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ORIGINAL RESEARCH

POST-OBTURATION PAIN EVALUATION AFTER NON-SURGICAL DEBULKING OF PERIAPICAL PATHOSIS AND INTRACANAL INJECTION OF GROWTH HORMONE (AN IN VIVO STUDY)

Mohamed Z. Abdel Aziz,[1] Motaz M. ElSadat,[1] Amr A. Bayoumi,[1] Moataz- Bellah A.M. Alkhawas[1]
[1] Department of Endodontics, Faculty of Dental Medicine, Al Azhar University, Cairo, Egypt.
Corresponding Author: Mohamed Z. Abdel Aziz Department of Endodontics, Faculty of Dental Medicine, Al Azhar University, Cairo, Egypt.Dr.mohamed.zakariaa@gmail.com
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Abstract

Background: This study aimed to evaluate and compare post-obturation pain following non-surgical debulking of periapical pathosis using XP-Endo Finisher and the intracanal injection of Growth Hormone in single-rooted necrotic teeth that were obturated using EndoSeal MTA sealer.

Methods: This single-blind randomized controlled clinical trial registered fifty-four patients presenting with necrotic, mature, permanent, single-rooted teeth associated with periapical lesions measuring 2–4 mm in diameter and classified as score 3 on the Cone Beam Computed Tomography Periapical Index (CBCTPAI). Following comprehensive clinical and radiographic assessment, participants were randomly assigned into three equal groups (n = 18). In Group I (GH-ES), growth hormone (SEDICO, 6 October, Egypt) (GH) was applied periapically prior to root canal obturation with EndoSeal MTA (Maruchi, Wonju, South Korea) (ES) sealer, Group II, (XP-ES) non-surgical debulking of periapical pathosis using XP-Endo Finisher (FKG,Dentrie Switzerland) file was done prior to root canal obturation with EndoSeal MTA (ES), whereas in Group III (ES), obturation was performed using ES sealer alone. Preoperative pain levels were assessed using the Arabic-translated version of the Verbal Descriptor Scale (VDS). Postoperative pain grades were noted at baseline (preoperatively), and at 6, 24, 48, and 72 hours, as well as 1 week after treatment.

Results: A statistically significant difference was observed between the three groups at 6, 24, and 48 hours postoperatively (p =0.001, 0.001, 0.005 respectively), with the GH-ES group showing lower pain scores and XP-ES group showing the highest pain scores. However, no significant differences were noted at 72 hours or at one week. All groups exhibited a progressive and significant decrease in pain scores over time (p =0.001).

Keywords**:** Growth Hormone, EndoSeal MTA sealer, XP-Endo Finisher, Non-surgical debulking, Bioceramics, Postoperative pain.

INTRODUCTION

Postoperative pain may appear after the endodontic therapy, within hours and last for many days [(i)]. According to reports, the prevalence of endodontic discomfort following treatment ranges from 3 to 58% [(ii,iii)], with fewer than 12% of the population experiencing severe pain following therapy [(iv)]. To avoid exacerbating pain throughout the postoperative phase, pain management must be a complementing phase of dental therapy [(v)]. One of the primary causes of endodontic postoperative severe pain that follows chemical, mechanical, or microbiological damage to periapical tissue was previously believed to be acute inflammation [(vi)]. Nevertheless, the various phases of therapy, from diagnosis to post-obturation, might affect the incidence of pain. Root canal sealers may cause local inflammation, due to their direct interaction among the periodontal tissues via the apical foramina and lateral canals, which possibly lead to post operative pain and impaired healing process in the periodontium [(vii)].

Pain evaluation is difficult because pain experiences are subjective and multifaceted, making them difficult to standardize or quantify. Additionally, it is impacted by several factors; psychological, physical, behavior and personality factors. Because of that, different pain scales were developed in this type of research to measure the degree of pain, direct treatment choices, and track efficacy. The common pain scales used in endodontics are: Visual Analog Scale (VAS), Numerical Rating Scale (NRS) and Verbal Descriptor Scale (VDS). The VDS is easy to finish since it is brief and straightforward. However, it is appropriate for all

patient groups and may be employed to quantify acute as well as chronic pain [viii,ix,x]. In 2010, Wang et al.[i] modified the VDS by adding a collection of terms that characterize various pain intensity in which each pain level was given a score from 0-10.

Calcium silicate-based endodontic sealers are thought to produce less inflammatory mediators and have minimal cytotoxicity [xi] and they are thought to reduce postoperative pain [xii]. The premixed injectable bioceramic sealer EndoSeal MTA (Maruchi, Wonju, South Korea) has attracted interest because of its ease of use and favorable results. The calcium silicate, calcium aluminates, and calcium sulfates that make up EndoSeal MTA have a number of benefits, including elevated alkalinity, excellent flowability, and biocompatibility [xiii]. Furthermore, unlike previous bioceramic sealers, it exhibits stability in dimensions throughout a 30-day trial period [xiii]. Several investigations conducted on animals in-vitro as well as in-vivo have demonstrated the advantageous physiobiological characteristics of bioceramic sealers [xiv,xv]. Nevertheless, despite their high attraction, there aren't many clinical research on how bioceramic sealers affect postoperative pain [vii].

XP-Endo Finisher (FKG Dentaire SA) has been introduced as an adjunctive approach to improve the effectiveness of irrigation and disinfection by reaching larger areas of the root canal walls that conventional methods are thought to miss, thereby maximizing bacterial removal and improving the healing of periapical pathosis [xvi]. Recently, another minimally invasive, non-surgical method was introduced that allows removal or debulking of chronically inflamed periapical tissues through a root canal access: a rotary instrument is inserted into the periapical area to mince the tissues, followed by aspiration using a large-gauge needle. This procedure is considered less traumatic than open-flap apical surgery [xvii,xviii, xix].

Growth hormone (GH) plays a complex role in postoperative pain. While it's secreted in response to surgical stress and trauma, potentially contributing to pain pathways, it also plays a role in tissue repair and can have analgesic effects. Research indicates that GH and related signaling molecules are implicated in both the onset of pain and pain relief [xx,xxi,xxii,xxiii].

To the best of our knowledge, not much research has examined how non-surgical debulking of periapical pathosis or growth hormone affects pain following obturation. The objective of the current study was to compare the effect of obturating root canals with EndoSeal MTA, with or without pre-application of Growth Hormone, or with non-surgical debulking of periapical pathosis on post-obturation pain. The null hypothesis of this research was that there would be no variation in post-obturation pain across teeth obturated with ES, with or without pre-application of GH, or with non-surgical debulking of periapical pathosis.

MATERIALS AND METHODS

Study design and sample size determination: This single-blind randomized clinical trial received ethical approval from the Ethical Committee of the Faculty of Dental Medicine, Al Azhar University for Research on Human Subjects (EC Ref No. 898/262) and was registered at *ClinicalTrials.gov* (NCT06433375). The required sample size was determined utilizing the G*Power software [xxiv], according to the prior research by Khandelwal et al. [xii], with a two-tailed α-error probability of 0.05 and a study power of 95%. The analysis denoted the lowest of 14 patients per group. To compensate for potential dropouts during the trial, the sample size was increased to 18 patients per group.

Patient selection: Out of one hundred, fifty-four healthy male patients between the ages of 18 and 40 were chosen from out-clinics visiting the Endodontic Clinic of the Faculty of Dental Medicine, Al-Azhar University Boys, Cairo, Egypt, to be assigned into the present research. After thorough clinical and radiographic assessments, patients with periapical lesion related to permanent single rooted necrotic teeth of a 2 to 4mm diameter and score 3 according to the Cone Beam Computed Tomography Periapical Index Score (CBCTPAI) [xxv] were selected. Each participant signed an informed consent document following exploring all steps of the research, suspected complications and follow-up then underwent Preoperative pain measurement was performed utilizing a translated modified verbal descriptor scale (VDS) into Arabic according to Hagras et al [xxvi] by the patient at preoperatively, 6, 24, 48, 72 hours as well as 1week after treatment. Only patients scoring between 0 and 6 were assigned into this research.

Randomization and grouping of patients: (Figure 1)

Participants were split into three groups randomly (n = 18) using research randomizer software (www.randomizer.org).

- Group I (GH-ES group): Teeth undergo Growth Hormone application before root canal obturation utilizing EndoSeal MTA sealer.
- Group II (XP-ES group): Teeth undergo non-surgical debulking of periapical pathosis using XP-Endo Finisher file before root canal obturation utilizing EndoSeal MTA sealer.
- Group III (ES group): Teeth undergo root canal obturation using EndoSeal MTA sealer without any additional intervention.

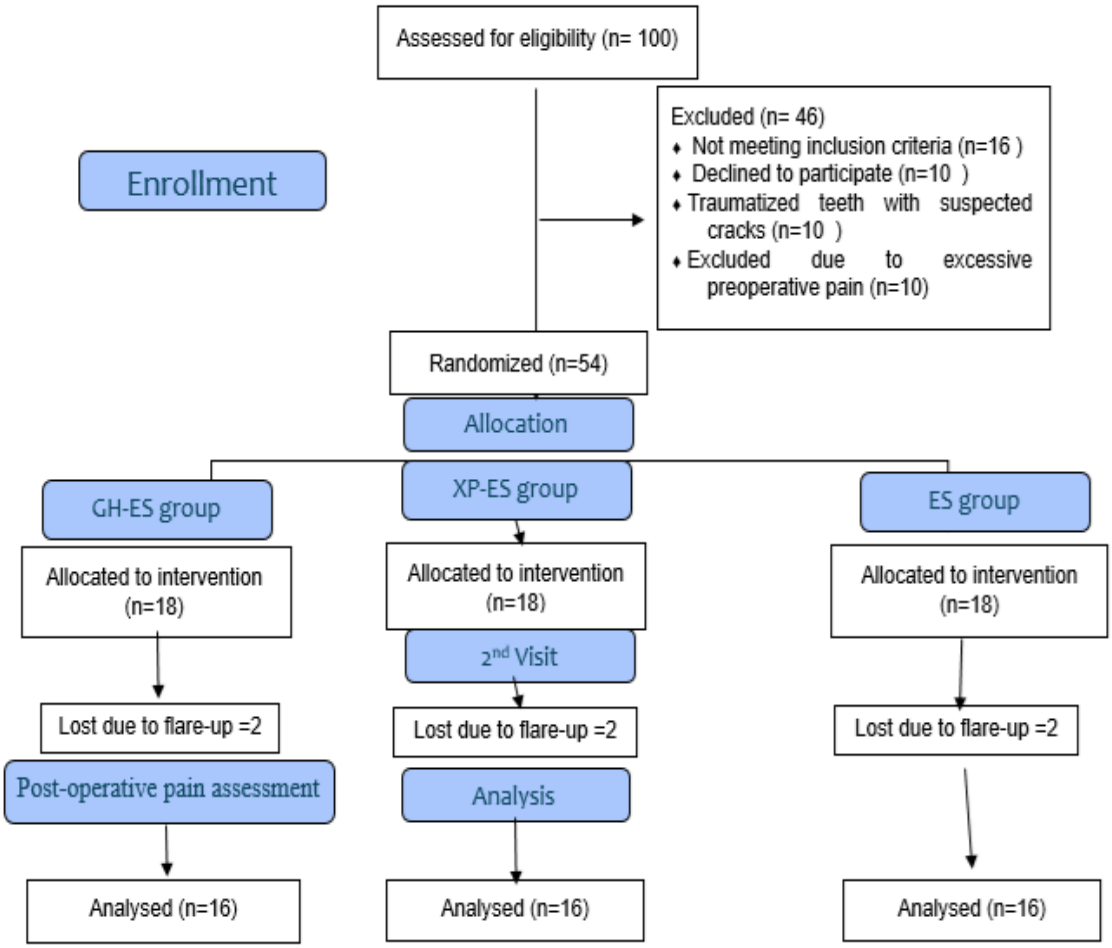

Figure (1): Patients Flow Diagram

Root canal treatment Procedure:

-During the first visit: Teeth in all groups were received to a conventional multiple endodontic therapy as follows:

The tooth was anesthetized, isolated using rubber dam, all dental caries or prior fillings were eliminated, and the crown was filled by composite resin restoration. Access cavity was prepared; the root canal was negotiated using #10 ISO K-file. Utilizing the apex locator device (Root ZXII, Morita, Japan), the working length was verified to be 1 mm below the radiography apex.

Root canal instrumentation was carried out using RACE EVO (FKG, Dentaire, Switzerland) up to a #35/.04 as a master apical file at 800rpm/ 1.5 Ncm as follow: Race EVO #15/0.4 (RE1) was used to create a glide path till reaching the working length, followed by irrigation and patency confirmation using #10 K-file. Then, size #25/0.4 (RE2) was used for initial shaping till reaching the working length, followed by irrigation and patency confirmation using #10 K-file. After that #30/0.4 (RE3) was used till reaching the working length, followed by irrigation and patency confirmation using #10 K-file. Finally, size #35/0.4 was used as master apical file.

Irrigation protocol of the root canals was done between each file using 3 ml 5.25% sodium hypochlorite solution followed by 3 ml 17% Ethylenediaminetetraacetic (EDTA) solution with intermittent 3 ml normal saline solution between them and as a final rinse of the canals. Root canals were then dried with sterile paper points equivalent to the size of the master apical file, the pulp chamber was lined with a sterile piece of Teflon (PTFE-Polytetrafluoroethylene), and the access cavity was temporarily filled till the second appointment with glass-ionomer cement.

-During the second visit:

After the first visit two patients from each group were lost due to flare-up that happened after first visit (Figure 1).

Access was reopened and checked for any exudate using sterile paper. (if any exudate was found patient was excluded from the research). Irrigation protocol of the root canals was performed utilizing 3 ml 5.25% sodium hypochlorite solution. Followed by manual dynamic activation using the master cone for 3-5 minutes in up and down motions. A 3 ml 17% Ethylenediaminetetraacetic (EDTA) solution with intermittent 3 ml normal saline solution between them. Followed by manual dynamic activation using the master cone for 3-5 minutes in up and down motions. A 3 ml of normal saline solution was utilized as a final rinse of the canals. Finaaly, Root canals were dried via sterile paper points equivalent to the size of the master apical file.

- **Group I (GH-ES group):**

Growth hormone (SEDICO, 6 October, Egypt) was prepared based on the manufacturer's instructions by injecting the accompanied diluent into the vial by aiming the steam of the liquid against the glass wall. The vial was swirled with a gentle rotary movement until the content was completely dissolved. After that a 4 IU (1.33 mg) was injected into the periapical area using a 3ml plastic syringe with 30-gauge open-ended needle slowly for 2 minutes. After that root canals were dried again via a sterile paper points equivalent to the size of the master apical file. Similarly, obturation of root canals was done using cold lateral compaction with Endoseal MTA sealer. At last, the access cavity was cleaned and sealed with a resin composite restoration as a final restoration after which a post-operative radiograph was taken.

- **Group II (XP-ES group):**

XP-endo Finisher file was used in non-surgical debulking of periapical tissues by inserting the file periapically. The file (size 25, taper zero) was mounted in a torque limiting motor at 800 rpm speed and 1 Ncm torque as recommended by manufacturer’s instructions up to the full working length, then inserted periapically to mince the periapical tissues for 30 seconds in a slow up and down motion, The tissue suspension was now washed out with sterile saline solution by using a syringe adapted with a 30-G blunt needle. The needle was passed through the enlarged apical foramen into the periapical space, and the saline solution was slowly and gently injected to flush the tissue suspension out. After that root canals were dried again via a sterile paper points equivalent to the size of the master apical file. Similarly, obturation of root canals was done using cold lateral compaction with Endoseal MTA sealer. At last, the access cavity was cleaned and sealed with a resin composite restoration as a final restoration after which a post-operative radiograph was taken. (Figure 2)

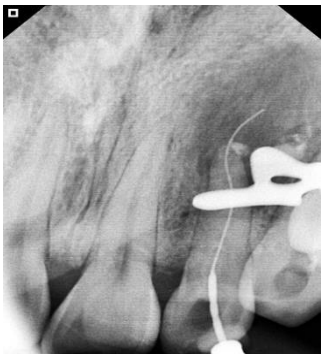

Figure 2. XP-endo Finisher inserted periapically

- **Group III (ES group):**

Obturation of root canals was done using cold lateral compaction with Endoseal MTA sealer.

Post-obturation pain assessment: Post-obturation pain evaluation was carried out as detailed previously in preoperative pain assessment. Patients were evaluated at six intervals: preoperatively and at 6, 24, 48, 72 hours, and 1 week afterward. The collected data was then tabulated and analyzed statistically.

Data management and analysis: Recorded data were analyzed using the statistical package for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA). The quantitative data were presented as median with inter-quartile range (IQR) was (non-parametric data). Data were explored for normality using Kolmogorov-Smirnov and Shapiro-Wilk Test. *The following tests were done: Kruskall Wallis test*: for multiple-group comparisons in non-parametric data & *Mann Whitney U test:* for two-group comparisons in non-parametric data and *Friedman test* was used to compare multiple within-group measures & the comparison between two periods for non-parametric data using *Wilcoxon Signed-Rank Sum test*. *The confidence interval was set to 95%* and the margin of error accepted was set to 5%. So, the p-value was considered

significant as the following: *Probability* P-value <0.05 was considered significant.

RESULTS

Pain scores: a) Inter-group comparison: Preoperatively, the three groups demonstrated comparable pain scores with no statistically significant differences (p = 0.594). At **6** hours postoperatively**,** a statistically significant difference was observed among the groups (Kruskal–Wallis test, p = 0.001). Group I (GH-ES) recorded the lowest pain scores**,** followed by Group II (ES), while Group III (XP-ES) exhibited the highest pain levels**.** At 24 hours, the difference between the groups remained statistically significant (p = 0.001). Again, pain was lowest in Group I**,** followed by Group II, whereas Group III demonstrated the highest postoperative pain**.** At 48 hours**,** pain further decreased in all groups, yet the difference remained statistically significant (p = 0.005). Group I reached complete pain resolution (0.0 ± 0.0)**,** Group II showed low pain levels, while Group III continued to present the highest scores**.** By 72 hours and at 1 week**,** postoperative pain resolved completely in all groups, with no statistically significant differences (p = 1.000). (Table 1)

a)Intra-group comparison:

Overall, all three groups exhibited statistically significant time-dependent decreases in pain. Within Group I (GH-ES), postoperative pain showed a significant and continuous reduction over time, beginning with a high preoperative score that dropped markedly at 6 hours and continued to decrease at 24 hours, reaching complete pain resolution by 48 hours and remaining at zero through 72 hours and 1 week. Similarly, Group II (ES) demonstrated a significant decline from the preoperative level to the 6-hour and 24-hour intervals, followed by an additional reduction at 48 hours, after which all patients became pain-free at 72 hours and 1 week. In Group III (XP-ES), although a significant decrease was also observed across the time intervals, pain levels remained higher than in the other groups during the early postoperative phase, with a notable reduction from preoperative to 6 hours, further improvement at 24 and 48 hours, and eventually complete resolution by 72 hours and at 1 week. (P-value < 0.001). (Table 1)**.**

Table 1 Median and IQR of postoperative pain score for each group and Kruskal Wallis test for non-parametric quantitative data between the three groups followed by Friedman test between time intervals in each group.

Post-operative Pain Score	Group I: GH-ES	Group II: ES	Group III: XP-ES	Test value	p-value
Pre-operative					
Mean±SD	5.36±0.84	5.00±1.04	5.07±0.92	1.041	0.594
Median (IQR)	6 (5-6)Aa	5 (4-6)Aa	5 (4-6)Aa		
Range	4-a6	4-a6	4-a6		
After 6 hrs.					
Mean±SD	2.86±1.03	3.14±1.29	4.57±1.28	13.141	0.001*
Median (IQR)	2 (2-4)Cb	3 (2-4)Bb	5 (4-5)Aa		
Range	2-a4	2-a6	2-a6		
After 24 hrs.					
Mean±SD	1.21±1.25	1.71±1.07	3.14±1.29	13.659	0.001*
Median (IQR)	1 (0-2)Cc	2 (2-2)Bc	3 (2-4)Ab		
Range	0-a4	0-a4	2-a6		
After 48 hrs.					
Mean±SD	0.00±0.00	0.57±0.94	1.21±1.25	10.761	0.005*
Median (IQR)	0 (0-0)Cd	1 (0-2)Bd	2 (0-2)Ac		
Range	0-a0	0-a2	0-a4		
After 72 hrs.					
Mean±SD	0.00±0.00	0.00±0.00	0.00±0.00	0.000	1.000
Median (IQR)	0 (0-0)Ad	0 (0-0)Ae	0 (0-0)Ad		
Range	0-a0	0-a0	0-a0		
After 1 week					
Mean±SD	0.00±0.00	0.00±0.00	0.00±0.00	0.000	1.000
Median (IQR)	0 (0-0)Ad	0 (0-0)Ae	0 (0-0)Ad		
Range	0-a0	0-a0	0-a0		
Friedman	64.596	61.555	61.878		

p-value	0.001*	0.001*	0.001*		

a) Using: Kruskal Wallis test for Non-parametric data "Median (Interquartile range: IQR) between three groups

b) Different capital letters indicate significant difference at (p<0.05) among means in the same row, using Mann-Whitney test

c) Different small letters indicate significant difference at (p<0.05) among means in the same column, using Wilcoxon test

*d) *: Significant level at P value < 0.*

DISCUSSION

Preventing post-obturation pain is still a problem for dentists. Only 4–10% of endodontic participants have moderate to severe post-obturation pain, based on specific investigations [xxvii], while some investigations reported that up to 50% of people experience post-obturation pain [xxviii]. Patients might experience main pain issues that significantly affect their quality of life. According to a few clinical trials, 5–12% of patients may endure constant pain for months or years following the endodontic therapy [xxix]. Post-obturation pain can occur for several causes, including bacterial, chemical, or mechanical damage to the periapical tissues that triggers the release of cell mediators (Substance P and Calcitonin Gene-related peptide, or CGRP), that result in inflammatory response [xxx, xxxi]. Also, the amount of root canal sealer and the obturation technique may arise post-obturation pain, which is associated with the local inflammatory reaction [xxxii].

Different pain scales have been developed in this type of research to measure the degree of pain, direct treatment choices, and track efficacy. modified verbal descriptor scale (VDS) developed by Wang et al. [i] and translated into Arabic by Hagras et al. [xxvi] was used. It was preferred over different methods of evaluation because of its simplicity, and easiness to be understood by the patients. When examining preoperative pain scores, the study focused exclusively on patients with scores between 0 and 6. This decision was informed by research indicating that elevated preoperative pain scores can profoundly impact postoperative pain experiences. [xxxiii].

The creation of novel calcium silicate-based endodontic compounds has been aided by the MTA's biocompatibility, bioactivity, and osteoconductive qualities. EndoSeal MTA is MTA based sealer which has favorable effect on postoperative pain [xxxiv,xxxv,xxxvi]

The purpose of the current trial was to compare the variation in post-obturation pain when EndoSeal MTA sealer (ES) was used in the obturation of root canals in single-rooted teeth with related periapical lesion with or without pre-application of GH, or with non-surgical debulking of periapical pathosis.

The findings of the current research demonstrated that the GH-ES, ES and XP-ES groups differed significantly with the lower scores at GH-ES group at 6, 24,48 hours. While following 72 hours and one week, there was no discernible variation between the three groups. But, within the same group there was a significant reduction in pain scores over different times.

When comparing the three groups, the GH-ES achieved a significantly lower pain score at 6, 24,48 hours. This may be attributed to the fact that EndoSeal MTA has been linked to lower postoperative pain, both in terms of frequency and intensity, than other sealers [xxxiv,xxxv,xxxvi]. This can be attributed to its favorable biological and physicochemical properties, including high biocompatibility, high alkalinity, and slight expansion [xxxvii].

With regards to Growth Hormone, it has shown that it downregulates pro-inflammatory cytokines such as TNF-α, IL-1β, and IL-6, while promoting anti-inflammatory mediators. This modulation reduces periapical inflammation, thereby lowering postoperative discomfort [xxxviii]. Also, GH stimulates fibroblast proliferation, collagen synthesis, and angiogenesis which accelerates the healing of periapical tissues damaged during root canal preparation, Faster tissue repair limits prolonged nociceptor activation. By supporting Schwann cell activity and axonal repair, aiding in recovery of nerve fibers affected during instrumentation or by infection. It helps to reduce peripheral sensitization and subsequent pain amplification. GH may prevent exaggerated central pain responses by decreasing sustained nociceptive input from inflamed periapical tissues [xxxix]. Also, GH improves immune response by enhancing macrophage and neutrophil function, aiding in faster elimination of microbial remnants, reducing the risk of flare-ups and associated pain [xl]. Finally, it has been shown that Growth Hormone administration after surgery may have a complex relationship with postoperative pain, impacting both pain perception and the body's hormonal responses to stress. GH can influence pain by affecting nociceptor sensitization and potentially reducing fatigue associated with pain[xx,xxi,xxii,xxiii].

Although there was a significant variation in pain scores at 6,24,48 hours, there were no significant differences at 72hours and 1 week. This may be explained by GH's dual role as an anti-inflammatory mediator and a pro-healing stimulator. As previously stated, root canal instrumentation and obturation typically provoke an acute inflammatory response which characterized by the release of TNF-α, IL-1β, and IL-6, which stimulate nociceptors in the periodontal ligament and periapical tissues, leading to pain [xli]. GH counteracts this response by inhibiting pro-inflammatory cytokines and increasing anti-inflammatory mediators

such as IL-10, thereby dampening nociceptor activity. Additionally, GH induces the expression of bone morphogenetic proteins (BMP-2, BMP-4) and enhances the osteogenic differentiation of periodontal ligament stem cells (PDLSCs), promoting accelerated repair and regeneration [xlii]. Moreover, GH exerts neuroprotective effects by modulating sensory neuron excitability and pain perception pathways. This explains the sustained analgesic benefit observed up to 48 hours postoperatively. However, by 72 hours, natural resolution of inflammation occurs even in untreated cases, as macrophages shift from a pro-inflammatory (M1) to a pro-healing (M2) phenotype, and baseline pain levels converge. Thus, GH's impact is most noticeable when inflammations are in their acute stages and repair.

Regarding, non-surgical debulking using XP-Endo Finisher file, as a minimally invasive endodontic procedure designed to remove chronically inflamed periapical tissue through the root canal, avoiding surgical access like an apicoectomy [xvii]. The findings of the current research demonstrated that the XP-ES group recorded the highest pain levels between the three groups. This may be attributed to many explanations; Enlarging the foramen likely stimulates periapical tissues more intensely by widening the canal's terminus, which can cause inflammation and pain [xviii]. Also, instruments like the XP-Endo Finisher, especially when used with foraminal enlargement, can force more debris and irrigant beyond the apex. This extrusion is a known trigger for postoperative pain due to peripheral irritation [xliii]. Non-surgical debulking with XP-Endo Finisher targets chronically inflamed periapical tissue. While effective in decontamination, this aggressive activity in inflamed tissue areas can elicit pain as inflammatory mediators are disturbed or released deeper into the periapical zone. In contrast, XP-Endo Finisher used alone (without foraminal enlargement) tends to produce only mild postoperative pain, indicating that it's the combination with apex widening that elevates pain levels [xix].At last, the local application of growth hormone before root canal obturation appears to create a more favorable healing environment in periapical tissues, leading to reduced inflammation, enhanced repair, and decreased nerve sensitization. These combined effects likely contribute to lower postoperative pain scores. While using of XP-Endo Finisher file in non-surgical debulking of chronically inflamed periapical tissue through the root canal appears to make high levels of postoperative pain. While preliminary data are promising, further clinical trials are required to establish standardized protocols and evaluate long-term safety in dental applications.

CONCLUSION

Growth Hormone application before root canal obturation in teeth with periapical lesion, effectively reduces post-obturation pain.

DECLARATIONS

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Competing Interests

The no competing interests .

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