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THE EFFICACY OF PROPHYLACTIC INTRALIGAMENTARY INJECTION OF PIROXICAM VERSUS MEPECAINE FOR MANAGEMENT OF POST-ENDODONTIC PAIN IN MANDIBULAR POSTERIOR TEETH WITH IRREVERSIBLE PULPITIS AND APICAL PERIODONTITIS A RANDOMIZED CLINICAL TRIAL (THERAPEUTIC STUDY) (PART 2)

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ABSTRACT

Aim: This study aimed to investigate the effect of prophylactic intraligamentary injection of piroxicam versus mepecaine on management of post-endodontic pain after single-visit treatment of mandibular posterior teeth with irreversible pulpitis and apical periodontitis.

Methodology: Twenty patients with symptomatic irreversible pulpitis and apical periodontitis in their mandibular posterior molars were included in the study. post-operative pain experienced after administration of prophylactic intraligamentary piroxicam in the experimental group or prophylactic intraligamentary mepecaine in the control group was evaluated after 6,12,24, and 48 hours using the numerical rating scale (NRS). Demographic data and NRS scores were collected from the patients and statistically analyzed.

Results: Results showed that the prophylactic administration of intraligamentary piroxicam before single-visit root canal treatment had no significant decrease in pain intensity at 6,12,24, and 48 hours postoperatively compared to mepecaine group. The piroxicam group showed no statistically significant decrease in pain on percussion after 7 days. The total number of analgesic tablets taken in the Piroxicam group was not statistically significantly different from the control group postoperatively.

Conclusion: It could be concluded that the prophylactic administration of intraligamentary piroxicam had no better potency in reducing post-endodontic pain than intraligamentary mepecaine for vital teeth with irreversible pulpitis and symptomatic apical periodontitis in mandibular molar teeth during the first 48 hours. Regarding postoperative pain on percussion, intraligamentary piroxicam has the same pain level as the mepecaine group. Participants in the piroxicam group used a comparable number of brufen tablets to the mepecaine group.

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INTRODUCTION

The International Association for the Study of Pain (IASP) established a definition of pain that recognized the link between tissue injury and pain as an unpleasant sensory and emotional experience linked with actual or possible tissue injury **Riganello et al. (2021).**

One of the main reasons that prevent patients from attending dental offices is anxiety and fear of pain during root canal treatment. For that reason, managing pain during and after root canal treatment (RCT) is of great importance. Prevention and management of post endodontic pain (PEP) is an integral part of endodontic treatment **Stevens et al. (2021).**

Endodontists, in particular, must frequently address the issue of odontalgia, the most common type of orofacial pain, before providing proper treatment. Once therapy is initiated, postoperative pain control is the concern **Pigg et al. (2021).** Post endodontics pain result from over instrumentation and/or obturation of the root canals, this pain can be severe but usually is moderate and doesn't need emergency treatment **Çiçek et al. (2017).** The skill of the clinician is often judged as patients usually link between dental care and pain **Gupta et al. (2021).**

For more than a decade, prostaglandins have been linked to the aetiology of pulp and periapical diseases. Inflamed pulps and periapical tissues of humans and animals have been found to contain elevated amounts of arachidonic acid metabolites. Therefore, Increased levels of these eicosanoids in the pulpal and periapical tissues are related to the occurrence of pain **Ribeiro-Santos et al. (2021).**

Non-steroidal anti-inflammatory drugs (NSAID) are now widespread all over the field of dentistry and they have been proved to be very effective in controlling PEP. Ketorolac Tromethamine is a potent inhibitor of prostaglandin synthesis and the first NSAID available for intramuscular injection. When compared to the standard method of delivery, ketorolac 60 mg/2 milliliters gave significantly better pain alleviation than placebo at 12 and 24 hours after several endodontic treatments (swallowing a tablet) Parenteral injection has the potential to provide increased analgesic effectiveness due to the faster onset of analgesic action and higher peak serum drug levels **Akhlaghi et al. (2019).**

Piroxicam is another NSAID that can be used to alleviate pain, fever, and inflammation in the body although its mechanism of action is incompletely known and has a half life of 50 hours in the plasma. within 2 to 4 hours, oral piroxicam reaches a peak plasma concentration **Suresh et al. (2020).**

The pain following endodontic therapy is commonly significant for the first 24 hours after treatment, then gradually fades till it disappears after 7-10 days in most cases. Since piroxicam has a long half-life and reaches a peak concentration rapidly, piroxicam will help to relieve the most severe pain that arises following endodontic therapy **Konagala et al. (2019).**

Administering medications such local anesthetics and NSAIDs before the onset of postoperative pain can provide the best clinical results. Administering these drugs before a surgical or an endodontic procedure may be of benefit for longer procedures or for minimizing peripheral sensitization, which is a result of the cascade of inflammatory mediators that are released by tissue injury and fuel the subsequent inflammatory process **Berhouma et al. (2021).**

To date, few studies have evaluated the efficacy of an intraoral injection of piroxicam. The purpose of the present study was to evaluate the effect of a single intraligamentary injection of piroxicam on postoperative pain associated with endodontic therapy.

AIM OF THE STUDY

The aim of this study was to investigate the effect of prophylactic intraligamentary injection of piroxicam versus mepecaine on management of post endodontic pain after single visit treatment

of mandibular posterior molars with irreversible pulpitis and apical periodontitis in a randomized controlled trial

MATERIAL AND METHODS

1. Description of research question (PICO):

P: Patient with irreversible pulpitis and symptomatic apical periodontitis.

I: Single dose of intraligamentary piroxicam.

C: Intraligamentary mepecaine.

O1: Postoperative pain.

O2: Incidence of analgesic intake and number of analgesic tablets.

O3: Pain on percussion.

2. Trial design:

Prospective, parallel and randomized double blinded clinical trial.

3. Trial setting and registration:

1. Recruitment, treatment and follow up:

Recruitment, treatment and follow up of the patients from the out clinic of the Endodontic Department, Faculty of Oral and Dental Medicine, Cairo University in the duration between august 2019 – January 2020.

2. Trial registration:

Website: www.clinicaltrials.gov

URL: http:/www.clinicaltrials.gov

Trial number: NCT03006107.

4. Participants:

1. Eligibility criteria for participants:

A-The inclusion criteria were:

1. Medically free patients.
2. Patient's age between 25-50 years with no sex predilection.
3. Mandibular molar teeth diagnosed clinically and radiographically with irreversible pulpitis and symptomatic apical periodontitis.
4. Positive patient's acceptance for participation in the study.

B- The exclusion criteria were:

1. Female patients who are pregnant or lactating.
2. Patients who are medically compromised.
3. Patient with multiple teeth that required endodontic treatment to eliminate the possibility of pain referral.
4. Patient who has taken analgesic or anti-inflammatory drugs 12 hours before treatment.
5. Teeth that had vertical root fracture, coronal perforation, calcification, mobile, mutilated teeth, internal or external resorption.
6. Teeth with extensive caries or root caries.

Sample size:

This sample size was approved by Medical Biostatistics Unit (Appendix 2) and calculated based on the previous research of (**Atabaei et al. 2011),** data were analyzed using SPSS ® advanced statistics, version 21 (SPSS Inc. Chicago, IL). Considering a standard deviation 1, a total sample size of 12 patients (6 in each group) was sufficient with power 90% and 5% significance level. This number was increased to 16 patients to correct for non-parametric usage. This number was increased again to total number 20 to compensate for losses during follow up. The sample size was calculated by PS power program.

Randomization steps

Sequence generation

Allocation sequence were generated using blocks of 4 on a Microsoft Excel sheet where the intervention and control were denoted A & B and randomly distributed.

Allocation concealment:

The table was retained and only the co-supervisor had access to it and concealed from the investigator.

Following local anesthesia, the operator contacted the assistant supervisor asking for IL injection protocol assigned to that patient, then endodontic treatment was completed.

Implementation:

The random sequence was generated by the co-supervisor, assigned the participants to the intervention or control groups and the co-supervisor knew whether A or B is the control or intervention. The operator enrolled the participants after they were diagnosed and found eligible and confirmed with the assistant supervisor.

Blinding:

Piroxicam vials were filled in anesthesia carpules after making them empty then autoclaved. The co-supervisor gave them to the operator who was blinded for both intervention and control groups and the outcome assessor who was the patient was also blinded.

Ethical considerations:

The protocol of this study and the template informed consent form (Appendix 6) were approved by the Ethics Committee of Scientific Research - Faculty of Oral and Dental Medicine – Cairo University.

The patients were informed about the therapy techniques, adverse effects, and treatment options. They were instructed to follow general instructions, sign a printed consent form that stated the study's purpose, and fill out the NRS chart (Appendix 7) accurately and honestly at 6, 12, 24, and 48 hours postoperatively, then deliver it to the operator on time. The pain levels were recorded using a numerical rating scale that was translated into Arabic.

Pain level was assigned to one of 4 categorical scores: None (0); Mild (1- 3); Moderate (4-6); Severe (7-10). The participants were asked to select the mark that best matched their level of pain. Patients were told to phone the operator if they were in moderate or severe pain, and they were given 400 mg of ibuprofen. They were also instructed to keep records of how many analgesics tablets they used.

Intervention:

Diagnostic procedure:

A. Personal information:

Patient's personal data as well as medical history were recorded (Appendix 8).

B. History of the chief complaint:

The dental history as well as the history of chief complaint were recorded by the investigator (Appendix 9). The chief complaint was recorded from the patient's own words. The history of the chief complaint included intensity, quality, onset, duration, location, course, initiating and relieving factors of pain.

C. Clinical and radiographic examination:

Patients were seated on the dental chair and clinical examination was done under the dental unit light source using disposable diagnostic set for assurance of presence of caries or old restoration and pain on percussion.

Radiographic examination using intra-oral bisecting angle technique with a periapical radiographic film was done to assure root morphology, the presence of periapical radiolucency, calcifications and resorption.

D. Diagnosis:

Patients were diagnosed for symptomatic irreversible pulpitis and apical periodontitis based on subjective and objective findings as follows:

Subjective findings:

Symptomatic irreversible pulpitis was diagnosed through history of severe, sharp throbbing pain

that is either spontaneous or provoked and lingers for some time after removal of the stimulus. Pain increases at night or when the patient lies down or on chewing.

Objective findings:

Cold thermal test

Cold thermal testing using ethyl chloride spray was used to confirm the vitality of the included molar teeth. Cotton rolls were applied into the vestibule for proper isolation. The tooth examined as well as its contralateral were dried with cotton rolls. Ethyl chloride spray was applied on a cotton pellet and applied on the middle third of the buccal surface of the examined tooth for 2-3 seconds. A sharp, severe, lingering painful response confirmed the diagnosis of symptomatic irreversible pulpitis, whereas no response indicated a non vital pulp.

Percussion test: positive

Percussion test was done to determine the health status of the periodontal ligaments and investigate any periodontal involvement. The testing was done initially gently with light pressure applied by finger tapping. If the patient could not detect any significant difference between any teeth, the test was repeated by tapping on occlusal surface of teeth using back end of a metal mirror handle.

The contralateral tooth was tested first, the patient was advised that sensation from this tooth was normal and was asked to scale degree of pain or tenderness from subsequent teeth on NRS. A painful response confirmed the diagnosis of symptomatic apical periodontitis

Palpation: may or may not be positive.

Radiographic examination: using periapical radiographic film using the bisecting angle technique, may be normal or widening in periodontal ligament space.

Endodontic procedure:

After diagnosis of the case with symptomatic irreversible pulpitis and apical periodontitis and confirming that the patient fulfilled all eligibility criteria, the patients were enrolled in the study and started the clinical treatment which was completed in one visit.

Pre operative pain assessment:

Patients were asked to fill a preoperative pain scale before starting the procedure. Patients were anesthetized by inferior alveolar nerve block local anesthesia.

Intervention

After obtaining profound anesthesia by anesthetizing the corresponding inferior alveolar nerve using local anesthesia of 2% mepecaine carpule containing 1:80 000 epinephrine. The experimental group (piroxicam group) received supplemental IL injection of 0.4 ml of 20mg mL piroxicam using a high pressure special ligamental syringe with a 27-gauge short disposable needle (Figure 1).

Fig. (1) Special ligamental syringe.

The needle was inserted in the gingival sulcus at a 30 degree angle to the long axis of the tooth then apical pressure was applied until the needle wedged into the periodontal ligament between the

tooth and the alveolar crest of the bone (0.2 ml on the distobuccal aspect of the target tooth and 0.2 ml on the mesiobuccal aspect).

The control group (mepecaine group) received supplemental IL injection of 0.4 ml of 2% mepecaine carpule containing 1:80 000 epinephrine (0.2 ml on the mesial aspect of the treated tooth and 0.2 ml on the distal aspect).

Access cavity preparation:

Access cavity preparation was started by removal of caries and/or coronal restorations completely, an access cavity was opened with a high speed handpiece using round bur size 2 and endo-z bur followed by isolation of the tooth using rubber dam.

Biomechanical preparation:

The canals were scouted with #06, #08 and #10 K-type hand files. The Working length (WL) was established by introducing a #10 K-file up to the apical constriction as determined by electronic apex locator, and confirmed radiographically.

Glide path was established using #15 and #20 k type hand files. Cleaning and shaping were done by crown down preparation technique with protaper universal files in the sequence of starting with S1 in brushing motion to laterally cut dentin in the coronal two thirds of the canal. Then SX file without pressure in the coronal two thirds of the working length, then S1 followed by S2 in brushing motion to the full working length, then F1, F2, F3 in picking motion in the mesial canals to the full working length and finishing with F4 in distal canals were used with x smart motor according to the manufacturer's instructions with a rotational speed of 300 rpm and torque 2.5 N/cm.

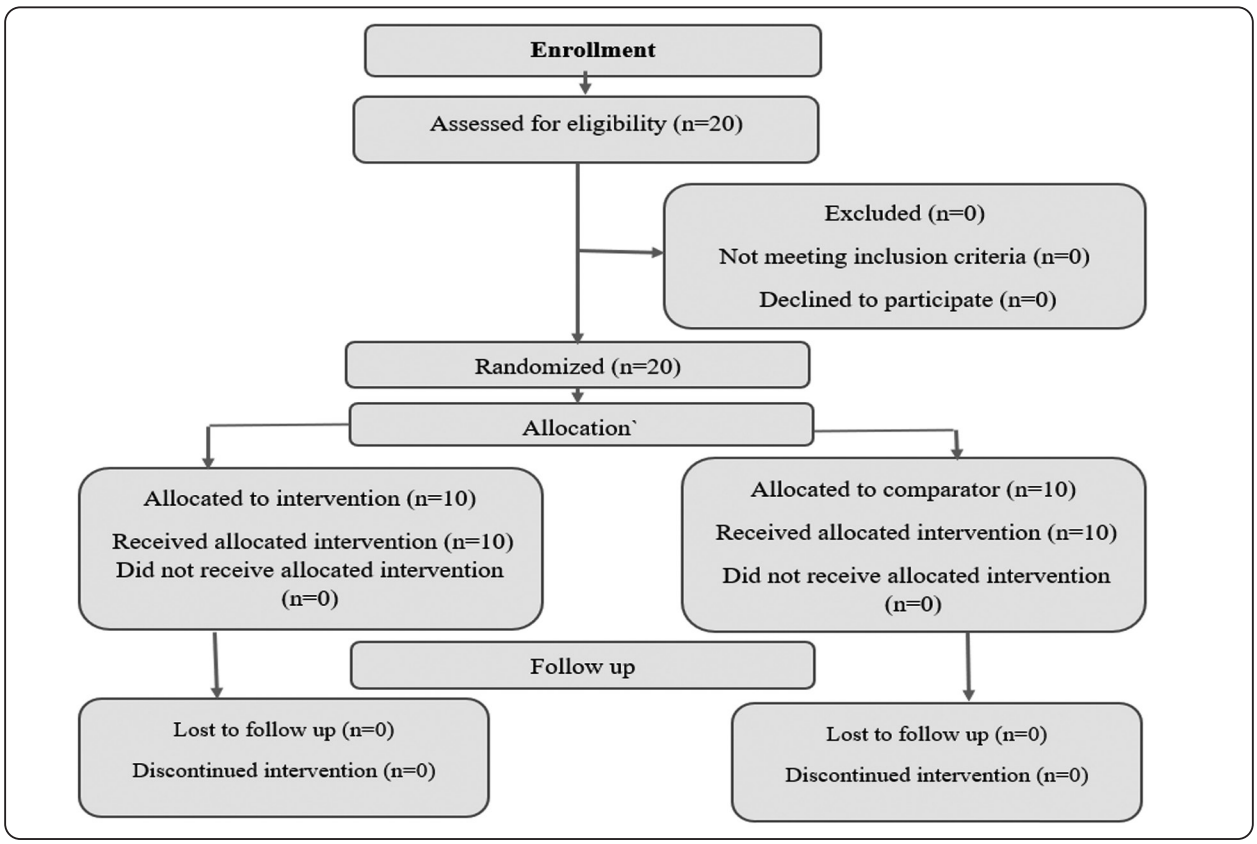

Fig. (2): CONSORT 2010 Flow diagram of the trial design

The canals were irrigated between two successive files with (3ml) using 1:3 diluted sodium hypochlorite (1.5%) in a plastic disposable syringe with side vented needle gauge 30. The needle was inserted 1 mm short from the working length, using a rubber stop as a guide, and the root canal was irrigated, whilst the needle was moved up and down followed by irrigation with 5 ml of 17% EDTA solution for 5 minutes as a final rinse.

The final file size used in the canal was determined by the size of the initial file. The mesial canals usually finished at F3 and the distal canals usually finished at F4. A 19% EDTA gel was used on each file as a lubricant. For the distal root, If the molar had only single distal canal, F4 file was used till full working length and if it had two canals, F3 file was used till full working length with progressive up and down movement.

Before obturation the canals were dried using protaper absorbent paper points and then filled with protaper gutta percha master cones corresponding to the master apical file. Periapical radiograph was done using the bisecting angle technique to confirm the proper length of gutta percha master cones.

Obturation was done by the previously checked master cones with resin based root canal sealer (Adseal) using cold lateral technique. After obturation a cotton pellet was inserted in the pulp chamber and the access cavity was closed with a temporary filling.

Post operative pain assessment:

The patients were given a NRS (Appendix 7) and asked to rate their pain level at 6, 12, 24 & 48 hours after root canal treatment. Postoperative instructions were given to all patients. Patients were told to phone the operator if they were in moderate or severe pain, and they were given 400 mg of ibuprofen. In addition, the number of analgesic tablets consumed must be recorded. The patients were asked to come after 7 days to deliver the NRS and to record the postoperative level of pain on percussion.

OUTCOMES

Primary outcome

The outcome of this trial was to measure the degree of the postoperative pain at 6, 12, 24 and 48 postoperative hours using the NRS. Primary outcome was recorded by the operator using the NRS, which is an 11-point scale with numbers ranging from 0 to 10; NRS categorized as follows: 0 reading represents “no pain”;1- 3 readings represent “mild pain”;4- 6 readings represent “moderate pain”;7- 10 readings represent “severe pain”.

Secondary outcomes:

Incidence and number analgesic tablets

The incidence of analgesic intake, Patients were allowed to take 400 mg of Ibuprofen and were told to keep record of how many tablets they took. the severity of pain and when they were taken ibuprofen.

Pain on percussion

Pain on percussion was measured using 11 point NRS at day 7 and was performed by the investigator through tapping in an apical direction on the tested tooth using the back of the mirror.

Statistical methods:

Data management and statistical analysis were performed using the Statistical Package for Social Sciences (SPSS) version 18. Numerical data were summarized using means and standard deviations or medians and ranges. Data were explored for normality by checking the data distribution and using Kolmogorov-Smirnov and Shapiro-Wilk tests. Categorical data were summarized as count and percentages.

Comparisons between the two groups with respect to normally distributed numeric variables were done using the independent t-test.

Non normally distributed numeric variables were compared by Mann-Whitney test. Comparisons over time regarding numeric variables were done

Table (1): Materials, instruments and devices used in this study:

Material	Company	Country
Devices		
Dental unit	Adec,200	USA
X-ray machine	ViVi, S.r.I	Italy
Endomotor	X-Smart, DentsplyMaillefer,	Switzerland.
Electronic apex locator	Root ZX,J.Morita USA, Irvine,	CA
Instruments		
Special ligamental syringe	AR instrument	Pakistan
Disposable diagnostic set	Kandil® disposable diagnostic set	Egypt
ProTaper rotary system	originals from the ProTaper Universal system; Dentsply Maillefer, Ballaigues,	Switzerland
Endo-Z™ Bur	DENTSPLY, Tulsa Dental, DENTSPLY Maillefer, TN	USA
Carbide round bur	DENTSPLY, Tulsa Dental, DENTSPLY Maillefer TN	USA
Stainless steel hand k files	Dentsply Maillefer, Ballaigues,	Switzerland
Materials		
Periapical radiographic film	Kodac Dental film, speed D, size 2	
Mepecaine carpule	Carpule Mepecaine, Alexandria Company for Pharmaceuticals and Chemical Industries	Egypt
ProTaper absorbent paper points	DENTSPLY, Tulsa Dental,DENTSPLY Maillefer,	TN
Gutta percha	DENTSPLY, Tulsa Dental, DENTSPLY Maillefer, TN	USA
Resin sealer	ADSEAL, META BIOMED CO., LTD,	Korea
Temporary filling	MD-Temp, META BIOMED CO., LTD,	Korea
Rubber dam	Dental Dam, Sanctuary Dental,	UK
Ibuprofen 400mg	Kahira Pharmaceuticals and Chem. Ind. Co., Abbott Laboratories	Egypt
Piroxicam	Pfizer Laboratories Div Pfizer Inc, FELDENE®	Egypt
2.6% Sodium hypochlorite	Clorox, Household cleaning products of Egypt,	10th of Ramadan, Egypt
17% EDTA solution	EDTA, 17% EDTA solution, Prevest DenPro Limited,	India

by Friedman test and pairwise difference were detected by the Wilcoxon rank test. For categorical variables, differences were analyzed with Chi-square test. Adjustments of p-value were done using the Bonferroni method for multiple testing. All p-values are two sided. P-values ≤0.05 were considered significant.

RESULTS

After recruitment of the patients, 20 patients were assessed for meeting the eligibility criteria of the study. A total of 20 patients met the inclusion criteria and were registered in the study. Patients were randomized into two groups of 10 patients per group.

Demographic Data (Table (2) and Figure (3,4))

Twenty patients participated in this study (17 females, 3 males). They were randomly divided into two equal groups of 10 patients each: Piroxicam Group (experimental) and Mepecaine Group(control).

TABLE (2): Mean, standard deviation (SD), frequencies (n), percentages (%) and results of independent t-test and Chi square tests for comparisons of demographic data in the two groups (Piroxicam; Mepecaine).

Variable \ Group		Piroxicam group	Mepecaine group	P value
Age in years	Mean (SD)	31.80 ±9.78	30.50 ±9.26	0.764ns
Gender [n (%)]	Female	9 (90.0%)	8 (80.0%)	0.531ns
	Male	1 (10.0%)	2 (20.0%)	

Significance level p≤0.05, ns=non-significant

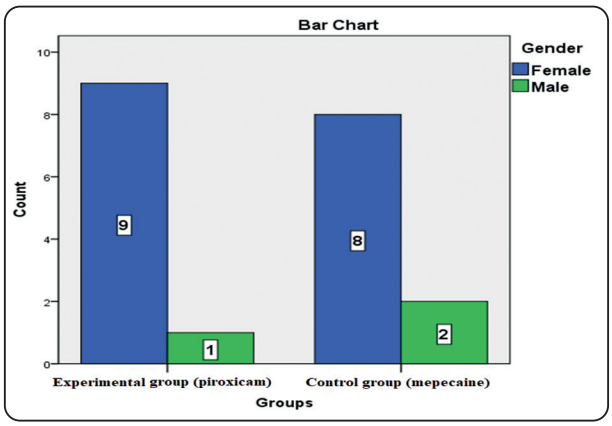

Fig. (3): Bar chart illustrating gender distribution in both groups

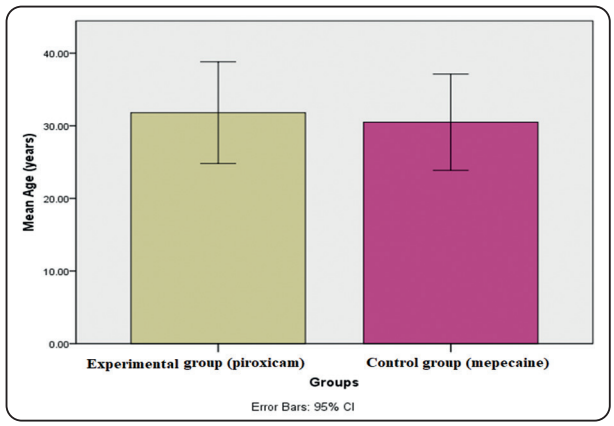

Fig. (4): Bar chart illustrating mean age in both groups

1-Age and Gender distribution in both groups:

There was no significant difference between mean age values between piroxicam group (experimental) and mepecaine group(control) (p=0.764). There was no statistically significant difference in gender distribution (P > 0.531) between the two groups.

2- Tooth type distribution and number of the canals in both groups (Table (3) and Figure (5)):

In the experimental group (piroxicam) and control group (mepecaine) 70% of the patients received endodontic treatment for the Lower 6 and 30% for the Lower 7 in both groups. There was no statistically significant difference between both groups for the treated tooth-type distribution (p=1.000). Numbers of canals were comparable in the piroxicam group and the mepecaine group with was no statistically significant difference between both groups (p=0.56).

Outcome data:

Pain intensity

1. Comparison of median scores in the tested groups (Table (4) and figure (6)):

Preoperatively, the pain scores had a median value of 9.5 with a range of (7-10) for experimental group (proxicam)and a median of 8.5, range 4-10 for control group (mepecaine), with no statistically significant difference between both groups (*p*= 0.17).

After 6 hours, the pain scores had a median value of 0 for piroxicam group, range (0-4) for group A and 1 for mepecaine group, range (0-5), with no statistically significant difference between both groups (p= 0.184).

Table (3): Frequencies (n), percentages (%) and results of independent t-test and Chi square tests for comparisons of number of canals distribution two groups (Piroxicam; Mepecaine).

Variable	Group	Piroxicam Group		Mepecaine Group		P-Value	Significance
		No.	%	No.	%		
Tooth type distribution	L6	7	70%	7	70%	1.00	NS
	L7	3	30%	3	30%		
Canals	3	6	60%	8	80%	0.56	NS
	4	4	40%	2	20%		

Table (4): Descriptive statistics of pain score at different time points and comparison of tested groups (Mann Whitney) and overtime in each group (Friedman Test).

		Pre	Post 6 hours	Post 12 hours	Post 24 hours	Post 48 hours	P Within the same group
Piroxicam Group	**Mean (SD)**	8.9	0.70	.60	.20	.00	0.00*
	Median	9.5	.00	.00	.00	.00	
	Minimum	7.00	.00	.00	.00	.00	
	Maximum	10.00	4.00	6.00	2.00	.00	
	Range	3.00	4.00	6.00	2.00	.00	
Mepecaine Group	**Mean (SD)**	7.90	1.60	.70	.00	.00	0.00*
	Median	8.50	1.00	.00	.00	.00	
	Minimum	4.00	.00	.00	.00	.00	
	Maximum	10.00	5.00	3.00	.00	.00	
	Range	6.00	5.00	3.00	.00	.00	
P (between groups)		.174ns	.184ns	.358ns	.317ns	1.00ns	

Significance level p≤0.05, *significant ns=non-significant

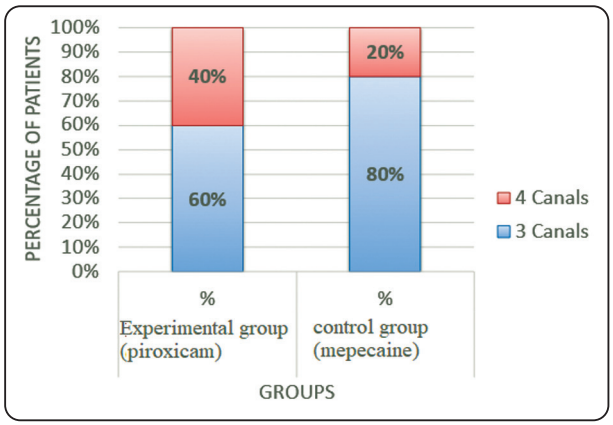

Fig. (5): Bar chart illustrating number of canals in both groups

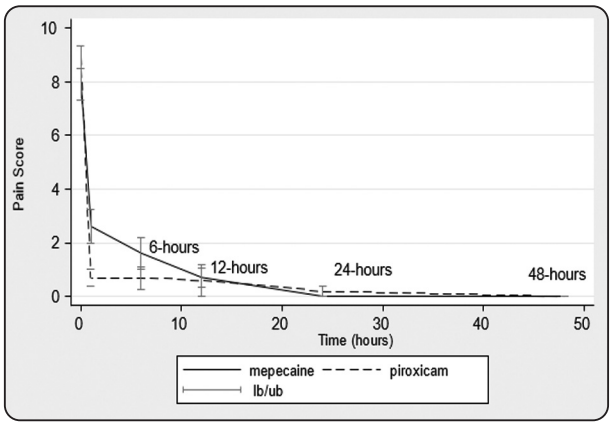

Fig. (6): Graph showing the median pain score in the tested groups at different time points. (Experimental group (piroxicam), Control Group (mepecaine))

After 12 hours, the pain scores had a median value of 0 for piroxicam group, range (0-6) for group A and 0 for mepecaine group, range (0-3), with no statistically significant difference between both groups (p= 0.358).

After 24 hours, the pain scores had a median value of 0 for piroxicam group, range (0-2) for group A and 0 for mepecaine group, range (0-0), with no statistically significant difference between both groups (p= 0.317).

After 48 hours, the pain scores had a median value of 0 for piroxicam group, range (0-0) for group A and 0 for mepecaine group, range (0-0), with no statistically significant difference between both groups (p= 1.00).

Comparing median pain score over time in each group was statistically significant (p≤0.05)

2. Changes with time in pain scores for piroxicam group (experimental group) (Figure (7)):

There was a statistically significant reduction in median pain scores comparing pre-operatively with all other time periods. However, there was no statistically significant decrease in median NRS scores comparing score at 6 h with 12h, 24 h and 48 h or comparing 12 h with 24 h and 48h or comparing 24 with 48h.

1.3. Changes with time in pain scores for mepecaine group (Control group) (Figure (8)):

There was no statistically significant decrease in median pain scores comparing score 6 hours and 12 hours post-operatively and no significant difference between 12 hours post-operatively and the subsequent observation times. Though, there was a statistically significant decrease in median pain scores comparing pre-operatively with all other time periods, as well as there was a significant difference between 6 hours and 24 or 48 hours.

1.5. Intensity scores (Table (5) and Figure (9)):

Comparison between groups: Using chi square test to compare the qualitative pain scores at different observation times revealed no statistically significant difference between both groups

Comparing median pain score over time in each group, chi square revealed a statistically significant difference (p ≤0.05).

2- Analgesic intake (Table 6, Figure 10):

In experimental group (piroxicam), 70% of the patients didn't receive Brufen, while 20% received Brufen once and 10% received twice. In control Group (mepecaine), 60% of the patients didn't receive Brufen, while 20% received Brufen once and 20% received twice. Chi square test displayed no statistically significant difference between groups (p=0.815).

3-Pain on percussion

Comparison of median scores in the tested groups (Table (7) and Figure (9)):

Preoperatively, the median and range of the NRS scores was 9.5 (8-10) for the piroxicam group and 9 (8-10) for the mepecaine group with no statistically significant difference between both groups (p= 0.446).

Post operatively, the median and range of the NRS scores was 0.00 (0-1) for the experimental group (piroxicam) and 0 (0-2) for the mepecaine group with no statistically significant difference between both groups (p= 0.818).

When each group's median pain score was compared over time, the difference was statistically significant (p=0.004 for piroxicam group, p=0.007 for mepecaine group).

Table (5): Qualitative Intensity scores at different observation times (Chi square test)

Time	Intensity	Piroxicam Group		Mepecaine Group		X^2	P
		No.	%	No.	%		
Pre-operative	**No pain**	0	0	0	0	1.05	0.78ns
	Mild	0	0	0	0		
	Moderate	0	0	1	10		
	Severe	10	100	9	90		
Post 6	**No pain**	7	70	4	40	1.818	0.44ns
	Mild	2	20	4	40		
	Moderate	1	10	2	20		
	Severe	0	0	0	0		
Post12	**No pain**	9	90	7	70	1.8	0.40ns
	Mild	0	0	3	30		
	Moderate	1	10	0	0		
	Severe	0	0	0	0		
Post 24	**No pain**	9	90	10	0	1.05	0.78ns
	Mild	1	10	0	0		
	Moderate	0	0	0	0		
	Severe	0	0	0	0		
Post 48	**No pain**	10	100	10	100	0	1ns
	Mild	0	0	0	0		
	Moderate	0	0	0	0		
	Severe	0	0	0	0		
	X^2	74.78		80.75		-----	
	P	0.00*		0.00*			

Significance level p≤0.05, *significant ns=non-significant

Table (6): Comparison of frequency of Brufen intake in both groups (Chi square test)

Groups		Piroxicam group		Mepecaine group		P value
		n	%	n	%	
Analgesic Intake	.00	7	70.0%	6	60.0%	0.815 ns
	1.00	2	20.0%	2	20.0%	
	2.00	1	10.0%	2	20.0%	

Significance level p≤0.05, *significant ns=non-significant

Table (7): Descriptive statistics of pain on percussion score pre and post operatively and comparison of tested groups (Mann Whitney) and overtime in each group (Wilcoxon Signed Rank test)

Groups Different times	Piroxicam group			Mepecaine group			P value (between groups)
	Median	Min.	Max.	Median	Min.	Max.	
Pre operative	9.50	8.00	10.0	9.00	8.00	10.0	.446ns
Post operative	0.00	0.00	1.00	0.00	0.00	2.00	.818ns
P value (Within the same group)	0.004*			0.007*			---------

Significance level p≤0.05, *significant ns=non-significant

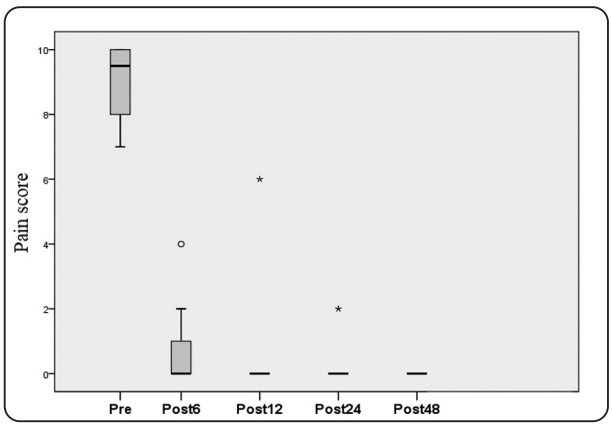

Fig. (7): Box plot showing the median pain score in experimental group (piroxicam) at different time points

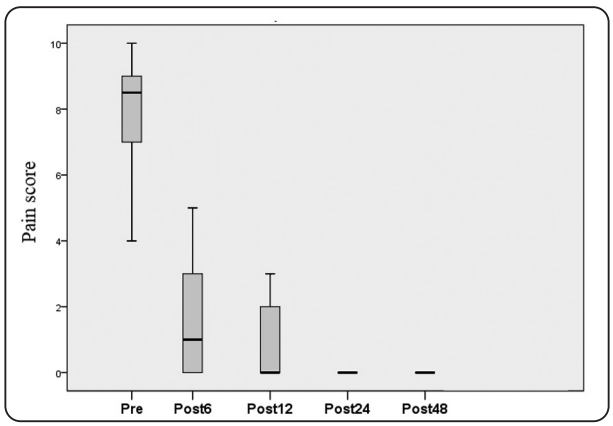

Fig. (8): Box plot showing the median pain score in the mepecaine group at different time points.

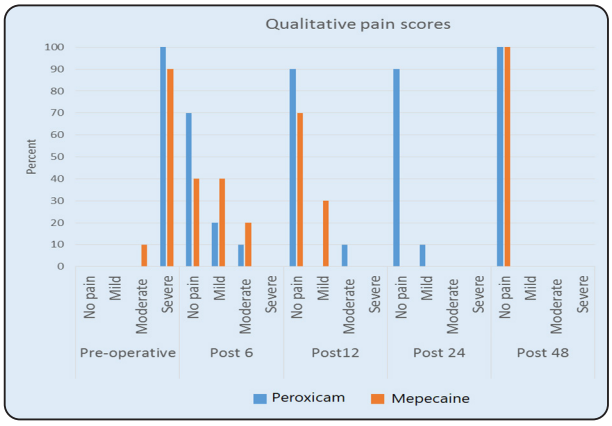

Fig. (9): Percentage values of qualitative pain scores of experimental (piroxicam group) and control (mepecaine group) groups.

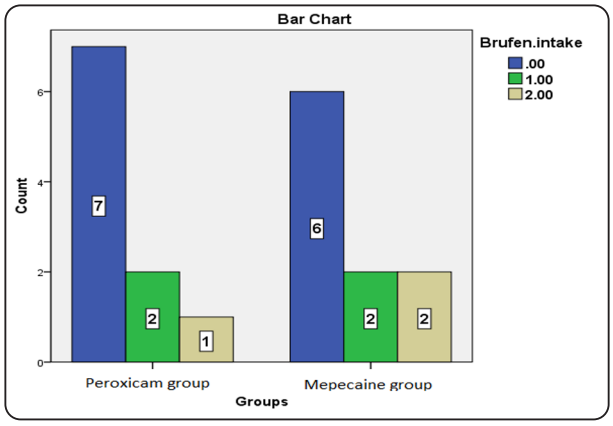

Fig. (10): Bar chart illustrating Brufen intake in experimental (piroxicam) and control (mepecaine) groups.

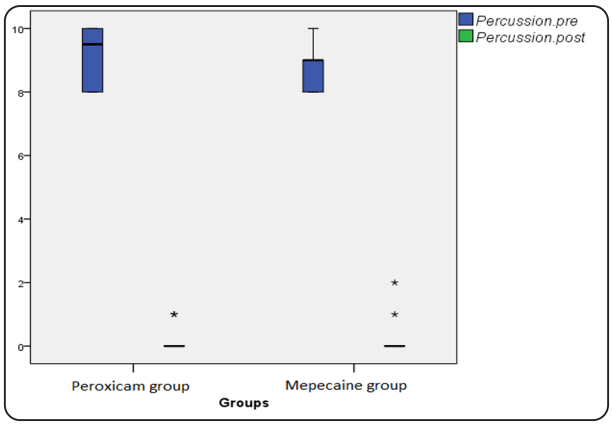

Fig. (11): Box plot showing the median pain on percussion scores in the tested groups pre- and post-operatively

DISCUSSION

Post operative pain is considered a common clinical predicament that can come to pass from a few hours to several days after endodontic treatment. If it is poorly managed, it may escalate patient fear and nervousness. So, Knowing the causes that induce pulpal and periapical pain could reduce the distress experienced by endodontic patients by implementing preventive or treatment strategies **Shabbir et al. (2021).**

The incidence of post operative pain in most cases is due to extrusion of dentine chips, pulp tissue fragments, necrotic tissue, pathogens and intracanal irrigants beyond apical foramen during instrumentation. Thus, irritation of periapical tissue was occurred and subsequent post operative pain and a flare up. Pain control usually involves occlusal reduction, administration of systemic analgesics and anti inflammatory drugs **Zajkowski et al. (2020).**

Endodontic treatment includes the management of postoperative pain and symptom that addresses both the patient's primary concern and potential long term sequelae such as chronic pain. Nonsteroidal anti inflammatory drugs, opioids, and pharmacological combinations have all been used to control postoperative pain **Smith et al. (2017).**

According to several systematic NSAIDs are one of the most commonly prescribed pain relievers in dentistry today. Their popularity is accredited to their over the counter accessibility, effectiveness in relieving pain and fever, and at therapeutic doses, it has a minimal side effect profile. NSAIDs function by decrease inflammation, inhibiting the COX enzymes and preventing the generation of new prostaglandin molecules, but they have no effect against existing molecules in circulation **Bindu et al. (2020).**

Piroxicam was used in this study as it is a non selective reversible anti inflammatory drug that inhibits COX enzymes. It also inhibits the synthesis of thromboxane in platelets, thus preventing the secondary phase of platelet aggregation. It has a half life of 50 hours in the plasma that has an advantage of decreasing the dose and improving compliance, particularly in elderly patients. According to **Konagala et al. (2019)** and **Suresh et al. (2020)** after premedication with dexamethasone and piroxicam, 83 percent of patients reported no discomfort after 12 hours.

Regarding using anti inflammatory agents locally adjacent to the inflamed tooth to decrease the production of inflammatory mediators, The IL injection technique of piroxicam (0.4 ml/20 mg/ml) was used in this study because it allows anti inflammatory agents to be applied directly in the periapical IL region without having to pass through the liver before reaching the target site, resulting in 100% bioavailability of the injected drug **Safwa et al. (2021).**

The IL injection was administered using specialized pressure syringe. Pressure syringes offer many advantages over the conventional syringe as they deliver a specified dose of local anaesthetic solution and anti-inflammatory solution. They also allow the administrator to overcome the significant tissue resistance encountered **Malamed (2019).**

Symptomatic irreversible pulpitis cases were chosen as a key inclusion criterion as pulpal pain (irreversible pulpitis) is the most feared among

patients due to its intensity and severity. When compared to asymptomatic teeth, these cases had a lower success rate of inferior alveolar nerve block anaesthesia and a higher incidence of postoperative discomfort, making their management a challenge for the clinician. **Safei Eldin et al. (2020).**

This study aimed at the evaluation of the effect of preoperative, prophylactic IL injection of piroxicam on post operative pain in patients with symptomatic apical periodontitis treated in a single visit. Twenty patients diagnosed with irreversible pulpitis and symptomatic apical periodontitis in their mandibular posterior teeth were randomly assigned to two groups; an experimental group where prophylactic IL piroxicam was tested for alleviating post operative pain and a control group utilizing prophylactic IL mepecaine. After obtaining profound anaesthesia, root canal treatment was performed in a single visit. Patients were instructed to record their pain experienced after endodontic procedure in a pain diary at 6, 12, 24, 48 and then they come back after 7 days to deliver the pain dairy and rate their pain of percussion. Patients were, also, asked to write down the number of analgesic tablets taken.

As a main inclusion criterion, cases with symptomatic irreversible pulpitis and apical periodontitis were chosen. These cases had a significantly lower IANB success rate and a higher incidence of postoperative pain than asymptomatic teeth. The presence of preoperative discomfort has been identified as a predictor of postoperative endodontic pain **Sudhakar et al. (2020)**

We choose mandibular molars since they are significantly more susceptible to cause postoperative pain, Because of the thick cortical mandibular plate, which allows for the accumulation of exudates and increases the intra-periapical pressure that causes pain, postoperative pain in the mandibular posterior teeth (42%) has been observed more frequently than in the maxillary posterior teeth (26%) **Ali et al. (2019).** Furthermore, mandibular molar teeth were associated with a higher prevalence level of post-endodontic pain due to greater number of canals and high frequency of bifurcated root canals in mandibular posterior teeth **Segura-Egea et al. (2009).**

In this study root canal treatment was completed in one visits which has several advantages, including a reduction in the number of appointments and treatment cost, familiarity with internal root canal anatomy, avoidance of inter appointment contamination and bacterial regrowth, which can result in pain and reinfection of the canals as a result of bacterial ingress from a leaky temporary restoration, and avoidance of inter appointment contamination and bacterial regrowth, which can result in pain and reinfection of the canals. A meta analysis conducted by **Almeida et al. (2017)** had shown that there was less post obturation pain in the single visit endodontic therapy group. Another randomized controlled trial by **Singh (2020)** had shown that the mean pain score in the single visit group was lower as compared to that of the multiple visit group

An informed consent would be obtained and signed from patients willing to participate in the trial. The goal of obtaining informed consent is to provide potential patients with easily understandable information about the research, confirm that they understand the research, and ensure that their willingness to participate is voluntary. The research operator will introduce the trial to patients and they will receive information sheets regarding the main aspects of the trial. Patients will then be able to have an informed discussion with the participating consultant. All information sheets and consent forms have been translated into Arabic. **Cocanour (2017)**.

After diagnosis we used numerical rate scale at 6, 12, 24, and 48 to measure postoperative pain. Evidence indicated that patients really want to give a pain number, rather than simply relate whether

they want analgesia **Karcioglu (2018)**. The NRS has become the more common choice because of its ease of use, superior reliability, a broader range of administration techniques, and evidence of consistent results across a wide range of languages and cultures **John et al. (2010)**. These times were chosen because symptomatic patients were more likely to have post-operative discomfort within the first 24 hours after root canal treatment. Piroxicam's 50-hour half-life may help to alleviate severe pain for up to 48 hours after treatment **Atbaei et al. (2011).**

In the present study, the working length was estimated using an electronic apex locator and checked with a radiograph as variations in root morphology and radiograph distortion could cause the radiographic apex to differ from the anatomic apex. The apex locator can reduce the risk of overestimation of the root canal length in these canals that is considered to be one of the reasons for postoperative pain. **Vanitha and Sherwood (2019).**

Crown down approach was applied in all cases of the present study due to many advantages. It allows more irrigant to be kept in the canal, making debris removal and disinfection easier; removes coronal curvatures and provides straight-line access; and reduces the possibility of instrument separation due to torsional failure **James (2015).**

The root canals were prepared using protaper universal Ni–Ti rotary system which is machined from conventional super elastic austenitic Ni–Ti wire. It features variable taper over the entire cutting blade length with convex triangular cross-sections **Nishad et al. (2018).** Their design favors debris removal and prevent the instrument from screwing into the dentinal walls of the canal. The extrusion of intracanal debris can lead to postoperative pain and swelling after root canal treatment **Koçak et al. (2014).**

The used irrigating solution between each rotary file was 2.6% sodium hypochlorite as it has bactericidal effect which plays an essential role in the microbial reduction by (98.07%) **Sergioluiz et al. (2017)**

This study was designed as a randomized, double-blind, clinical trial on 20 patients with irreversible pulpitis and symptomatic apical periodontitis in mandibular molar teeth. The three elements of randomization (sequence generation, allocation concealment and implementation) ensure that all patients have an equal probability of being assigned to one of the study groups.

This design is for assessment of the effects of different medical interventions without selection or allocation bias. The aim of randomization is to prevent bias in the judgement or systematic planning of treatment, and to afford a solid base for statistical analysis such as significance of results. In this study, the participants and the investigator were blinded to the preoperative intervention used that decreases the performance bias. **Bridgeman et al. (2003)**

The baseline data for the two groups in this study were similar in terms of age, gender, pre-operative pain, tooth type distribution and number of canals, therefore the effect of these variables on the study outcome was limited.

Regarding the overall reduction in postoperative pain in the current study, there was a significant gradual reduction in postoperative pain in both intervention and control group (piroxicam and mepecaine) from 6 to 48 hours. These results were similar to those of **Atbaei and Mortazavi (2012)** who reported a significant postoperative pain reduction after prophylactic IL injection with piroxicam during the same time interval

Results obtained from the present study showed that the prophylactic IL injection of piroxicam failed to display any better potency in decreasing post endodontic pain compared to IL injection of mepecaine, as no statistically significant difference was found among the pain score between the two groups ($p>0.05$).

Our results are in disagreement with **Atbaei et al. (2012)** who randomly separated 65 patients with irreversible pulpitis into two groups in a study. The group that received IL piroxicam showed a significant reduction in post operative pain intensity compared to the control group (lignocaine group). The author used a concentration of lignocaine of 0.4 mL of 2 percent carpule containing 1:80,000 epinephrine, whereas we employed mepecaine carpules with a concentration of 1:80,000 epinephrine in our trial. In both experiments, the piroxicam concentration was the same. The key reason for the disagreement is that mepivacaine increased the success rate of IANB as compared to lidocaine in a network meta-analysis **Nagendrababu et al. (2019)**. Another variable which could cause significant different is the presence of apical periodontitis among our subject unlike the cases in **Atbaei** study.

The outcomes of this study were likewise in contrast to the findings of **Subhan and Shami (2016)**, who grouped 120 patients with symptomatic irreversible pulpitis into two groups. After 48 hours, the piroxicam group showed a significantly reduction in pain intensity (Mean SD=0.40 0.49) compared to the lignocaine group, which had mean pain values of 1.37 (0.93). Between the two groups, there was a statistically significant difference in pain reduction (p0.001). This difference was most probably due to significant different in sample size between the two studies which can amplify any subtle finding.

The findings of this study contradicted those of **Joshi et al. (2016)**, who examined the efficacy of oral and IL piroxicam administration in reducing post endodontic pain. The difference in pain management between oral and IL piroxicam was not significant in the first 8 hours, but IL piroxicam was considerably more effective in reducing post treatment pain at time points 12, 24, and 48 hours. These differences can be explained as **Joshi** used a placebo with no pharmacological intervention as a control group, whereas we employed mepecaine carpules with a concentration of 1:80,000 epinephrine in our trial.

One of the drawbacks of research assessing post endodontic pain is that it is subjective and differs from person to person. As a result, evaluating a drug's efficacy by comparing pain perception in different people is inappropriate. this explains the discrepancy between our study results and others **Akilan et al. (2018).**

Regarding postoperative pain on percussion IL piroxicam has the same level of pain compared to the control group these results was in disagreement of **Paredes et al. (2018)** that showed that a single dose of preoperative ketorolac was as effective as NSAIDs for the relief of pain after single visit root canal treatment in teeth with symptomatic apical periodontitis. These differences can be explained by that in our study we used mepecaine as control group in contrary to **Paredes** who used no pharmacological intervention as control group.

In the current study, participants in the piroxicam group used comparable number of Brufen tablets with control group. There was no statistically significant difference between the two groups (p=0.815).

The primary cause for discrepancy in results between the final outcome here and the above-mentioned papers is due to the diversity in cases selection. In the present study, cases with apical periodontitis were included and on the other hand the previous studies included only symptomatic irreversible pulpitis.

We concluded that prophylactic IL injection of piroxicam was effective in decreasing post endodontic pain but with no statistically significant difference between both groups.

SUMMARY:

This study is randomized controlled, double blinded clinical trial, two parallel groups to assess the

efficacy of Prophylactic intraligamentary injection of piroxicam versus Mepecaine for management of post-endodontic pain in posterior teeth.

Twenty patients were diagnosed with irreversible pulpitis and symptomatic apical periodontitis in their mandibular posterior teeth, were included. Each patient had mandibular molar that experiencing pain on percussion, and selected from those attending or referred for root canal treatment to post-graduate clinic students in the Department of Endodontics, Faculty of Dentistry, Cairo University, Egypt.

Patients are divided randomly into two groups each group contain ten patients:

Each participant will complete the treatment in a single visit.

In that visit the patient will be screened and approved by the assistant supervisor if eligible. Then the patient will be anaesthetized and then will be given an intraligamentary injection of Piroxicam or Mepecaine as a prophylactic medication, access shall be done, placing a rubber dam for isolation, then working length determination, cleaning and shaping, dryness of the canals, obturation and closing the access cavity using temporary filling.

The patient is then asked to rate the intensity of pain pre-operatively and after 6, 12, 24 &48 hours after root canal treatment using a NRS and informing the investigator with the results.

The results of the present study showed that:

1. Results showed that the prophylactic administration of intraligamentary piroxicam before single visit root canal treatment has no significant decrease in pain intensity at 6, 12, 24, 48 hours post operatively compared to mepecaine group.
2. piroxicam group showed no statistically significant decrease in pain on percussion after 7 days.
3. It was found that the total number of analgesic tablets taken in the Piroxicam group was not statistically significantly different from the mepecaine group postoperatively.

From the results of the present study, it could be concluded that:

1. Prophylactic intraligamentary injection of Piroxicam was effective in decreasing post endodontic pain but with no statistically significant difference between the Piroxicam and Mepecaine groups after 6, 12, 24 and 48 postoperatively.
2. Regarding postoperative pain on percussion, intraligamentary piroxicam has the same level of pain compared to the control group.
3. Participants in the Piroxicam group used comparable number of Brufen tablets with control group. There was no statistically significant difference between the two groups (p=0.815).

From the results of the current study, the follow could be recommended:

1. Administer of prophylactic intraligamentary piroxicam in severe cases such as hot tooth for reducing the post operative pain could be beneficial.
2. Repeat the study with larger patient population to evaluate the efficiency of piroxicam intake in pain management intraoperatively and post operatively.

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