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COMPARATIVE EFFECT OF BUPIVACAINE VERSUS LIGNOCAINE ANAESTHETIC AGENTS USED FOR SURGICAL REMOVAL OF MANDIBULAR IMPACTED THIRD MOLARS. – A SYSTEMATIC REVIEW

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ABSTRACT

BACKGROUND

Impacted third molars are commonly encountered clinical finding in the general population. Surgical removal of impacted mandibular third molars is a mandatory to prevent any complications such as occurrence of any pathologies like cyst or any sought of benign tumours pertaining to the impacted molar, and TMJ pain pertaining to the impacted tooth. Thus in recent years removal of impacted mandibular teeth has become almost mandatory due to its variations in morphology which results in impaction and also due to its less and less usage cause of which its almost becoming vestigial. In past decades there has been various techniques in removal of impacted tooth using various anaesthetic agents, among which commonly used was lignocaine.

In the recent years, the usage of bupivacaine is becoming more common due to its long action and reduced post-operative pain during treatment. After the removal of impacted third molars the most common postoperative sequelae are pain, swelling, trismus, alveolar osteitis (dry socket).Various studies have shown that the postoperative discomfort is related to the type of anaesthetic agent used. It is widely accepted that lignocaine has been used commonly as a common choice of anaesthetic agent due to its short duration of action and being less cost effective, but studies have shown better post-operative compliance using bupivacaine as an anaesthetic agent. Thus the aim of this systematic review is to compare the effect of bupivacaine and lignocaine anaesthetic agents used for surgical removal of impacted third molars.

OBJECTIVES

The objective of this systematic review is to compare the effectiveness between bupivacaine and lignocaine anaesthetic agents in surgical removal of mandibular impacted third molars.

MATERIALS AND METHODS

The Data Bases of PubMed, Cochrane and Google scholar were searched for the related topics along with a complimentary manual search of all oral surgery journals till December 2018. Articles were selected based on the inclusion criteria, which included all randomized controlled trials.

RESULTS

From this systematic review it can be concluded that bupivacaine is comparatively more effective than lignocaine as a choice of anaesthetic agent for surgical removal of mandibular impacted third molar.

CONCLUSION

The surgical removal of mandibular impacted third molar teeth is one of the most common procedures in oral and maxillofacial surgery. The absolute indication for removal of impacted third molar is infection, pain difficulty in mouth opening or presence of any cysts and benign tumours and for therapeutic purposes such as orthodontic treatment. Other common indications include un-restorable caries, pulpal and periapical pathology.

Most commonly the benefits of surgical removal of a third molar include alleviation of the symptoms and signs of pericoronitis and its potential consequences. However, surgery is frequently associated with postoperative pain, swelling and trismus. To minimize the post–operative complications a right choice of anaesthetic agent is must

to provide a painless treatment. And after thorough reviews of all the six articles, this systematic review concludes by saying bupivacaine is comparatively a better anaesthetic agent to that of lignocaine in surgical removal of mandibular third molar.

Keywords: Bupivacaine, lignocaine, local anaesthetic agent, third molar removal surgery, molar impactions

INTRODUCTION

Impaction of third molar is relatively more common clinical finding and surgical removal of impacted third molar is one of the most commonly performed procedure in the field of oral surgery, and this procedure has few post-operative sequelae, some common ones include post-operative pain, swelling and trismus.

Among the post-operative sequelae, Pain is a horrifying experience which a person wants to avoid and it is pain associated with the procedure which makes a person very anxious about dental procedures .Dentistry has been made pleasant with the introduction of many local anaesthetic drugs.

Introducing the concept of painless dentistry is a rewarding experience not only for the operator but also for the patient.

Lignocaine was introduced in the year 1948 and until today its considered as the gold standard of all the local anaesthetic agents **[1]**, And few years down the lane bupivacaine was introduced as an anaesthetic agent in the year 1957 **[2]**.

Among the various anaesthetic agents introduced till date, by far lignocaine is still one of the most widely used anaesthetic agents. Lignocaine is used widely because of its low cost and small time of onset after injection **[3]**. However there has been always a tendency to use a local anaesthetic for extended procedures like 3rd molar surgeries which often last longer **[4]**. Some authors suggest use of bupivacaine as local anaesthetic because of its extended duration of action and less post -operative requirement of analgesic post-operatively **[5]**.

Local anaesthetic agents and its effectiveness have been explained

using a pain model theory, as the pain model's reproducibility has been well-established **[6]**. Pain intensity following third molar surgery generally reaches a maximum between 3 and 5 hours following the procedure **[7]**. Due to its high lipid solubility and protein binding characteristics, bupivacaine tends to have duration of action of over 200 minutes hence its anaesthetic effect is longer compared to that of lignocaine **[8]**. This would suggest that bupivacaine would be an appropriate anaesthetic agent for third molar surgery, which is associated with prolonged periods of post-operative pain.

In the past decades **[9]**, several studies have been done which includes comparing the action of various anaesthetic agents at various concentrations for third molar surgeries, all of these were clinically evaluated in an effort to minimize the post-operative sequelae and among all of these studies bupivacaine as an choice of anaesthetic agent has shown better and promising results.

AIM

The aim of this systematic review was to analyse the existing literature to compare the effectiveness of bupivacaine and lignocaine as an anaesthetic agent in surgical removal of mandibular impacted third molars.

STRUCTURED QUESTION

Is there any difference in the comparative effect of bupivacaine and lignocaine anaesthetic agent for the postoperative control of pain, during the surgical removal of mandibular impacted third molars?

PICO Analysis

Population: Patients undergoing mandibular third molar surgery

Intervention: Bupivacaine

Comparison: lignocaine

Outcome: Postoperative control of pain

MATERIALS AND METHODS

INCLUSION CRITERIA

Different criteria for considering studies for the Review -

Types of studies -

- Randomized controlled trials
- Clinical trials.

Types of Participants –

Patients undergoing surgical removal of impacted lower third molar.

Types of Intervention

Postoperative discomfort is evaluated using bupivacaine as an anaesthetic agent for surgical removal of mandibular third molar surgery.

Types of Comparison

Postoperative discomfort is evaluated using lignocaine as an anaesthetic agent for surgical removal of mandibular third molar surgery.

Types of Outcome Measures

Post-operative pain was evaluated following mandibular third molar surgery.

EXCLUSION CRITERIA

The following studies were excluded,

- Case reports / Case series
- Review articles
- Animal studies
- In-vitro studies
- Studies not meeting inclusion criteria

SOURCES USED:

The Data Bases of PubMed, Cochrane and Google scholar were searched for the related topics.

We used free-text terms to search the following journals"

- British Journal of Oral and Maxillofacial Surgery
- International Journal of Oral and Maxillofacial Surgery
- Journal of Oral and Maxillofacial Surgery
- Journal of Cranio-Maxillofacial Surgery
- Quintessence International Journal

Only articles in English and human species were applied during the electronic search to include all the possible clinical trials that are relevant for the search phase of the systematic review. Reference list of the identified randomized trials were also checked for possible additional studies.

SEARCH METHODOLOGY

History

Download history Clear history

Search	Add to builder	Query	Items found	Time
#55	Add	Search ((((((((((((((third molar) OR wisdom tooth) OR third molar extraction) OR third molar removal) OR third molar removal) OR third molar impaction) OR wisdom tooth extraction) OR wisdom tooth removal) OR wisdom tooth impaction) OR wisdom tooth surgery) OR mandibular third molar surgery) OR mandibular third molar impaction)) AND ((((((((((((lignocaine) OR xylocaine) OR lignocaine hydrochloride) OR local anaesthetic) OR anaesthetic) OR local) OR amide) OR amide anaesthetic) OR amide local anaesthetic) OR anaesthetic agent) OR short acting) OR anodyne) OR shot)) AND ((((((((((((bupivacaine) OR marcaine) OR sensorcaine) OR local anaesthetic) OR anaesthetic) OR local) OR amide) OR amide anaesthetic) OR amide local anaesthetic) OR anaesthetic agent) OR long acting) OR anodyne) OR shot)) AND (((((((pain) OR dental pain) OR tooth pain) OR post operative pain) OR post surgical pain) OR post extraction pain) OR vas score) Filters: Clinical Trial; Free full text; Abstract; Humans; English	115	07:17:37
#41	Add	Search ((((((pain) OR dental pain) OR tooth pain) OR post operative pain) OR post surgical pain) OR post extraction pain) OR VAS score	763671	05:25:06
#40	Add	Search VAS score	13562	05:24:33
#39	Add	Search post extraction pain	757	05:23:55
#38	Add	Search post surgical pain	19726	05:23:29
#37	Add	Search post operative pain	100197	05:23:12
#36	Add	Search tooth pain	9699	05:22:51
#35	Add	Search dental pain	20184	05:22:40
#34	Add	Search pain	759857	05:22:28
#33	Add	Search ((((((((((((bupivacaine) OR marcaine) OR sensorcaine) OR local anaesthetic) OR anaesthetic) OR local) OR amide) OR amide anaesthetic) OR amide local anaesthetic) OR anaesthetic agent) OR long acting) OR anodyne) OR shot	1837227	05:22:14
#26	Add	Search shot	15346	05:20:39
#25	Add	Search anodyne	557326	05:20:31

Continued...

#25	Add	Search anodyne	557326	05:20:31
#32	Add	Search long acting	36527	05:20:19
#23	Add	Search anaesthetic agent	242778	05:20:07
#31	Add	Search analgesic	577318	05:19:50
#22	Add	Search amide local anaesthetic	40813	05:19:39
#21	Add	Search amide anaesthetic	43100	05:19:23
#20	Add	Search amide	461139	05:19:08
#19	Add	Search local	734806	05:18:59
#18	Add	Search anaesthetic	256405	05:18:50
#17	Add	Search local anaesthetic	131361	05:18:40
#30	Add	Search sensorcaine	15862	05:18:28
#29	Add	Search marcaine	15964	05:18:18
#28	Add	Search bupivacaine	16147	05:18:07
#27	Add	Search ((((((((((lignocaine) OR xylocaine) OR lignocaine hydrochloride) OR local anaesthetic) OR anaesthetic) OR local) OR amide) OR amide anaesthetic) OR amide local anaesthetic) OR anaesthetic agent) OR short acting) OR anodyne) OR shot	1819491	05:17:52
#24	Add	Search short acting	14380	05:16:18
#16	Add	Search lignocaine hydrochloride	31043	05:14:38
#15	Add	Search xylocaine	31352	05:14:23
#14	Add	Search lignocaine	31829	05:14:12
#13	Add	Search ((((((((((third molar) OR wisdom tooth) OR third molar extraction) OR third molar eemoval) OR third molar removal) OR third molar impaction) OR wisdom tooth extraction) OR wisdom tooth removal) OR wisdom tooth impaction) OR wisdom tooth surgery) OR mandibular third molar surgery) OR mandibular third molar impaction	10763	05:13:56
#12	Add	Search mandibular third molar impaction	1651	05:12:52
#11	Add	Search mandibular third molar surgery	2723	05:12:34
#10	Add	Search wisdom tooth surgery	5839	05:12:16

Continued...

#28	Add	Search bupivacaine	16147	05:18:07
#27	Add	Search ((((((((((((lignocaine) OR xylocaine) OR lignocaine hydrochloride) OR local anaesthetic) OR anaesthetic) OR local) OR amide) OR amide anaesthetic) OR amide local anaesthetic) OR anaesthetic agent) OR short acting) OR anodyne) OR shot	1819491	05:17:52
#24	Add	Search short acting	14380	05:16:18
#16	Add	Search lignocaine hydrochloride	31043	05:14:38
#15	Add	Search xylocaine	31352	05:14:23
#14	Add	Search lignocaine	31829	05:14:12
#13	Add	Search ((((((((((third molar) OR wisdom tooth) OR third molar extraction) OR third molar eemoval) OR third molar removal) OR third molar impaction) OR wisdom tooth extraction) OR wisdom tooth removal) OR wisdom tooth impaction) OR wisdom tooth surgery) OR mandibular third molar surgery) OR mandibular third molar impaction	10763	05:13:56
#12	Add	Search mandibular third molar impaction	1651	05:12:52
#11	Add	Search mandibular third molar surgery	2723	05:12:34
#10	Add	Search wisdom tooth surgery	5839	05:12:16
#9	Add	Search wisdom tooth impaction	3064	05:12:03
#8	Add	Search wisdom tooth removal	2094	05:11:46
#7	Add	Search wisdom tooth extraction	4216	05:11:31
#6	Add	Search third molar impaction	2933	05:11:13
#5	Add	Search third molar removal	2025	05:10:53
#4	Add	Search third molar eemoval	10374	05:10:37
#3	Add	Search third molar extraction	4055	05:10:22
#2	Add	Search wisdom tooth	10763	05:10:00
#1	Add	Search third molar	10374	05:09:47

Figure 1: Screenshot of PubMed search

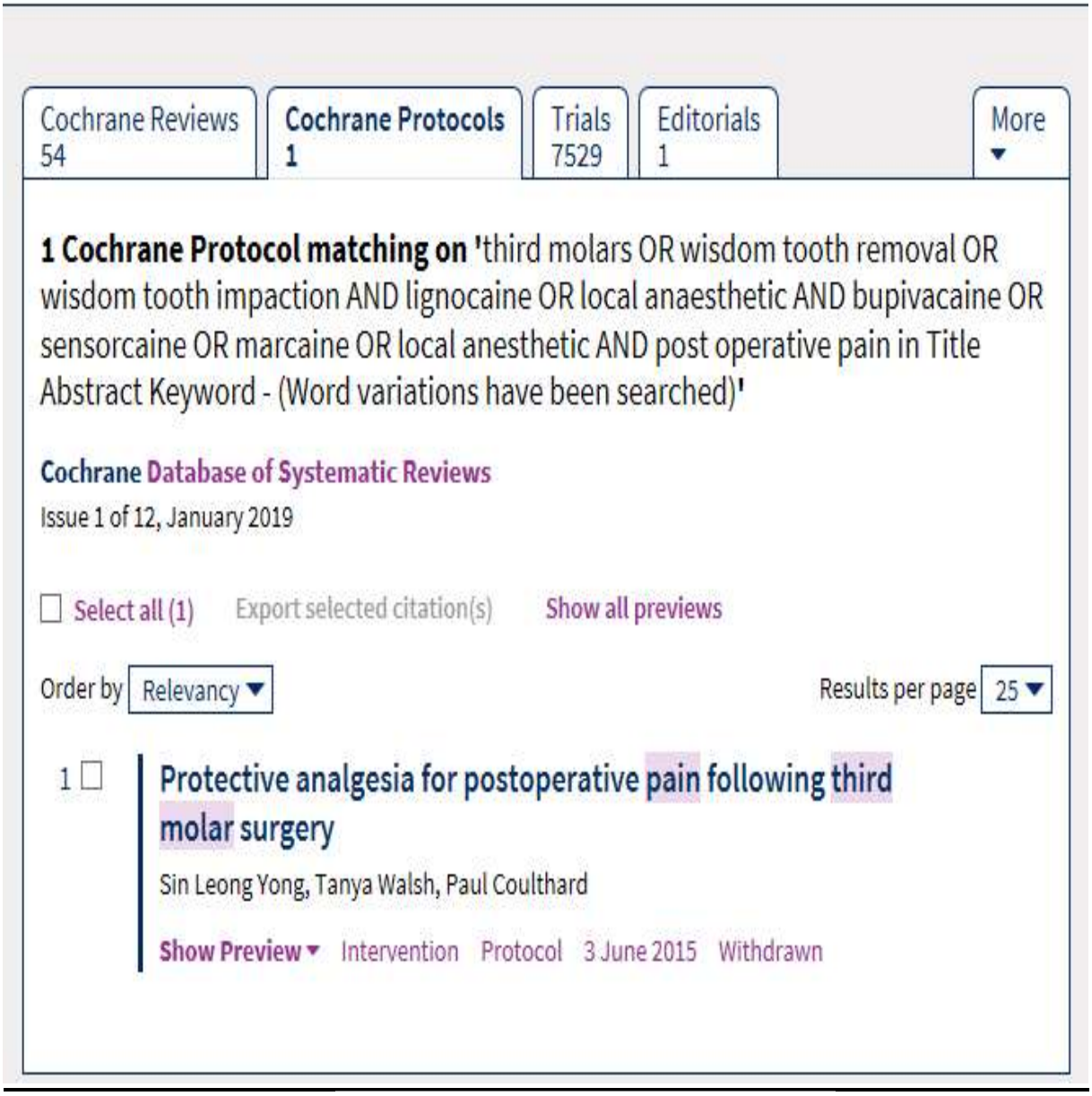
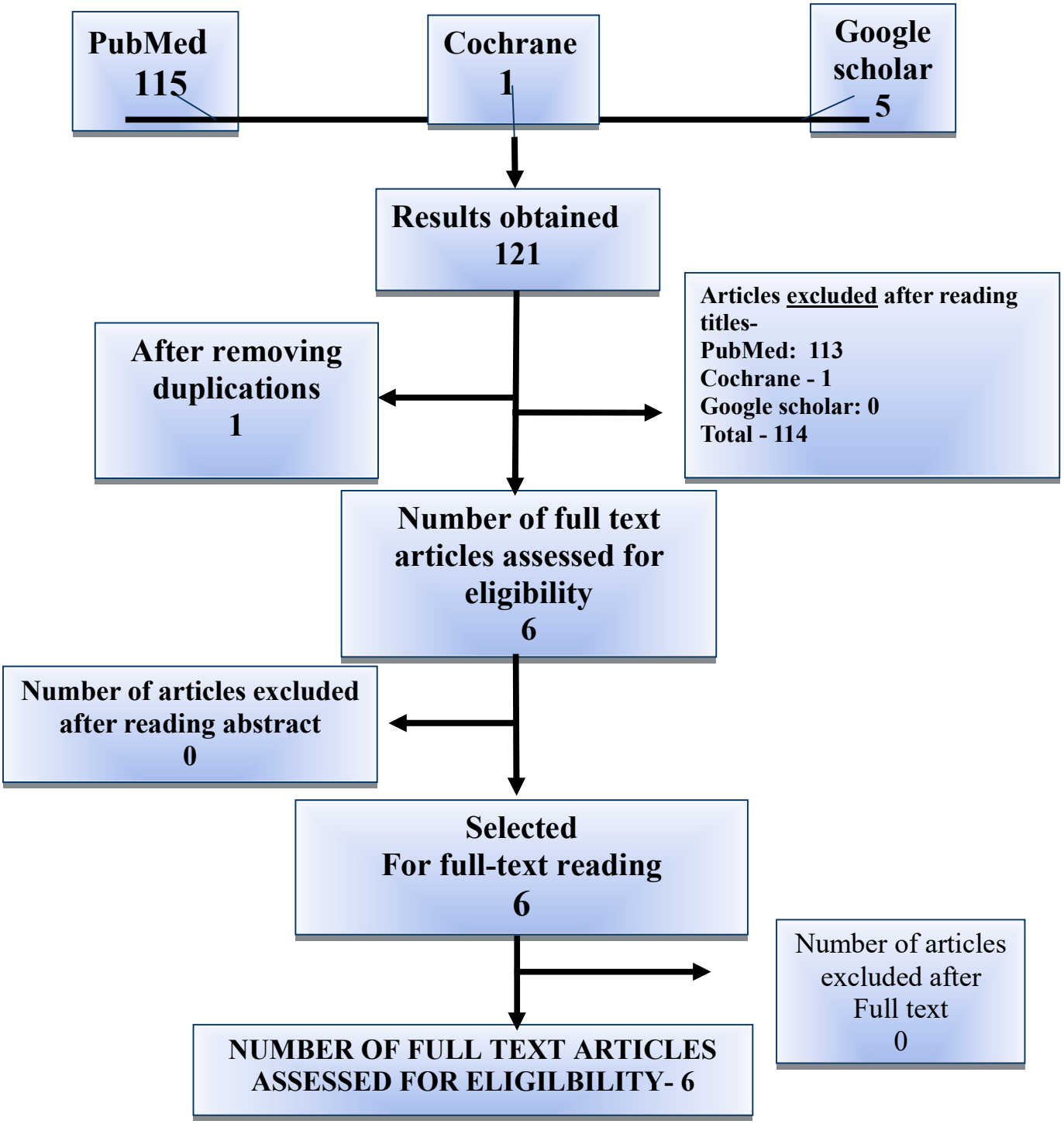


Figure 2: Screenshot of Cochrane search

Search Flow Chart



Data Collection and Analysis

Screening and Selection

Electronic search was carried out using the keywords in the Search engines- PubMed, Cochrane and Google Scholar which yielded a total of 120 articles. Based on pre-set inclusion and exclusion criteria, the titles of the studies identified from the search were assessed independently by two review authors **(Dr. Swetha Murali, Dr.M.Madhulaxmi)**. Conflicts concerning inclusion of the studies were resolved by discussion. Hundred and fourteen articles were excluded after reading titles. Six titles were identified from the search after excluding one duplication. Abstracts of selected articles were reviewed independently. No articles were excluded after reading abstract. Full text articles were retrieved for six relevant studies.

The reference list of the full text articles were reviewed for identifying additional studies. Titles of articles relevant to the review were selected by discussion. Quality Assessment criteria to evaluate the studies were decided by two review authors in accordance with CONSORT guidelines. The risk of bias for each study was independently assessed by the review authors and conflicts concerning risk of bias were sorted by discussion.

Data Extraction

Data extraction for general characteristics of studies and variables of outcome was done

For each trial the following data were recorded:

- Author and Journal
- Study Design
- Sample Size
- Participants and Group
- Methodology
- Parameters
- Statistical Analysis
- Results

Table 1: Variables Of Interest

S. No	VARIABLES OF INTEREST
1.	Post-operative pain

QUALITY ASSESSMENT

(Higgins and Green. Cochrane reviewer's hand book 2009)

The quality assessment analysis of the included trials was evaluated independently as a part of data extraction process. Out of which Four main quality criteria were examined.

1. **Method of Randomization**, was recorded as

a) YES- Adequate as described in the text

b) NO- Inadequate as described in the text

c) Unclear in the text

2. **Allocation Concealment**, was recorded as

a) YES- Adequate as described in the text

b) NO- Inadequate as described in the text

c) Unclear in the text

3. **Outcome assessors Blinded to intervention**, was recorded as

a) YES- Adequate as described in the text

b) NO- Inadequate as described in the text

c) Unclear in the text

4. **Completeness of Follow up** (was there a clear explanation for withdrawals and dropouts in each treatment group) assessed as

a)YES- Dropouts were explained

b) NO- Dropouts were not explained

c) None- No Dropouts or withdrawals.

Other methodological criteria examined included:

1. Presence or Absence of sample size calculation.
2. Comparability of Groups at the start.
3. Clear Inclusion or Exclusion criteria.
4. Presence or Absence of estimate of measurement error.

RISK OF BIAS IN INCLUDED STUDIES

The bias in the study was assessed into three categories one as high risk group, or moderate risk group or low risk group, It was categorised as "High risk" group of bias if the studies did not record a "Yes" in three or more out of the four main categories listed according to the quality assessment tool, and similarly

for "Moderate Risk" group of bias the studies need to record a minimum of two out of four categories according to the quality assessment tool. And it was categorised as “Low Risk” group of bias if all the four categories recorded did not meet the quality assessment criteria, along with blinding and Completeness of all the inclusive studies and its follow up were considered in the assessment of risk of bias. And in case of non-randomized and clinical trials without control group, it was directly recorded as not applicable.

RESULTS

Table 2: general Characteristics of The Studies

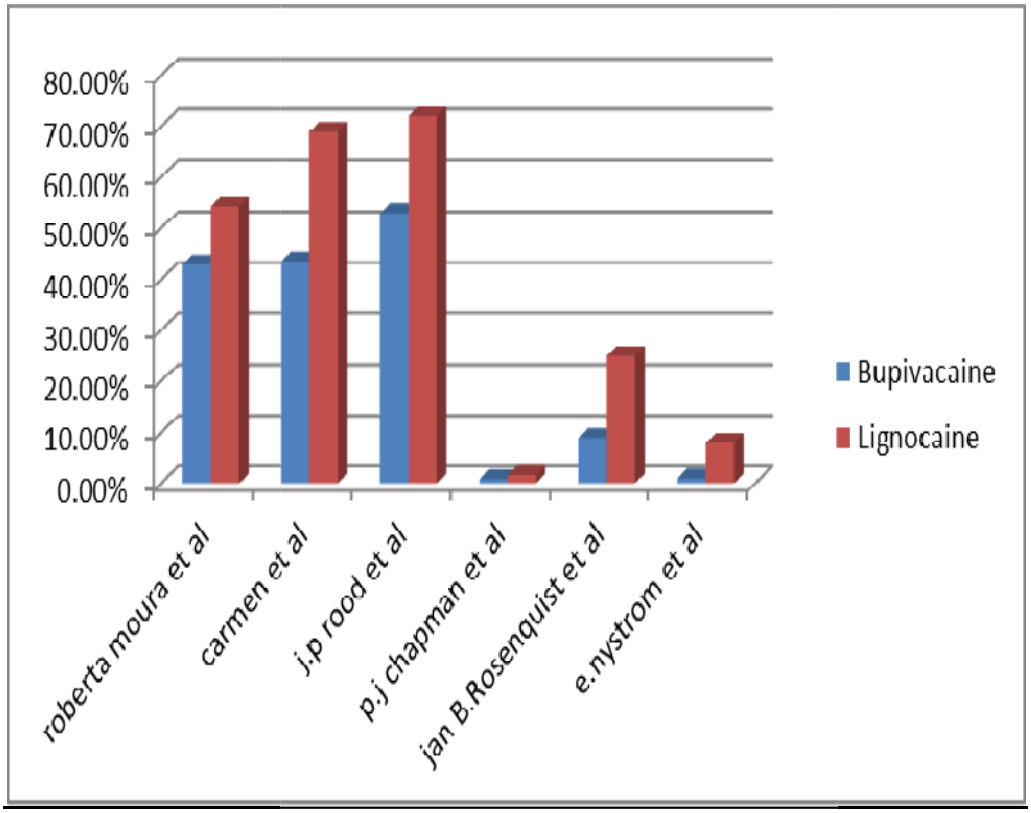
S.No	Author	Year	Study design	Sample size	Age	Technique used	Method of evaluation
1.	Roberta Moura Sampaio *et al.*	2012	Randomized double blinded clinical study	N=70	16-40years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was evaluated using VAS score.
2.	Carmen Fernandez *et al.*	2005	Randomized double blinded clinical study	N=39	20-30 years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was evaluated using VAS score.
3.	J.P Rood *et al*	2002	Randomized double blinded clinical study	N=93	18-41 years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was evaluated using VAS score.
4.	Jan B. Rosenquist *et al*	1988	Randomized double blinded clinical study	N=26	19-43years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was evaluated using VAS score.
5.	P.J. Chapman *et al.*	1988	Randomized double blinded cross over study	N=20	17 – 33 years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was evaluated using VAS score.
6.	E.Nystrom *et al.*	1987	Randomized double blinded clinical study	N=48	19– 43 years	One group receiving lignocaine and another group receiving bupivacaine	Post -operative pain was assessed using VAS score.

Table 3: Characteristics Of The Excluded Studies

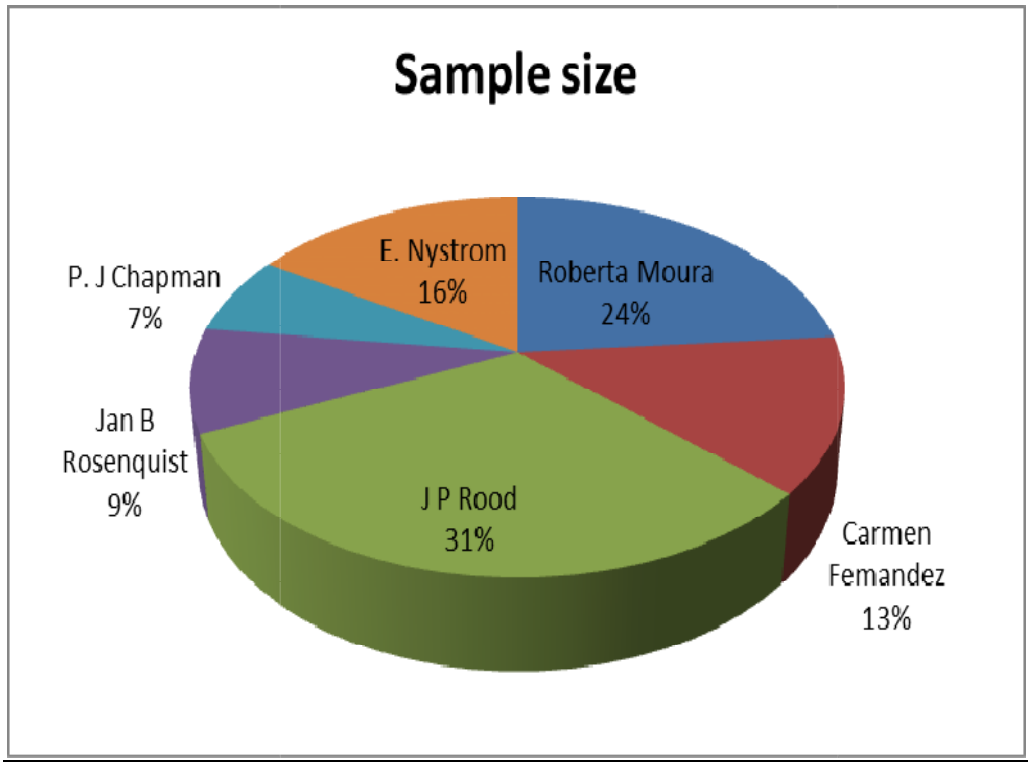
S.NO	AUTHOR	TITLE	REASON FOR EXCLUSION
1.	Lieblich S E 2017	Liposomal bupivacaine used in third molar impaction surgery:Innovate study.	Not relevant to this systematic review, as they did not mention in detail about the search method.
2.	Da Siva Junior GP 2017	Comparison of articaine and lidocaine for buccal infiltration after inferior alveolar nerve block for intraoperative pain control during impacted mandibular third molar surgery.	Not relevant to this systematic review, as the study group did not match according to the review title.
3.	Karm M H *et al* 2017	Comparison of the efficacy and safety of 2% lidocaine HCL with different epinephrine concentration of local anaesthesia in participants undergoing surgical extraction of impacted mandibular 3rd molar. A multicentrerandomized double blinded cross over phase-1V trial.	Not relevant to this systematic review, as the lignocaine used as a choice of anaesthetic agent was without adrenaline.
4.	Crincolive *et al* 2015	The effectiveness of ropivacaine and mepivacaine in the post-operative pain after 3rd lower molar surgery.	Not relevant to this systematic review, as two different anaesthetic agents were used
5.	Yadav S 2013	Buccal injection of 2% lidocaine with epinephrine for the removal of maxillary third molar	Not relevant to this systematic review, as only one anaesthetic agent was used in the study
6.	Lima JL 2013	Comparision of buccal infiltration of 4% articaine with 1:100000 and 1:200000 epinephrine for extraction of maxillary 3rd molars with pericoronitis-a pilot study	Not relevant to this systematic review, two different anaesthetic agents were used at different concentrations
7.	Silva LC 2012	articaine versus lidocaine for 3rd molar surgery a randomized clinical study	Not relevant to this systematic review, two different anaesthetic agents were used.
8.	Sancho-Puchades M 2012	Bupivacaine 0.5% versus articaine 4% for the removal of lower third molars a crossover randomized controlled trial.	Not relevant to this systematic review, as concentrations of anaesthetic agents used were different.
9.	Trullenque Eriksson A 2011	Comparative study of two local anaesthetics in the surgical extraction of mandibular third molars : bupivacaine and articaine	Not relevant to this systematic review, one of the choice of anaesthetic agents used is not relevant to the study.
10.	Sierra Rebolledo A 2007	Comparative study of anaesthetic efficacy of 4% articaine versus 2% lidocaine in inferior alveolar nerve block during surgical extraction of impacted lower third molars.	Not relevant to this systematic review, the concentration of anaesthetic agent used is different than the one used in the study.
11.	Porto GG 2007	Evaluation of lidocaine and mepivacaine for inferior third molar surgery.	Not relevant to this systematic review, due to different anaesthetic agents used
12.	El-Sharrawy E 2006	Anaesthetic efficacy of different ropivacaine concentrations for inferior alveolar nerve block.	Not relevant to this systematic review, as two different anaesthetic agents used.
13.	Campbell WI 1997	The effect of pre-operative administration of bupivacaine compared with its post-operative use	Not relevant to this systematic review, the concentration of anaesthetic agent used is different.
14.	Wilson I H 1986	Regional analgesia with bupivacaine in dental anaesthesia.	Not relevant to this systematic review, due to different concentration of anaesthetic agent used
15.	Hyrkas T *et al* 1994	Effective post-operative prevention through administration of bupivacaine diclofenac	Not relevant to this systematic review, single anaesthetic agent used in this study.

Table 4: Data Extraction Table

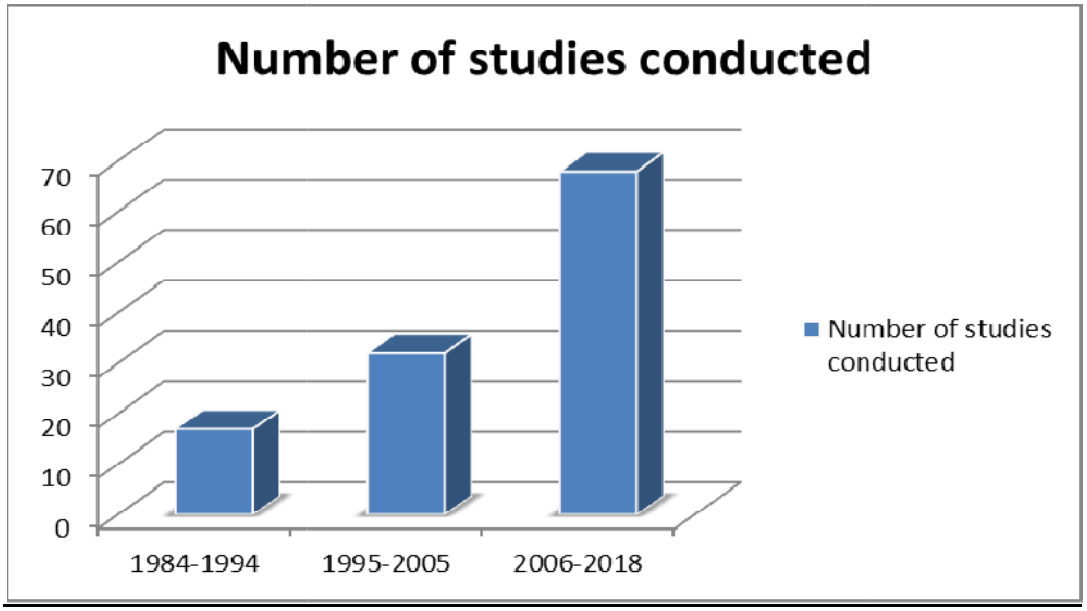
S. No	Author and Year	Technique used	Method of evaluation	Mean Values	Outcomes
1.	Roberta Moura Sampaio *et al.* 2012	Comparative anaesthetic effect between lignocaine and bupivacaine.	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 54.3% Bupivacaine group =42.9%	Post-operative pain experienced in bupivacaine group was significantly less
2.	Carmen Fernandez *et al.* 2005	Comparative anaesthetic effect between lignocaine and bupivacaine	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 54-84% Bupivacaine group =31-56%	Post-operative pain experienced in bupivacaine group was significantly less
3.	J.P Rood *et al* 2002	Comparative anaesthetic effect between lignocaine and bupivacaine	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 72% Bupivacaine group =53%	Post-operative pain experienced in bupivacaine group was significantly less
4.	P.J Chapman *et al.* 1988	Comparative anaesthetic effect between lignocaine and bupivacaine	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 4hrs-1.1%,8hrs-0.9%,12hrs-1.6% Bupivacaine group =4hrs-0%,8hrs-0.5%,12hrs-0.8%	Post-operative pain experienced in bupivacaine group was significantly less
5.	Jan B. Rosenquist *et al.* 1988	Comparative anaesthetic effect between lignocaine and bupivacaine	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 25% Bupivacaine group 9%	Post-operative pain experienced in bupivacaine group was significantly less
6.	E.Nystrom *et al.* 1987	Comparative anaesthetic effect between lignocaine and bupivacaine	Post-operative pain measured using VAS score	Post-operative pain Lignocaine group= 8% Bupivacaine group =1%	Post-operative pain experienced in bupivacaine group was significantly less



Graph 1: Comparison Of Post Operative Pain



Graph 2: Comparison of Sample Size



Graph 3: Number Of Articles Suggestive Of Using Lignocane And Bupivacaine As Anaesthetic Agent During Various Time Lapse

Table 5: Evidence Level of Selected Articles

S No	Author & Year	Study Design	Level of Evidence
1	Roberta mourasampaio *et al.* 2012	Randomised double blinded clinical study	1
2	Carmen Fernandez *et al.* 2005	Randomised double blinded clinical study	1
3	J P Rood *et al* 2002	Randomised double blinded clinical study	1
4	P J Chapman 1988	Randomised double blinded clinical study	1
5.	Jan B Rosenquist *et al* 1988	Randomised double blinded cross over study	1
6.	E.Nystrom *et al.* 1987	Randomised double blinded clinical study	1

(The United States department of health and human services 2012)

Table 6: Risk of Bias- Major Criteria

S. No	Study	Randomization	Allocation concealment	Assessor Blinded	Drop outs described	RISK OF BIAS
1	Roberta mourasampaio *et al.* 2012	YES	NO	YES	NONE	MODERATE
2.	Carmen Fernandez *et al.* 2005	YES	NO	YES	NONE	MODERATE
3.	J P Rood *et al* 2002	YES	NO	YES	NONE	MODERATE
4.	P J Chapman 1988	YES	NO	YES	NONE	LOW
5.	Jan B Rosenquist *et al* 1988	YES	NO	YES	NONE	LOW
6.	E.Nystrom *et al.* 1987	YES	NO	YES	NONE	LOW

Table 7: Risk Of Bias- Minor Criteria

S. No	Study	Sample justified	Baseline comparison	I/ E criteria	Method of error
1	Roberta mourasampaio *et al*. 2012	NO	YES	YES	NO
2	Carmen Fernandez *et al*. 2005	NO	YES	YES	NO
3	J P Rood *et al* 2002	YES	YES	YES	NO
4	P J Chapman 1988	NO	YES	YES	NO
5.	Jan B Rosenquist *et al* 1988	NO	YES	YES	NO
6.	E.Nystrom *et al*. 1987	NO	YES	YES	NO

Table 8: Summation Table For Individual Parameters

S. No	Author	Year	Evaluation period	Outcome
1.	Roberta mourasampaio *et al*.	2012	POD 7^{TH} DAY	There was significant difference between the two groups, results are in favour of bupivacaine group.
2.	Carmen Fernandez *et al*.	2005	POD 3^{RD}, 7^{TH} DAY	There was significant difference between the two groups, results are in favour of bupivacaine group.
3.	J P Rood *et al*	2002	POD 1^{ST},3^{RD},7^{TH} DAY	There was significant difference between the two groups, results are in favour of bupivacaine group.
4.	P J Chapman	1988	POD- 4HOURS, 8HOURS, 12 HOURS AND 24 HOURS.	There was significant difference between the two groups,results are in favour of bupivacaine group.
5.	Jan B Rosenquist *et al*	1988	POD 3^{RD}, 7^{TH} DAY	There was significant difference between the two groups, results are in favour of bupivacaine group.
6.	E.Nystrom *et al*.	1987	POD 1^{ST}, 3^{RD}, 7^{TH} DAY	There was significant difference between the two groups, results are in favour of bupivacaine group

DISCUSSION

Adequate and efficient post-operative analgesia is a pre-requisite for any successful pain less surgery pertaining to maxillofacial procedures. Third molar removal is one such procedure which is not without morbidity and definitely has some degree of post-operative pain and swelling. Such complications can have significant effect on patient's quality of life and should not be neglected **[10]**. Pain is one of the most commonly encountered post-operative sequelae after a minor oral surgical procedure, and acute pain is provoked by a specific disease or injury, and serves as a useful tool for biologic purpose, in spite being is self-limited. Third molar removal

typically requires surgery which results in tissue injury which may be soft tissue only or also involving the alveolar bone. Due to the presence of an complex and dynamic nervous system in the head and neck region there can be several possibilities of pain transmission from various nerve endings such as inferior alveolar nerve, lingual nerve and sometimes from the mylohyoid nerve, and sometimes pain continues to be perceived even after the transient stimulus of the surgical procedure has ceased or removed may be due to the pain perceived by the patient during the procedure or in adequate pain control measures were taken can result in presence of prolonged stimulus. Hypothetically, inhibition of nerve sensitisation should work to reduce pain experience which supports nerve blockade with local anaesthesia to prevent development of a hyper excitable state.

Local anaesthetic agents have long been compared using the third molar pain model, as the pain model's reproducibility has been well-established **[11]**. Pain intensity following third molar surgery reaches a maximum between 3 and 5hours following surgery. Due to its high lipid solubility and protein binding characteristics, bupivacaine tends to have duration of action of over 200 minutes[12]. In the following six articles each and every author have suggested that bupivacaine have significantly shown better results compared to that of lignocaine in reducing post-operative pain after removal of impacted third molar. In the study conducted by **Roberta mourasampario *et al*.** in the year 2012 he conducted a study in approximately 70 individuals who were undergoing third molar surgery he divided the sample size into two groups, one group receiving lignocaine and the other receiving bupivacaine, and he evaluated the effect of the anaesthetic agent post-operatively by evaluating pain score using VAS score index, and duration of action of each anaesthetic agent, and other post-operative sequelae, In this study the only drawback remained was the type of impaction the patients were undergoing wasn't mentioned in the article.

In the study conducted by **Carmen Fernandez *et al*.,** in the year 2005 was a double blinded randomized clinical study comprising of 39 subjects, and the study was conducted between two groups, each group received either one of the anaesthetic agent, and post–operative pain was evaluated, the drawback of this study was the participants in each groups were not equally divided. And the other studies had shown results with bupivacaine being a better choice of anaesthetic agent than lignocaine for impacted mandibular third molar surgeries. Overall, from these articles we would suggest that bupivacaine would be an appropriate anaesthetic for third molar surgery, which is associated with prolonged periods of post-operative pain.

INTERPRETATION OF RESULTS

There were 6 randomized controlled trials included in this systematic Review.

According to **Roberta mourasampario *et al***, a total sample size of 70 was taken with the each group consisting of 35 participants. In bupivacaine group after the removal of the mandibular impacted third molar procedure showed significant difference in pain score levels compared to that of the lignocaine group. The significant VAS score between the two groups were, lignocaine group showed a overall value of 54.3% in pain score, whereas the bupivacaine group showed an value of 42.9%.thus the post-operative pain score was evaluated and the bupivacaine group showed significantly better results.

According to **Carmen Fernandez *et al*,** a total sample size of 39was taken with the one group consisting of 18 participants, the other group consisting of 19 participants. In bupivacaine group after the removal of the mandibular impacted third molar procedure showed significant difference in pain score levels compared to that of the lignocaine group. The significant VAS score between the two groups were, lignocaine group showed a overall value of 54-84% in pain score, whereas the bupivacaine group showed an value of 31-56%.thus the post-operative pain score was evaluated and the bupivacaine group showed significantly better results

According **J.P Rood *et al***, a total sample size of 93 was taken with the one group consisting of 46 participants and the other group consisting of 37 participants. In bupivacaine group after the removal of the mandibular impacted third molar procedure showed significant difference in pain score levels compared to that of the lignocaine group. The significant VAS score between the two groups were, lignocaine group showed a overall value of 72% in pain score, whereas the bupivacaine group showed an value of 53%.thus the post-operative pain score was evaluated and the bupivacaine group showed significantly better results

According to **Champman *et al***, a total sample size of 20 was taken with the each group consisting of 10 participants. In bupivacaine group after the removal of the mandibular impacted third molar procedure showed significant difference in pain score levels compared to that of the lignocaine group. The significant VAS score between the two groups were, lignocaine group showed a overall value of VAS score at POD 4HRS-1.1%, 8HRS-0.9%, 12HRS-0.7% >24HRS-1.6% in pain score, whereas the bupivacaine group showed an value of VAS SCORE AT POD 4HRS-0%,8HRS-0.5%,12HRS-0.7%,>24HRS-0.8%. .thus the post-operative pain score was evaluated and the bupivacaine group showed significantly better results

According to **Jan Rosenquist *et al*,** in this study published by this author, a total sample size of 26 participants was taken with the each group consisting of 13 participants each. In bupivacaine group after the removal of the mandibular impacted third molar procedure the results showed significant difference in pain score levels compared to that of the lignocaine group. The significant VAS score between the two groups had shown a significant difference, the lignocaine group showed an overall value of 25% in pain score, whereas the bupivacaine group showed a value of 9% in pain score. Post-operatively the post-operative pain score was evaluated and the bupivacaine group showed significantly better results

According to **Nystron *et al***, in this authors study a total sample size of 48 was taken with the each group consisting of 24 participants. In bupivacaine group after the removal of the mandibular impacted third molar procedure showed significant

difference in pain score levels compared to that of the lignocaine group. There was significant difference in VAS score between the two groups. The lignocaine group showed an overall value of 8% in pain score, whereas the bupivacaine group showed a value of 1% in pain score.

The post-operative pain score was evaluated and the bupivacaine group showed significantly better results

DEFENDING THE RESULT

Among Six clinical trials, one clinical trial compared the anaesthetic effect between the two study groups along with a placebo as a third intervention group, and had also given the anaesthetic agent at different concentrations so as to observe its onset of action and total duration of actions and accordingly post-operative pain parameter was evaluated at post-operative intervals of 4hours, 8hours, 12 hours and more than 12hours respectively. Whereas the other articles evaluated the post-operative pain at 24hours, 2day and 7^{th} post-operative day.

In this study the initial investigation conclusively showed a significant difference in pain experience during the immediate post-operative period with the use of local anesthesia in third molar removal procedure. Time frame played a particular importance in preparation for patient discharge, and for the overall procedure time, where pain control is paramount during this process by minimizing the procedural time and with proper administration of anaesthetic agent it can drastically influence the post-operative sequelae in minor oral surgical procedures such as third molar removal surgery. With the proper use of right anaesthetic agent had shown significant results in third molar surgery.

With more statistically significant results in every clinical study that was included in this systematic review had proven bupivacaine to be more effective than lignocaine anaesthetic agent in treatment of impacted mandibular third molars.

QUALITY OF EVIDENCE

All the six trials included in this review have a level of evidence 1. All are randomised clinical trials, thus the level of evidence is high. Risk of bias of included three trials (Roberta moura *et al*, Carmen Fernandez *et al*, J P Rood *et al*) are moderate, the other three trials (P J Chapman *et al*, Jan B Rosenquist *et al*, E Nystrom *et al*) are low. Hence the interpretations obtained from these studies are indicative that in-spite of lignocaine being the gold standard

anaesthetic agent, bupivacaine has significantly shown better results in reducing the post-operative pain following surgical removal of impacted mandibular third molar.

INFERENCE

Implications for practice -

There is some evidence there hasn't been significant differences noted between the modes of action of the two anaesthetic agents, but the group receiving bupivacaine as an anaesthetic agent has significantly shown better results when compared to the lignocaine group, but due to many recent advances in various concentrations of anaesthetic agents, one cannot definitely say one particular anaesthetic agent will work wonders, and in this evidence based study that was done in all these articles it's has proven better results with bupivacaine group in management of post-operative pain parameter.

Implications for Research -

The number of good quality randomized controlled trials included in this review is very limited. There is lack of evidence supporting the findings. And due to many recent advances in anaesthetic administration and the types of anaesthetic agent's present, more elaborate and longer term randomized controlled trials are required to prove the effectiveness of the anesthesia, and hence have a pain less practice in the field of oral surgery.

CONCLUSION

The clinical evidence in this review is inadequate to state that there is difference in the Post- operative complications following third molar surgery with lignocaine and bupivacaine as an anaesthetic agent.Hence, more properly designed randomized clinical trials are needed to evaluate the usage of these anaesthetic agents to reduce post-operative complications, such as post-operative pain.

SUMMARY

The aim of this systematic review was to compare the effect of bupivacaine and lignocaine anaesthetic agents used for surgical removal of mandibular impacted third molars. There were 6 randomized controlled trials included in this systematic review, all the six studies have used two anaesthetic agents and have evaluated the post-operative sequelae after the surgical removal of the impacted mandibular third molar. In one study they compared the effect of these two anaesthetic agents at different concentrations and evaluated the pain score at 4^{th} hourly, 8^{th} hourly , 12^{th} hour and at post-operative 24 hours, whereas in other studies the post-operative complication was

evaluated at 24hours, 2nd day and 7th day of post-operative period. in few studies proper allocation of the participants were not stated, and the methodology wasn't mentioned in few studies, also the type of impaction included for comparing the effect of anaesthetic agent wasn't mentioned, apart from few of these setbacks, overall to evaluate and conclude which anaesthetic agent has significantly reduced post-operative pain was clearly stated in each of the srticles, Thus from this systematic review it can be concluded that even though lignocaine is commonly used anaesthetic agent in our clinical practice, but bupivacaine has evidently shown better results.

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REFERENCES

[1] Adams, H. J., Kro:-: Derg G. H. & Takman B. H.: Local anesthetic activity and acute toxicity of (+)-2-(N-ethylpropyl·amino)-2,6-bu. tyroxylidide, a new long-acting agent J. Pharm, Sci. 1972: 61: 1829-1831.

[2] Ahlstrom, U. & Dahl, E.: The effectivity of Carbocainc> and Marcaine> in oral surgery. A comparative clinical examination of Carbocaine I% and Marcaine 0.25%.Odont, Rev. 1971: 22: 251-256.

[3] Covino, B. G. & Vassallo, H. G.: Local anesthetics. Mechanisms ofaction and clinical lise.Grune& Stratton: New York 1971.

[4] Feldman, G. & Nordenram, A.: Marcainef in oral surgery. A clinical and comparative study with Carbocaine>.ActaAnaesthesiol. Scand. 1966: Suppl XXIII: 409--413.

[5] Gissen, A. J., Covino, B. G. & Gregus, J.: Differential sensitivities of mammalian nerve fibers to local anaesthetic agents. Anesthesiology 1980: 53: 467--474.

[6] Hellden, L, Blmiberg, S., Woxberg, B. & Ohman, A.: A controlled trial of a long-actinglocal anaesthetic (Marcainc") in oral surgery for relief of post-operative pain. Sired. Dent. J. 1974: 67: 223-228.

[7] Henn, E & Bratisand, R.: Some pharmacological and toxicological properties of a new long-acting local analgesic, LAC-43 (Marcaine1» in comparison with mepivacaine and tetracaine. ActaAnaesthesiol. Scand. 1966: Suppl XXI: 9-30.

[8] Jensen, O. T., Upto~, L. G., Hayward, J. R. & Sweet, R. B.: Advantages of long-acting local anesthesia using etidocaine hydrochloride. J. Ora! Surg, 1981: 39: 35G-353.

[9] Laskin, J. L., Wallace, W. R. & Deleo, B.: Use of bupivacaine hydrochloride in oral surgery - a clinical study. J. Ora! Surg, 1977: 35: 25-29.

[10] Laskin, J. L.: Use of etidocaine hydrochloride in oral surgery: a clinical study. J. Ora! Surg, 1978: 36: 863-865. II. LOFSTRO~I, B. (ED.).: Clinical experience with long-acting local anaesthetics. ActaAnaesthesiol. Scand. 1975: Suppl LX.

[11] Lofstro~I, B.: Blocking characteristics of etidocaine (Durancst"). ActaAnaesthesiol. Seand. 1975: Suppl LX: 21-24.

[12] Lund, P. C., Cwik, J. C. & Pagdanganan, R. T.: Etidocaine - a new long-acting local anestheticagent: a clinical evaluation. Anesth.Ana!g. 1973: 52: 482-493.

[13] Moore, P. A. & Dunsky, J. L.: Bupivacaine anesthesia - a clinical trial for endodontic therapy. Ora! Surg, 1983: 55: 176—17

[14] Moore PA. Bupivacaine: a long-acting local anaesthetic for dentistry. Oral Surg 1984; 58: 369-74.

[15] American Dental Association. Accepted dental therapeutics.40th edn. Chicago: American Dental Association.

[16] Chapman PJ, Gordon Macleod AW. A clinical study of bupivacaine for mandibular anesthesia in oral surgery. Anesth Prog 1985; 32: 69-72.

[17] Laskm JL, Wallace WR, De Leo B. Use of bupivacaine hydrochloride in oral surgery - a clinical study. J Oral Surg

[18] Pricco DF. An evaluation ofbupivacaine for regional nerve block in oral surgery. J Oral Surg 1977; 35: 126-9.

[19] Trieger N, Gillen GH. Bupivacaine anesthesia and post- operative

analgesia in oral surgery. Anesth Prog.

[20] Buckley FP, Simpson BR. In: Cousins MJ, Bridenbaugh PO, eds. Neural blockade in clinical anesthesia and management of pain. Philadelphia: JP Lippincott, 1980:586.

[21] Seymour RA, Walton JG. Pain control after third molar surgery. Int J Oral Surg 1984; 13: 457-85.

[22] Pedersen A. Interrelation of complaints after removal of impacted mandibular third molars. Int J Oral Surg.

[23] Chapnick P, Baker G, Munro CO. Bupivacaine anaesthesia.

[24] Huskisson EC. In: Melzack R, ed. Pain measurement and oral surgery. J Can Dent Assoc 1980; 46: 441-3.