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Original Article

Evaluation Of Postoperative Pain andExtrusion Following Ultrasonic Activation of Bioceramic Sealer with Symptomatic Irreversible Pulpitis: A Randomized Clinical Trial

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Abstract

Aim: To evaluate postoperative pain and extrusion after ultrasonic activation of CeraSeal bioceramic sealer in symptomatic irreversible pulpitis. **Subjects and methods:** Thirty-two mandibular premolars (single root/canal) with irreversible pulpitis were included after confirmation of the diagnosis. Standard endodontic treatment was done in a single visit. Patients were placed into two groups (n=16) ; in the intervention group, ultrasonic activation of CeraSeal (20 seconds) while no activation was done in the control group. Obturation was performed using modified single cone technique, and pain was evaluated preoperatively, after 6,12, 24 and 48 hours using modified Visual Analogue Scale (VAS). Analgesic intake was recorded for 48 hours. Baseline and outcome data were statistically analyzed. **Results:** Postoperative pain incidence was significantly affected by ultrasonic activation at 6 hours (6% reported severe pain in intervention group to 37.5 % in control group)(P =.01) while the effect was not significant at 12, 24 and 48 hours. Analgesic consumption and sealer extrusion were not affected by ultrasonic activation. **Conclusion:** Postoperative pain was less after 6 hours when CeraSeal was ultrasonically activated compared to the control. Ultrasonic activation of CeraSeal did not negatively affect postoperative pain analgesic intake or sealer extrusion compared to the control group.

Keywords: Postoperative pain, Ultrasonic activation, bioceramic sealer , extrusion, irreversible pulpitis.

Introduction

Root canal treatment aims to minimize microorganisms in root canals which is one of the main contributing factors behind development of postoperative pain. The International Association for the Study of Pain (IASP) stated that pain is “An unpleasant sensory and emotional experience associated with or resembling that associated with actual or potential tissue damage”(1). Hence, optimum root canal treatment should aim to minimize pain postoperatively which is a regularly experienced patient-related hurdle.

A variation in reported postoperative pain from 3-58% was described (2, 3). Pain typically progresses to its maximum levels within first 24 hours, then starts subsiding after 48 hours till its minimum values are reached (4).

Postoperative pain following endodontic therapy may be precipitated by an incitement of the inflammatory process periapically due to the potential extrusion of infected dentine chips from the apical terminus during filing, irrigants, or materials as gutta percha or endodontic sealers. The nerve fibers located in the periodontal ligament increase their neuropeptide expression as a consequence (5).

After the cleaning and shaping processes, the main canal, ramifications and lateral canals must be sealed in three dimensions to prohibit bacterial colonization and multiplication inside the root canals or in the periodontium (6). Traditionally, endodontic sealers and gutta-percha have been used to fill root canals. Such sealers may come into immediate contact with the periapical tissues through lateral canals and apical terminus even though they are designed to be employed inside the root canal. So, it became sensible to suppose that sealers would trigger inflammatory reactions and excite sensory nerves. Accordingly, postoperative pain accompanying root canal therapy may be attributable to endodontic sealers (7).

According to studies of cytotoxicity, resin-based sealers emit noxious monomers that can exacerbate oxidative stress in living cells (8). This emission of reactive oxygen species may be correlated to the pain-inducing tissue inflammation that is caused by it. As opposed to resin-based sealers, calcium silicate-based bioceramic sealers display limited cytotoxicity, yet they still show some cytotoxicity (9).

Bioceramic sealers being biocompatible and hydrophilic, expand during setting, creating a "self-seal." Such expansion can result in up to 0.2% upon conclusion of the setting reaction, coupled with chemical and micromechanical binding, all contribute to the BC's increased adherence to root canal walls. Furthermore, the high pH (12.8) during the first 24 hours allows the environment to be exceedingly antimicrobial. As a result, superior three-dimensional obturation will ensue, hence, an improved seal and achievement of goals of root canal therapy will be realized (10).

The inadequacy of the sealer penetration into anatomical variances of root canal system, particularly in the apical portion, is a shortcoming of all traditional obturation approaches. Ultrasonic activation of the bioceramic sealer promotes superior sealer projection into anatomical intricacies, and further inwardly into the dentinal tubules with fewer gaps (11). In vitro testing showed that ultrasonically agitated sealer placement yielded a far greater percentage of sealer penetration depth in relation to other sealer placement techniques (12).

Owing to the promising results shown by in-vitro studies (13,14), the aim of this trial was to evaluate the effect of ultrasonic activation of bioceramic sealer CeraSeal on postoperative pain, analgesics intake and sealer extrusion when compared to non-activated placement of sealer in symptomatic irreversible pulpitis in mandibular premolars. The null hypothesis was that ultrasonic activation of bioceramic sealer would have no effect on postoperative pain, analgesics intake and extrusion compared to non-activated sealer.

Subjects and Methods

This prospective, double-blinded, parallel, and randomized clinical study was approved by the Ethics Committee of Cairo University Faculty of Dentistry, Giza, Egypt (Approval No. 10/4/22). The study protocol was recorded in the www.clinicaltrial.gov, with the NCT number (NCT05289791) and the PRIRATE guidelines (2020) for randomized trials were followed (15).

Patient Selection

The patients with a noncontributory medical history and who were referred to the Endodontic Department of Cairo University Faculty of Dentistry between April 2022 and September 2022 were screened. Patients were between 18 and 50 years old, had no allergies to local anaesthetic agents or systemic diseases, and had no previous root canal treatment. The inclusion criteria were as follows: Mandibular premolar teeth with preoperative sharp (moderate or severe) pain according to the pain score indicated on modified VAS chart preoperatively (modified VAS scale is divided into 4 categories 0 no pain, 1-3 mild ,4-6 moderate, 7-9 severe and 10 most excruciating pain), positive response to cold sensibility test by ethyl chloride (Egyptian Pharmaceutical Trading Company, Egypt) and normal periapical radiographic appearance or slight widening in lamina dura. The exclusion criteria included: Teeth having necrotic pulp, history or presence of swelling or fistulous tract, acute / chronic periapical abscess, evidence of periodontal bone loss, non-steroidal anti-inflammatory drug allergy and taking analgesics, anti-inflammatories, or antibiotics within 7 days. All patients included in this trial were informed about the study, and consent forms were obtained.

Sample Size

Based on a pilot study conducted on 10 patients (since no previous studies matched the intervention), and using a statistical power of 80% and alpha error of 5%, 14 patients were to be included in each group. Given the possibility of dropouts throughout the study, it was planned to recruit 15% more participants and conduct the study on 16 patients per group. Finally, 32 patients (7 men and 25 women) were included.

Randomization of groups

The study had two treatment groups (Ultrasonic activation or control group). A random sequence generator software (http://www.random.org/) was used to randomly place patients in each group. A single clinician executed all root canal treatments in one visit. Numbers of patients was written on 8 folded papers and placed in an opaque sealed envelope. When an outpatient met the eligibility criteria, the patient was asked to draw from the concealed envelope containing a number which determined his assignment to one of the 2 groups according to the randomized sequence. The assistant supervisor generated the random sequence and assigned the study participants to one of the 2 groups of the trial (Intervention or control).

The study was patient- and statistician-blind; where the participant and the statistician were not informed of the intervention used.

Root canal procedure

After confirming with cold sensibility testing using ethyl chloride spray that teeth were vital, a pain scale chart modified Visual Analogue Scale (VAS) was given to the patient and the patient was taught how to record the pain level. Consequently, the patient was instructed to note the pain level before treatment. An initial radiograph was taken (FONA Digital ScaNeo imaging plate size 2), then the tooth was anaesthetized using inferior alveolar nerve block technique by 2% mepivacaine hydrochloride with 1:100,000 levonordefrin (1.8 ml, Alexandria for Pharmaceuticals, Egypt), and intrapulpal injection was the supplemental anesthesia of choice when needed. Access cavity was done using an endo-Z bur (Dentsply Maillefer, Ballaigues, Switzerland). Further confirmation of the diagnosis was achieved upon visualization of bleeding from access.

The tooth was isolated with a rubber dam (Dental Dam, Sanctuary Dental, UK), and the canal was explored for patency with #8 or #10 K- files (MANI. Industrial Park, Tochigi, Japan) in a watch-winding motion. Working length (w.l) was determined using a Root ZX

electronic apex locator (J. Morita, USA), and it was confirmed using a periapical radiograph to be within 0.5 -1 mm from the radiographic apex. Mechanical preparation was done by crown-down technique using EdgeEndo rotary instruments (EdgeEndo, Albuquerque, New Mexico) in continuous rotary brushing motion using endodontic gear reduction torque-controlled x-smart motor at speed 400 rpm, torque 2 Ncm ending the preparation at size 40.04.

The canal was irrigated with 3 ml 2.5% sodium hypochlorite solution (Medical company, Egypt) between every subsequent instrument, and introduced to the canal using a 27-gauge side-vented needle placed without binding; short 1mm of the w.l. Canal was dried, and master cone radiograph was taken.

According to the randomization sequence, patients were assigned to one of 2 groups: interventional group (Ultrasonic activation of CeraSeal group, n=16): Injection of CeraSeal (Meta Biomed, Korea) in coronal third of the canal, then non-cutting ED 62 ultrasonic tip (Guilin Woodpecker Medical Instrument) was introduced to the canal 2 mm short of the w.l and activated for 20 seconds; 10 seconds buccolingually and 10 seconds mesiodistally prior to obturation because the ultrasonic tip oscillates in single plane.

Control group (Non-activated CeraSeal group, n=16): CeraSeal was injected into the canal in the same manner as the interventional group without activation. To facilitate patients blinding, the ultrasonic tip was activated in the patients' mouth above the tooth to mimic the intervention group. Master cone was then seated in place and modified single cone technique was used (a spreader size 30 was introduced next to master cone to ensure proper coronal sealing and accessory points were placed till spreader could no longer be placed). Access cavity was sealed with temporary restoration and patient instructed to return for final restoration placement.

Pain was assessed immediately after obturation, at 6, 12, 24 and 48 hours postoperatively using modified VAS (it takes the form of 10 cm line tethered by two limits "No pain" and "pain as bad as could be" and numbered from 0 to 10. The level of pain was classified into 4 categorical scores: None(0); Mild(1-3); Moderate(4-6); Severe((7-10) (16). In case of severe or persistent pain, they were instructed to take Ibuprofen 400 mg (Abbott Pharma, Egypt) not less than 6 hours apart, and to record their tablet intake within 48 hours post-operatively. The postoperative radiograph was examined by the clinician and a 3rd party investigator to assess the presence of sealer extrusion.

Statistical analysis

All data were collected and tabulated. Baseline data about age and gender was collected from each patient. Preoperative pain intensity and Modified VAS for postoperative pain intensity was collected for each group. Numerical data were presented as mean, standard deviation (SD). Data were explored for normality by checking the data distribution using Kolmogorov-Smirnov and Shapiro-Wilk tests. Parametric data were analyzed using independent t-test for comparisons between two groups , Mann Whitney test for non-parametric data, categorical data were analyzed by chi2 test. The significance level was set at $p \leq 0.05$.

Results

All 32 patients were included in the statistical analysis; the process of patient enrollment and each phase of the trial is shown in Figure 1. Age and gender distribution were comparable between the groups, and no statistically significant differences were found ($P > .05$) as seen in Table 1.

The incidence of postoperative pain is presented in Figure 2 and was significantly lower in the intervention group compared with the control group at 6 hours ($P=.01$), while the other tested intervals showed no statistical significance ($P > .05$). At 6 hours postoperative, the intervention group had 6 %

reporting severe pain to 37.5 % in control group. There was no significant difference in pain intensity between the 2 groups at all time intervals as seen in Table 2.

There was a decrease in mean pain score of intervention group compared to control group over time at 6 hours which was not statistically significant while it was nearly equal in the remaining intervals as seen in Figure 3.

In terms of incidence of analgesic intake (31.2% in intervention group versus 50% in control group), there was no statistically significant difference between the 2 groups, (P=.2).

Table (1):The frequency & percentage of gender and mean and standard deviation of age for tested groups

ns; non-significant (P >.05)

Variables		**Demographic data**				
		Non-activated group		**Ultrasonic activation group**		**p-value**
		N	**%**	**N**	**%**	
Gender (N, %)	Males	3	18.8%	4	25%	0.6ns
	Females	13	81.2%	12	75%	
Age (Mean ± SD)		35 ± 6.354		31.375 ±10.048		0.23ns

Table (2):Intensity of pre & post-operative pain of the tested groups after 6 hours, ,12 hours, 24 hours , and 48 hours.

	Non-activated group		**Ultrasonic activation group**		**P value**
	Median (mini-max)	**Mean ±SD**	**Median (mini-max)**	**Mean ±SD**	
Preoperative	**8(5-10)**	**8.13±1.75**	**8(6-10)**	**8.13±1.54**	**0.9ns**
immediate post operative	**0(0-4)**	**0.94±1.34**	**0(0-7)**	**1.44±2.61**	**0.8ns**
After 6hrs	**4(0-10)**	**4.88±3.22**	**3.5(0-8)**	**3±2.34**	**0.9ns**
After 12hrs	**2.5(0-7)**	**2.94±2.35**	**3(0-8)**	**3.13±2.36**	**0.7ns**
After 24hrs	**1(0-6)**	**1.88±2**	**1(0-8)**	**1.88±2.25**	**0.9ns**
After 48hrs	**0(0-5)**	**1.25±1.84**	**0(0-8)**	**1.25±2.29**	**0.8ns**

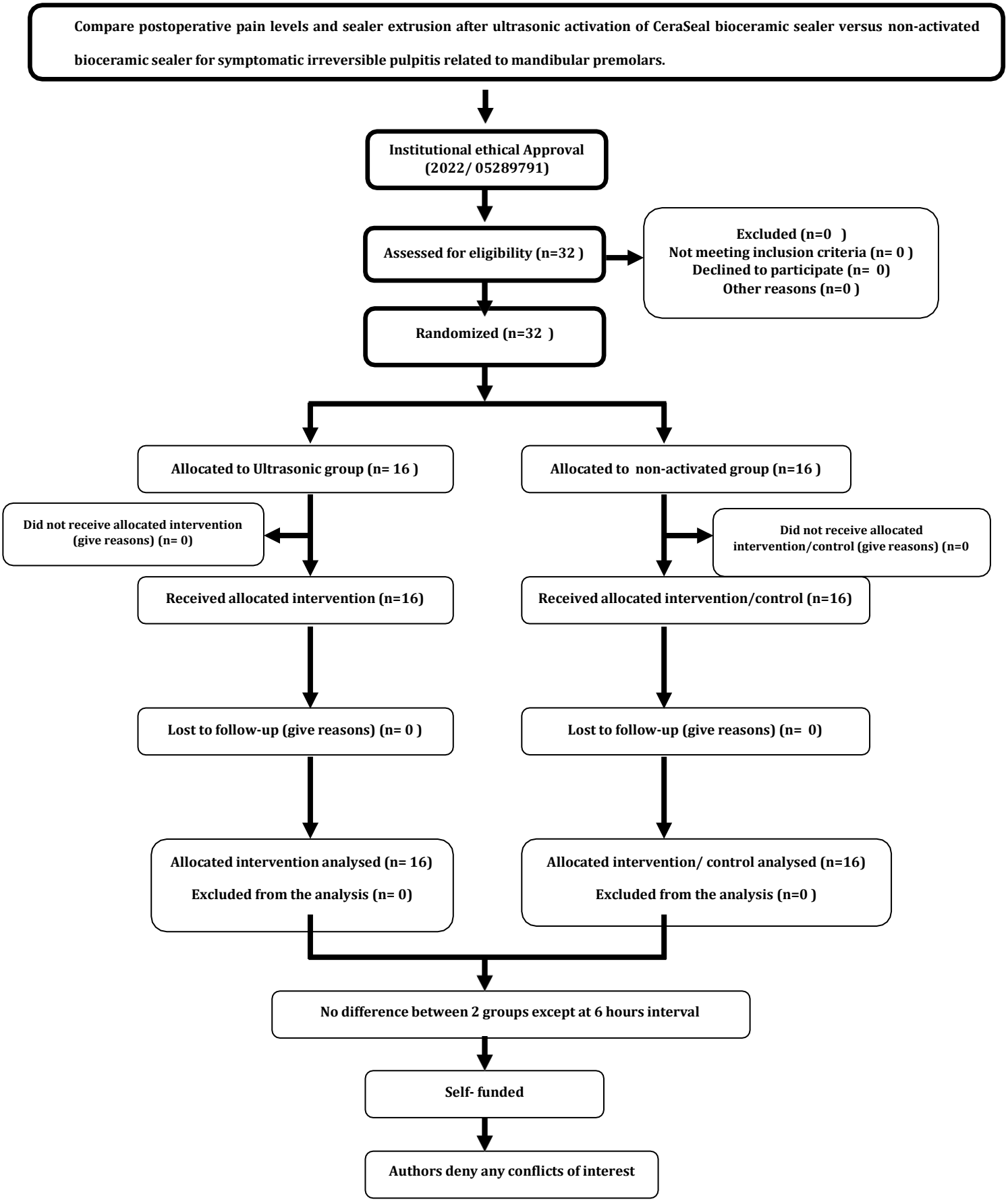

Figure (1): PRIRATE 2020 flowchart

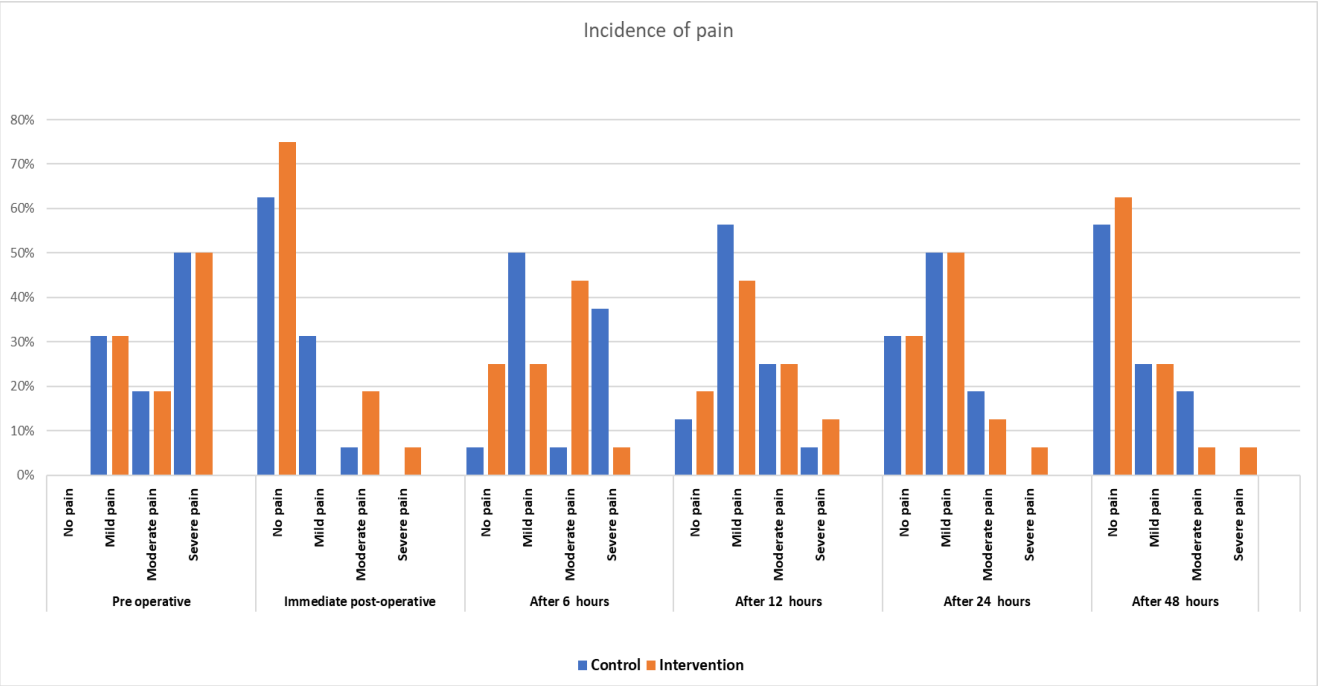

Figure (2):Bar chart representing the incidence of pain at different time intervals for each group.

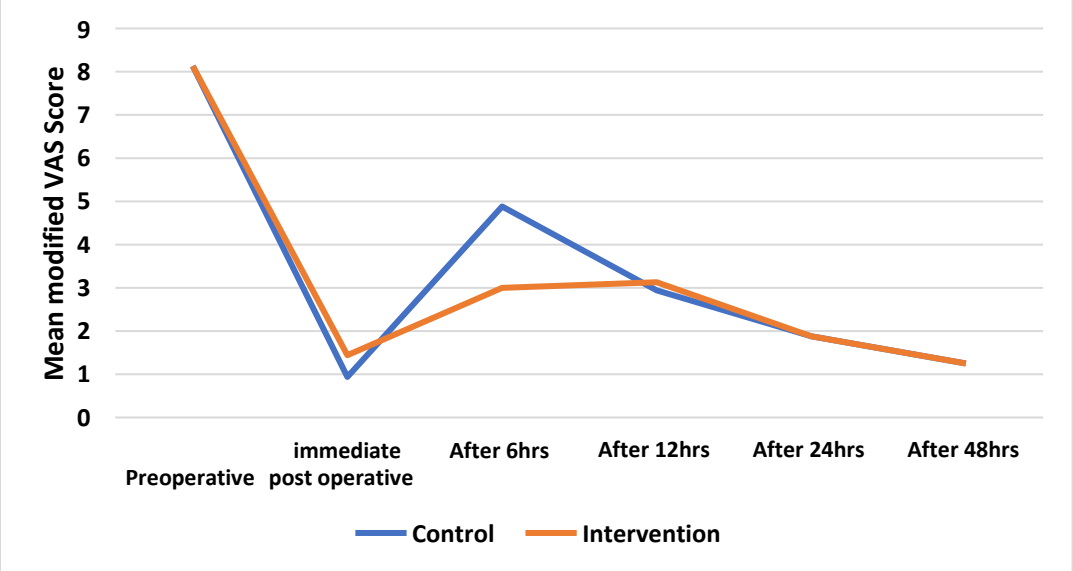

Figure (3):Line chart for intensity of post-operative pain at different time intervals for studied groups.

There was no statistically significant difference in incidence of sealer extrusion (25% in intervention group versus 12.5% in control group) between the tested groups (P= .3) as observed in Figure 4.

The correlation between preoperative pain and postoperative pain at 6 hours was insignificant (r= -.063, P value >.05),and the correlation between preoperative pain and pain at 12 hours was non-significant as well (r =-.06, P value >.05).

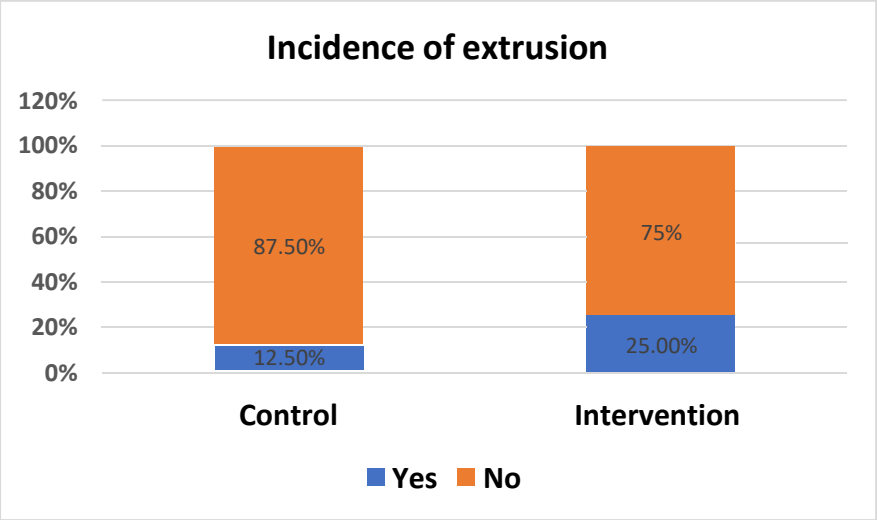

Figure (4):Bar chart representing incidence of extrusion.

Discussion

Endodontic treatment should hinder bacterial infiltration, decrease the chance of reinfection, and maintain low bacterial residual levels. Because of the elliptical outline of the radicular space (17), it is challenging to ensure

dense root canal filling which is well adapted without voids to entomb bacteria depriving it of nutrition and space through three-dimensional obturation (18).

The use of ultrasonic activation for sealers (19) was recommended particularly for bioceramic sealers (13, 14, 20). This is owing to increase in pushout bond strength of bioceramic sealers (21), better adaptation and penetration into dentinal tubules (22), and less gaps and voids formed (19) when bioceramic sealers were ultrasonically agitated. This is bound to ensure 3-D obturation of root canals and better achieving of endodontic goals.

Sealers can play a vital role in post-operative pain by interacting with the periapical tissues via the apical foramen and lateral canals. This occurs in form of a localized inflammation with the sealer's composition directly affecting the degree of inflammation and thus, affecting postoperative pain intensity (23). Sealers were found to directly stimulate trigeminal nerve cells, resulting in a large release of calcitonin gene-related peptide (CGRP) and, consequently, causing pain and neurogenic inflammation. However, bioceramic sealers were observed to fail in stimulation of trigeminal neurogenic cells and obstructed the release of CGRP, thus may positively affect post-operative pain and inflammation (7).

Additionally, the high pH established for calcium silicate-based sealers promotes antibacterial effect (24). Some bioceramic sealers were found to release Calcium ions, thus, encouraging mineralization (25,26). This coupled with their ability to reduce pro-inflammatory mediators (26) could be predictive of reduction in post-operative pain due to periapical inflammation.

The effect of sealer extrusion is controversial in literature. Some authors claim that as long as there is no periapical lesion, the apical extent of the root canal filling material has no effect on the endodontic outcome (27). Others, however, have reported that sealer extrusion does not interfere with healing regardless (28).

CeraSeal is a premixed sealer composed of calcium silicates, aluminates and thickening agents. It was found that CeraSeal had better cell viability, attachment, migration rates, significantly higher mineralization capacity (higher calcium ion release) than Endoseal (25). The bioactivity of CeraSeal can neutralize acids and play an active role in mesenchymal cell differentiation and tissue mineralization promoting healing (29). These results were corroborated by Oh et al. where cell viability with CeraSeal markedly increased after 7 days compared to other groups (26). Moreover, the level of proinflammatory cytokines of CeraSeal was similar to those of control proving their high biocompatibility, and CeraSeal showed high levels of an anti-inflammatory cytokine which was interpreted as an indication of anti-inflammatory effect of CeraSeal.

Ultrasonic activation resulted in better marginal adaptation to root dentine, greater intratubular penetration, and greater bond strength (11).When compared to sonic activation and lentulospiral, Usta & Punia demonstrated that ultrasonic activation of CeraSeal yielded the highest push-out bond particularly in the apical third of the root (30). Abo El-Mal recommended the use of single cone with ultrasonic agitation of CeraSeal since it resulted in better sealing and filling quality (14).

Post operative pain incidence was not statistically significant between the 2 groups except at 6-hour interval where ultrasonically activated group showed less pain incidence. The fact that ultrasonic activation increased calcium ion release and pH of bioceramic sealer (31) combined with the anti-inflammatory potential of CeraSeal (26) could explain the decrease in postoperative pain after 6 hours. Conversely, various studies on postoperative pain with bioceramic and resin sealers showed no significant difference in first 48 hours postoperatively (9).

The number of analgesic tablets consumed was statistically not significant between both tested groups which was in line with results of a study by Fonseca et al.(9). According to Sponchiado Jr. et al., a small number of patients required analgesics throughout their postoperative period regardless of sealer type which supported that calcium silicate-based sealers and resin-based sealers do not differ in postoperative pain intensity (4).

Although, ultrasonic agitation enhanced the flow of sealers in in-vitro tests which could predispose to higher sealer extrusion, there was no significant difference in sealer extrusion for both groups. This is supported by Song et al. where sealer extrusion of Ceraseal was found not statistically significant compared to tested sealers (32). Additionally, various studies are in agreement that there was no significant correlation between bioceramic sealer extrusion and incidence of postoperative pain or its intensity (9). This is explained by the fact that the amount of extruded cement reported in the studies was miniscule, and insufficient to cause substantial inflammatory reaction in the periapical tissues (33). Unfortunately, there are no clinical studies evaluating effect of ultrasonic activation on extrusion of CeraSeal to date.

Correlation between preoperative pain and incidence of postoperative pain after 6 and 12 hours was insignificant. A study by Albashaireh and Alnegrish depicted similar results (34). However, this is in contrast with findings of Tan et al. where moderate to severe preoperative pain was found to be a prognostic factor of postoperative pain (35).

On studying the available literature concerning ultrasonic activation of bioceramic sealers, it was worth noting the lack of standardization in

the technique and duration of ultrasonic activation (from 3 seconds (19) to 10 (36) or 20 seconds (21)), and whether it was applied in direct contact with the sealer (21) or indirectly (19). In some studies, ultrasonic activation was carried out with a tip (21) while in others it was done with a file attached to an ultrasonic handpiece. Only a handful of studies noted the level to which the ultrasonic tip was introduced inside the canal and the activation in both buccolingual and mesiodistal planes (21,36). This variation in methodology could explain the variability in results of available studies and calls for a standard protocol with regards to activation of sealers to allow results to be easily compared and more acceptable to scientific community.

This trial is the first in-vivo study evaluating the effect of ultrasonic activation of bioceramic sealer CeraSeal on postoperative pain and sealer extrusion in mandibular premolars. The results were encouraging showing less postoperative pain at 6-hour interval in the ultrasonic group. However, more studies are needed with larger sample size and other tooth types to reach a more definitive conclusion. Longer follow-up intervals is needed to evaluate the outcome of sealer extrusion. A comparison between direct and indirect application of ultrasonic activation is required to determine the most effective method to enable the adoption of a standard protocol regarding optimum power setting of ultrasonic energy, the level to be introduced to, the time of activation and technique.

Conclusion:

Within the limitations of this study, it can be concluded that:
Postoperative pain was less after 6 hours when CeraSeal was ultrasonically activated compared to the control. Ultrasonic activation of CeraSeal did not negatively affect postoperative pain analgesic intake or sealer extrusion compared to the control group.

Conflict of Interest:

The authors declare no conflict of interest.

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This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors

Ethics:

This study protocol was approved by the ethical committee of the faculty of dentistry- Cairo university on: 26/4/2022, approval number: 10/4/22

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