EUROPEAN ENDODONTIC JOURNAL

ORIGINAL ARTICLE

Effectiveness of Lignocaine with and without Pre-operative Oral Ibuprofen in Controlling Pain in Primary Mandibular Molars with Irreversible Pulpitis in 5 to 9-Year-Old Children: A Randomized Controlled Trial

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ABSTRACT

Objective: Childhood experiences of pain associated with dental treatment can induce dental anxiety. Inferior alveolar nerve blocks are eight times more likely to fail in patients with irreversible pulpitis. The objective was to compare the effectiveness of lignocaine with and without pre-operative oral ibuprofen for controlling pain in primary mandibular molars scheduled for pulpectomy procedures in 5 to 9-year-old children.

Methods: One hundred and twenty-two children diagnosed with irreversible pulpitis in mandibular posterior teeth and scheduled for pulpectomy procedures were included. The children were assigned to one of the two groups, Treatment group A: Pre-operative with oral ibuprofen and local anaesthesia with 2% lignocaine (with adrenaline 1:80000); Treatment group B: Pre-operative with oral placebo and local anaesthesia with 2% lignocaine (with 1:80000 adrenaline). Pain and pulse rate were recorded at baseline, one hour after administration of oral medication, fifteen minutes following administration of Inferior Alveolar Nerve Block (IANB), and also during the course pulpectomy. The results were statistically analysed using chi square test and repeated measures analysis of variance (ANOVA).

Results: In treatment group A, 90.16% children had IANB success compared to 9.83% in group B.. The difference in the success rate between two groups was statistically significant ($p<0.001$) with an odds ratio of 84.

Conclusion: Oral medication with ibuprofen is effective in increasing the success rate of IANB with lignocaine for the treatment of irreversible pulpitis of 5 to 9-year-old children.

Keywords: Ibuprofen, inferior alveolar nerve block, irreversible pulpitis, NSAIDs, pain, pulp

HIGHLIGHTS

- Release of inflammatory and pro-inflammatory mediators sensitize the nerve endings within the pulp of the inflamed tooth, which increases pain production.
- Chances of failure of nerve block is higher in teeth with irreversible pulpitis.
- Hence achieving profound local anaesthesia in primary teeth with irreversible pulpitis is challenging.
- Poor pain management may impact child behaviour and attitude towards dentistry.
- Pre-operative administration of Ibuprofen greatly increased success rate of nerve block in irreversibly inflamed primary teeth and reduced the need for supplemental anesthesia.

Please cite this article as: Gandhi Z, Nagaraj Gowda SH. Effectiveness of Lignocaine with and without Pre-Operative Oral Ibuprofen in Controlling Pain in Primary Mandibular Molars with Irreversible Pulpitis in 5 to 9-Year-Old Children: A Randomized Controlled Trial. Eur Endod J 2024; 9: 191-7

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Received : September 05, 2023,
Revised : December 22, 2023,
Accepted : December 31, 2023

Published online: August 09, 2024
DOI 10.14744/eej.2023.18480

INTRODUCTION

Pain is one of the oldest medical problems and perhaps the universal physical affliction of humanity. Childhood experiences of pain associated with dental treatment can induce dental anxiety and affect a child's attitude towards den-

tistry throughout his or her lifetime (1). The role of local anaesthesia to allay the pain during dental procedures is irreplaceable.

Patients most often seek treatment for irreversible pulpitis (2). Teeth with irreversible pulpitis are eight times more likely to experience failure of profound pulpal anaesthesia compared to non-inflamed teeth (2). Currently, most commonly used block to anesthetize the mandibular teeth is the inferior alveolar nerve block (IANB) (3). Clinical studies have revealed that the failure rate of IANB in teeth with irreversible pulpitis ranged from 44%–81% (4) The unpredictable spread of anaesthetic solution, needle deflection and inaccurate injection technique are plausible factors for such high failure rate. There are also patient factors including anatomic variations, accessory innervations and psychological issues (5, 6).

Failure of neve block in teeth with irreversible pulpitis primarily occurs due to inflammation (7). Release of inflammatory and pro-inflammatory mediators sensitize the peripheral nociceptors within the pulp of the inflamed tooth, which increases pain production (8). Other reasons suggested in the literature are changes in the resting potentials and reduced excitability thresholds of inflamed nerves; tetrodotoxin resistant sodium channels (resistant to anaesthetics); increased expression of sodium channels in irreversibly inflamed pulps; and anxious patients with lower pain thresholds (9). To address the shortcomings of IANB in managing pain in patients with irreversible pulpitis, various techniques have been considered, including the use of different anaesthetic agents, topical anaesthetics, and supplementary anaesthetic techniques (10). Pre-operative oral administration of steroidal or nonsteroidal anti-inflammatory drugs (NSAIDs) is another such method proposed as an approach to improve IANB success (4, 7). Ibuprofen, a propionic acid derivative, is a NSAID used in mild to moderate pain (11). Ibuprofen is safe and well tolerated than other non-steroidal anti-inflammatory drugs (NSAIDs) especially in children (11).

The efficacy of NSAIDs to improve the success rate of IANB has been investigated by many clinical studies in adults (4, 12–20). Results of which are not in cohort. Meta-analysis by Li et al. (21) reported moderate level of evidence for effectiveness of NSAIDs in improving the success of IANB in adults. Another meta-analysis by de Geus et al. (22) compared the preventive ibuprofen administration to placebo on the efficacy of IANB in patients with irreversible pulpitis showed Ibuprofen as premedication is beneficial for the success of inferior alveolar nerve block. However, there is a paucity of literature on efficacy of preoperative analgesics on improving efficiency of IANB in children with irreversible pulpitis.

Hence, this study evaluated the role of pre-operative oral NSAID (ibuprofen) on the effectiveness of IANB with lignocaine, which can in turn help us in effective pain management for endodontic therapy in a paediatric population. The objective was to assess and compare the success rate of IANB, severity of pain (if any) and pulse rate in 5 to 9-year-old children with primary mandibular molars diagnosed with irreversible pulpitis using:

- 2% lignocaine (with adrenaline 1:80000).
- 2% lignocaine (with adrenaline 1:80000) with pre-operative oral ibuprofen.

MATERIALS AND METHODS

Institutional Ethics Committee approved the protocol (YMTDCH/IEC/OUT/072/2016 on 16/11/2016) for this triple blinded (patient, evaluator, statistician), two parallel arm randomized controlled trial with 1:1 allocation ratio. The study was conducted in accordance with the Declaration of Helsinki.

Sample Size Calculation

The sample size estimation was based on the primary outcome variable. In a previous study by Parirokh et al. (17), the reported success rates of IANB with pre-operative ibuprofen was 35% higher than lignocaine alone. Adjusting alpha at 0.05 and beta at 0.20, the sample required in each group to detect a minimal difference of 35% between two groups was 55. To compensate for any dropouts, a 10% of additional sample that was 6 children, were added to each group. Therefore, a total of 122 children were included in the study.

Study Setting

Three hundred and eleven, 5 to 9-year-old children, who visited the department of Pediatric and Preventive Dentistry of the institute with at least one primary molar tooth indicated for pulpectomy were screened from May 2017 to June 2018. A total of 122 children were recruited based upon the inclusion and exclusion criteria.

Inclusion Criteria

- Healthy children with primary mandibular molar indicated for pulpectomy.
- Clinical examination revealed deep dental caries on primary mandibular molars and provided history of pain in mandibular molar.
- Positive pain response to cold refrigerant test (Endofrost cold spray m/s Coltene Whaledent Pvt Ltd. Taloja, Panvel, Maharashtra, India).
- Children belonging to Frankl behaviour rating – negative, positive and definitely positive.

Exclusion Criteria

- Physically, intellectually and medically compromised children.
- Children with history of allergy or sensitivity to NSAIDs or local anaesthesia.
- Non vital teeth. Cold test (Endofrost cold spray m/s Coltene Whaledent Pvt Ltd. Taloja, Panvel, Maharashtra, India) was used to determine the vitality of the tooth.
- Children presented with any signs of abscess, extra oral swelling and draining sinus.
- Children who had taken NSAIDs in the past 12 hours.
- Children unwilling to participate in the study or for whom the parents/guardians refused to give consent.

Along with a written consent from the parents/legal guardian, additional assent was taken from the children in the presence of a witness.

Randomization, Allocation and Sequence Generation
The selected children were randomly allocated to two groups (1:1 allocation ratio, n=61) using sealed opaque envelope containing computer generated random alpha numeric code (http://www.randomization.com, seed- 1260) (23).

- Treatment group A: Pre-operative with oral ibuprofen and local anaesthesia with 2% lignocaine (with adrenaline 1:80000) (LIGNOX - M/s INDOCO Remedies Ltd, Gandhinagar, Gujarat, India)
- Treatment group B: Pre-operative with oral placebo and local anaesthesia with 2% lignocaine (with adrenaline 1:80000).

Children allotted to treatment group A received ibuprofen (M/s Cipla Ltd by golden cross pharma Pvt. Ltd. Plot no. 3, MIDC, Shiroll, Kohlapur, 416122, India) (10 mg/kg) mixed with the 15 ml juice and treatment group B received 15ml plain fruit juice. This helped us mask the children to intervention.

Allocation Concealment
Each patient picked an envelope after their enrolment in the study and before the start of intervention. Alpha numeric code in the envelope determined which group was assigned for the child. A trained nurse, blinded to the treatment and assessment protocol verified the code against the allocation sheet and dispensed fruit juice mixed with ibuprofen or plain fruit juice, so that operator and evaluators remained blinded to the study groups. The evaluator who showed Wong-Bakers FACES pain scale and recorded pulse rate was blinded to the treatment groups.

Procedure
Prior to the administration of any juice, baseline pain using the Wong-Bakers FACES pain scale (24), and pulse rate using a fingertip pulse oximeter was recorded. Subsequent to one hour of oral administration of medication/plain fruit juice, pain and pulse rate were recorded again and IANB was administered. The IANB was administered by a single operator. Total of 2.2 ml of local anaesthetic solution (Lignox 2% A, Indoco Remedies ltd, Gandhinagar, India) was utilized to complete IANB and lingual nerve block and long buccal nerve block. Fifteen minutes following administration of IANB, pain and pulse rate were recorded, lip numbness was confirmed and were undertaken for access opening and pulp extirpation. Complete pulp extirpation was done with 21 mm stainless steel K files (Mani Inc. India). If the child experienced pain during the procedure, supplemental anaesthesia was administered.

Outcomes
Inferior alveolar nerve block was considered successful if the child did not experience any pain during access opening and pulp extirpation and the operator was able to complete the procedure without any supplemental anaesthesia.

Wong-Baker FACES Pain rating and pulse rate were recorded at different intervals.

- On penetrating the dentine
- On penetrating the pulp
- During pulp extirpation

Statistical Analysis
Statistical analysis was carried out using windows based MedCalc Statistical Software' version 13.3.1 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2014). Chi-square test was used to compare the difference between the success rate of IANB in treatment group A and B. Paired t –test was used for inter group comparison of mean pain rating and at different intervals during pulpectomy. Repeated measures analysis of variance (ANOVA) was employed to access pain rating and pulse rate at different time intervals and the effect of age and gender on pain rating and pulse rate. P value < 0.05 was set as statistically significant.

RESULTS
The patients were accessed for eligibility, and randomly assigned to one of the two groups using simple randomization (Fig. 1). There were 33 males and 28 females in treatment group A. There were 34 males and 27 females in treatment group B. The mean age in treatment group A was 6.82 years and in treatment group B was 6.89 years. The mean age difference of children in both treatment groups was not statistically significant (p=0.791). Based on their Frankl behaviour rating scale, there was no statistically significant difference in the distribution of children between two groups (p=0.47).

Success Rate
In treatment group A, IANB was successful in 90.16% children and in treatment group B, IANB was successful only in 9.83% children. The difference was statistically significant (p<0.001) with an odds ratio of 84 (276.68–25.52) (Table 1).

Pain Rating during Pulpectomy in Both Treatment Groups
The difference in the mean pain rating of treatment group A and B was statistically significant at one hour after oral pre-operative ibuprofen or placebo administration, fifteen minutes after block administration, on dentine penetration and on pulp penetration (p<0.001). However, the difference was not statistically significant at baseline(p=0.058) and on pulp extirpation (p= 0.63) (Table 2).

Pulse Rating during Pulpectomy in Both Treatment Groups
The mean pulse rate in treatment group A was 106.92 and in treatment group B was 99.80. The difference between the pulse rate in both treatment groups was significant (p=0.043). Therefore, 103.36 beats/minute was used as a co-variate which is the arithmetic mean of baseline pulse rates in treatment group A (106.92) and B (99.80).

Using 103.36 beats/minute as a co-variate, the difference in the mean pulse rate of treatment groups A and B is statistically significant at fifteen minutes after block administration (p=0.001), on dentine penetration (p=0.002), pulp penetration (p=0.001) and on pulp extirpation (p=0.003). However, the difference is insignificant at one hour after oral medication administration (p=0.36) (Table 3).

Difference in Pain and Pulse Rate at Different Intervals of Time
Repeated measurements of pain and pulse rate at five different specified intervals as compared to pain and pulse rate at baseline were statistically significant [Repeated measures ANOVA, Pain rating (p=0.03), Pulse rate (p<0.001)]. There was no effect of

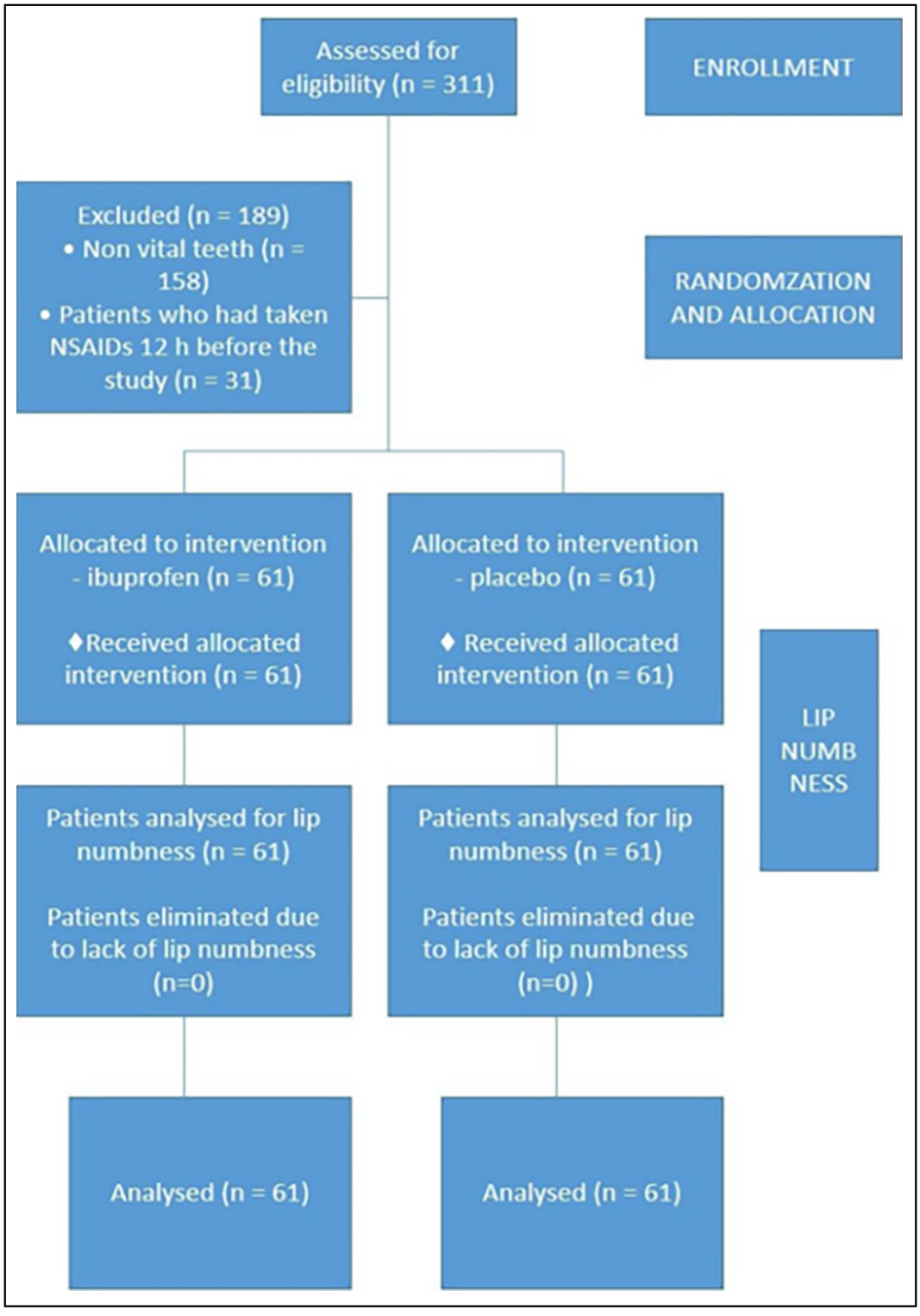

Figure 1. Consort diagram

age, gender and baseline pulse rate on the pain rating (p=0.22, p=0.68, p=0.09) or on pulse rate (p=0.13, p=0.93) (Table 4).

No child reported any adverse effect to either the anaesthesia or ibuprofen.

DISCUSSION

The success rate of IANB has been reported to range from 38% to 85% (25–28). Supplemental anaesthesia techniques like intra-ligamentary and intra pulpal injection are relied upon when pulpal anaesthesia fails. However, supplemental injection is associated with fear and anxiety and an additional dose of anaesthetic solution is needed (29).

Various studies which have shown that severe pain at the beginning of the treatment may affect the success of anaesthesia (30), Age and behaviour can also influence the perception of pain. However, in this study, the child's age group

TABLE 1. Success of anesthesia in treatment group A and B

Success of anesthesia	Treatment group A		Treatment group B		p	Odds ratio (CI, upper bound – CI, lower bound)
	n	%	n	%		
Yes	55	90.16	6	9.83	<0.001*	84 (276.68–25.52)
No	6	9.83	55	90.16		
Total	61	50	61	50		

*: Statistically significant. Statistical test: Chi-square test. CI: Confidence interval

TABLE 2. Assessment and comparison of pain rating at different intervals during pulpectomy for treatment group A and B

	Treatment group A (n=61)		Treatment group B (n=61)			Confidence interval		p
	Mean	SD	Mean	SD	Mean difference	Upper	Lower	
Baseline	6.39	2.42	5.67	1.68	0.72	-0.025	1.47	0.058
One hour after oral administration	2.46	1.52	4.92	1.99	-2.46	-3.10	-1.83	<0.001*
Fifteen minutes after block	0.33	0.75	2.27	2.30	-1.94	-2.56	-1.33	<0.001*
After block, on dentine penetration	0.10	0.44	2.13	2.25	-2.03	-2.61	-1.46	<0.001*
After block, on pulp penetration	0.26	0.93	2.52	1.86	-2.26	-2.79	-1.74	<0.001*
During pulp extirpation	0.23	0.90	0.16	0.55	0.07	-0.20	0.33	0.63

*: Statistically significant. Statistical test: Paired t test. SD: Standard deviation

TABLE 3. Comparison of mean pulse rate between the two treatment groups at different intervals during pulpectomy

	Treatment group A (n=61)			Treatment group B (n=61)			p
	Mean	95% CI		Mean	95% CI		
		Upper	Lower		Upper	Lower	
One hour after oral administration	96.69	93.25	100.13	99.02	95.58	102.45	0.036
15 minutes after block	100.19	95.35	105.04	111.79	106.95	116.64	0.001*
After block, on dentine penetration	103.86	99.97	107.77	112.59	108.69	116.50	0.002*
After block, on pulp penentration	106.66	103.54	109.82	114.16	111.02	117.30	0.001*
During pulp extirpation	105.02	101.67	108.37	112.43	109.08	115.78	0.003*

*: Statistically significant. Statistical test: ANCOVA. Here covariate appearing in the model are evaluated at baseline being 103.36 beats/minute. CI: Confidence interval

TABLE 4. Difference in pain and pulse rate at different intervals of time

Variable	Mean square for pain rating	F	p	Mean square for pulse rating	F	p
Intervention	39.152	4.989	0.03*	252825.73	226.51	<0.001*
Time*Age	11.795	1.503	0.22	2616.33	2.34	0.13
Time*Gender	1.373	0.175	0.68	8.45	0.01	0.93
Time*Baseline Pulse Rate	23.316	2.971	0.09	–	–	–

*: Statistically significant. Satistical test: Repeated Measures ANOVA. Covariates appearing in the model are evaluated at the following values: Age (yrs.) = 6.842, Baseline pulse rate = 103.22. ANOVA: Analysis of variance, F: F Value of ANOVA statistical test

and Frankl behaviour rating and baseline pain rating were not significantly different between the treatment group A and treatment group B.

This study has revealed that pre-operative ibuprofen significantly improved the success rate of IANB anaesthesia with irreversible pulpitis which is in accordance with several

other studies in adults (13, 15, 17), but no studies have been done previously in children. A study by Riaz et al. (31) compared four groups - placebo, Diclofenac sodium, Piroxicam 20 mg and Tramadol 50 mg. Results found all the analgesic groups showed a significant effect on the efficacy of the inferior alveolar nerve block in contrast to the control group ($p<0.05$). The overall effectiveness of the preoperative drug in improving IANB efficacy was observed in 69.2% of patients, with the remaining 30.8% reporting pain during the root canal procedure. Furthermore, no significant difference was found between the drug groups on the effectiveness of the IANB ($p>0.05$). Parirokh et al. (17) found that premedication with ibuprofen and indomethacin significantly improved the success rates of inferior alveolar nerve block in teeth with irreversible pulpitis. Placebo, ibuprofen and indomethacin had success rates of 32%, 78% and 62%, respectively. Ibuprofen and indomethacin were significantly better than placebo ($p<0.01$). There was no difference between ibuprofen and indomethacin ($p=0.24$) (17). Another study by Elnaghy et al. (32) evaluated the effectiveness of meloxicam 7.5 mg, ketorolac 10 mg, dexamethasone 0.5 mg, ibuprofen 600 mg, or placebo on two hundred and fifty emergency patients in moderate to severe pain diagnosed with symptomatic irreversible pulpitis. The overall success rates for the meloxicam 7.5 mg, ketorolac 10 mg, dexamethasone 0.5 mg, and ibuprofen 600 mg groups were 52%, 64%, 54%, and 58%, respectively, with no significant differences in success rates among the premedication groups ($p>0.05$). However, the tested premedication revealed significant differences compared with the placebo group (32% success rate) ($p<0.05$). Pre-operative administration of drugs can help to alleviate the inflammation. The anti-inflammatory and analgesic effect of ibuprofen is primarily from their ability to block cyclooxygenase activity, leading to the inhibition of PG synthesis (33) and the secondary inhibition of the sensitisation of nociceptive nerve endings (34). Ibuprofen is commonly prescribed, because it is safe, cost-effective, and possesses an effective analgesic and anti-inflammatory action (35).

On the contrary, few other studies showed no significant difference with pre-operative ibuprofen for successful anaesthesia (18, 19). These are reported by Ianiro et al. in 2010 (19). They found that placebo, acetaminophen, and acetaminophen plus ibuprofen had success rates of 46.2%, 71.4%, and 76.9% respectively, but the differences were not statistically significant. A study by Mahajan et al. (36) demonstrated that tramadol group showed significantly higher success rates but ibuprofen and combination of ibuprofen and acetaminophen groups were not significant with placebo. A systematic review and network meta-analysis (NMA) of different drugs, dexamethasone was the most effective in improving the outcome of a nerve block procedure (21). Non-steroidal anti-inflammatory drugs (NSAIDs) came in second place in terms of overall performance in enhancing the success of a nerve block (21).

The mean pain rating at different intervals during pulpectomy between treatments group A and B is statistically significant indicating pain management with pre-operative oral ibuprofen is better in children with irreversible pulpitis. If the child experienced pain during dentine or pulp penetration, the block was considered as a failure and supplemental anesthesia was administered. Thus, we did not find a significant difference in the pain rating between treatment group A and B during pulp extirpation. There was a greater difference in the mean baseline pain rating and mean pain rating of other intervals, in treatment group A when compared to treatment group B. This again indicates better pain management in children receiving pre-operative oral ibuprofen.

There was a significant difference in the baseline pulse rate between treatment group A and B. Analysis of covariance (ANCOVA) test was applied to compare the treatment groups at various intervals with the covariate baseline pulse rate as 103.36 beats/minute. After adjusting baseline value, the difference was non-significant at one hour after oral medication administration. However, the mean difference in pulse rate between treatment groups A and B was statistically significant at fifteen minutes after block administration, on dentine penetration, pulp penetration and on pulp extirpation. This indicates better pain control in treatment group receiving pre-operative oral ibuprofen. There was greater and statistically significant difference observed in the pulse rate when baseline was compared with other treatment intervals in treatment group B. This could be attributed to lesser pain control in the treatment group B.

Limitations

Children always tend to objectively inform absolute degrees of pain that is, either painful or painless. The best possible way to address this limitation was to display (through the Wong-Baker's pain rating scale) the emotion which children can easily point towards. Hence, we used Wong- Baker's pain rating scale which is considered highly reliable and reproducible in children (37). The major concern with the Wong-Baker's pain rating scale was the confounding of emotion with pain intensity in the representation of the faces (38). Since this was a parallel arm study, there is a possibility of children with high or low pain threshold being allocated to either of the treatment groups, which could affect the pain assessment. However, it is expected that randomization of children into two groups eliminated this possibility.

Pulse rate was measured as proxy measure to assess pain experience. Pain experience increases the pulse rate. However, other factors like anxiety and fear can also contribute to increase in pulse rate.

In cases of healthy children suffering from irreversible pulpitis with no swelling or abscess, oral administration of Ibuprofen can improve the success of IANB with lignocaine. Effect of this intervention in children with high level of anxiety, disruptive behaviour which may adversely affect the pain threshold needs be to further studied.

CONCLUSION

Oral administration of ibuprofen an hour before IANB administration greatly increases the success rate of IANB with lignocaine for the management of irreversible pulpitis in children, and reduces the need for supplemental anaesthesia.

Disclosures

Ethics Committee Approval: The study was approved by the Dr G.D.Pol Foundation YMT Dental College and Hospital, Navimumbai Ethics Committee (no: YMTDCH/IEC/OUT/072/2016, date: 16/11/2016).

Authorship Contributions: Concept – S.H.N., Z.G.; Design – S.H.N.; Supervision – S.H.N., Z.G.; Materials – Z.G.; Data collection and/or processing – Z.G.; Data analysis and/or interpretation – S.H.N., Z.G.; Literature search – Z.G.; Writing – Z.G., S.H.N.; Critical review – S.H.N., Z.G.

Conflict of Interest: All authors declared no conflict of interest.

Use of AI for Writing Assistance: Not declared.

Financial Disclosure: The authors declared that this study received no financial support.

Peer-review: Externally peer-reviewed.

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