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Long Acting Local Anaesthetic Agents as Alternative or Adjuvants to Systemic Analgesics in Management of Immediate Postoperative Pain Following Cleft Palate Surgeries-A Systematic Review

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ABSTRACT

To systematically identify, evaluate and assess the efficacy of systemic analgesics with that of long acting local anaesthetic agents in management of post-operative pain in patients undergoing palatoplasty.

Objective: To identify, appraise and assess the available evidence in literature on the use of long acting amide local anaesthetic agent as an alternative and/or adjuvant to systemic analgesics in management of post-operative pain in paediatric patients undergoing palatoplasty which in turn may lead to reduction in complications associated with opioid/ NSAIDs consumption.

Methods: A comprehensive search was done using electronic databases of PubMed, Google Scholar and Cochrane central register of controlled trials were searched for related studies along with a complementary manual search of relevant journals using PICO terms. The title scan was done to identify relevant articles, which were further evaluated for inclusion by reading the abstract. Bibliography of all the identified studies was scanned to include studies published outside the electronic database.

Results: Electronic database search identified 29 articles. Out of which, 19 were excluded after removing duplication and 15 were excluded after reading titles. 4 studies were evaluated in detail after reading the abstract and full text. A final of 2 studies were included based on the inclusion criteria to meet the research question. The studies analysed quantity and need for post-operative rescue analgesia in patients undergoing palatoplasty.

Conclusion: Cleft palate repair is a painful procedure which needs a standardised approach to address post-operative pain in children. The available evidence based on the included studies show those loco-regional nerve blocks with long acting amide local anaesthetic agents are a safe, effective and simple measure for management of postoperative pain in a predictable manner after palatoplasty. Regional anaesthesia also reduces the total consumption of systemic analgesics in the first 48 hours post operatively. However, limited number of studies is available, hence we can only draw a guarded conclusion that postoperative complications associated with systemic analgesics can also be reduced in children.

Key words: Cleft Palate, Palatoplasty, Local anaesthetic agents, Bupivacaine, Ropivacaine

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INTRODUCTION

Clefts of the lip and/or palate are one of the most common craniofacial malformations characterised by complete or partial cleft of the lip and/or palate, with severity ranging from notching of lip to a complete non-fusion of lip, primary cleft palate or secondary cleft palate [1, 2]. Orofacial clefts may not be lethal but are psycho-socially debilitating due to the effect on stomatognathic functions and facial aesthetics. Worldwide the burden of all oral clefts is estimated to be about 1 in every 700 live births [3]. But the incidence of isolated cleft palate is difficult to assess, due to a huge overlap between cases of cleft lip and palate with that of cleft palate alone. An incidence range of 0.1-1.1 per 1000 births is reported for all cleft palates. Prevalence also has a racial variation with Asiatic races exhibiting higher rates of cleft palate [4,5].

Cleft palate surgical repair was first performed not until the 19th century despite descriptive evidence of the anomaly in ancient texts [6,7]. Primary surgery or palatoplasty varies greatly depending upon the surgical technique used, the age of the patient at the time of operation, anaesthetic technique used, and the postoperative management [8]. Early surgery is necessitated by the fact that there is a need to reduce difficulty in phonation, feeding and at the same time

reduce complications such as sinusitis and respiratory tract infections in affected children [9].

Palatoplasty is usually performed when the child is between 6 months to 1 year of age [10]. Repair of the hard palate is performed using a bi-layer closure with a bi-pedicled or posteriorly based mucoperiosteal flap and nasal mucosal flaps sutured in the midline. These flaps are based on the palatine vessels [11]. Soft palate is approximated in a bilayer manner and intravelar veloplasty involving dissection with retro-positioning of levator veli palatini muscle is also a part of this repair. The push back technique provides increased length for the palate and places the levator muscle in a more favourable position. Often releasing incisions are placed laterally to aid in dissection and to reduce mid-line tension during closure. These lateral incisions are commonly not sutured at the time of closure. It is thought that a combination of aggressive dissection and open releasing incisions are the main contributors to postoperative pain following palatoplasty [10].

Inadequate postoperative analgesia in combination with vigorous crying may lead to wound dehiscence and pulmonary complications [12]. These might lead to a delayed recovery and prolonged hospital stay. Postoperative analgesia in patients undergoing cleft lip and palate repair is associated with a potential risk of airway obstruction secondary to soft tissue swelling, bleeding, and reduced respiratory drive from administration of peri operative opioids to control pain [13,14]. Administration of opioids requires close monitoring and a longer duration of hospital due to the risk of postoperative airway obstruction and respiratory depression which requires vigilant monitoring, particularly during the first 24 hours postoperatively [15-17].

The use of regional nerve blocks for postoperative pain relief in infants and children has gained popularity in recent years as it provides a longer duration of pain free period and avoids the complications of opioids and/or non-steroidal anti-inflammatory drugs (NSAIDs) [18-20]. Combination of nerve blocks produces effective prolonged analgesia and reduces the dose of postoperative systemic analgesics [21-23]. Guidelines for management of post-operative analgesia following palatoplasty have not been established. As there is no universally accepted mode of opioid/NSAIDs sparing, this study focuses on identification and appraisal of available evidence in existing literature regarding the use of long acting amide local anaesthetic agents for analgesia in palatal repair cases post operatively.

Aim

To systematically evaluate the efficacy of systemic analgesics with that of long acting local anaesthetic agents in management of post-operative pain in patients undergoing palatoplasty.

Structured question

Is the use of long acting anaesthetic agents such as bupivacaine and ropivacaine injected as regional blocks an effective alternative and/or adjuvant to systemic analgesics such as NSAIDs or opioids when used to manage immediate post-operative pain in patients undergoing cleft palate repair surgery?.

PICO analysis

- Population: Patients undergoing cleft palate repair surgery.
- Intervention: Long acting amide local anaesthetic agents (Bupivacaine/Ropivacaine).
- Comparison: Systemic Analgesics (NSAIDs/Opioids).
- Outcome: First dose of rescue analgesia.

MATERIALS AND METHODS

This review was done in accordance with guidelines given by Cochrane Handbook of Systematic Review.

Sources

Inclusion criteria

Studies were selected using the following inclusion criteria,

All studies including:

- All study designs in paediatric patients up to 6 years of age undergoing primary palatoplasty.
- All randomised controlled studies including patients undergoing primary palatoplasty for repair of cleft palate.
- Studies using long acting amide anaesthetic agents for post-operative pain management in cleft palate surgeries.
- Studies published in English language only.

Exclusion criteria

Studies were excluded based on the following exclusion criteria.

- Studies involving older children or adults.
- Studies involving comparison of systemic analgesics with other methods of pain management.
- Ongoing studies in which results have not yet been published.

Search method for the identification of studies

To identify the studies to be included for detailed evaluation in systematic review, following search strategy was developed for each database searched:

- PubMed (All types of study design published till December 2019).
- The Cochrane Central Register of clinical Trials (All types of study design published till December 2019).
- Google Scholar (All types of study design published till December 2019).

PUBMED search strategy (Figure 1a to 1c)

Advanced search of PubMed search engine was used using the following keywords:

(cleft palate) OR cleft palates) OR isolated cleft palate) OR isolated cleft palates) OR cleft palate repair) OR cleft palate repair surgery) OR cleft palate repair surgical procedure) OR cleft palate operation) OR cleft palate operative procedure) OR palatoplasty) OR primary palatoplasty) OR palatal cleft repair) OR palatal repair) OR palatal cleft closure) OR palatal cleft closure surgery) OR palatal cleft closure operation) OR palatal cleft operative procedure)) AND (analgesics) OR analgesic) OR systemic analgesic) OR systemic analgesics) OR pain killers) OR pain medication) OR pain killer drugs) OR short acting analgesics) OR non-steroidal anti-inflammatory drugs) OR non-steroidal anti-inflammatory agents) OR NSAIDS) OR non-narcotic analgesics) OR narcotics) OR narcotic analgesics) OR opioids) OR opioid analgesics) OR opiates) OR opiate analgesics) and (local anesthesia) OR LA) OR local anesthetic agent) OR local anesthetic agents) OR amide local anesthesia) OR amide local anesthetic agent) OR amide local anesthetic agents) OR long acting local anesthesia) OR long acting local anesthetic) OR long acting local anesthetic agents) OR long acting amide local anesthetic agent) OR long acting local amide anesthetic agents) OR bupivacaine) OR levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH bupivacaine) OR ropivacaine) OR 3-OH ropivacaine) and (pain) OR post-operative pain) OR post-surgical pain) OR post-operative pain management) OR post-surgical pain management) OR post op pain) OR post op pain management) OR post-operative pain management in cleft palate repair) OR post-surgical pain management in cleft palate repair) OR post-operative pain management in cleft palate surgery) OR post-surgical pain management in cleft palate surgery) OR rescue analgesia)) AND (Clinical Trial [ptyp] OR Controlled Clinical Trial[ptyp]) AND Humans[Mesh]). The search yielded 10 studies.

Search	Add to builder	Query	Items found	Time
#60	Add	Search ((((((((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery)) AND ((((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics))) AND ((((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine)) AND (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia)) Filters: **Clinical Trial; Humans**	10	10:14:08
#59	Add	Search ((((((((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery)) AND ((((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics))) AND ((((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine)) AND (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia)) Filters: **Clinical Trial**	10	10:13:49

Figure 1A: Image showing the PubMed search strategy.

#59	Add	Search ((((((((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery)) AND ((((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics))) AND ((((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine)) AND (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia)) Filters: **Clinical Trial**	10	10:13:49
#58	Add	Search ((((((((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery)) AND ((((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics))) AND ((((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine)) AND (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia))	20	10:13:41
#57	Add	Search ((((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine)) AND (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia)	37592	10:13:00
#56	Add	Search (((((((Pain) OR Post surgical pain) OR Post operative pain) OR Post operative pain management) OR Post surgical pain management) OR Post op pain) OR Post op pain management) OR Rescue analgesia	800731	10:12:42
#55	Add	Search **Rescue analgesia**	2741	10:12:06
#54	Add	Search **Post op pain management**	26101	10:11:55
#53	Add	Search **Post op pain**	101888	10:11:27
#52	Add	Search **Post surgical pain management**	4128	10:10:57
#51	Add	Search **Post operative pain management**	27339	10:10:44
#50	Add	Search **Post operative pain**	106912	10:10:30
#49	Add	Search **Post surgical pain**	21361	10:10:14
#48	Add	Search **Pain**	800461	10:10:05
#47	Add	Search ((((((((((((((((Local anaesthesia) OR Local anaesthetic agent) OR Local anaesthetic agents) OR LA) OR Amide local anaesthesia) OR Amide local anaesthetic agent) OR Amide local anaesthetic agents) OR Long acting local anaesthesia) OR Long acting local anaesthetic agents) OR Long acting amide local anaesthetic agents) OR Long acting amide local anaesthetic agent) OR Bupivacaine) OR Levobupivacaine) OR 3-hydroxybupivacaine) OR 3-OH Bupivacaine) OR Ropivacaine) OR 3-OH Ropivacaine	585575	10:09:50

Figure 1B: Image showing the PubMed search strategy.

#46	Add	Search 3-OH Ropivacaine	7	10:08:18
#45	Add	Search Ropivacaine	4739	10:08:00
#44	Add	Search 3-OH Bupivacaine	7	10:07:42
#43	Add	Search 3-hydroxybupivacaine	7	10:06:56
#42	Add	Search Levobupivacaine	1390	10:06:38
#41	Add	Search Bupivacaine	16664	10:06:23
#40	Add	Search Long acting amide local anaesthetic agent	73	10:06:11
#39	Add	Search Long acting amide local anaesthetic agents	77	10:05:30
#38	Add	Search Long acting local anaesthetic agents	170	10:05:12
#37	Add	Search Long acting local anaesthesia	393	10:04:58
#36	Add	Search Amide local anaesthetic agents	6631	10:04:33
#35	Add	Search Amide local anaesthetic agent	1438	10:04:21
#34	Add	Search Amide local anaesthesia	11839	10:04:08
#33	Add	Search LA	513381	10:03:48
#32	Add	Search Local anaesthetic agents	17436	10:00:42
#31	Add	Search Local anaesthetic agent	3481	10:00:28
#30	Add	Search Local anaesthesia	47586	09:59:34
#29	Add	Search ((((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery)) AND ((((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics)	204	09:59:01
#28	Add	Search ((((((((Analgesics) OR Analgesic) OR Short acting analgesics) OR Non steroidal anti inflammatory drugs) OR NSAIDS) OR Non steroidal anti inflammatory agents) OR Non narcotic analgesics) OR Narcotic analgesics) OR Opioids) OR Opioid analgesics	616068	09:57:51
#27	Add	Search Opioid analgesics	121286	09:56:53
#26	Add	Search Opioids	135704	09:56:43
#25	Add	Search Narcotic analgesics	137789	09:56:33
#24	Add	Search Non narcotic analgesics	360003	09:53:02
#23	Add	Search Non steroidal anti inflammatory agents	229130	09:50:58
#22	Add	Search NSAIDS	234372	09:50:41
#21	Add	Search Non steroidal anti inflammatory drugs	73187	09:50:30
#20	Add	Search Short acting analgesics	1284	09:48:48
#19	Add	Search Analgesic	594731	09:48:30
#18	Add	Search Analgesics	573401	09:47:51
#17	Add	Search ((((((((((Cleft palate) OR Cleft palates) OR Isolated cleft palate) OR Isolated cleft palates) OR Cleft palate repair) OR Palatoplasty) OR Cleft palate repair surgical procedure) OR Palatoplasty) OR Primary palatoplasty) OR Palatal repair) OR Palatal cleft repair) OR Palatal cleft closure) OR Palatal cleft closure surgery	28574	09:46:58
#16	Add	Search Palatal cleft closure surgery	1341	09:46:01
#15	Add	Search Palatal cleft closure	1641	09:45:28
#14	Add	Search Palatal cleft repair	2928	09:45:16
#13	Add	Search Palatal repair	3856	09:45:01
#12	Add	Search Primary palatoplasty	327	09:40:33
#11	Add	Search Palatoplasty	1033	09:38:41
#10	Add	Search Cleft palate repair surgical procedure	1586	09:38:21
#9	Add	Search Cleft palate repair	2921	09:38:05
#8	Add	Search Isolated cleft palates	1521	09:37:14
#7	Add	Search Isolated cleft palate	1519	09:37:01
#6	Add	Search Cleft palates	27484	09:36:47
#5	Add	Search Cleft palate	27411	09:36:39

Figure 1C: Image showing the PubMed search strategy.

Cochrane search strategy (Figure 2)

Cochrane trial for clinical registry was searched using following keywords:

(Cleft palate):ti, ab, kw OR (Cleft palate repair):ti, ab, kw OR (Cleft palate surgery):ti, ab, kw OR (Palatoplasty):ti, ab, kw OR (Palatal cleft repair):ti, ab, kw with Cochrane Library publication date Between Jan 1990 and Dec 2019, in Trials AND (Analgesics):ti,ab,kw OR (Opioid analgesics):ti, ab, kw OR (Non-steroidal anti-inflammatory agents): ti, ab, kw OR (NSAIDs):ti,ab,kw OR (Short acting analgesics):ti, ab, kw with Cochrane Library publication date Between Jan 1990 and Dec 2019, in Trials AND (Local anaesthetic agents):ti, ab, kw OR (Long acting local anaesthetic agents):ti, ab, kw OR (Amide anaesthetic agents):ti,ab,kw OR (Bupivacaine):ti, ab, kw OR (Ropivacaine):ti,ab,kw with Cochrane Library publication date Between Jan 1990 and Dec 2019, in Trial AND (Pain):ti,ab,kw OR (Post-operative pain):ti, ab, kw OR (Post-surgical Pain):ti, ab, kw OR (Post-surgical pain management):ti, ab, kw OR (Rescue analgesia):ti, ab, kw with Cochrane Library publication date Between Jan 1990 and Dec 2019, in Trials. The search yielded 6 studies.

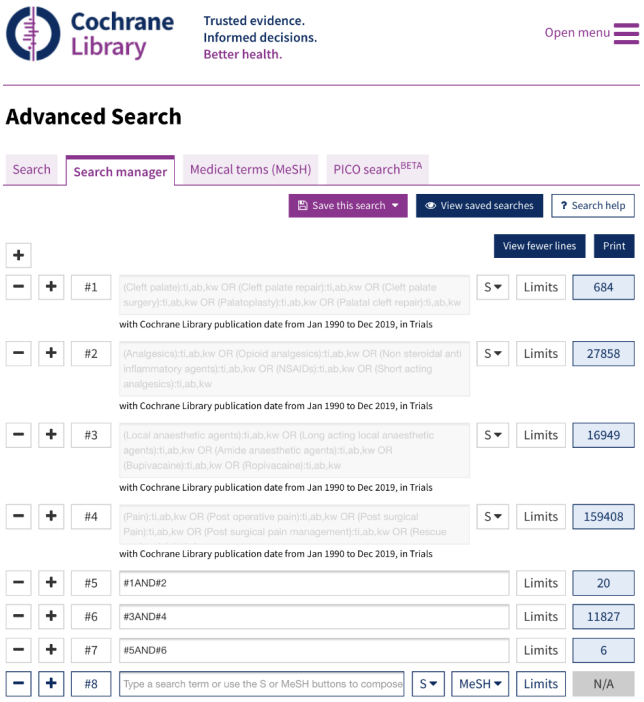

Figure 2: Image showing the Cochrane search strategy.

Google scholar search strategy (Figure 3)

Google Scholar search engine was searched using the following keywords with year of publication range set as 1990 to 2019:

Nerve block, Palatoplasty, Bupivacaine, Ropivacaine, Bilateral, Greater palatine, Analgesia, Cleft. The search yielded 13 studies.

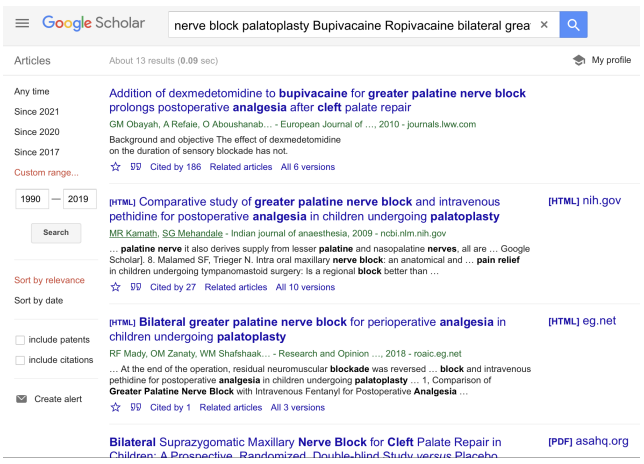

Figure 3: Image showing the google scholar search strategy.

DATA COLLECTION AND ANALYSIS

Selection of studies

One author (SHIVANGI GAUR (SG)) carried out the search strategy for the individual data bases. The total number of titles obtained were scanned and evaluated independently by two authors, SG and [MADHULAXMI M

(MM)) to identify the relevant studies. The studies duplicated in the different data bases were excluded. In case of any disagreement between the two authors, final decision was obtained by discussion between the two authors.

Abstracts of the studies were evaluated when complete information regarding the groups and participants included was not mentioned in the title. The abstract evaluation was carried out independently by two authors SG and MM to identify the final studies to be included based on the inclusion and exclusion criteria. Full text articles were evaluated when the abstracts did not provide adequate information regarding the groups compared.

Figure 4 gives the PRISMA flow diagram for the included studies (Figure 4). All the irrelevant studies were excluded and the reasons for the exclusion were noted in the characteristics of excluded studies (Table 1). The final studies included by the discussion of both the authors were further evaluated for the quality of studies following the guidelines given by Cochrane Handbook of systematic review. This was done independently by both the authors and any discrepancy was resolved by discussion between both the authors.

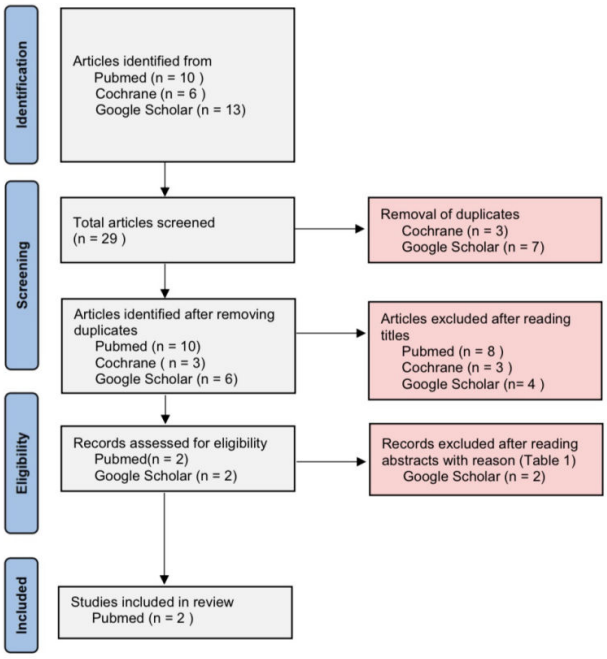

Figure 4: PRISMA flowchart showing included studies.

Table 1: Characteristics of excluded studies.

S.No	Study	Reason for exclusion
1	Moustafa et al.	Two local anaesthetic agents were compared
		No group received systemic analgesic or placebo
2	Mady et al.	No group received systemic analgesic or placebo

Data extraction and management

Data for the included studies were evaluated for the characteristics of the study. Following characteristics were included:

- Author and year of study.
- Journal.
- Study design.
- Sample size.
- Type of groups.
- Outcome assessed.
- Results.
- Conclusion.

The variables observed are mentioned in (Table 2). A detailed evaluation of the variables observed in the study was noted by their mean values and statistical significance.

Table 2: Variables of interest.

Variables of interest	
Clinical parameters	Post-operative pain control
	Duration of post-operative analgesia
	Need for rescue analgesia

Assessment of the quality of included studies

The quality of the included studies was assessed using the guidelines given by the Cochrane Handbook of systematic review. The parameters used to evaluate the included studies are as follows:

- Random sequence generation (Selection bias).
- Allocation concealment (Selection bias).
- Blinding of participants and personnel (Performance bias).
- Blinding of outcome assessment (Detection bias).
- Free of Incomplete outcome data assessment (Attrition).
- Free from baseline imbalance (Reporting bias).
- Adequate reliability.

Individual parameter was assessed for high risk, low risk and unclear risk (Table 3). The final risk of bias of individual study was determined as low risk if all the studies showed low risk for the individual parameters. In case of high risk or unclear risk for one or two parameters, moderate risk was considered for the included study. If more than 2 parameters showed high risk or unclear risk, the included study showed to have a high risk of bias.

Table 3: Criteria for the assessment of risk of bias.

S.No	Criteria	Inference
1.	Adequate random sequence generation	Yes : Random number table, computer random number generator, stratified or lock randomization, low tech-coin toss, shuffling cards, envelopes, throwing dice
		No: Quazi random- date of birth, day of visit, ID or record number, alternate allocation Non-random- choice of clinician or participant, availability
		Unclear
2.	Allocation concealment	Yes : Central allocation, sequentially numbered, sealed, opaque envelopes, identical containers
		No : Random sequence known to staff in advance, envelope or packing without any safe guard, random predictable sequence
		Unclear
3.	Blinding participants and personnel	Yes : Blinding and unlikely that blinding could have been broken, No blinding but outcome cannot be influenced
		No: No blinding, incomplete or broken blinding and outcome likely to be influenced
		Unclear
4.	Blinding of outcome assessment	Yes : Blinding and unlikely that blinding could have been broken, No blinding but outcome cannot be influenced
		No: No blinding, incomplete or broken blinding and outcome likely to be influenced
		Unclear
5.	Free of incomplete outcome data assessment (attrition, exclusion	Yes: No missing data. Reason for missing data not related to outcome and missing data balanced across the group
		No : Reason of missing data influencing the outcome
		Unclear
6.	Free from baseline imbalance	Yes: Protocol is available and all the pre-specified outcome is reported. Protocol is not available but all the outcome of interest are reported
		No : Outcome are not reported as pre-specified or outcome are reported incompletely
		Unclear
7.	Adequate reliability	Yes : Study free of any other source of bias
		No:Non-randomized studies, blocked randomization in unblinded trials.
		Unclear
	Risk of bias in the included studies	A) Low risk of bias (plausible bias unlikely to seriously alter the results) if all criteria were met. (B) Moderate risk of bias (plausible bias that raises some doubt about the results) if one or more criteria were partially met. (C) High risk of bias (plausible bias that seriously weakens confidence in the results) if one or more criteria were not met

RESULTS

Study selection

The systematic search from the electronic databases of PubMed revealed 10 studies, Cochrane library revealed 6 studies and Google Scholar revealed 13 studies. No studies were obtained from hand searching. After removal of duplicates 19 studies were identified. After title scanning, 4 studies were identified. After abstract scanning 2 articles were eliminated as they did not meet the inclusion and exclusion criteria. Full text articles for the other 2 studies were obtained for more detailed evaluation. The bibliography of these full text articles was scanned to include studies apart from the electronic databases. No relevant studies were found from the cross-reference. A total of 2 studies met the inclusion and exclusion criteria of the intended research.

Study characteristics

Characteristics of the included studies were mentioned and the Outcome of these studies were assessed using clinical parameters (Table 4 and 5).

According to Chiono et al, post cleft palate repair there is a significant difference during first 48 hours of between the nerve block and placebo groups. Morphine doses also drop by 50% in the Ropivacaine group, which was administered bilateral supra zygomatic maxillary nerve block (104.3 [68.9 to 139.6] vs. 205.2 [130.7 to 279.7] µg/kg; P=0.033). Continuous IV morphine was significantly lower in Ropivacaine group(1 patient [3.6%] vs. 9 patients [31%]; P=0.006). The SMB technique allowed lesser morphine administered which was observed in the Ropivacaine group within 2 to 12 hours postoperatively. After the 12th hour, there was a rebound of morphine consumption in the Ropivacaine group, which was related to the anaesthesia wearing off. However, the study was limited by the number of patients enrolled in the study to have a statistically significant difference between the two groups during this time interval.

Jonnavithula et al assessed the efficacy of palatal nerve block in children undergoing palatoplasty by evaluating intra operative anaesthetic requirement, postoperative analgesia and parental satisfaction. Median time for the first demand of analgesia was 6 hours postoperatively in group given with No block (NB), 18 hours in group Saline (SB) and 18 hours in the group administered with Bupivacaine (B). The mean Face Legs Activity Cry and Consolability (FLACC) scores in group NB were found to be higher when compared with the scores groups S and B. The number of patients requiring anaesthesia for pain relief for group NB was 3, group S was 0 and in group B it was 0. The analgesic requirement was significantly higher in NB compared to the group B and S. The parental satisfaction of children who received block in the group S was good in 66.6% of parents and 93% in group B but in group NB all the parents (100%) were poorly satisfied with postoperative pain management. The parental satisfaction was good in group B and S (P-0.000) and they recorded no significant complications following the administration of nerve block (Figures 5 and Figure 6).

Table 4: Characteristics of included studies.

S. No	Author and Year	Study design	Sample size and Age group	Study Groups		Outcomes assessment
				Intervention	Control	Variables Evaluated
1	Chiono et al, 2014	Prospective double blind single site randomised controlled study	60 children (Less than 5 years of age)	Ropi group- 0.15ml/kg of 0.2% Ropivacaine	Saline group- 0.15ml/kg of isotonic saline	CHIPPS Score
2	Jonnavithula et al, 2010	Prospective randomized controlled study	45 children (Less than 5 years of age)	Group B- 0.5ml of 0.25% Bupivacaine	Group NB- No block group	FLACC Score
				Group S- 0.5ml plain saline		

Table 5: Characteristics of included studies.

S. No	Author and Year	Journal	Results	Conclusions
1	Chiono et al, 2014	Anesthesiology: The Journal of the American Society of Anesthesiologists	Morphine consumption decreased by 50% in the Ropi group. CHIPPS score statistically insignificant	Bilateral SMB along with general anaesthesia reduces total consumption of morphine in 48 hours post operatively and also reduces postoperative respiratory complications.
2	Jonnavithula et al, 2010	Pediatric Anesthesia	Demand for rescue analgesia and mean post-operative pain were lower in experimental groups- B,S. FLACC scores similar in B and S group, more in NB	Palatal blocks with long acting local anaesthetic agents as well as saline produce equivalent results although duration of blockade was not consistent in

saline group. Palatal blocks are safe, effective and easy to perform for post-operative pain relief in children.

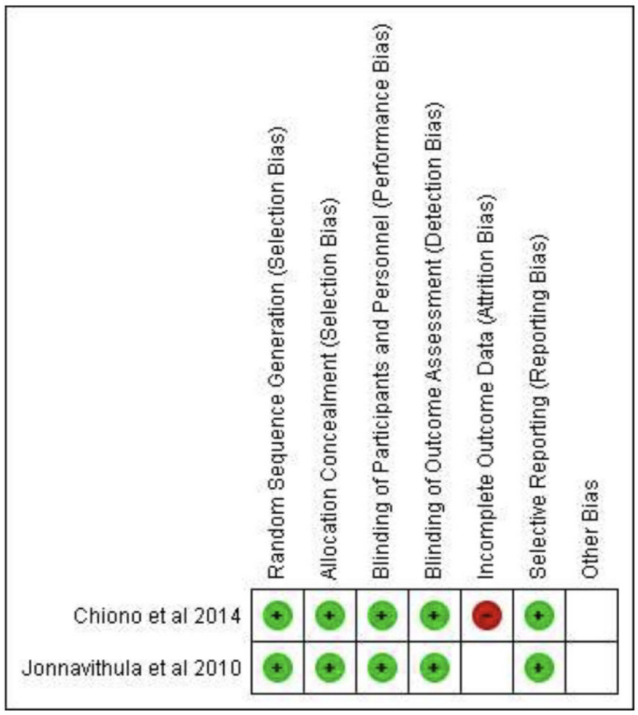

Figure 5: Risk of bias summary: Judgement about each risk of bias item for each included study.

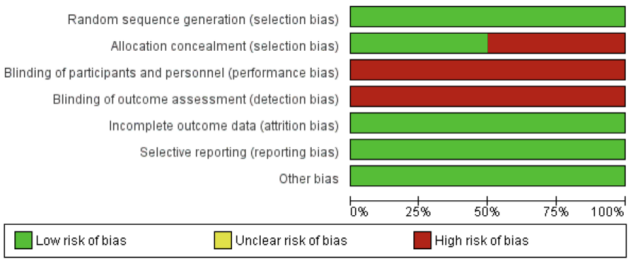

Figure 6: Risk of bias Graph: Judgement about each risk of bias item presented as percentage among included studies.

DISCUSSION

Successful ambulatory paediatric cleft lip and palate repair surgery relies on predictable postoperative recovery which is interplay of sufficient analgesia, management of postoperative nausea and adequate nourishment. Powerful nociceptive impulses are generated not only by the surgical procedure itself but also by the action of Proteolytic and inflammatory agents such as histamine, serotonin, bradykinin, and prostaglandins released into the wound tissues after cleft palate repair [24]. These inflammatory mediators act directly by activation of free nerve endings of afferent A-delta and C-fibers and indirectly by sensitisation of nerve receptors to stimulation. This inflammatory reaction at the surgical site has the onus for the activation and maintenance of pain pathway for several days after surgery. Post operatively for the paediatric age group, adequate analgesia can prevent complications like venous congestion, wound dehiscence, and blood pressure surges. All these events have the potential to risk the healing of a repaired cleft palate.

Infants have a varying sensitivity to opioids, therefore, so it becomes obligatory to decrease morphine consumption so that morphine-related respiratory depression can be avoided [25]. Surgery to repair cleft palate can lead to postoperative hypoxic episodes as the infants have a narrow upper respiratory passage which becomes severely restricted post operatively. Takemura et al [9] compared the risk of airway obstruction to the preoperative airway level after cleft palate surgery and found it to be increased in patients receiving opiates as continuous infusion. This justifies the closer monitoring of the Post-Anaesthesia Care Unit (PACU). One of the simplest methods available to reduce this burden of respiratory depression due to opiate consumption is by infiltration using long acting local anaesthetic agents intra-operatively or postoperatively. With this systematic review we aimed to evaluate the evidence in literature which supports the administration of long acting local anaesthetic agents in the management of postoperative pain following cleft palate repair in children.

Administration of long acting local anaesthetic agents is becoming the norm in managing immediate postoperative pain in all surgical cases. Long-acting agents, such as ropivacaine, bupivacaine are safe when administered in weight- based doses. The use of local anaesthetics in cleft palate surgery was first studied by Bateman, et al. [26] where all patients in his study was administered intra-operative injection of lignocaine and epinephrine, while the treatment group receiving a long-acting local anaesthetic (marcaine) and dexamethasone intra-operatively. The treatment group was found to have a shorter length of hospital stay, 86% of the patients were discharged early after 24 hours and had a faster time of first feed postoperatively.

In a study by Mostafa et al [27], they compared the effect of levobupivacaine with bupivacaine for bilateral SMB in surgeries involving cleft palate repair under general anaesthesia, FLACC pain scale scores to determine the differences between the two groups. They observed that levobupivacaine was of had the similar safety index and efficacy as bupivacaine when used for bilateral SMB.

Studies in patients undergoing bone grafting for management of alveolar clefts from anterior iliac crest and posterior iliac crest have found that bupivacaine is effective in reducing the post-operative pain as well as reduction in the need for traditional postoperative analgesia [3,28].

Ropivacaine exists as an S-enantiomer and exhibits less central nervous system and cardiovascular toxicity than bupivacaine in healthy individuals [29-32]. It has been shown that combined use of ropivacaine and Bupivacaine yields lower postoperative pain scores [33]. The systemic absorption of Ropivacaine is slower when it is given via an extradural route as compared to its analogue, bupivacaine [34]. In literature, there have been limited numbers of studies where ropivacaine was used in the oropharynx [35,36].

A study done by Coban et al [37], used ropivacaine infiltration as preemptive analgesia in patients undergoing cleft palate repair and monitored the pain scores using Children and Infants Postoperative Pain Scale (CHIPPS) at definitive observation time period. The study showed results which were favourable for reducing early postoperative pain.

A mean cumulative dose of sufentanil of 0.59 μg/kg and a mean cumulative postoperative morphine consumption of 400 μg/kg was observed in a study by Roulleau et al in 40 children undergoing cleft palate surgery [38]. Fenlon and Somerville compared mean opiate consumption in the form of IV morphine (50 μg/kg) with intramuscular codeine (1 mg/kg) in 40 children after cleft palate repair. Mean morphine consumption in PACU was found to be around 320 in the morphine group while 420 μg/kg was consumed by the codeine group [39,40].

Literature is not short on the role of a comfortable postoperative period in successful cleft palate repair surgeries. Since the age of the patients undergoing cleft palate repair is such that they are unable to communicate the degree of pain or discomfort, it becomes even more essential to see to their needs. This novel method of postoperative pain control with long acting local anaesthetic agents that have minimal side effects as compared to NSAIDs/opioids should become the standard of care worldwide while treating patients with cleft palate.

CONCLUSION

Palatal nerve blocks are easy to perform and yield a very high success rate along with being very efficacious in delivering a significant postoperative period of analgesia. Long acting local anaesthetics are used for palatal blocks, the duration of which can be determined by the type of drug being used. By administering regional field techniques, the patient's stay in the postoperative period can be made more comfortable while avoiding the complications related with conventional analgesic agents. Both Bupivacaine and Ropivacaine have been used independently in patients to manage immediate postoperative pain in patients undergoing cleft palate repair. The authors suggest that for standardisation and further validation of postoperative pain management protocols in children undergoing palatoplasty, more randomised controlled trials need to be undertaken.

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