgroup analysis

Subgroup analysis indicated no statistically significant differences between the groups with regards to routine administration of intravenous sedation or additional pharyngeal lignocaine administration on cough outcome between the cricothyroid and the spray-as-you-go methods [Figure 7].

DISCUSSION

One of the most important aims while performing a flexible bronchoscopy is to ensure optimum patient comfort so that a complete airway examination may be performed and diagnostic sampling is undertaken. Vigorous coughing can ensue if the vocal cords and upper trachea are not properly anesthetized, which can make the patient uncooperative and compromise the yield of the procedure. The findings of this meta-analysis indicate that the cricothyroid method of lignocaine administration during flexible bronchoscopy is associated with less cough, greater operator satisfaction, and less time for upper airway negotiation at a significantly lower dose of lignocaine administered. There was no statistically significant difference observed between patient discomfort and total procedure duration between the groups.

A plausible explanation for the advantage of the cricothyroid method is that when lignocaine is instilled through the bronchoscope working channel, a part of it is swallowed while a part of it suctioned out, leading to a nonuniform deposition and a lower amount of drug being delivered. The cricothyroid method effectively deposits lignocaine near the vocal cords. Akin to the explanation regarding the cricothyroid technique, a recent RCT has demonstrated that lignocaine instillation using a dedicated spray catheter during bronchoscopy is associated with reduced cough and improved operator satisfaction as compared with the direct spray-as-you-go injection

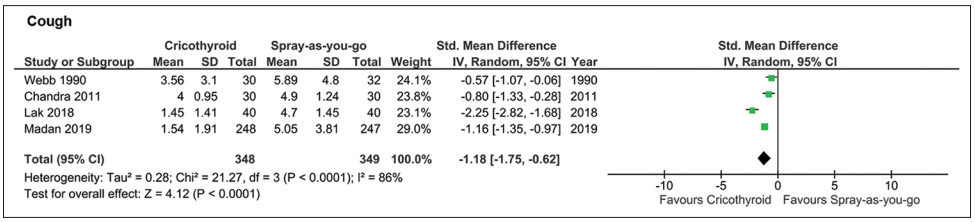

Figure 3: Forest plot showing the comparison of cough between the cricothyroid versus the spray-as-you-go method

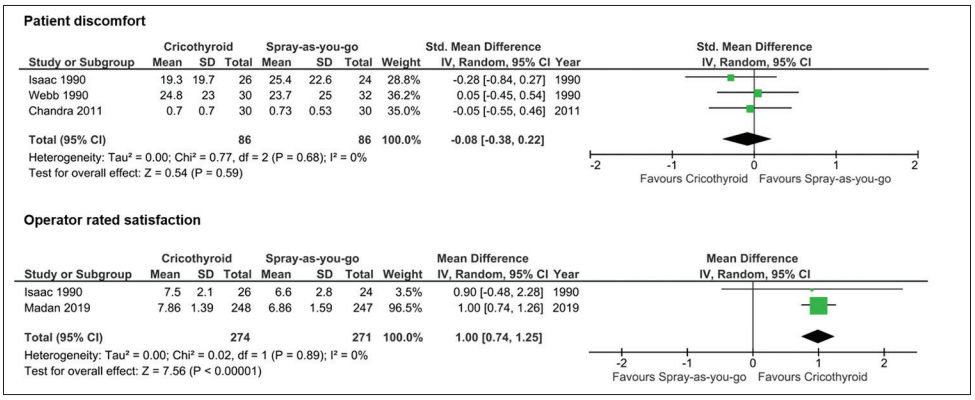

Figure 4: Forest plot showing the comparison of patient comfort and operator satisfaction between the cricothyroid versus the spray-as -you-go method

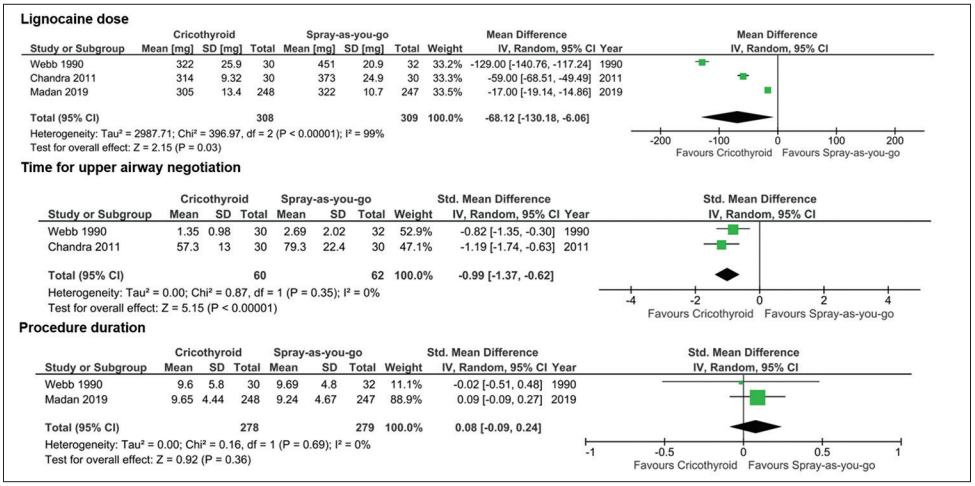

Figure 5: Forest plot showing the comparison of cumulative lignocaine dose, time for upper airway negotiation, and the total procedure duration between the cricothyroid versus the spray-as-you-go method

through the working channel of the bronchoscope.[18] A targeted and more uniform deposition of lignocaine is therefore ideal. Second, the transcricoid puncture is performed before insertion of the bronchoscope and allows a sufficient time for the drug to act. The time required for upper airway negotiation was also lower in the cricothyroid group. This is probably as a result of reduced cough which enables proper visualization and easy negotiation. However, our analysis found that the overall time required for completion of bronchoscopy was not different. This could be since a combination of different procedures (such as BAL, and Biopsy) was performed in each study.

This is the first meta-analysis to study the comparative characteristics of these two methods of lignocaine administration during bronchoscopy. Certain proceduralists argue against the use of cricothyroid method citing its invasive nature and the possibility of injuring the neighboring structures and vocal cords. However, none of the RCTs reported any complications with the cricothyroid puncture method. Therefore, it is appropriate to infer that if anatomical landmarks are well adhered to, this method is safe. Recent studies have also described the use of ultrasonography for accurate localization of the cricothyroid membrane, thereby improving the overall safety of the procedure.[19] Following cricothyroid injection,

there is a transient cough which is short lasting. A small amount of blood in the trachea may be noticed following cricothyroid injection which does not interfere with the procedure. Operators can gain confidence relatively easily with the injection technique, and a quicker procedure turnaround time with the cricothyroid method has also been reported.[16] The lower dose of lignocaine administered with the cricothyroid method is one of the important advantages. Lignocaine toxicity often manifests unpredictably and can be life-threatening.

No-sedation bronchoscopy is commonly performed. We believe that the cricothyroid method is especially important for settings wherein sedation is not routinely used for diagnostic flexible bronchoscopy. Although, there results seem consistent regardless of administration of intravenous sedation, further studies are required in settings where heavy sedation is used during bronchoscopy. In these situations, the differences between the two methods may not be marked.

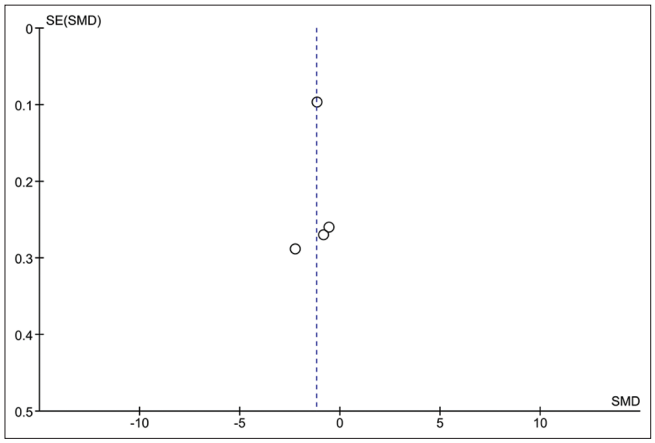

Figure 6: Funnel plot for publication bias: Funnel plot for publication bias

There are certain limitations of the interpretation of the findings of the meta-analysis. There was significant heterogeneity in the findings of the primary outcome which may be due to the different methods of cough measurement. In two out of the four studies reporting this outcome, a dedicated assistant counted the cough, while in one study, the cough was recorded by an assistant using a counting device and the method was not specified in one study. Another limitation is that not all studies reported all the study outcomes of interest. Regarding operator satisfaction, although there was no heterogeneity, only two studies report this outcome and in the study, the operators were not blinded to the intervention used. The use of sedation was not consistent and most of the studies did not have an objective method to record the cough count. The cricothyroid method leads to easier upper airway negotiation; however, it is not clear whether this helps in improving the efficiency of the procedure overall. This is because there was no difference in the overall procedure duration and patient comfort.

CONCLUSIONS

The cricothyroid method for topical anesthesia of the vocal cords during flexible bronchoscopy was associated with less cough, enhanced operator-rated procedure satisfaction, and a shorter duration of upper airway

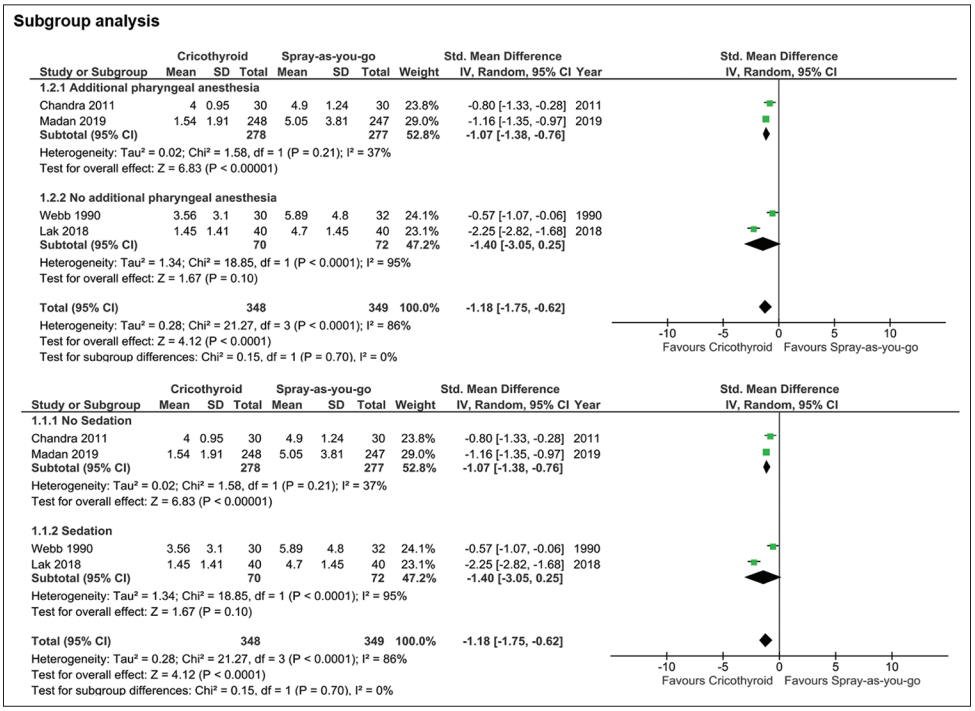

Figure 7: Forest plot of cough in two methods by subgroups

negotiation at a lower dose of lignocaine in comparison to the spray-as-you-go method.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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