

## Post Operative Pain and Expression of Substance P, IL8 After the Use of Ketorolac Irrigant in Teeth with Symptomatic Irreversible Pulpitis with Apical Periodontitis (Clinical Trial)

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### Abstract

**Introduction:** Endodontic post-treatment pain management is one of the most challenging problems in the clinical practice of endodontics. Although this pain is decreased after root canal treatment, there may be residual symptoms due to inflammation. It has been reported that up to 80% of patients with preoperative pain will report pain after endodontic treatment, which might range from mild to severe. Therefore, pain control is an important aspect of root canal treatment before, during and after intervention

**Aim of the study:** To assess the influence of ketorolac tromethamine versus sodium hypochlorite irrigant as a final rinse on, Postoperative pain in patients with symptomatic irreversible pulpitis with apical periodontitis in single visit root canal treatment and Periapical substance P and IL-8 level post- instrumentation and pre obturation.

**Methods:** Forty-four patients were included. After confirming the diagnosis clinically and radiographically, patients were assigned into two irrigant groups (n=22), 2.5% sodium hypochlorite and ketorolac tromethamine. The pain was assessed using the verbal rating scale (VRS) preoperatively, and postoperatively after 6, 12, 24 and 48 hours. All demographic, baseline and outcome data were collected and statistically analyzed. Periapical blood samples (sample 1) were collected on post instrumentation, and periapical blood samples (sample 2) were collected pre- obturation. Quantification of substance P and IL8 was done by ELISA test.

**Results:** There was no statistically significant difference between the two groups regarding age, gender distribution, pre-operative pain and post operative pain at 6 hours, 12 hours, 24 hours, 48hours. There was no statistically significant difference in the levels of IL8 and substance P between the two irrigant groups.

**Conclusion:** Sodium hypochlorite used as a root canal irrigant to reduce bacterial count could be contributed to the reduction in inflammation and postoperative pain. The level of IL8 and substance P showed no statistically significant difference between the two irrigant groups.

**Keywords:** Single Visit Root Canal Treatment; Irrigation; Ketorolac; Interleukin 8; Substance P

## Abbreviation

IL8: Interleukin 8; sub-P: Substance P

## Introduction

Endodontic post-treatment pain management is one of the most challenging problems in the clinical practice of endodontics [1].

Although this pain is decreased after root canal treatment, there may be residual symptoms due to inflammation [2,3]. It has been reported that up to 80% of patients with preoperative pain will report pain after endodontic treatment, which might range from mild to severe [4,5]. Therefore, pain control is an important aspect of root canal treatment before, during and after intervention [6].

Many mechanisms have been proposed to explain the reason for postoperative pain, including the sensitization of nociceptors by inflammatory mediators [3,7]. Among these chemical inflammatory mediators are the prostaglandins, which are the terminal product of arachidonic acid metabolism through the cyclooxygenase (COX) pathway. Endodontic treatment can cause the release of inflammatory mediators (e.g., prostaglandins, leukotrienes, bradykinin, platelet-activating factor, and substance P) into the surrounding periapical tissues, causing pain fibers to be directly stimulated (by bradykinin, for instance) or sensitized (by prostaglandins) [8]. In addition, the vascular dilation and increased permeability as a consequence of periradicular inflammation cause oedema and increased interstitial tissue response [7].

The role of irrigating solutions used during root canal treatment to help control postoperative pain is unclear [9]. While specific studies have observed a reduction in postoperative pain with particular types and concentrations of irrigating solutions, other studies have reported no difference in postoperative pain with the different irrigating solutions [10,11].

Most postoperative pain is usually well managed with non-steroidal anti-inflammatory agents (NSAID). Ketorolac tromethamine, a potent NSAID available in both oral and injectable forms, is over 400 times more potent as a non-selective inhibitor of COX-1 over COX-2 than many other drugs. When ketorolac tromethamine was used as an intracanal medicament in teeth with irreversible pulpitis undergoing root canal treatment, it contributed to significant post-operative pain relief [12]. An earlier study by the

authors revealed that when ketorolac tromethamine was used as a root canal irrigant in teeth with irreversible pulpitis, it was able to control the expression of substance P in the periapical tissue [13].

To our knowledge, there was a lack of studies investigating the effect of irrigation by NSAID on the control of post endodontic pain and (Sub P, IL8) reduction. Thus, this study is conducted to assess the effect of ketorolac tromethamine irrigant compared with sodium hypochlorite irrigant on postoperative pain and inflammatory mediators (Sub P, IL8) level.

## Material and Methods

### Trial design

The trial design of this study is a non-randomized clinical trial with a superiority framework.

### Study setting

Study setting This study was conducted in outpatients who presented to clinic of Endodontic Department, Faculty of Dentistry, Cairo University.

### Sample size

The minimum proper sample size was 18 patients in each group. The increased number for anticipated drop out was four patients per group (total 44 patients) to detect a 0.7 difference with 80% power at  $\alpha = 0.05$  level using Student's *t* test. Sample size calculation was done using G\*Power software version 3.1.2 for MS Windows, Franz Faul, Kiel University, Germany.

### Ethical consideration

The protocol for this parallel designed trial was reviewed and approved by the ECs [Ethics committee], Faculty of Dentistry, Cairo University, with respect to scientific content and compliance with applicable research and human subjects' regulations. Site-specific informed consent forms (Arabic language and English versions), participant education, recruitment materials, other requested documents and any subsequent modifications were also reviewed and approved by the ethical committee. The treatment procedures, aim of the study and possible side effects were thoroughly explained to all the participants.

### Participants

- Inclusion criteria
- Age between 15-60 years old.
- Systemically healthy patient.
- Male & female.
- Molar or premolar teeth with:
  - Preoperative moderate to severe pain.
  - With or without slight widening in the periodontal membrane space.
- Patients' acceptance to participate in the trial.

### Exclusion Criteria

- Patients allergic to anesthetics.
- Patients having significant systemic disorder.
- Hemostatic disorders or anticoagulant therapy during the last month.
- Retreatment cases
- Pregnant women: Avoid radiation exposure, anesthesia, and medication.
- No re-storability: Hopeless tooth.

### Endodontic procedure

When the participant was diagnosed as symptomatic irreversible pulpitis with apical periodontitis and confirming that the patient conforms to all eligibility criteria, the patient was enrolled in the study and asked to mark his/her level of pain on the verbal rating scale in the pain diary.

Each tooth was anaesthetized before treatment by 1.7ml of 4% Articaine HCl (Articaine-L, Alexandria Company for Pharmaceuticals and Chemical Industries, Egypt) with 1:100,000 epinephrine. Single visit endodontic treatment was done where access cavity preparation was performed with minimal removal of dentine wall and complete deroofing of the chamber by using a round bur and Endo-Z bur. A rubber dam was applied immediately after access cavity preparation.

The patency of canals was established and verified with K file size 10 and 15. Determination of the working length was done using an electronic apex locator and confirmed with an intraoral

periapical x-ray 1mm shorter than the apex. Canal lubrication and smear layer management were done with EDTA.

Canal preparation was done in a crown-down approach using a rotary nickel-titanium system" MPRO" (IMD, Shanghai, CH) that was used in a gentle in and out motion.

The canals of each group were thoroughly irrigated using 2.5% sodium hypochlorite between every subsequent instrument. After completion of the root canal preparation, apical patency was checked using a size 10 k file.

A pulp and periapical blood sample (sample 1) was taken with a sterile paper point that was placed 1-2 mm beyond the apical foramen. The collected sample was placed in an Eppendorf tube and stored at -80 C for further analysis.

The patients were divided into two groups. Intervention groups (ketorolac tromethamine final irrigant) and control group (2.5% sodium hypochlorite root canal final irrigant) as a final rinse. The canals were irrigated using 5ml of ketorolac tromethamine (ketolac ampoules, AMRIYA pharmaceutical, Egypt) as a final rinse in the experimental group. The canals were irrigated using 5ml of 2.5% sodium hypochlorite as a final rinse in the control group. After completion of the final root canal irrigation, the apical patency was checked using a size 10 k file.

A pulp and periapical blood sample (sample 2) was taken with a sterile paper point that was places 1-2 mm beyond the apical foramen. The paper point was left for the 30s; the collected sample was placed in an Eppendorf tube and stored at -80C for further analysis. The canals were dried with paper points. Obturation was carried out using a modified single-cone technique with resin-based root canal sealer (Adseal, Meta Biomed CO., LTD, Korea).

In case of severe pain or persisting pain, patients were instructed to take a prescribed analgesic (Ibuprofen 400mg), not to take it less than 6 hours apart, and to record the number of tablets taken.

The rating of postoperative pain was recorded by a verbal rating scale (VRS) in sheets given to the patients to mark their level of pain after 6hrs, 12hrs, 24hrs, and 48hrs. Checking the records was done by calling the patients at different time intervals. Preoperative assessment of pain was also included.

**Biochemical analysis**

The paper points were fractionated and diluted by using 200ul (pH 7.4) phosphate-buffered saline. Then, the samples were vortexed and centrifuged at 5000 xg for 10 min. Quantification of substance P and IL-8 was completed according to the manufacturer’s instructions using an enzyme-linked immunosorbent assay (ELISA) kit. The kit was provided by Bioassay Technology Laboratory (Cat.No E1528Hu), China). and Human IL-8 The kit was provided by SunLong Biotech Co., LTD (Catalogue Number:SL3409Hu), (China). The absorbency of each sample was read at 420–450 nm wavelengths in a microplate reader. A standard curve was created using the standard concentrations of substance P and IL-8. The concentrations of substance P and IL-8 for each sample were calculated using the standard curve.

**Gender**

There was no significant difference in gender distribution between the two groups ( $p = 0.34$ ).

	Ketorolac group		Sodium hypochlorite group		P-Value
	Frequency	Percentage	Frequency	Percentage	
Males	9	40.9%	6	27.3%	0.340
Females	13	59.1%	16	72.7%	

**Table 2:** Frequencies, percentages and the results of Chi square test for comparison of gender distribution between the two groups.

**oth type**

There was no significant difference in tooth type distribution between the two groups ( $p = 0.763$ ).

	Ketorolac group		Sodium hypochlorite group		P-Value
	Frequency	Percentage	Frequency	Percentage	
Premolars	10	45.5%	11	50.0%	0.763
Molars	12	54.5%	11	50.0%	

**Table 3:** Frequencies, percentages and the results of Chi square test for comparison of tooth type distribution between the two groups.

**Incidence of pain categories**

**Incidence of preoperative pain categories**

There was no statistically significant difference between the two groups. ( $p = 1.0$ ).

**Results**

**Age**

There was no significant difference in age between the two groups ( $p = 0.775$ ).

	Ketorolac group	Sodium hypochlorite group	P - Value
Mean	34.68	35.41	
SD	9.10	7.63	
Median	36.00	35.00	0.775
Min	20.00	23.00	
Max	46.00	49.00	

**Table 1:** Descriptive statistics and the result of independent t test for comparison of age between the two groups.

**Incidence of pain categories at 6 hours postoperatively**

There was no significant difference in incidence of pain categories at 6 hours postoperatively between the two groups. ( $p = 0.934$ ).

Ketorolac group			Sodium hypochlorite group		P - Value
	Frequency	Percentage	Frequency	Percentage	
Moderate	14	63.6%	14	63.6%	1.0
Severe	8	36.4%	8	36.4%	

**Table 4:** Frequencies, percentages and the results of Chi square test for comparison of incidence of preoperative pain categories between the two groups.

Ketorolac group			Sodium hypochloritegroup		P - Value
	Frequency	Percentage	Frequency	Percentage	
No Pain	7	31.8%	6	27.3%	0.934
Slight	8	36.4%	7	31.8%	
Moderate	6	27.3%	8	36.4%	
Severe	1	4.5%	1	4.5%	

**Table 5:** Frequencies, percentages and the results of Chi square test for comparison of incidence of pain categories at 6 hours postoperatively between the two groups.

**Incidence of pain categories at 12 hours postoperatively**

There was no significant difference in incidence of pain categories at 12 hours postoperatively between the two groups.

( $p = 0.831$ ).

Ketorolac group			Sodium hypochlorite group		P - Value
	Frequency	Percentage	Frequency	Percentage	
No pain	12	54.5%	10	45.5%	0.831
Slight	6	27.3%	7	31.8%	
Moderate	4	18.2%	5	22.7%	

**Table 6:** Frequencies, percentages and the results of Chi square test for comparison of incidence of pain categories at 12 hours postoperatively between the two groups.

**Incidence of pain categories at 24 hours postoperatively**

There was no significant difference in incidence of pain categories at 24 hours postoperatively between the two groups.

( $p = 0.648$ ).

Ketorolac group			Sodium hypochlorite group		P - Value
	Frequency	Percentage	Frequency	Percentage	
No pain	15	68.2%	12	54.5%	0.648
Slight	5	22.7%	7	31.8%	
Moderate	2	9.1%	3	13.6%	

**Table 7:** Frequencies, percentages and the results of Chi square test for comparison of incidence of pain categories at 24 hours postoperatively between the two groups.

**Incidence of pain categories at 48 hours postoperatively**

There was no significant difference in incidence of pain categories at 48 hours postoperatively between the two groups. ( $p = 0.68$ ).

Ketorolac group			Sodium hypochlorite group		P - Value
	Frequency	Percentage	Frequency	Percentage	
No Pain	19	86.4%	18	81.8%	0.680
Slight	3	13.6%	4	18.2%	

**Table 8:** Frequencies, percentages and the results of Chi square test for comparison of incidence of pain categories at 48 hours postoperatively between the two groups.

**Concentration of substance P**

**Concentration of post-instrumentation substance P between the two groups**

There was no significant difference in the concentration of post-instrumentation substance P between the two groups. ( $p = 0.077$ ).

	Ketorolac group	Sodium hypochlorite group	P - Value
Mean	4.33	3.69	0.077
SD	0.83	1.41	
Median	4.45	3.75	
Min	2.71	1.70	
Max	5.81	5.95	

**Table 9:** Descriptive statistics and the result of independent *t* test for comparison of concentration of post-instrumentation substance P between the two groups.

**Concentration of pre-obturation substance P between the two groups**

There was no significant difference in the concentration of pre-obturation substance P between the two groups. ( $p = 0.411$ ).

	Ketorolac group	Sodium hypochlorite group	P - Value
Mean	3.04	2.76	0.411
SD	1.02	1.18	
Median	3.18	3.21	
Min	0.70	0.39	
Max	4.88	4.49	

**Table 10:** Descriptive statistics and the result of independent *t* test for comparison of the concentration of pre-obturation substance P between the two groups.

**Change in concentration of substance P within ketorolac group**

There was a significant reduction of substance P concentration between post-instrumentation and pre-obturation within group A ( $p < 0.001$ ).

	Post- instrumentation	Pre- obturation	P - Value
Mean	4.33	3.04	<0.001
SD	0.83	1.02	
Median	4.45	3.18	
Min	2.71	0.70	
Max	5.81	4.88	

**Table 11:** Descriptive statistics and the result of paired *t* test for comparison of post-instrumentation and pre-obturation concentrations of substance P within group A.

**Change in concentration of substance P within sodium hypochlorite group**

There was a significant reduction of substance P concentration between post-instrumentation and pre-obturation within sodium hypochlorite group ( $p = 0.002$ ).

	Post- instrumentation	Pre- obturation	P - Value
Mean	3.69	2.76	0.002
SD	1.41	1.18	
Median	3.75	3.21	
Min	1.70	0.39	
Max	5.95	4.49	

**Table 12:** Descriptive statistics and the result of paired *t* test for comparison of post- instrumentation and pre-obturation concentrations of substance P within Sodium hypochlorite group.

**Concentration of IL-8**

**Concentration of post-instrumentation IL-8 between the two groups**

There was no significant difference in the concentration of post-instrumentation IL-8 between the two groups ( $p = 0.841$ ).

	Ketorolac group	Sodium hypochlorite group	P - Value
Mean	14.36	14.43	
SD	1.12	1.26	0.841
Median	14.54	14.40	
Min	12.68	12.68	
Max	16.43	16.92	

**Table 13:** Descriptive statistics and the result of independent *t* test for comparison of concentration of post-instrumentation IL-8 between the two groups.

**Concentration of pre-obturation IL-8 between the two groups**

There was no significant difference in the concentration of pre-obturation IL-8 between the two groups. ( $p = 0.193$ ).

	Ketorolac group	Sodium hypochlorite group	P - Value
Mean	12.15	12.86	
SD	1.47	2.03	0.193
Median	11.85	12.18	
Min	10.28	10.05	
Max	16.28	16.24	

**Table 14:** Descriptive statistics and the result of independent *t* test for comparison of the concentration of pre-obturation IL-8 between the two groups.

**Change in concentration of IL-8 within ketorolac group**

There was a significant reduction of IL-8 concentration between post-instrumentation and pre-obturation within ketorolac group ( $p < 0.001$ ).

	Post- instrumentation	Pre- obturation	P - Value
Mean	14.36	12.15	
SD	1.12	1.47	<0.001
Median	14.54	11.85	
Min	12.68	10.28	
Max	16.43	16.28	

**Table 15:** Descriptive statistics and the result of paired *t* test for comparison of post-instrumentation and pre-obturation concentrations of IL-8 within ketorolac group.

**Change in concentration of IL-8 within sodium hypochlorite group**

There was a significant reduction of IL-8 concentration between post-instrumentation and pre-obturation within sodium hypochlorite group ( $p < 0.001$ ).

	Post- instru- mentation	Pre- obturation	P - Value
Mean	14.43	12.86	
SD	1.26	2.03	0.000
Median	14.40	12.18	
Min	12.68	10.05	
Max	16.92	16.24	

**Table 16:** Descriptive statistics and the result of paired *t* test for comparison of post-instrumentation and pre-obturation concentrations of IL-8 within sodium hypochlorite group.

**Discussion**

Post operative pain management is one of the most challenging aspect of endodontic clinical practice [1]. The post-endodontic flare up has poly etiological predisposing factors; mechanical, chemical, and microbial factors [14]. Many studies were performed to assess pain prevalence during and after root canal treatment, the prevalence of pain after root canal treatment has been reported between 3% and 58% of the patients [15].

Various classes of drugs have been studied to manage post treatment endodontic pain, including NSAID's, acetaminophen, opioids and steroids [12]. Non-steroidal anti- inflammatory drugs (NSAIDs) have been used to control severe pain after endodontic treatment.

Ketorolac tromethamine was used in this study as it is a potent NSAID, is a selective inhibitor of COX1 and COX-2, it reduces prostaglandin synthesis, and their anti-inflammatory effect can indirectly relieve nociceptive pain by reducing inflammation and tissue swelling [16].

The pain was recorded using the verbal rating scale (VRS). It's easy to administer, valid, and take less time, and is preferred by the less educated and elderly [17].

Treatment was completed in a single visit, 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 bacteria regrowth resulting in pain and reinfection of the canals as a sequence of bacteria ingress from leaky temporary restoration [18,19].

In this study, the pain intensity was recorded preoperatively as baseline data and postoperatively at different time intervals. Six hours was chosen as it was the time that the effect of the anesthetic solution would start to fade. 12, 24, and 48 hours were chosen as it was proven that the most of the postoperative pain occurred between these time intervals [20].

Patients who had already consumed preoperative medication, such as steroidal or non-steroidal anti-inflammatory drugs and analgesics, within 12 hours before treatment were excluded from the study to avoid misinterpretation of the diagnosis or the post-treatment pain scores [21,22].

After access cavity preparation, isolation by rubber dam was conducted before instrumentation of the root canal system to minimize the risk of saliva contamination and ingestion of chemicals or aspiration of instruments. Using a rubber dam during root canal treatment is considered the standard of care because it enhances patient safety, a pivotal aspect of healthcare, and improves the odds of a successful treatment [23].

In the present study, the working length (WL) was determined by Root ZX mini electronic apex locator due to its high accuracy, which had been asserted *in vitro* and *in vivo*. The radiograph further confirmed this working length. It greatly confines the instrumentation within the root canal system [24,25]. One of the iatrogenic factors causing the postoperative pain and flare-up of the endodontic treatment is incorrectly measured working length of the root canal [26].

In the present study, root canal instrumentation was achieved using the M-Pro rotary system (Innovative Materials and Devices, Shanghai, China), consisting of one opener file, 18/.09, and two shaping files, 20/.04 and 25/.06. The files have a convex triangular cross-section which has high fracture resistance, high adaptability to root canal curvatures, and also the files can be pre-curved [27].

In the current study, a standardized irrigation protocol was done using 5 ml of 2.5% NaOCl solution between every subsequent instrument. It was proved to have lesser cytotoxicity than 5.25% sodium hypochlorite [28].

Furthermore, the reduction of intracanal microbiota is not any greater when 5.25% NaOCl is used as an irrigant compared to

2.5% NaOCl [29]. During root canal preparation, a potent irrigating solution is mandatory for the cleaning procedure since it facilitates cleaning and shaping, which benefits root canal enlargement for subsequent filling [30].

NaOCl has been widely used in endodontics as an irrigant as it covers most of the requirements for an endodontic irrigant than any other known compound. It has a broad-spectrum antimicrobial activity with the ability to rapidly kill vegetative bacteria, spore-forming bacteria, fungi, protozoa, and viruses (including HIV, rotavirus, HSV-1 and -2, and hepatitis A and B viruses) [31]. At the end of the chemo-mechanical preparation, 5 ml of 17% EDTA. This irrigation regimen was used in order to remove both the organic and inorganic parts of the smear layer [32] and followed by a final rinse of NaOCl or ketorolac tromethamine according to the groups.

Irrigation was done using a side-vented 30-gauge needle fitted to a 3ml disposable plastic syringe. The needle was introduced into the canal space without binding, 1mm short of the working length; this seemed to have a lowering effect on irrigant extrusion into the periapical space, as regular needle irrigation proved to cause the highest fluid extrusion [33,34].

According to previous studies [35], Inflammatory mediators sampling in the present study were performed by introducing paper points into the periapical area through root canals, which were retained in position for 30 seconds. This procedure was repeated with three paper points for standardization. Immediately afterward, the sample was placed in a sterile plastic Eppendorf tube and stored at -80°C.

After the completion of cleaning and shaping of the root canal system, master cones corresponding to the size and taper of the final NiTi instrument were fitted inside the canals, and a master cone confirmatory radiograph was taken to confirm that the master cones reach the working length and further instrumentation will not be needed. Afterwards, root canals were dried with sterile absorbent paper points and obturated using the modified single cone technique with an Adseal resin sealer at the same visit. This technique showed a lower incidence of postoperative pain than warm obturation techniques [36,37]. Adseal was used in this study as previous studies showed that it provides a good apical sealing ability, biocompatibility, and adaptability to root canal walls [38,39].

The patients were afterwards asked to record their pain level on the verbal rating scale at 6, 12, 24 and 48 hours after root canal obturation.

Human Elisa Kit was used to measure the inflammatory mediators in the root canal and periapical area by the Sandwich-ELISA method. ELISA (enzyme-linked immunosorbent assay) is a plate-based assay technique designed for detecting and quantifying substances such as peptides, proteins, antibodies, and others. The key advantage of a sandwich ELISA is its high sensitivity; it is 2-5 times more sensitive than direct or indirect ELISAs. In addition to this, it delivers high specificity as two antibodies were used to detect antigen [40].

There was no statistically significant difference between the two groups regarding age, gender, and pre-operative pain in the present study regarding the demographic data. These factors were considered to be homogenous in all groups. This was in accordance with [41] and [42], who showed no effect of the patient's age and gender on endodontic postoperative pain. Our findings were in disagreement with [43] and [44] who reported that age and gender are factors that may influence postoperative pain.

The effect of using sodium hypochlorite, as a root-canal irrigant, in decreasing the bacterial count as well as its better tissue dissolving capability has been documented in the literature [11,45]. [12] revealed that the use of ketorolac tromethamine as an intracanal medicament was able to provide significant pain relief. Conversely [13,35], reported no significant changes in post-operative pain levels using different root canal irrigants. In agreement, our results demonstrated no statistically significant reduction in postoperative pain intensity in the ketorolac group compared to the sodium hypochlorite group at 6, 12, 24, and 48 hours. As both ketorolac and sodium hypochlorite irrigants act by reducing inflammation and pain intensity.

In the present study, the level of IL8 and substance P showed no statistically significant difference between the two irrigant groups. Our findings agreed with [35], who evaluated the influence of ketorolac tromethamine, dexamethasone, saline, and sodium hypochlorite irrigants on substance P and IL8 expression. The study concluded that there was no statistically significant difference in the levels of IL8 and substance P between the two irrigant groups.

These findings are in contrast to [13], who evaluated the effect of ketorolac tromethamine when compared with sodium hypochlorite and saline on substance P expression. The study concluded the ketorolac tromethamine group had a more significant reduction in substance P expression.

The diversity of the results in different studies support the idea that the production of inflammatory mediators differs from site to site and from subject to subject, and their levels may be influenced by several factors, such as genetic factors, and bacterial composition [46,47].

These results also showed a statistically significant reduction in sub P, IL8 between Sample 1 and Sample 2 within the same group. Both groups showed a significant decrease in the mean value of sub P, IL8 between each two samples (post-instrumentation and pre-obturation). These findings are in agreement with [48], who investigated the effects of root canal debridement (cleaning and shaping) on periapical inflammation by measuring the levels of inflammatory cytokines, Interleukin-8 (IL-8) and Interleukin-10 (IL-10). The study concluded that root canal debridement appears to be effective in decreasing the levels of both pro- and anti-inflammatory cytokines.

## Conclusion

Within the limitations of this study, it could be concluded that

- There was no statistical difference regarding using either ketorolac or sodium hypochlorite irrigants regarding the decrease of endodontic postoperative pain.
- Sodium hypochlorite used as a root canal irrigant to reduce bacterial count could be contributed to the reduction in inflammation and postoperative pain.
- The level of IL8 and substance P showed no statistically significant difference between the two irrigant groups

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### Conflict of Interest

I declare that this thesis has been composed solely by myself and there is no conflict of interest.

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