Lidocaine for pain relief during nasogastric intubation: systematic review and meta-analysis

Lidocaína para o alívio da dor durante a intubação nasogástrica: revisão sistemática e meta-análise

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ABSTRACT

BACKGROUND AND OBJECTIVES: Procedural acute pain is a common experience associated with nasogastric tube insertion. Nevertheless, there is an important gap in the knowledge on its management. Lidocaine seems an effective option for relieving procedural pain. The objective of this study was a systematic review with metanalysis to evaluate the analgesic efficacy of jelly, spray, atomized and nebulized lidocaine during nasogastric intubation in adult patients.

CONTENTS: The Pubmed, LILACS, Scopus, CINAHL and Cochrane databases were searched using the keywords: pain, acute pain, pain management, lidocaine and gastrointestinal intubation. The identified articles were then screened according to the population, intervention, comparison, outcome and type of study. A total of 192 people were included, 30 of whom were healthy, while 162 had gastrointestinal disorders. The data revealed heterogeneity between the studies regarding the presentation and administration route of lidocaine, as well as the comparison groups. The group pain scores that received atomized lidocaine were significantly different from those of the control group (37.4 vs 64.5), the lidocaine spray group (23.6±16.6 vs 43.1±31.4) and the lidocaine gel group (33±29 vs 48±27). In the study evaluating lidocaine gel, atomized lidocaine and cocaine, the results were 19.3±24.9, 23.9±26.4, 30.5±29.6, respectively.

CONCLUSION: Thus, the metanalytic estimate showed that lidocaine led to a significant reduction in pain compared to the control group in all studies.

Keywords: Gastrointestinal intubation, Lidocaine, Pain, Pain measurement.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor aguda procedural é uma experiência comum associada à inserção da sonda nasogástrica. No entanto, existe uma lacuna importante no conhecimento sobre sua gestão. A lidocaína parece uma opção eficaz para aliviar a dor procedural. O objetivo deste estudo foi realizar uma revisão sistemática com meta-análise para avaliar a eficácia analgésica da lidocaína durante a intubação nasogástrica em pacientes adultos.

CONTEÚDO: As bases de dados Pubmed, LILACS, Scopus, CINAHL e Cochrane foram pesquisadas utilizando as palavras-chave: dor, dor aguda, manejo da dor, lidocaína e intubação gastrointestinal. Os artigos identificados foram selecionados de acordo com a população, intervenção, comparação, resultado e tipo de estudo. Foram incluídas 192 pessoas, 30 das quais saudáveis, enquanto 162 apresentavam distúrbios gastrointestinais. Os dados revelaram heterogeneidade entre os estudos sobre a apresentação e via de administração da lidocaína, bem como os grupos de comparação. Os escores de dor do grupo que recebeu lidocaína atomizada foram significativamente diferentes daqueles do grupo controle (37,4 vs 64,5), do grupo spray de lidocaína (23,6±16,6 vs 43,1±31,4) e do grupo gel de lidocaína (33±29 vs 48±27). No estudo que avaliou gel de lidocaína, lidocaína atomizada e cocaína, os resultados foram 19,3±24,9, 23,9±26,4, 30,5±29,6, respectivamente.

CONCLUSÃO: Assim, a estimativa meta-analítica mostrou que a lidocaína levou a uma redução significativa da dor em comparação com o grupo controle em todos os estudos.

Descritores: Dor, Intubação gastrointestinal, Lidocaína, Mensuração da dor.

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage and frequently occurs during therapeutic procedures, such as venous and arterial puncture, collection of tracheal aspirate and urinary and nasogastric tube insertion[1-5].

Pain associated with nasogastric intubation (NI) is attributable to mechanical trauma to the nasal mucosa. Despite the existence

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of scales to measure pain and pharmacological and nonpharmacological methods for pain relief, procedural pain management remains neglected[6,7].

Unlike endoscopic procedures for which patients are sedated, NI is performed with lidocaine jelly, without previous preparation, and only the tube tip is lubricated with the anesthetic, facilitating advancement of the device without providing an analgesic effect[8,9].

Randomized controlled trials have demonstrated that atomized lidocaine spray or nebulized lidocaine may effectively mitigate pain during NI, thus providing increased comfort and reducing pain during the procedure[8,9].

Given the scarcity of studies on the subject, a systematic review to evaluate the analgesic efficacy of lidocaine (jelly, spray, atomized and nebulized) during NI was performed.

This is a systematic review following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and is registered in the International Prospective Register of Systematic Reviews (PROSPERO) - CRD42018091999.

The objective of this study was a systematic review with meta-analysis to evaluate the analgesic efficacy of lidocaine (jelly, spray, atomized and nebulized) during NI in adult patients.

CONTENTS

Eligibility criteria

The elements of the PICOT (population, intervention, comparison, outcome and type of study) strategy were chosen as the eligibility criteria:

1. Population – adult patients who underwent gastrointestinal intubation.
2. Intervention – lidocaine jelly, spray/atomized lidocaine or aerosol/nebulized lidocaine.
3. Comparison – placebo or control without lidocaine.
4. Outcome – pain relief.
5. Type of study – randomized controlled trials (RCTs).

Studies published until November 2017 in English, Spanish and Portuguese were included. Studies in which pain was not clearly defined or those in which validated scales for measuring pain were not used were excluded. Thus, the strategy generated the following question: is jelly, spray, atomized or nebulized lidocaine effective for pain relief during NI in adult patients?

Search strategy

A systematic search was conducted in November 2017 by two reviewers at different times and locations to identify RCTs in the following databases: Pubmed, Scopus, Bireme, CINAHL and Cochrane Library. The PROSPERO and ClinicalTrials.gov were also referred to identify possible ongoing studies on the topic. Additionally, searches in Google Scholar and manual searches of the reference lists of the included articles were conducted to identify relevant references that had not been retrieved in previous searches.

The following MeSH terms were used for the search: "Intubation, gastrointestinal", "Lidocaine", "Pain", "Acute pain", "Nociceptive pain", "Pain management", "Pain measurement" and "Analgesia".

Study selection

The reviewers independently screened the studies retrieved by reading the titles and abstracts. The studies considered relevant were read in full and included in the review when they met the eligibility criteria. The degree of agreement between the reviewers was assessed using the Cohen (k) Kappa coefficient as follows: $k<0.10$ – no agreement, $k<0.40$ – weak agreement, $k=0.40$ to 0.75 – good agreement and $k>0.75$ – excellent agreement. Any disagreements were resolved by a third reviewer.

Data extraction

Data was extracted from the studies using an instrument created by the principal investigator, which included the location and year of the study, sample size, subject ages, the male to female ratio, the pain scale used, tube size, the intervention protocol, secondary variables and main outcomes.

Analysis of the risk of bias

To analyze the risk of bias, RevMan 5.3 software was used according to the Cochrane guidelines using the following domains: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of the outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias) and other sources of bias (other biases). The risk was classified into three categories according to the evaluation of each domain: low risk of bias, high risk and uncertain risk.

Meta-analysis

The efficacy of lidocaine was assessed according to the pain parameters reported by the patients using a visual analog scale (VAS). The results were combined to increase statistical power and were summarized using a meta-analysis of the mean differences between the two groups.

The heterogeneity of the meta-analysis was assessed using Cochran's Q test and the Higgins I^2 test. The assumption that the studies included in the meta-analysis would be homogeneous was considered the null hypothesis in Cochran's Q test. The Higgins I^2 test result was categorized on a scale where a value close to 0% indicates no heterogeneity between studies, a value close to 25% indicates low heterogeneity, a value close to 50% indicates moderate heterogeneity, and a value close to 75% indicates high heterogeneity.

After the analysis of heterogeneity, the model to be used in each of the meta-analyses, the fixed-effects model or the random-effects model was selected. The fixed-effects model assumes that the effect of interest is the same in all studies and that the observed differences between them are due only to sampling errors. The random-effects model assumes that the effect of interest is not the same in all studies and considers that the studies included in the meta-analysis form a random sample of a hypothetical population of studies. The random-effects model was used in cases of moderate or high heterogeneity (Higgins I^2 greater than 50%).

The meta-analysis was then performed using the mean differences between the two groups as effect measures. Meta-effect estimates of the mean differences with the respective 95% confidence intervals were reported. A funnel plot was used to evaluate the publication bias potential. A significance level of 0.05 was adopted. All analyses were performed in R version 3.5.1 (R Core Team, 2018) using the "etaphor" package[10,11].

RESULTS

Study eligibility

The search strategy identified 101 records, 22 of which were excluded because they were duplicates. Screening by reading titles and abstracts resulted in the exclusion of 69 articles. During the full-text reading phase, six articles were excluded because they were not clear regarding pain evaluations. The final sample consisted of four articles (Figure 1). The reliability and eligibility analyses of the studies based on Cohen's Kappa coefficients for titles and abstracts yielded moderate results 0.41-0.47, respectively, and excellent results for inclusion of the final studies in the analysis (1.0).

Among the four articles selected, one study evaluated pain during NI in healthy patients and three studies evaluated pain in patients with gastrointestinal disorders during feeding or due to upper or lower gastrointestinal bleeding and intestinal obstruction[9,10-15]. The VAS was used in all studies.

Sociodemographic and clinical data

A total of 192 people were included in the four studies. Among them, 30 patients were healthy and 162 presented with gastrointestinal disorders. The procedures were performed in outpatients and clinical inpatients (Table 1).

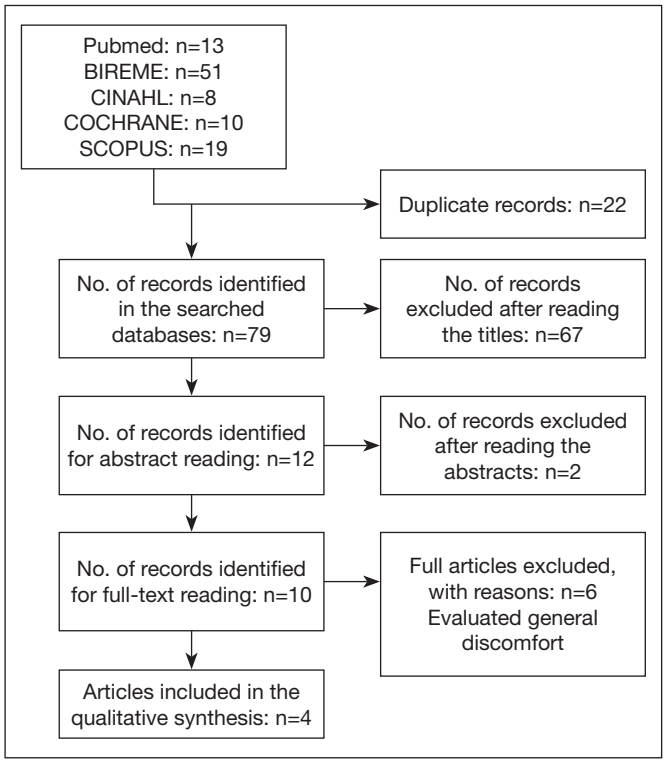

Figure 1. Flowchart of the articles included in the study

Table 1. Baseline data

Characteristics	Studies			
	Wolf et al.[18]	Ducharme and Matheson[8]	Pongprasobchai et al.[27]	Uri et al.[17]
Year of publication	2000	2003	2007	2011
Country	USA	Canada	Thailand	Israel
Sample size	40	30	60	62
Type of tube	NGT	NGT	NGT	NGT
Tube diameter	18F	Not reported	14F and 18F	16F
Pain scale	VAS	VAS	VAS	VAS
Age (mean±SD)				
Lidocaine	49±19.2	Not reported	55±16.4	68±19
Placebo	40.1±18.4		55±16.2	64±17
M/F ratio [n (%)]				
Lidocaine	7 (35) 13 (65)	Not reported	11 (35.5) 20 (64.5)	19 (61.3) 12 (38.7)
Placebo	9 (45) 11 (55)		21 (72.4) 8 (27.6)	21 (67.7) 10 (32.3)

NGT = nasogastric tube; VAS = visual analog scale; SD = standard deviation; M/F = males/females.

Protocols used in the studies

The diameter of the nasogastric tube ranged from 14F to 18F according to the indication for intubation, and one of the studies did not report this variable (Table 1).

Table 2 shows the intervention protocols of the four RCTs included in the final analysis. The data reveals heterogeneity between the studies regarding the presentation and administration of lidocaine, as well as the comparison groups. In addition, the studies diverged on the timing of intubation, which was performed immediately after the analgesic intervention or after an interval standardized in the protocol. The pain scores of the atomized lidocaine group differed significantly from those of the control group (37.4 vs 64.5), the lidocaine spray group (23.6±16.6 vs 43.1±31.4) and the lidocaine gel group (33±29 vs 48±27). In the study evaluating lidocaine gel, atomized lidocaine and cocaine, the pain scores were 19.3±24.9, 23.9±26.4 and 30.5±29.6, respectively (Table 3).

Risk of bias

The risk of bias in the studies was assessed according to Cochrane's guidelines for RCTs. The risk of bias was classified as low, especially for the selection, performance and detection biases (Figure 2).

Description of the meta-analysis results

The analysis of the mean differences in pain scores showed heterogeneity, with a significant Cochran's Q test result (Q(df=3)

Table 2. Protocols of the studies

Authors	Presentation	Experimental intervention	Control intervention	Form of administration
Wolf et al.[18]	4% atomized L; 2% L gel; 0.9% saline.	4.5mL of 4% atomized L + 5mL of 2% L gel.	4.5mL of SSN + 5mL of L gel 2%.	1.5mL of the solution was atomized in the nostril and 3 mL was atomized in the oropharynx. Shortly after, 5mL of atomized 2% L gel was administered to both groups, and the tube was inserted immediately.
Ducharme and Matheson[8]	4% atomized L; 4% atomized C; 2% L gel.	1.5 mL of 4% atomized L; 1.5mL of 4% atomized C; 5mL of 2% L gel.	The patient was under his own control.	The atomized agents and gel were administered into the nostril and then the tube was inserted. The nostril was flushed and an interval of one hour was adopted until the next intubation.
Pongprasobchai et al.[27]	10% L spray; 2% L gel; 0.9% saline.	1.4mL of 10% L spray + 3mL of 2% L gel.	1.4 mL of saline spray + 3 mL of 2% L gel.	Two puffs of spray agent in the nostril and six puffs in the oropharynx. Three minutes later, the tube was inserted with 3mL of 2% L gel in both groups.
Uri et al.[17]	2% L gel; K-Y gel.	5mL of 2% L gel	5 mL of placebo gel.	The agent was administered into the nostril, and after a five-minute wait, the tube, whose tip had been lubricated with the placebo gel, was inserted.

L = lidocaine; C = cocaine.

Table 3. Description of the pain results

Authors	Mean±SD
Wolfe et al.[18]	37.4 vs 64.5
Pongprasobchai et al.[27]	23.6±16.6 vs 43.1±31.4
Uri et al.[17]	33±29 vs 48±27
Ducharme and Matheson[8]	
Lidocaine gel	19.3±24.9
Atomized lidocaine	23.9±26.4
Atomized cocaine	30.5±29.6

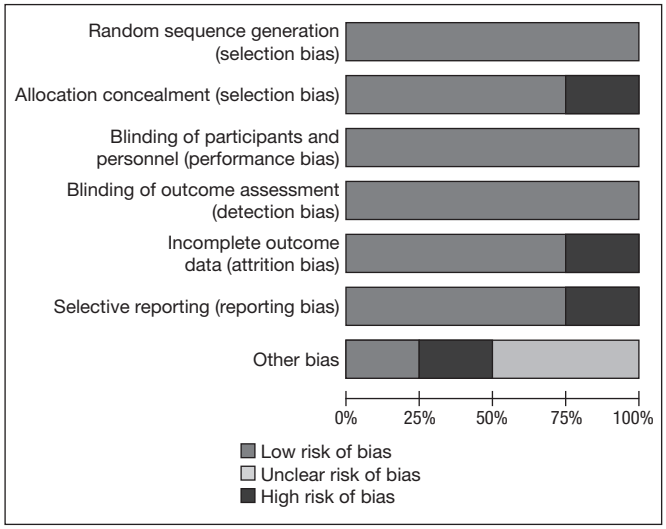

Figure 2. Risk of bias summary showing the review authors' judgments about each risk of bias domain for each included study

= 7.9701, p value=0.0466) and a Higgins I^2 value of 62.13%. Therefore, the random-effects model was used. The meta-analysis (Figure 2) yielded a significant meta-analytic estimate of -16.56 (95% CI: -25.88 to -7.24). The funnel plot (Figure 3) used to assess the publication bias showed some asymmetry.

DISCUSSION

The present systematic review demonstrated a favorable effect of lidocaine on pain relief during NI. Nasogastric tube insertion is frequently performed in individuals who need help with feeding or who have some gastrointestinal disorder. Although nasogastric tube insertion is a very important tool for health recovery, it also causes the patient pain[2,12].

Procedural pain has several consequences, such as changes in physiological parameters, anxiety, fear and discomfort[13]. Thus, nonpharmacological and pharmacological therapies during painful procedures, such as lidocaine spray or nebulized lidocaine, are important tools to promote patient well-being and satisfaction.

Considered the fifth vital sign, pain is a multidimensional, subjective, perceptive, sensorial and emotional experience of varied etiologies. Although studies have shown that nasogastric tube insertion is one of the most painful procedures, the pain associated with this procedure remains neglected by many professionals and is not systematically assessed; consequently, this pain is often undertreated[4,8,14-18].

Pain should be properly investigated, evaluated, treated, re-evaluated and recorded. Adequate pain treatment is a patient's right and should not be neglected by health professionals, especially since persistent pain causes important organic changes with systemic and psychological effects[19-21].

Unlike endoscopic procedures for which analgesia is used together with sedation, NI is performed daily in emergency and medical departments without prior preparation, and only the tube tip is lubricated with anesthetic[2,12]. The results of the meta-analysis indicate that the use of lidocaine, whether in the form of jelly or spray, atomized lidocaine or a combination of forms, significantly reduces pain when following a protocol, rendering this agent an important ally in the management of pain during intubation[8,14,17,18]. Thus, the use of lidocaine in its various presentations should be incorporated into institutional clinical protocols to ensure adequate pain management and humanization of patient care.

The reasons for undertreatment include a lack of knowledge of the pain process, inexperience with the use of scientifically validated scales to measure pain, normalization of the pain associated with NI and unavailability of local anesthetic preparations[7,14,15,22-27]. Ineffective use of pain relief strategies during painful procedures can cause patients to have unpleasant experiences, jeopardizing their adherence to treatment or even causing them to refuse to undergo the procedure in the future, as well as increasing the risk of chronic pain[26].

One of the limitations of this systematic review was the heterogeneity of the intervention protocols used in the studies. The tube diameter and the indication for the procedure diverged between studies, and the timing of tube insertion may have contributed to the differences in the results[8,14,17,18].

The research results reveal that the analgesic technique widely used for nasogastric tube insertion in daily clinical practice is insufficient for pain relief[8,14,17,18]. Some studies recommend the use of new techniques, such as a combination of anesthetic spray or nebulizers with a topical gel agent and sufficient time to allow the analgesic effect to occur[14]. However, further studies using the same analgesic protocol during NI are needed. The establishment of institutional protocols and policies for analgesia, coupled with adequate methods of evaluation, treatment and re-evaluation of pain, should be routine in health services.

The strength of this study is the methodological rigor adopted for the selection of articles and presentation of the results, as well as the use of two reviewers to evaluate the titles, abstracts and summaries of the results. The PRISMA guidelines were followed, therefore, the suggestion is to incorporate the results of this systematic review into clinical practice as recommended by the International Association for the Study of Pain (IASP).

CONCLUSION

Lidocaine may be an important analgesic agent for pain management during nasogastric intubation. However, it is strongly recommend that further RCTs should be conducted using the same study protocol so that the results are comparable and meta-analyses can be carried out.

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