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The application of lidocaine to alleviate the discomfort of nasogastric tube insertion A systematic review and meta-analysis

You-Chen Lor, MD^a, Pei-Ching Shih, MD^a, Hsin-Hao Chen, MD, MS^a, Shu-Jung Liu, MA^b, Hsingchu-Chu Chao, MD^c, Lee-Ching Hwang, MD, PhD^{d,e}, Yen-Fen Hsu, BN^f, Tzu-Lin Yeh, MD^{a,*}

Abstract

Background: Nasogastric (NG) tube insertion is a common procedure in the clinical setting that causes much discomfort and pain for the patient. Pain control is often suboptimal, as many NG tube insertions are performed without any pain-relieving supplements. The aim of this study was to summarize and critically evaluate the evidence from randomized controlled trials (RCTs) on the effect and adverse effects of lidocaine agents in reducing pain and discomfort associated with NG tube insertion.

Methods: Databases from the Cochrane Library, MEDLINE, EMBASE, Airiti Library, PerioPath Index to Taiwan Periodical Literature, and Cumulative Index of Nursing and Allied Health (CINAHL) were searched from inception to April 2017. RCTs focusing on lidocaine before NG tube insertion were appraised. The primary outcome was the visual analog scale (VAS) score. The modified Jadad scale was used for quality assessment. Mean difference (MD) with 95% confidence intervals (95% CIs) and odds ratio (OR) for binary outcomes were assessed by a random effects model. Heterogeneity was determined by using the Cochran Q test and *I*² statistics. Publication bias was analyzed by using a funnel plot analysis.

Results: Ten RCTs enrolling 734 patients were included in the meta-analysis. Eight of the 10 RCTs reporting VAS scores had sufficient quantitative data to be pooled through meta-analysis. Results revealed a significant reduction in VAS score, with a MD of -26.05 and a Cl of -28.21 to -23.89 with moderate heterogeneity (P < .001, $l^2 = 56\%$). There were no significant changes in difficulty of NG tube insertions (MD=-0.30, 95% Cl, -1.30 to 0.70, P = .55), number of NG tube insertion attempts (MD=-0.22, 95% Cl, -0.98 to 0.53, P = .56), nasal bleeding (OR=0.62, 95% Cl, 0.11-3.41, P = .59), and vomiting (OR=0.30, 95% Cl, 0.07-1.27, P = .10).

Conclusion: This meta-analysis suggests that applying lidocaine before NG tube insertion can alleviate pain and discomfort by 26% without increasing nasal bleeding or vomiting.

Abbreviations: CI = confidence interval, CINAHL = Cumulative Index of Nursing and Allied Health, MD = mean difference, NG = nasogastric, OR = odds ratio, PRISMA-P = Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols, RCT = randomized controlled trial, VAS = visual analog scale.

Keywords: lidocaine, meta-analysis, nasogastric intubation, visual analog scale

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^a Department of Family Medicine, Hsinchu MacKay Memorial Hospital, Hsinchu City, ^b Medical Library, Tamsui MacKay Memorial Hospital, New Taipei City, ^c Department of Pediatrics, ^d Department of Family Medicine, Taipei MacKay Memorial Hospital, Taipei City, ^e MacKay Medical College, New Taipei City, ^f Department of Nursing, Hsinchu MacKay Memorial Hospital, Hsinchu City, Taiwan.

* Correspondence: Tzu-Lin Yeh, Department of Family Medicine, Hsinchu MacKay Memorial Hospital, No. 690, Section 2, Guangfu Road, East District, Hsinchu City, Taiwan (e-mail: 5767@mmh.org.tw).

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1. Introduction

Nasogastric (NG) tubes are flexible lumen tubes that are passed proximally from the nose into the stomach. NG tube insertions are common medical procedures performed in the clinical setting. They are used for both diagnostic and therapeutic purposes such as bowel obstruction, administration of medications, enteral nutrition, or stomach lavage.^[1,2] Pain and discomfort associated with the procedure has long been recognized and reported and has even been described as the single most painful routine procedure in the emergency department.^[3] Many patients experience oropharyngeal discomfort. However, pain control is often suboptimal, as many NG tube insertions are performed with ordinary lubricant jelly alone, without any additional painrelieving supplements. Reasons for inadequate pain control measures include poor recognition of pain, inconvenience, unavailability, and insufficient research on alternative treatment options.[4-6]

A previous systematic review and meta-analysis in 2010 concluded that nebulized lidocaine introduced before NG tube insertion significantly reduced the associated pain and discomfort of the procedure.^[7] Gallagher^[8] reviewed 6 randomized clinical trials that have all demonstrated that the application of various forms of lidocaine helps alleviate some of the discomfort associated with NG tube placement. A randomized controlled trial (RCT) demonstrated that lidocaine gel significantly reduces pain and gagging sensations associated with the procedure but is associated with more difficult NG tube insertion than the use of lubricant gel.^[9] However, adverse effects were not documented. To date, there are no agreed upon guidelines or international consensus in the provision of local anesthesia in patients undergoing NG tube insertion. The aim of this study was to perform an updated systematic review and meta-analysis to evaluate the benefits and adverse effects of lidocaine agents in reducing pain and discomfort associated with NG tube insertion.

2. Methods

2.1. Database and search strategy

This systematic review and meta-analysis were conducted in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) guidelines (Supplement 1, http://links.lww.com/MD/C97).^[10] We searched the following databases from inception to the end of April 2017: the Cochrane Library, MEDLINE, Cumulative Index of Nursing and Allied Health (CINAHL), EMBASE, Airiti Library, and PerioPath Index to Taiwan Periodical Literature. We searched for RCTs using the search terms: "nasogastric tube," "NGT," "lidocaine," "lignocaine," "lidocaine hydrochloride," and "xylocaine." For the Airiti Library and PerioPath Index to Taiwan Periodical Literature databases, we used the Chinese search terms: "liduokayin" (English translation: lidocaine), "weiguan" (English translation: gastric tube), "biweiguan" (English translation: nasogastric tube) (Supplement 2, http:// links.lww.com/MD/C97). The search was supplemented by reviews of reference lists of all relevant studies. Two reviewers (PCS and SJL) conducted the search independently, and disagreements were resolved through discussion with the third author (TLY). As this meta-analysis collected data from published articles, ethical approval was not necessary.

2.2. Inclusion and exclusion criteria

In our search for eligible studies, no restriction was placed on language. All authors are literate in both English and Chinese. HCC is also a native Korean speaker. Duplicate publications and those irrelevant to the topic of this study are excluded. Inclusion criteria for the studies were RCTs on human subjects, the effect of lidocaine on NG tube insertion, normal saline or K-Y lubricant gel or no intervention used for the control group, and the visual analog scale (VAS) score as the primary clinical outcome assessed. Studies were excluded if they were non-RCTs or crossover studies, lacked VAS scores, or if the control group used any substance other than the ones mentioned above.

2.3. Data extraction and statistical analysis

The authors independently used the modified Jadad scale to assess the methodological quality of each included study (Supplement 3, http://links.lww.com/MD/C97). The modified Jadad scale includes 8 items to evaluate if randomization was done (score range 0–1), if randomization was appropriate (score range -1 to 1), if blinding was done (score range 0–1), if blinding

was appropriate (score range -1 to 1), if withdrawals and dropouts were described (score range 0–1), if inclusion and exclusion criteria were described (score range 0–1), if adverse reactions were assessed (score range 0–1), and if the statistical analysis was described (score range 0–1).^[11] The score of each study ranges from 0 (the lowest quality) to 8 (the highest quality). Studies were classified as moderate if they had a score of 4 or 5. If 2 authors had different opinions when assessing and selecting the included studies, agreement was reached by consensus with a third author.

The authors independently extracted the data from all included studies and the following data were collected: first author's name, year of publication, country, patient source, number of patients, age, type of intervention, control intervention type, clinical outcomes, and adverse effects. We have tried contacting the authors of certain studies to request for more in-depth study data that we felt would be beneficial to our research, but we were unable to obtain the raw data.

Data were analyzed using the mean difference (MD) with 95% confidence intervals (95% CIs) for continuous outcomes and odds ratio (OR) for binary outcomes. RevMan version 5.3.5 software (The Nordic Cochrane Center, The Cochrane Collaboration, Copenhagen, Denmark) was used for all data analyses. Meta-analysis was conducted when the trials had acceptable clinical homogeneity and statistical heterogeneity. Because of the significant heterogeneity expected among the studies, a random effects model was employed using the DerSimonian and Laird method.^[12] Heterogeneity was quantified using the Cochran Q test and I^2 statistics.^[13] A P value < .10 for Chi-square testing of the Q statistic or an $I^2 > 50\%$ was considered as a statistically significant heterogeneity. In accordance with the Cochrane methodology,^[14] we performed a sensitivity analysis by individually removing each study to investigate whether choice of summary statistic is critical to the results of the meta-analysis. Subgroup analyses were also performed to determine sources of heterogeneity. Potential publication bias was assessed by observing the symmetry of funnel plots.^[15]

3. Results

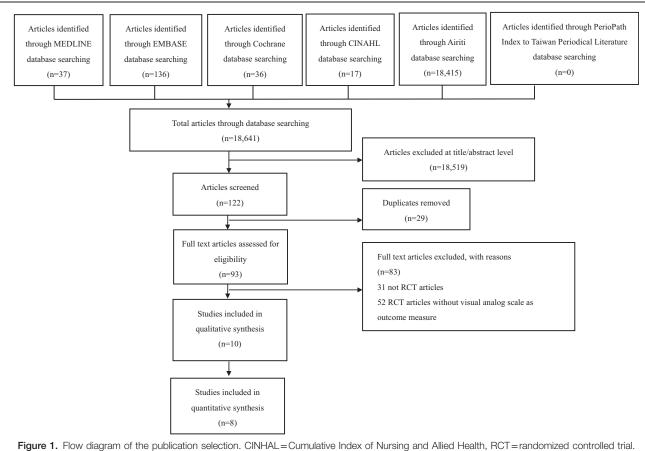
A total of 10 RCTs were included for quality assessment using the modified Jadad scale.^[5,9,16-23] Seven of the 10 included RCTs achieved a full or nearly full score (modified Jadad score ≥ 6 ; Table 1).^[5,9,16,18,19,21,22] Two RCTs had a moderate quality rating (modified Jadad score ≥ 4 ; Table 1).^[17,20] One study had a Jadad score of 3 (Table 1).^[23] The characteristics of the included trials are summarized in Table 1. A total of 734 participants were enrolled in the 10 studies and the mean age of the treatment and control group was 49 and 50 years, respectively. Only 1 of the 10 studies was conducted on children and had an age range of 1.0 to 3.8 years.^[16] Five of the studies were conducted in Asia, 2 in Australia, 2 in the United States, and 1 in Israel. Six studies were written in English,^[5,9,16,18,21,22] 3 studies in Chinese, ^[17,19,23] and 1 study in Korean.^[20] Eight of the 10 studies recruited patients from the emergency department, 1 study allocated patients from the surgery department, and 1 study did not clarify their patient source. All patients required NG intubation with the most common indication being related to gastrointestinal diseases. The size of the NG tubes used was cited in all of the studies except for 2.^[17,23] In adult patients, the sizes ranged from 14F to 20F, while in child patients, the sizes ranged from 6F to 10F.

We used the VAS scores as the main outcome. Eight of the 10 RCTs reporting VAS scores had sufficient quantitative data to be

Table 1 Characteristics of the included studies.	of the inclu	ded studi	es.						
Studies	Country	Patient source	No. of patients	Age (T:C)	Intervention	Control	Description	Outcome	Modified Jadad score
Chao ^[17]	China	SD	126	54:52	5 mL 2% L nasal spray	5mL NS spray	Both nostrils, 5 min before NG	AE, failure number, time of intubation VAS	5.5
Hsu and Tang ^[19]	China	E	60	46:50	5 mL 2% L nebulized	5mL NS solution	Aerosol mask with 8 L/min flow for 10 min.16F NG	AE, VAS (100)	7
Uri et al ^[9]	Israel	ED	62	68:64	5 ml 2% L topical gel	5mL K-Y gel	Insertion nostril, 5 min before 16F NG	AE, Likert scale, no. of attempts, VAS(100)	8
Chan and Lau ^[5]	Hong Kong	E	206	60:60	10% L nasal and pharynx spray	NS spray	1 mL KY jelly, both nostrils 1spray (1 mL), 2 sprays (2 mL) to the throat, 5 min before 16F NG	AE, Likert scale, no. of attempts, VAS(25), vital signs	ω
Babl et al ^[16]	Australia	E	36	2:2	4 mg/kg 2% L nebulized	0.9% NS solution	Aerosol mask with 8 L/min flow for 5 min, 6/8/1 0F NG	AE, FLACC, no. of attempts, VAS (100)	80
Yang and Hu ^[23]	China	NA	43	48:48	2–3 mL 2% L pharynx spray	No intervention	1 spray (2-3 mL) to throat x 2 times, 5 and 10 min before NG	First time success rate, VAS (100)	ო
Cullen et al ⁽¹⁸⁾	Australia	ED	50	67:55	4 mL 10% L nebulized	4 mL NS solution	Aerosol mask with 6 L/min flow, K-Y jelly, 18 F NG	AE, Likert scale, VAS(100)	ω
Kim et al ⁽²⁰⁾	Korea	ED	71	48:46	10% L nasal and pharynx spray	No intervention	Both nostrils 2 sprays, 3 sprays to throat, 16~20F NG tube insertion with lubricant ielly	AE, VAS(100)	5.5
Wolfe et al ^{t22]}	USA	E	40	44:49	4% L Atomized, 5mL 2% L topical gel	0.9% NS solution, 5 mL 2% L topical gel	1.5 mL atomized in nasopharynx, 3 mL atomized in oropharynx, 5 mL 2% L del insertion nostril. 18F NG	VAS(100)	ω
Singer and Konia ⁽²¹⁾	USA	E	40	53:57	5 mL 2% L topical gel; nasal and pharynx spray	5mL of intranasal lubricant	Insertion nostril 2 sprays 0.5% phenylephrine, 5 mL of 2% L gel intranasal, throats sprayed with 2% tetracaine, 2% buth aminobenzoate, 14% benzocaine, 16F NG	AE, Likert scale, no. of attempts, VAS(100)	Q

3

AE = adverse effect, C = control group, ED = emergency department, F = female, FLACC = Face, Legs, Activity, Cry, and Consolability pain and distress assessment tool, L = lidocaine, M = male, Mins = minutes, NA = not available, NG = nasogastric tube, No = number, NS = normal saline, SD = surgery department, T = treatment group, VAS = visual analog scale.



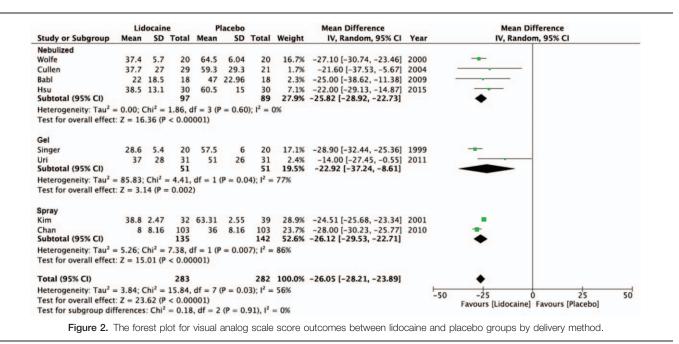
pooled through meta-analysis.^[5,9,16,18-22] The other 2 RCTs were excluded, as 1 study did not clarify the measurement of the VAS score used,^[17] while the other study did not provide sufficient information on the study design used.^[23] The flowchart of the study selection process is summarized in Fig. 1. Thus, the analysis from the 8 included RCTs consisted of a total of 565 subjects. The primary outcome of most RCTs was to measure pain during NG insertion. Two studies^[5,18] assessed discomfort that was considered as synonymous with pain. Seven studies used the VAS 100 mm measurement and 1 study^[5] used the VAS 25 mm measurement, which for the purpose of our analysis was converted to the 100 mm scale by multiplying the result by 4. Overall, the meta-analysis showed a significant reduction in VAS score in the lidocaine group with a MD = -26.05, 95% CI, -28.21 to -23.89, P < .001, $I^2 = 56\%$; forest plot is shown in Fig. 2.

To explore the cause of heterogeneity, we performed a subgroup analysis according to the lidocaine concentration (Fig. 3) and method of delivery (Fig. 2). In 4 of the 8 studies, lidocaine used in 2% concentration as the intervention was effective in reducing discomfort (MD = -24.18, 95% CI, -30.25 to $-18.12, P < .001, I^2 = 55\%$).^[9,16,19,21] Results from 1 study using 4% lidocaine were also shown to decrease pain (MD = -27.10, 95% CI, -30.75 to -23.45, P < .001)^[22] and 3 studies using 10% lidocaine yielded a similar outcome (MD = -25.94, 95% CI, -29.07 to $-22.81, P < .001, I^2 = 74\%$).^[5,18,20] In the subgroup analysis of the different delivery methods of lidocaine, 4 studies employing the use of nebulized/atomized lidocaine showed reduction in pain (MD = -25.82, 95% CI, -28.92 to

-22.73, P < .001, $I^2 = 0\%$).^[16,18,19,22] Two studies comparing lidocaine gel to K-Y and lubricant gel also found lidocaine to be more effective in decreasing discomfort (MD = -22.92, 95% CI, -37.24 to -8.61, P = .002, $I^2 = 77\%$).^[9,21] The remaining 2 studies testing the effect of nasal and pharynx spray of lidocaine also had lower VAS scores than the control group (MD = -26.12, 95% CI, -29.53 to -22.71, P < .001, $I^2 = 86\%$).^[5,20]

Sensitivity analysis was also performed to determine whether the outcomes were altered after the removal of any of the studies. All results were stable and no significant difference was found. These results indicated that no single study carried enough weight to significantly influence the pooled results. Given the asymmetry of the funnel plot on visual inspection, publication bias is likely to be present (Supplement 4, http:// links.lww.com/MD/C97).

The difficulty of NG tube insertion was assessed using a 5-point Likert scale in 4 studies.^[5,9,16,18] The scale marked "minimal," "slight (less difficult than usual)," "moderate (usual amount of difficulty)," "substantial (more difficult than usual)," and "extreme." The meta-analysis did not show a significant reduction in Likert scale (MD=-0.30, 95% CI, -1.30 to 0.70, P=.55) nor an increase in the number of NG tube insertion attempts (MD=-0.22, 95% CI, -0.98 to 0.53, P=.56).^[5,9,16] For the adverse effect of nasal bleeding, no significant difference was found between the lidocaine group and the placebo group when all the patients were pooled into our meta-analysis, OR = 0.62; 95% CI, 0.11–3.41, P=.59.^[5,16,18,19,21] There was also no detectable difference in vomiting between the 2 groups (OR = 0.30; 95% CI, 0.07–1.27, P=.10).^[5,9,17–19,21]



4. Discussion

NG tube insertion is a common procedure in the clinical setting for all ages of patients. Although a useful tool, it is also a procedure that causes much discomfort and pain for the patient. The aim of this paper is to create a comprehensive up-to-date summary of the studies done on methods to minimize patient discomfort in NG tube insertions.

In our review, we did not limit our search on method of lidocaine delivery; rather, methods included nebulized, atomized, spray or topical gel, etc. All of the selected publications used a randomized placebo-controlled design, which reduced the risk of bias, and were critically appraised using the modified Jadad scale. We selected 10 articles of moderate and high-quality RCTs with 5 articles achieving a full score of 8.^[5,9,16,18,22] We expanded our

search to incorporate papers in all languages and all age groups. Our study demonstrated that the application of lidocaine before NG tube insertion was associated with 26% less pain and discomfort as evaluated by the VAS score and should be considered in daily medical practices.

Previously, Li et al^[24] reviewed 6 RCTs involving 384 patients and reported that the administration of intranasal lidocaine spray reduced the discomfort of NG tube insertion. Kuo et al^[7] also conducted a systemic review and meta-analysis of 5 RCTs with 212 subjects regarding the use of nebulized and atomized lidocaine to reduce the pain of NG tube insertion. In this study, they concluded that nebulized lidocaine decreased pain in patients by 57.7% as assessed by the VAS. However, they focused solely on the adult population and only included studies

	Li	docaine	2	P	lacebo			Mean Difference		Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	Year	IV, Random, 95% CI
2%										
Singer	28.6	5.4	20	57.5	6.02	20	17.1%	-28.90 [-32.44, -25.36]	1999	
Babl	22	18.52	18	47	22.96	18	2.3%	-25.00 [-38.63, -11.37]	2009	
Jri	37	28	31	51	26	31	2.4%	-14.00 [-27.45, -0.55]	2011	
Hsu Subtotal (95% CI)	38.5	13.1	30 99	60.5	15	30 99		-22.00 [-29.13, -14.87] -24.18 [-30.25, -18.12]	2015	•
Heterogeneity: Tau ²	= 19.45:	Chi ² =	6.64. 0	f = 3 (F)	9 = 0.08	(); $ ^2 = 1$	55%			370
Test for overall effect							10.008			
4% Wolfe Subtotal (95% CI)	37.4	5.73	20	64.5	6.04	20		-27.10 [-30.75, -23.45] -27.10 [-30.75, -23.45]	2000	-
Heterogeneity: Not a	oplicable					1. 77. 77. 7				
Test for overall effect			< 0.000	01)						
10%										
Kim	38.8	2.47	32	63.31	2.55	39	29 0%	-24.51 [-25.68, -23.34]	2001	
Cullen	37.7		29					-21.60 [-37.53, -5.67]		
Chan	8	8.16	103	36				-28.00 [-30.23, -25.77]		+
Subtotal (95% CI)		0.10	164	50	0.10	163		-25.94 [-29.07, -22.81]	2010	•
Heterogeneity: Tau ² =	= 4.51: 0	$chi^2 = 7$.58. df	= 2 (P	= 0.02)	$ ^2 = 74$	4%			1. A A A A A A A A A A A A A A A A A A A
Test for overall effect										
Total (95% CI)			283			282	100.0%	-26.05 [-28.21, -23.89]		•
Heterogeneity: Tau ² =	- 3 84.0	⁻ hi ² - 1		IF - 7 (0	- 0.03					
Test for overall effect					- 0.03	, i = .	0/0/0			-50 -25 0 25 50
Test for subgroup dif					P - 0 7	1) 12 -	0%			Favours [Lidocaine] Favours [Placebo]

Figure 3. The forest plot for visual analog scale score outcomes between lidocaine and placebo groups by concentration.

written in the English language. Their review did not discuss the adverse effects, difficulty of NG insertions, or number of NG tube insertion attempts.

Moderate heterogeneity was noted in our meta-analysis. Different doses and delivery methods of anesthesia may explain some of the heterogeneity. We conducted a subgroup analysis in delivery methods of anesthesia to reduce heterogeneity. In the subgroup analysis, the nebulized, gel, and spray form of lidocaine were all shown to decrease VAS pain score (MD= 25.82 vs 22.92 vs 26.12). Likewise, a subgroup analysis of the different concentrations of lidocaine all had a significant reduction in pain during NG tube insertions (MD=2%:24.18 vs 4%:27.10 vs 10%:25.94). Thus, the use of lidocaine, regardless of concentration or method of delivery, can decrease patient discomfort. Although it seems that lidocaine is a feasible method to alleviate the pain felt by NG intubation, we are unable to recommend the exact dose or preferred method of delivery. Ducharme and Matheson ^[25] studied 30 healthy volunteers, comparing the anesthetic effects of 1.5 mL 4% atomized lidocaine, 1.5 mL 4% atomized cocaine, and 5 mL 2% lidocaine gel in NG intubations. All 3 medications were effective in decreasing pain as shown by VAS scores. However, overall discomfort was noted less in lidocaine gel and the subjects seemed to prefer this method above the other 2 atomized agents. More head-to-head studies of the many concentrations and methods of lidocaine delivery may be needed to determine the best protocol. We also realize that the different methods of lidocaine delivery are dependent on the cost, availability, and preparation time in each clinic setting. Thus, the emphasis is on individualized therapy and health care providers should make a recommendation best regarding each patient.

Difficulty of NG tube insertion as measured by the 5-point Likert scale and number of NG tube insertion attempts did not show a significant difference between the treatment and control groups. These findings suggest that the application of lidocaine before NG intubation was not associated with more difficult tube insertions nor did it increase the number of insertion attempts. This was in contrast to the study done by Uri et al,^[9] where topical lidocaine gel used was associated with an increase in difficulty of NG tube insertions. On the contrary, Chan and Lau^[5] found that the application of lidocaine spray reduced NG intubation difficulty, duration, and number of attempts.

In our analysis, there was no detectable difference regarding the adverse effect of nasal bleeding or vomiting between the 2 groups. Thus, applying lidocaine before intubation can reduce pain and discomfort without increasing nasal bleeding or vomiting. In contrast, Cullen et al^[18] found that although nebulized lidocaine was shown to be effective in reducing the discomfort of NG intubation, it was also associated with an increased incidence of epistaxis. However, studies done by Chan and Lau,^[5] Chao,^[17] and Hsu and Tang^[19] all demonstrated that lidocaine use was associated with a decreased frequency of nausea and vomiting. Future studies should consider further investigation of the adverse effects of lidocaine on NG tube insertions.

There are some limitations to our study. Only 10 publications were selected for our study but most of them were moderate and high-quality RCTs. Due to the small number of data collected from the included RCTs, the following variables were not assessed: chest pain, cough, shortness of breath, and endotracheal intubation. Additional research is needed to determine the most efficient method with the least adverse effect. Furthermore, only 1

study out of the 10 assessed was a pediatric RCT, thus we are unable to make a strong recommendation for child patients.^[16] Most of the RCTs included in this meta-analysis focused on the effects of lidocaine on an adult population. Thus, more studies are needed to make a final conclusion on the benefits of lidocaine in children during NG intubations.

5. Conclusion

Current evidence confirms the clinical benefit of lidocaine in reducing pain associated with NG tube insertions as assessed by the VAS and that every health care provider should consider using some form of anesthesia before attempting this procedure.

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