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ASSESSMENT OF THE PRETREATMENT EFFICIENCY WITH DEXAMETHASONE VS PLACEBO ON POST-OPERATIVE PAIN IN TEETH WITH SYMPTOMATIC IRREVERSIBLE PULPITIS

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ABSTRACT

This study aimed to assess the clinical efficiency of administrating one oral preoperative dose of dexamethasone vs placebo on post-operative pain which is a primary outcome demonstrated directly after the root canal treatment procedure, and also respectively after 6, 12, 24, 48 hours in teeth with symptomatic irreversible pulpitis. **Methods:** Thirty-two adults, with age range of 25-45 years old, complaining from symptomatic irreversible pulpitis were involved in our clinical study. Thorough clinical and radiographic diagnosis was performed, then the candidates were blindly assigned into 2 main equal groups with 16 patient in each group. The procedure of pain levels recording was properly discussed to the patients and they were asker to record the pain levels after applying a thermal pulp test (cold test) before proceeding in the root canal procedure utilizing the Numerical Rate Scale (NRS). Access cavity preparation followed by extirpating all the pulp tissues were performed. Pain records directly after the treatment is completed, then at 6, 12, 24, and 48 hours postoperatively. All demographic data and categorical scores were collected from the patients and statistically analysed. **Results:** it was shown that there was no statistically significance differences between the 2 main groups regarding pain records obtained pre-operatively, during access cavity preparation, extirpating the pulp tissue, immediate postoperative, after 6, 12, 24 and 48 hours.

Conclusions: Pretreatment with oral dose of dexamethasone 0.5mg administrated preoperatively did not modify or decrease the level of post-operative pain at any time interval in patients with lower molars with symptomatic irreversible pulpitis.

INTRODUCTION

Post-operative pain is very common, affecting from 2.5% to almost 60% of subjects that have undergone endodontic treatments [(1)], and it shows a tendency to increase between 6 and 12 h after treatment, reaching a prevalence of about 40% in 24 h and falling to 11% one week after treatment. Moreover, post-operative endodontic pain is highly

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unpreventable, being affected by a variety of factors related to the subject [2].

Glucocorticoids have been used in endodontics for their potent anti-inflammatory effects. After the administration of the glucocorticoid, reductions in pulpal levels of both PGE2 and IL-8 which are elevated in inflamed dental pulp have been demonstrated [3]. Glucocorticoids have been used as an intracanal medication either alone or in combination with antibiotics/ antihistamines, and systemically to decrease pain and inflammation in endodontic patients [4].

Glucocorticoids are well- known to reduce the acute inflammatory response by suppressing vasodilation, the migration of polymorphonuclear leukocytes, and phagocytosis and by inhibiting the formation of arachidonic acid from neutrophil and macrophage cell membrane phospholipids, thus blocking the cyclooxygenase (cox) and lipoxygenase pathways and the respective synthesis of prostaglandins (PGs) and leukotrienes [5].

The anti-inflammatory properties of glucocorticoids were first appreciated and utilized as an adjunct in endodontic therapy almost half a century ago. The anti-inflammatory action of glucocorticoids can neutralize the inflammatory mediators [6].

Dexamethasone is a synthetic form of the glucocorticoid class of steroid drugs. It is 25 times more potent in reducing inflammation than the naturally occurring cortisol hormone [7].

So, this study assess the efficiency of administrating one oral dose of dexamethasone preoperatively vs placebo and its effect on the post-operative pain which is a primary outcome demonstrated immediately after the treatment, 6, 12, 24, 48 hours postoperatively and success of inferior alveolar nerve block which is the secondary outcome demonstrated at access preparation and pulp extirpation in mandibular molars with symptomatic irreversible pulpitis.

MATERIALS AND METHODS

Trial design

This study was set as a prospective, parallel, randomized clinical trial.

Ethical protocol

The treatment plan steps with thoroughly discussed and a printed informed consent form had been signed by the patients then properly revised and approved by the ethical committee, Faculty of oral and dental medicine, Future University in Egypt.

Patients

Number of samples:

Thirty-two participants were randomly selected and equally divided into two main groups (sixteen per group)

Eligibility criteria:

A) Inclusion criteria:

1. Patients not suffering from any systematic diseases.
2. Patients who had one lower molar with symptomatic irreversible pulpitis.
3. Patients aged 25 to 45 years old.
4. Patients who were able to record the pain levels and aware of the treatment procedure.

B) Exclusion criteria:

1. Patients who are complaining of pain rather than single lower molar.
2. Patients who were taking routine pain killers or at least had taken within the 6 hours before the treatment.
3. Complicated systematic illness.
4. Allergic patients or those hypersensitive to dexamethasone.

5. Mobility grade 2 or more in the lower molars.

C. Setting & location:

32 patients were enrolled from the clinic of Endodontics at the Faculty of Dentistry, Future Egypt. All the interventions were performed by a single operator. The endodontic treatment procedures were done on the same dental units and X-ray machine.

· **X-ray machine:** Belray II 097, Belmont, Japan.

· **X-ray film:** Intraoral periapical Kodac Dental film, speed D, size 2.

IV. Subjects and Methods Sequence

A. Diagnosis

The diagnosis of symptomatic irreversible pulpitis depended on the patient complain, thermal pulp testing, clinical examination and radiographic picture.

B. Randomization:

After patients were found eligible, randomization was performed. The 32 patients were randomly divided into two groups (n = 16). The randomization was done in the following steps:

C. Blinding:

The study was double-blinded (participants and operator). Operators and participants didn't know which group they were assigned to.

Endodontic procedural steps

Preparing the medication

Preparing the oral capsules was performed by a skilled pharmacist to make sure that both the operator and the participants do not know the type of the medication administrated. Those capsules were containing dexamethasone 0.5mg for Group 1 and a powder of lactose (Placebo) for Group 2.

Endodontic treatment was performed in one session

- Utilizing the widely used Numerical Rate Scale (NRS), participants were directed to record the pain intensity level after applying the cold thermal pulp test prior to beginning the root canal procedure. The scale was numerical, visual, and verbal to facilitate its use by the participants which was a horizontal line of 11 marks and 10 intervals each took numbers from 0 to 10 where 0 = no pain, 1-3 =mild pain, 4-6 = moderate pain, 7-10 = severe pain.
- 30 minutes after taking the oral medication, local anaesthesia was given through IANB using 1 or 2 carpules of Mepivicaine 2% containing 1:100.000 epinephrine LA solution. Intra-ligamentary injections was the supplemental LA when required.
- A round bur #2 was used for preparing and deroofing the access cavity, then a tapered diamond stone with safe end was used for flaring and toileting the access cavity.
- A composite resin filling material was used to build up any missing walls and a strict rubber dam isolation was appropriately applied to the tooth. Then, st.st. K-files #10 and #15 were used to negotiate the canals and for glide path preparation in a watch-winding motion till the estimated working length.
- Exact working length determination was carried out by utilizing an electronic apex locator and then PA x-ray was taken for WL confirmation of 0.5-1mm short than the radiographic apex.
- Mechanical instrumentation was done utilizing Pro-taper Next (PTN) Niti rotary files with their innovative M-wire technology and the unique offset mass of rotation. They were used in a pick-and-brush motion according to the manufacturing instructions regarding the torque and speed starting with the X1 (17/0.04),

followed by X2 (25/0.06), then X3 (30/0.07) for the full working length in all the canals. In cases where the distal root had only one distal canal, X4 (40/0.06) rotary file was used.

- Chemical disinfection was carried out using the most commonly used irrigating solution (sodium hypochlorite). 5ml of NaOCl (2.5%) in a side vented needle was used to minimize the risk of irritant extrusion and the subsequent post-operative pain. Irrigation was performed during chemomechanical preparation between every rotary file. Afterwards, canals were irrigated by 1ml of EDTA (17%) [8], and then followed by saline as the final flush.
- Selection of the master gutta percha cone corresponds to the last rotary file used (MAF); X3 in all canals and X4 in case of single distal canal. After insertion of the master gutta percha cones in all canals, PA x-ray was taken for confirmation.
- Sterile suitable sized paper points were then used for dryness of the root canals. Obturation was then performed utilizing the cold lateral condensation method using the well fitted gutta percha master cones with a resin sealer (AD-seal). A suitable-sized hand spreader was selected to allow room for auxiliary gutta percha cones to be laterally condensed beside the master gutta percha cone. Afterwards, intermediate restorative filling material (GI) was used to properly seal the access cavity. Finally, post-operative X-rays were taken .

E. Outcomes

Outcomes include the pain recording directly after the root canal treatment, also post-treatment at time intervals 6, 12, 24 and 48 hours.

Statistical analysis

Presentation of data was as follows; mean, standard deviation (SD), median and range values. The T tests were utilized for the values comparison within the 2 main groups regarding the para-metric data. However, the U tests (M-Witney) were utilized for comparison of the of the 2 main groups regarding the non parametric data. Time changes in every group was studied by the Fredman test. Also, comparing the periods of time was carried out through the Duun test.

After setting of the significant value at P≤0.05, Statistics was carried out by using IBM® SPSS® Windows version 20.

RESULTS

Pain scores

Intergroup comparisons

Preoperatively pain level was 7.4 for the intervention and 7.5 for the control where no statistic significance differences was observed in-between the 2 main groups (*P* - value = .83) while pain level at access was 4.9 for the intervention group and 4.9 for the control group with no statistically significant difference between two groups (*P*-value=0.969). The pain level at pulp extirpation was 4.5 for the intervention group and 5.2 for the control group with no statistically significant difference between two groups (*P*-value=0.419) followed by immediate post-operative pain level 1.4 for the intervention group and 2.1 for the control group with no statistically significant difference between two groups (*P*-value=0.535). Pain level after 6 hours was 2.3 for the intervention group and 2.9 for the control group with no statistically significant difference between two groups (*P*-value=0.906) followed by pain level after 12 hours 0.7 for the intervention group and 2.5 for the control group with also no statistically significant difference between two groups (*P* value=0.094). After 48 hours, the pain level was 0.1 for the intervention group and 0 for the control group with no statistically significant difference between two groups (*P*-value=0.317).

TABLE (1): Comparing the pain level scoring of the two groups

(Time)	Dexamethasone n=16	Placebo n=16	P- value
Pain level post-operatively (Immediate)			
Mean (SD)	1.4 (1.6)	2.1 (2.4)	0.535
Median (Range)	0.5(0–4)	(0–7)	
6-hours pain scores			0.906
Mean (SD)	2.3(2.3)	2.9(3.5)	
Median (Range)	(0–8)	(0–9)	
12-hours pain scores			0.093
Mean (SD)	0.6(1.6)	2.4(3.2)	
Median (Range)	(0–5)	(0–9)	
24-hours pain score			0.733
Mean (SD)	0.6(1.6)	0.5(1.1)	
Median (Range)	(0–5)	(0–3)	
48-hours pain scores			0.317
Mean (SD)	0.1(0.5)	(0)	
Median (Range)	(0–2)	(0–0)	

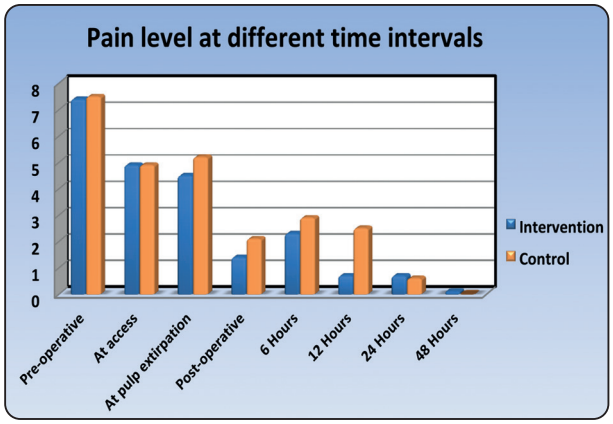

Fig. (1): showing mean pain level scoring of the 2 groups

Intra-group comparison

Group 1 : Dexamethasone (intervention group)

By time, A statistical significance differences were found in pain level scoring within the dexamethasone group.

Pair-wise comparisons between the time periods revealed that there was a statistically significant decrease in pain scores at access (P-value=0.969). There was no statistically significant change in pain scores at pulp extirpation (P-value=0.419) compared to pain at access followed by a statistically significant decrease in pain scores post-operatively (P-value=0.535). After 6 hours, a statistical significance increased pain level score was shown in comparison to that of the postoperative (P-value=0.906). However, the median pain score after 6 hours showed statistical significance lower value in comparison to that of the preoperative status; the access cavity preparation as well as at pulp extirpation (P- value=0.906). From 6 hours to 12 hours, there was a statistical significance decrease in pain level scoring followed by nonstatistically significant change from 12 hours to 24hours (P-value=0.094) as well as from 24 hours to 48 hours 90 (Pvalue=0.734). Pain scores after 12, 24 and 48 hours had shown a statistical significance lower values in comparison to the preoperative, access cavity preparation, pulp extirpation & 6 hours and non-statistically significant difference from pain scores post-operatively.

Group 2 : Placebo (control group):

By time, A statistical significance differences were found in pain level scoring within the placebo group Pair-wise comparisons between the time periods revealed that there was a statistically significant decrease in pain scores at access (P-value=0.969). No statistical significance change regarding pain level scoring at pulp extirpation in comparison to pain at access (P-value=0.419) followed by a statistically significant decrease in pain scores post-operatively (P-value=0.535). After 6 hours as well as from 6 to 12 hours, no statistical significance change in pain level scoring in comparison to postoperative pain level scoring (P-value=0.906). However, the median pain score after 6 and 12 hours showed statistical significance lower value compared to pain level preoperative

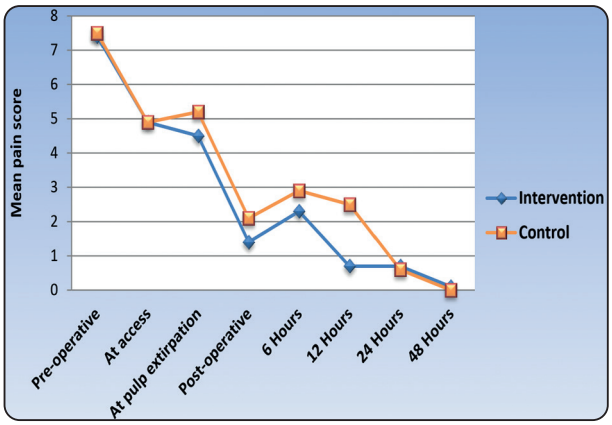

Fig. (2): Showing the by-time changes in pain level scoring within every group

score, access cavity preparation as well as at pulp extirpation (P-value=0.094). From 12 hours to 24 hours (Pvalue=0.734), a statistical significance decrease in pain level scoring followed by a nonstatistical significance change from 24 hours to 48 hours (Pvalue=0.317). Pain level scoring after 24 and 48 hours showed statistical significance lower values in comparison to pain level preoperative score, at access cavity preparation, pulp extirpation, postoperative, 6 and 12 hours.

DISCUSSION

This study aimed to assess the clinical efficiency of administrating one oral preoperative dose of dexamethasone vs placebo on post-operative pain which is a primary outcome demonstrated directly after the root canal treatment procedure, and also respectively after 6, 12, 24, 48 hours and also the efficiency of the IANB in lower molars with symptomatic irreversible pulpitis.

This clinical study was designed as a prospective double-blinded parallel randomised clinical trial in which neither the participants nor the clinician knew knows which intervention or pretreatment were administrated until the clinical trial was over. It is the gold standard and the most reliable type of studies as they provide the strongest possible evidence of causation[9]. Randomisation makes the study groups as similar as possible and makes the results of the study less likely to be biased [10].

Symptomatic irreversible pulpitis cases were selected as a main inclusion criterion as pain of pulpal origin (irreversible pulpitis) is the most feared among patients due to its intensity and severity. This severity is most likely because of increased exudative (acute) forces that cause an increase in the intrapulpal pressure within the unyielding, closed pulpal space that surpasses the threshold limits of sensory fibers. [11]. The management of such cases was always a challenging as they reveiled decreased efficiency of IANB [12] with greater possibility of postoperative pain in comparison to the asymptomatic non-painful teeth [13] .

In our study, the participants that were selected have not taken any kind of analgesics or pain killers at least 6 hours prior to the root canal treatment to prevent any interactions between medications and to record the exact pain level scores without any variations due to drug actions[14]. Lower molars were selected as they are more subjected for intra-operative and post-operative pain, Since the age was found to have a significant effect on postoperative pain, participants aged between 25 and 45 were only eligible to participate in the study[15] .

Regarding the number of treatment sessions, root canal was performed in a single session as it posses many advantages over treatments performed in multiple sessions such as less stressful for patients suffering from anxiety, decreased possibility for leakage or infection in-between the visits. In addition that it had been proved that no differences in prognosis and success rate between single visit and multiple visits root canal treatments.[16] Moreover, systematic review and meta-analysis concluded that patients experienced much less pain intensity and frequency after the single session endodontics than patients who had assigned for multiple sessions endodontics.[17].

In the present study, pain level scores were recorded using the Numerical Rating Scale (NRS) due to its simplicity, reproducibility, easy comprehensibility, and sensitivity to small changes in pain in comparison to the Visual Analogue Scale (VAS) or Verbal Rating Scale (VRS) [18].

Mepivacaine was chosen as the local anaesthetic agent for the standard IANB. A waiting period was allowed for the onset of the local anaesthesia [7].

Dexamethasone is a glucocorticoid medication that was used to inhibit the synthesis of prostaglandins by decreasing the release of arachidonic acid from the membranous phospholipids and consequently its availability for cyclooxygenase resulting in minimizing pain by reducing inflammation and edema along with depolarization of damaged nerves [19].

Also, It has been claimed that no harm or side effects were expected from taking one oral dose of dexamethasone as long as the medical status is normal [20].

In our study, Morita Root ZX II EAL was used for exact working length determination, because of its ease of use being a reliable EAL which has been confirmed in in vivo study [21], then confirmed by the radiograph. Root canals were prepared using Protaper Next (PTN) rotary system as it could preserve the original canal in a satisfactory way without causing canal transportation, shape curved canals safely and produce satisfactory root canal instrumentation.

Root canals were irrigated using 2.5% sodium hypochlorite (NaOCl) between every subsequent file for its potent antimicrobial effect [21]. Irrigation was done using a side-vented disposable needles, to minimize the risk of extrusion of the irrigant (NaOCl) beyond the apex and irritation of the periradicular tissues with subsequent post operative pain [22].

Obturation was done using cold lateral compaction technique and sealed with resin-based root canal sealer (AD seal sealer) because of its biocompatibility, easy to dispense and mix, hermitic seal ability, non staining to the teeth, acceptable radio-opacity and insolubility [23].

In the current study, the reduced efficiency of preoperative administration of dexamethasone on the local anaesthetic success may be due to several factors. Breakdown of damaged cell membrane in inflamed pulp triggers the release of arachidonic acid (AA). This is then acted on cyclooxygenase or prostaglandin H synthase enzymes, which in turn transform it into eicosanoids to produce PGS. Voltage-gated sodium channels are the target of local anaesthesia, and the PGS increase the expression, depolarization, and activity of theses channels. Drugs which inhibit PGS tend to inhibit the effect of local anaesthesia in patients with symptomatic irreversible pulpitis. [24]

At the 6-hours time interval, a statistical significance increase in pain level scoring was revealed. in comparison to the postoperative pain level scoring for the dexamethasone group and the placebo group. This was in agreement with the study outcomes of Maingret test al [25] and Attar et al[26] who stated that the greatest scores postoperative pain was recorded 6 hours post-treatment, when the action of the LA had been completely vanished.

Moreover, a statistical significance differences were observed in the pain level scoring at the 12, 24 and 48 hours time intervals a statistical in comparison to the pre-operative pain level scoring for the dexamethasone group and the placebo group, also during access cavity preparation, extirpating the pulp tissue & at 6 hours time interval. This might be attributed to that the pulpal inflammation resulting from extirpating the pulp along with the chemo-mechanical preparation had been subsided and resolved and the subsequent decrease of prostaglandins at the peri-radicular region [27].

In the current study, a non-significant differences were observed on the postoperative pain that may be due to the existence of the preexisting status of the pulp that may have an action on the outcome of the

clinical trial. Also, the active inflammatory action of the preexisting status of the inflamed pulp with the associated periapical inflammation dramatically increase the reception field of the sensory A delta fibres. [26] .

Our results were in agreement with **Jorge-araújo *et al***, [28] who revealed that no statistical significance between the different groups regarding the pain level scored at different time intervals (4h, 8h, 12h, 24h &48h). This might be attributed to the fact that corticosteroids have an anti-inflammatory effect by activation of cytoplasmic glucocorticoid receptors which regulate the transcription of some primary responses. At this cellular level, regulation of the immune system takes place, including regulation of several pro inflammatory cytokines. This mechanism is helpful in the suppression of glucocorticoids on COX-2 thus prolonging the time required for changes in the gene expression, all of which responsible for its delayed action. Dexamethasone thus having a plasma half life of 1.5-4 hours exhibits its action for 24-36 hours. Therefore, dexamethasone is advised to be administrated 1 hour prior to the procedure.

However, on the other side our study was not in agreement with ***Sharma et al*****,** [29] & ***Bidar et al,*** [30] who revealed that premedication with dexamethasone results in lower pain level scores than placebo. This might be attributed to the potent anti inflammatory action and the inhibitory effect of the dexamethasone that inhibit the production of the potent mediators responsible for the inflammation by preventing the arachidonic acid breakage. On the other side, the placebo has no analgesic nor anti inflammatory action, thus has no effect on the postoperative pain.

CONCLUSIONS:

In patients with symptomatic irreversible pulpitis in lower molars, oral premedication with dexamethasone preoperatively does not have a role to play when it comes to reducing the post endodontic pain.

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