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Comparative Evaluation of Pre-Operative Ibuprofen and Acetaminophen on the Success of Inferior Alveolar Nerve Block in Irreversible Pulpitis –A Systematic Review

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ABSTRACT

Introduction

Pain control particularly during the early phases of endodontic treatment is of paramount importance and makes both the dentist and the patient confident and comfortable for the treatment. The inferior alveolar nerve block (IANB) is the conventional method for anesthetizing mandibular molar teeth. Research have shown that, gaining anesthesia in mandibular molars with irreversible pulpitis is much more difficult in comparison to the teeth with normal healthy pulp. Some investigations have been performed to overcome pulpal pain that remains, despite having had an inferior alveolar nerve block injection. Numerous investigations have been performed to increase the success rate of anesthesia during dental and particularly endodontic procedures such as the use of various anesthetic techniques and solutions, as well as pretreatment with analgesics. The concept of using preoperative analgesic drugs to increase the effectiveness of inferior alveolar nerve block is based on reports of their beneficial effects on reducing postoperative pain.

Objective

To evaluate the effect of pre-operative ibuprofen and acetaminophen on the success of the inferior alveolar nerve block in patients with irreversible pulpitis.

Search Strategy

We searched Pubmed Central and Medline for the related topic from 1996 to June 2012.

Selection Criteria

Trials were selected if they met the following criterias: Randomized controlled clinical trials comparing the effect of preoperative placebo, ibuprofen and acetaminophen on the success of the inferior alveolar nerve block in patients with irreversible pulpitis only.

Data Collection and Analysis

All the studies included were based on the data extraction and analysis of the studies for quality and publication bias. The data collection form was customized. The primary outcome measures were the pre-operative medication in reduction of operative pain in anaesthetic success of inferior alveolar nerve block in irreversible pulpitis.

Main Results

The reviews found some clinical evidence that, there is no significant difference in the use of pre-operative ibuprofen or acetaminophen on the success of inferior alveolar nerve block in irreversible pulpitis.

Conclusion

The clinical evidence in this review is inadequate to state that, there is a difference in anaesthetic success on the use of pre-operative ibuprofen and acetaminophen in irreversible pulpitis. Hence, more properly designed randomized clinical trials are needed to evaluate the usage of pre-operative medication on success of inferior alveolar nerve block in irreversible pulpitis.

Key-words:- Ibuprofen, Acetaminophen, Inferior alveolar nerve block, irreversible pulpitis, pre-operative.

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BACKGROUND

The inferior alveolar nerve (IAN) block is the most frequently used mandibular injection technique for achieving local anesthesia for endodontic treatment. However, the IAN block does not always result in successful pulpal anesthesia. Clinical studies in endodontics have found failure with the IAN block occurring between 44% and 81% of the time. Therefore, it would be advantageous to improve the success rate of the IAN block in endodontics.

One theory regarding the high rate of local anesthetic failure in symptomatic teeth diagnosed with irreversible pulpitis is the prostaglandin-induced sensitization of peripheral nociceptors caused by inflammation (*Henry et al 2007*)**.** Inflammation also induces changes in the central nervous systems pain processing system.

The use of acetaminophen, a combination of acetaminophen and ibuprofen, and a placebo, in 40 patients diagnosed with irreversible pulpitis. The medications were administered 30 minutes before administering local anesthesia. If the patient had no pain to cold test or on endodontic access, the IAN block was considered successful.

The authors found a 71% success rate for the acetaminophen group, a 76% success rate for the combination acetaminophen and ibuprofen group, and a 46% success rate for the placebo group. Although the authors stated that there was a trend toward higher success in the medication groups, they found no significant differences among the groups *(Ianiro et al 2007).*

AIM

The aim of this systematic review was to compare and evaluate the effect of pre-operative ibuprofen and acetaminophen on the success of the inferior alveolar nerve block in patients with irreversible pulpitis.

Search Methodology

Search Time		Add to builder	Query	Items found
#50	Add	Search **(#37) AND #49**	9	14:11:24
#49	Add	Search **((((((((((#38) OR #39) OR #40) OR #41) OR #42) OR #43) OR #44) OR #45) OR #46) OR #47) OR #48**	362260	14:10:59
#48	Add	Search **acetaminophen**	15734	14:08:33
#47	Add	Search **ibuprofen**	9405	14:08:08
#46	Add	Search **preemptive analgesics**	421	14:07:29
#45	Add	Search **pre-operative oral medication**	74	14:07:06
#44	Add	Search **oral pain killer**	16	14:06:26
#43	Add	Search **pre treatment analgesics**	6978	14:06:01
#42	Add	Search **prophylactic drug**	19234	14:05:34
#41	Add	Search **NSAID**	169770	14:05:01
#40	Add	Search **oral analgesics**	29454	14:04:33
#39	Add	Search **pain killer**	379	14:04:13
#38	Add	Search **placebo**	155560	14:03:30
#37	Add	Search **(((#27) AND #16) AND #32) AND #36**	46	14:03:12
#36	Add	Search **((#33) OR #34) OR #35**	9389	14:02:32
#35	Add	Search **anaesthetic efficacy**	8097	14:02:10
#34	Add	Search **inferior alveolar nerve block success**	106	14:01:01
#33	Add	Search **anaesthetic success**	1579	14:00:31
#32	Add	Search **(((#28) OR #29) OR #30) OR #31**	867955	13:59:57
#31	Add	Search **controlled clinical trial**	172924	13:59:33
#30	Add	Search **clinical trial**	867955	13:59:11
#29	Add	Search **randomized control clinical trial**	142270	13:58:56
#28	Add	Search **randomized clinical trial**	402055	13:58:31
#27	Add	Search **(#26) OR #25**	29550	13:57:52
#26	Add	Search **endodontic treatment**	6746	13:57:30
#25	Add	Search **(((((((#17) OR #18) OR #19) OR #21) OR #20) OR #22) OR #23) OR #24**	29279	13:56:26
#24	Add	Search **symptomatic irreversible pulpitis**	32	13:55:41
#23	Add	Search **pain irreversible pulpitis**	109	13:55:19
#22	Add	Search **irreversible pulpitis**	220	13:55:00
#21	Add	Search **non surgical root canal therapy**	459	13:53:28
#20	Add	Search **endodontic therapy**	5818	13:54:36
#19	Add	Search **endodontics**	26001	13:51:57
#18	Add	Search **root canal treatment**	16602	13:51:39
#17	Add	Search **root canal therapy**	17355	13:51:23
#16	Add	Search **((((((((((((((#15) OR #14) OR #13) OR #12) OR #11) OR #10) OR #9) OR #8) OR #7) OR #6) OR #5) OR #4) OR #3) OR #2) OR #1**	498670	13:51:03
#15	Add	Search **post instrumentation pain**	987	13:49:39
#14	Add	Search **operative pain**	18803	13:49:13
#13	Add	Search **post operative endodontic pain**	38	13:48:41
#12	Add	Search **endodontic pain**	614	13:48:20
#11	Add	Search **post operative pain relief**	7918	13:47:58
#10	Add	Search **post operative pain management**	13776	13:47:28
#9	Add	Search **post operative pain control**	16284	13:46:59
#8	Add	Search **post operative pain**	61522	13:46:39
#7	Add	Search **dental pain management**	2083	13:46:07
#6	Add	Search **tooth ache**	2499	13:45:50
#5	Add	Search **tooth pain**	6566	13:45:30
#4	Add	Search **dental pain**	12259	13:45:13
#3	Add	Search **pain management**	59530	13:44:59
#2	Add	Search **pain control**	120005	13:44:45
#1	Add	Search **pain**	498446	13:43:43

STRUCTURED QUESTIONS
What is the difference in anesthetic success between placebo, acetaminophen and ibuprofen?

PICO ANALYSIS
- **Population-** Patients having irreversible pulpitis.
- **Intervention-**Ibuprofen and acetaminophen in anaesthetic success.
- **Comparison-** Placebo in anaesthetic success.
- **Outcome-** Anesthetic efficacy in irreversible pulpitis.

NULL HYPOTHESIS
There is no difference in anaesthetic success of inferior alveolar nerve block in irreversible pulpitis using pre-operative placebo or Acetaminophen or Ibuprofen administration.

MATERIALS AND METHODS

Sources Used
For identification of studies included or considered for this review, detailed search strategies were developed for the database searched. The MEDLINE search used the combination of controlled vocabulary and free text terms.

Searched Databases
- PUBMED (from February 1996 till June 2012)
- PUBMED Advanced Search (from February 1996 to June 2012)
- MEDLINE

Language
There were no language restrictions.

Hand Searching
The following journals were hand searched
- Journal of Endodontics
- International Endodontic Journal
- Oral Surgery Oral Medicine Oral Pathology Oral Radiology Endodontology

INCLUSION CRITERIA

Criteria for considering studies for this review
Types of Studies
1. Randomized controlled trials or clinical trials.
2.Anaesthetic success is evaluated after administration of inferior alveolar nerve block.

Types of Participants
Patients of age greater than 18years having irreversible pulpitis.

Types of Interventions
Anaesthetic is evaluated after the administration of inferior alveolar nerve block.
Types of Outcome Measures
Pre-operative medication in irreversible pulpitis to check the anaesthetic success after administration of Inferior alveolar nerve block.

EXCLUSION CRITERIA
The following studies were excluded,
- Case reports/case series
- Animal studies
- In vitro studies
- Studies not meeting the inclusion criteria

Table 1: Variables of interest

S. No	Variables Of Interest
1.	Anaesthetic success

Table 2:Characteristics of Included Studies

S. No	Author And Year	Materials Used	Method of Evaluation	Mean Values	Outcome
1.	Michael Simpson et al 2011	Placebo and combination of acetaminophen and ibuprofen. 45 minutes before local anaesthesia administration.	Heft-Parker Visual Analog Scale.	Combination tablet-32%. Placebo-24%.	No significant difference between two groups.
2.	Masoud Parirokh et al 2010	Placebo, ibuprofen, or indomethacin. One hour before local anaesthesia administration.	Heft-Parker Visual Analog Scale.	Placebo-32% Ibuprofen-78% and Indomethacin-62%.	Ibuprofen and indomethacin groups showed significantly higher success rates compared with the placebo group. There was no significant difference between ibuprofen and indomethacin.
3.	Mark Oleson et al 2010	Ibuprofen or Placebo.45minutes before local anaesthesia administration.	Heft-Parker Visual Analog Scale.	Ibuprofen - 41% and Placebo 35%.	No significant difference between the two groups.
4.	Vivek Aggarwal et al 2010	Ibuprofen, Ketorolac and Placebo.One hour before local anaesthesia administration.	Heft-Parker Visual Analog Scale.	Placebo -29% Ibuprofen-27% and Ketorolac-39%.	No significant difference between the three groups.
5.	Staci R Ianiro et al 2007	Acetaminophen or Combination of Acetaminophen and Ibuprofen and Placebo.30 minutes before local anaesthesia administration.	Visual Analog Scale.	Acetaminophen-71.4% Combination-75.9% and Placebo-46.2%.	No significant difference between the three groups.

Table 3: Characteristics of Excluded Studies

S. No	Author	Year	Reason for Exclusion
1.	Penniston SG, Hargreaves KM	1996	Not relevant to topic.
2.	Lindemann M, Reader A, Nusstein J, Drum M, Beck M	2008	Discussed about anaesthetic success but pre-operative medication was different.
3.	Prasanna N, Subbarao CV, Gutmann JL	2011	Discussed about anaesthetic success but pre-operative medication was different.
4.	Aggarwal V, Singla M, Rizvi A, Miglani S	2011	Discussed about anaesthetic success but pre-operative medication was different.

RESULTS

Description of Studies

The search identified 9 publications out of which 1 was excluded after reviewing the title or abstract. Full articles were obtained for 8 studies, 3 of these publications were excluded after reading the full text article. Therefore, a total of 5 publications fulfilled all criteria for inclusion.

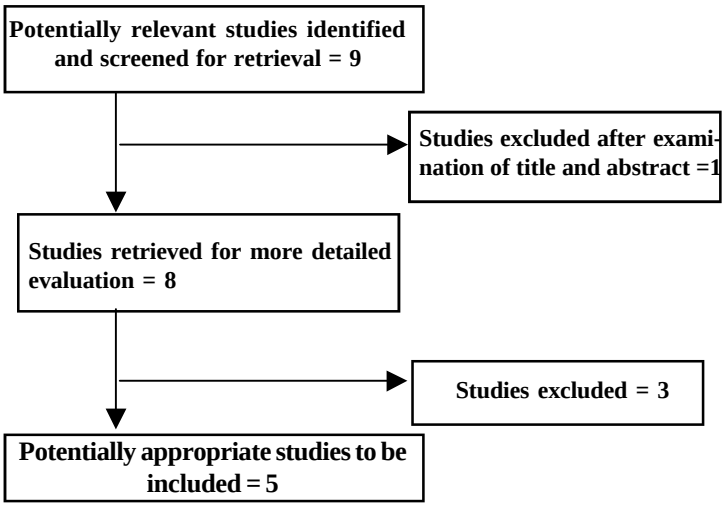

Chart 1: Search Flow Chart

Quality Assessment

The quality assessment of included trials was undertaken independently as a part of data extraction process. Four main quality criteria were examined:

1. Method of Randomization, 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, recorded as
   a. Yes – Adequate as described in the text
   b. No – Inadequate as described in the text
   c. Unclear in the text
3. Outcomes assessors blinded to intervention, 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/ exclusion criteria

Presence/ absence of estimate of measurement error. The validity and reproducibility of the method of assessment (table 4).

Risk of Bias in Included Studies

The assessments for the four main methodological quality items are shown in table. The study was assessed to have a "High risk" of bias if it did not record a "Yes" in three or more of the four main categories, "Moderate" if two out of four categories did not record a "Yes" and "Low" if randomization assessor blinding and completeness of follow – up were considered adequate.

Table 4: Evidence of Selected Article

S. No	Author	Year	Study Design	Level of Evidence
1	Michael Simpson et al	2011	Randomized double blinded clinical trial	Level 2
2	Masoud Parirokh et al	2010	Randomized double blinded clinical trial	Level 2
3	Mark Oleson et al	2010	Randomized double blinded clinical trial	Level 2
4	Vivek Aggarwal et al	2010	Randomized double blinded clinical trial	Level 2
5	Staci R Ianiro et al	2007	Randomized double blinded clinical trial	Level 2

Table 5: Risk of Bias – Major Criteria

Study	Randomization	Allocation Concealed	Assessor Blinding	Dropouts Described	Risk of Bias
Michael Simpson et al	Yes	No	No	None	Moderate
Masoud Parirokh et al	Yes	No	No	None	Moderate
Mark Oleson et al	Yes	No	No	None	Moderate
Vivek Aggarwal et al	Yes	No	No	Yes	Moderate
Staci R Ianiro et al	Yes	No	No	None	Moderate

Table 6: Risk of Bias – Minor Criteria

Study	Sample Justified	Baseline Comparison	I/ E Criteria	Method Error
Michael Simpson et al	No	Yes	Yes	No
Masoud Parirokh et al	Yes	Yes	Yes	No
Mark Oleson et al	No	Yes	Yes	No
Vivek Aggarwal et al	Yes	Yes	Yes	No
Staci R Ianiro et al	No	Yes	Yes	No

DISCUSSION

Interpretation of Results

First trial *Michael Simpson et al (2011),* 100 patients (50 per group) with irreversible pulpitis mandibular posterior teeth were given placebo, combination dose of 800 mg ibuprofen and 1000 mg acetaminophen 45 minutes before the administration of a conventional inferior alveolar nerve block. Result shows that, the success rate for the inferior alveolar nerve block was 32% for the combination of ibuprofen and acetaminophen group and 24% for the placebo.There was no significant difference ($p = 0.37$) between the two groups. For mandibular posterior teeth, a combination dose of 800 mg ibuprofen and 1000 mg acetaminophen was given 45 minutes before administration of the inferior alveolar nerve block did not result in a statistically significant increase in anesthetic success in patients with symptomatic irreversible pulpitis.

Second trial *Masoud Parirokh et al (2010),* 150 patients (50 per group) with irreversible pulpitis of mandibular posterior teeth were given placebo, 600 mg ibuprofen or 75mg indomethacin 1 hour before the administration of a conventional inferior alveolar nerve block. Result shows that, the overall success rates of inferior alveolar nerve for placebo, ibuprofen and indomethacin were 32%, 78% and 62% respectively ($p < 0.001$). Ibuprofen and indomethacin were significantly better than placebo ($p < 0.01$). There was no difference between ibuprofen and indomethacin ($p = 0.24$). Premedication with ibuprofen and indomethacin significantly increased the success rates of inferior alveolar nerve block anesthesia for teeth with irreversible pulpitis.

Third trial *Mark Oleson et al (2010),* 100 endodontic emergency patients diagnosed with irreversible pulpitis of a mandibular posterior tooth, were given 800 mg ibuprofen or placebo 45 minutes before the administration of a conventional inferior alveolar nerve block. Result shows that the success rate for the inferior alveolar nerve block was 41% with ibuprofen and 35% with placebo, with no significant difference ($p = 0.57$) between the two groups. For mandibular posterior teeth, a dose of 800 mg of ibuprofen given 45 minutes before the administration of the inferior alveolar nerve block did not result in a statistically significant increase in anesthetic success in patients with irreversible pulpitis.

Fourth trial *Vivek Aggarwal et al (2010),* 69 patients diagnosed with irreversible pulpitis of mandibular posterior tooth, were given 2 capsules of 300 mg of ibuprofen, 2 capsules 10 mg ketoroloc, 2 capsules placebo 1 hour before the administration of a conventional inferior alveolar nerve block. Result shows that the success rate for the inferior alveolar nerve block, placebo gave 29% success rate. Premedication with ibuprofen gave 27% and premedication with ketorolac gave 39% success rate. There was no significant difference between the three groups. Preoperative administration of ibuprofen or ketorolac has no significant effect on success rate of inferior alveolar nerve block in patients with irreversible pulpitis.

Fifth trial *Staci R Ianiro et al (2007),* 40 patients with irreversible pulpitis of mandibular posterior teeth were given 1000 mg of acetaminophen, combination of 1000 mg of acetaminophen and 600 mg of ibuprofen or placebo group 30 minutes before the administration of a conventional inferior alveolar nerve block. Result shows that, the success rate for the inferior alveolar nerve block was 60% for all three groups. Success was 71.4% for the acetaminophen group, 75.9% for the acetaminophen and ibuprofen group and 46.2% for the placebo group. There was no significant difference between the groups. However, there was a trend toward higher success in the medication groups.

Three clinical trials compared the use of placebo and ibuprofen as a pre-operative medication, two clinical trials compared the use of placebo and combination (acetaminophen and ibuprofen), one clinical trial compared the use of placebo, combination (acetaminophen and ibuprofen) and acetaminophen as a pre-operative medication on the success of inferior alveolar nerve block in irreversible pulpitis.

The result of anaesthetic success of inferior alveolar nerve block in the studies using ibuprofen in comparison to placebo is inconsistent as one trial shows significant difference and the other two trials, shows no significant difference. This heterogenicity of results may be due to lack of predetermination of sample size.

Moreover, the studies using the combination of acetaminophen and ibuprofen in comparison to placebo showed no significant difference in anaesthetic success of inferior alveolar nerve block suggesting no beneficial effect.

In another trial using acetaminophen and placebo also showed no significant difference in anaesthetic success of inferior alveolar nerve block.

Defending the Results

Premedication with ibuprofen or acetaminophen did not significantly increase the success rate because of acute inflammatory reaction.The inflammatory mediators had already activated the nociceptors. Medication with NSAIDs only inhibits the formation of prostaglandins but has no effect on already activated nociceptors.

Prostaglandins are one of a vast array of inflammatory mediators found in the dental pulp in patients experiencing irreversible pulpitis. A study by *Maingret et al (2008)* demonstrated that when inflammatory mediators such as prostaglandins, serotonin and histamine were applied singly to neurons, up-regulation of Nav 1.9 isoform did not occur. However, when the inflammatory mediators were combined and then applied to the neuron, the Nav 1.9 isoform was up-regulated. It was found that, the synergistic action of multiple inflammatory mediators was most likely responsible for the up-regulation of the Nav 1.9 isoform.

Therefore, the removal of a single inflammatory mediator might not be enough to overcome the effects of the other inflammatory mediators involved. Another possible explanation is the degree and duration of the damage and up-regulation occurring before the prostaglandins are inhibited by the ibuprofen. Prostaglandins are effectively blocked by ibuprofen and they have a relatively short half-life.

However, even if all of the new prostaglandin production were inhibited, the inflammatory damage previously created is still present, as well as the concerted action of the other inflammatory mediators. Therefore, even if preoperative ibuprofen inhibited prostaglandin production, the previous damage along with the action of multiple other inflammatory mediators, might explain the high rate of local anesthetic failure.

Quality of Evidence

All the studies included in this review has a level of evidence 2. All are randomized clinical trials, thus the level of evidence is high. Risk of bias of included studies included five trials *(Michael Simpson et al, Masoud Parirokh et al, Mark Oleson et al, Vivek Aggarwal et al, Staci R Ianiro et al)* is moderate. Hence, the interpretations obtained from these studies are proposed to be reliable.

INFERENCE

Implications for Practice

There is some evidence that pre-operative medication shows there is an increase in success of inferior alveolar nerve block in irreversible pulpitis.

Implications for Research

However, the number of good quality randomized controlled clinical trials included in this review is very limited. This shows the lack of evidence supporting the findings. Hence, more long term clinical trials are required to prove that there is an increase in success of inferior alveolar nerve block in irreversible pulpitis when pre-operative medications are used.

Report of Outlier Data

No outlier data obtained.

SUMMARY

The aim of this systematic review was to compare and evaluate the effect of preoperative ibuprofen and acetaminophen on the success of the inferior alveolar nerve block in patients with irreversible pulpitis.

Trials were selected if they met the following criteria. Randomized controlled clinical trials comparing pre-operative medication using placebo, ibuprofen and acetaminophen in irreversible pulpitis. The studies for inclusion in this review represents comparison of pre-operative medication on anaesthetic success of inferior alveolar nerve block.

The databases PUBMED CENTRAL and MEDLINE were searched for the related topic from 1996 to till June 2012.The search identified 9 publications out of which 1 was excluded after reviewing the title or abstract. Full articles were obtained for 8 studies 3 of these publications were excluded after reading the full text article. Therefore, a total of 5 publications fulfilled all criteria for inclusion.

CONCLUSION

The clinical evidence in this review is inadequate to state that there is a difference in anaesthetic success on the use of pre-operative ibuprofen and acetaminophen in irreversible pulpitis. Hence, more properly designed randomized clinical trials are needed to evaluate the usage of pre-operative medication on success of inferior alveolar nerve block in irreversible pulpitis.

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