



REVIEW ARTICLE

Endodontic postoperative flare-up: An update



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Abstract Endodontic treatment corresponds to a combined chemical and mechanical approach, followed by a three dimensional hermetic obturation, that eliminate the pulpal and periradicular disease and boost healing and repair of periradicular tissue. Despite the advances in the endodontic field, the inter-appointment flare up remains a true nightmare that encounters every dentist. This complication commences a few hours or days after root canal procedures and it is characterized by the development of pain and/or swelling, requiring an unscheduled appointment for emergency treatment. Different studies showed that flare-ups represent a multifactorial phenomenon including mechanical, chemical and microbial factors. In addition, a correlation was found between flare-up and age, gender, tooth type, presence of preoperative pain, tooth condition before treatment, irrigation techniques, number of visits as well as intracanal medication. Moreover, some medicine intake was proved to be efficient in controlling this postoperative pain. However, a clear procedure to avoid its occurrence is yet to be established. In this review, we summarize knowledge about the etiology of flare-up and its related factors. This could be effective in helping dentists to adapt some strategies to prevent it.

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1. Introduction

Dentists always seek to preserve a tooth. Once a tooth disorder is encountered, endodontic therapy can be applied as one of the routinely employed procedures. Endodontic treatment is a chemo-mechanical method of disinfection of root canals followed by three dimensional hermetic obturation. It is employed to eradicate the pulpal and *peri*-radiculare disease-causative agents and to enhance *peri*-radiculare tissue recovery (Udoye Ch, 2010).

Despite the modern root canal procedures and new rotary systems, the inter-appointment flare up remains a major issue

that encounters every dentist. Flare up is a postoperative pain that starts shortly after root canal therapeutic procedures and is manifested as pain and/or swelling episodes, requiring urgent treatment with an unscheduled appointment (Siqueira, 2003).

Reports showed that the rate of flare up after endodontic treatment ranges from 1,4% to 16% and can reach 50% in some cases (Ehrmann et al., 2003; Udoye Ch, 2010; Onay et al., 2015; Azim et al., 2017). Many factors (such as the protocol followed by the researchers, the criteria of evaluation of pain and swelling and the experience skills of the dentist) can explain this difference of rates (Iqbal et al., 2009; Gotler et al., 2012). According to Iqbal et al. (2009), comparison of flare-up incidence among studies remains challenging due to both the absence of any gold standard and the variable definitions (Iqbal et al., 2009).

The best way to face the existence of such risk “flare up” is by adopting some strategies of prevention. But first we should know the etiology of this distress. It is widely established that flare up is a multifactorial phenomenon that could be associated with microbial, mechanical, chemical, host and treatment factors as well as endodontic infection (Gondim et al., 2010; Azim et al., 2017).

2. Causes of flare-ups

Flare up is a result of the periradicular tissues damage during endodontic treatment. Once this damage happens, a fighting response arises via the body defensive system, leading to pain and swelling (Siqueira, 2003; Siqueira and Barnett, 2004). It is a multifactorial event, influenced by the severity of the periapical lesion and its irritation (Siqueira and Barnett, 2004; Gondim et al., 2010). (Fig. 1)

2.1. Microbial factors

The root canal system complexity presents a challenge during the endodontic procedure (cleaning and shaping). Endodontic

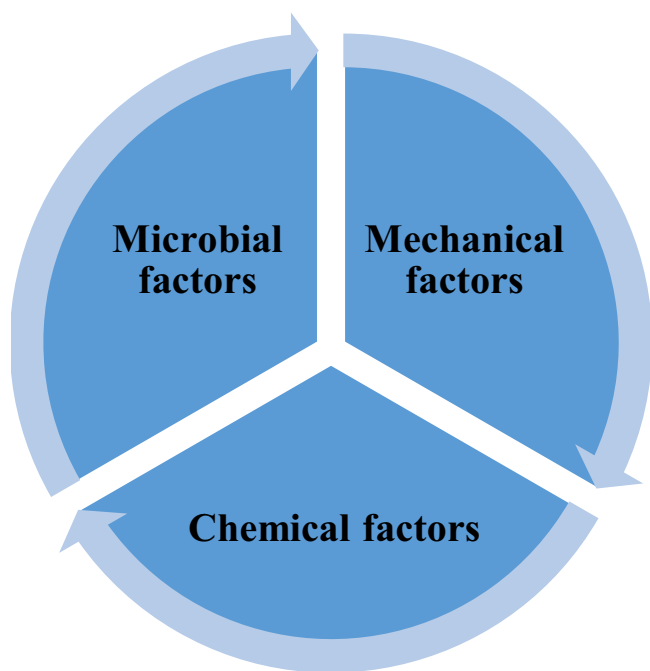


Fig. 1 Factors that influence the development of the post-endodontic flare-up.

treatment attempt to eliminate pathogenic microorganisms. A balance exists between the microflora and the human immune system, called “local adaptation syndrome” (Gondim et al., 2010). This balance that exists in the asymptomatic apical periodontitis could be corrupted during the endodontic treatment after the extrusion of infected debris in the periradicular tissues, thus causing flare up (Siqueira, 2003; Siqueira and Barnett, 2004). Flare up intensity is, therefore, affected by the quantity and virulence of the microorganisms in the periodontal tissues (Siqueira, 2003).

In flare ups associated with symptomatic apical periodontitis cases, species of *Porphyromonas endodontalis*, *Porphyromonas gingivalis*, *Prevotella* and *F. nucleatum* bacteria were frequently isolated (Siqueira et al., 2001). Flare ups in such cases might be attributed to: (1) inadequate chemomechanical preparations; (2) disuse of intracanal medications between appointments; (3) insufficient asepsis during the procedure; (4) uncleaned carious tissue; or (5) non hermetic temporary filling between appointments or after treatment if left for more than two weeks (Naoum and Chandler, 2002; Siqueira and Barnett, 2004; Gondim et al., 2010).

2.2. Mechanical factors

Mechanical factors, during the endodontic treatment, could be associated with flare up mechanism, since during this stage, an amount of debris, necrotic pulp masses, irrigative solutions and microorganisms can be pushed from the root canal to the apical periodontal tissues, leading to inflammation and postoperative pain that disturbs healing of periradicular tissues (Tinaz et al., 2005).

Previous studies showed that, a combination of crown-down technique with engine-driven nickel titanium Ni-Ti systems will lead to a minimal extrusion of debris (Siqueira, 2003).

Reddy and Hicks showed that cleaning canals with manual instruments using step-back technique leads to a higher amount of extrusion of debris (2.58 mg) into the periradicular tissues than NiTi rotational mechanical instruments (0.5 mg) with crown-down technique (Pasqualini et al., 2012). These results are consistent with other studies showing that rotary instruments application during endodontic treatment leads to a lower incidence of flare up compared to manual instruments (Kashefinejad et al., 2016).

Recently, with the introduction of the reciprocating instruments into the endodontic market, many studies compared them with rotary instruments, regarding their association with the flare up issue. Remarkably, reciprocating instruments showed a higher incidence of post-operative pain than Rotary instrument (Eyuboglu and Ozcan, 2019). However, Garcia et al. showed that endodontic retreatment with Reciprocating instruments resulted in lower values of postoperative pain compared to ProFile (Garcia-Font et al., 2018).

During endodontic treatment, it is essential to determine the working length (WL) accurately. Any wrong working length can lead to flare up (Iqbal et al., 2009). According to the endodontic glossary, working length is defined as: “the distance from a coronal reference point to a point at which the canal preparation and obturation should terminate”. Various methods are used to establish correct working length. These include use of conventional or digital radiography, tactile method, moisture on paper point and the apex locator

(Ruddle, 2002). An overestimation of WL leads to over instrumentation, so infected debris and filling material will be extruded in the periodontal tissues, causing their irritation, and leading to flare up (Siqueira and Barnett, 2004). Alternately, an underestimation of WL leads to an incomplete debridement of the endodontic system, and consequently to a less efficient treatment and prognosis (Tinaz et al., 2005). So a simultaneous control of WL during endodontic treatment will help to prevent a postoperative pain (Arslan et al., 2017).

During endodontic treatment, it is recommended to maintain the apical patency, by using a K-file instrument (#6, #8 OR #10) and make it go deeper than the WL measured; In order to avoid debris accumulation and thus obstruction formation during treatment. And this technique will improve the irrigation process by allowing the irrigation solution to access the apical third of the root canal and ensure a direct contact of the intracanal dressing and the periapical tissues. This would lead to a better outcome of the treatment concerning the post-operative pain (Yaylali et al., 2018). However, this technique may lead to apical extrusion of debris by the k-file and cause irritation of the apical periodontal tissues leading to post-operative pain (Goldberg and Massone, 2002). Some studies showed no significant relation between maintaining an apical patency and pain occurrence after treatment (Garg et al., 2017). Apical foraminal enlargement seems to be a promoting factor for flare-ups occurrence, because it is linked to higher level of debris extrusion during treatment (Borges Silva et al., 2017; Albuquerque et al., 2020).

2.3. Chemical factors

Substances used in endodontic treatment (such as: intracanal medicaments, irrigation solutions and sealer) might be toxic, causing irritation and flare up if they reached the periradicular tissues. The inflammatory response intensity is proportional to the amount of substances extruded (Hawker et al., 2011).

It has been shown that flare ups are often related to the use of resorcinol – formaldehyde resin in the obturation in endodontic retreatment. Moreover formaldehyde is considered cytotoxic, causing necrosis of living tissue and if extruded in the periradicular area will lead to pain and swelling (Moline, 2006).

Table 1 Studies findings about correlation between gender and flare-ups.

Study	Finding
(Naoum and Chandler, 2002) (Garcia-Font et al., 2018) (Walton, 2002) (Ali et al., 2016) (Nair et al., 2017) (Shresha et al., 2018) (Ng et al., 2004)	Women are more susceptible to develop flare ups than men
	No correlation between gender and pain after endodontic treatment

The type of solution used for irrigation during treatment has no influence on the incidence of flare-ups (Onay et al., 2015). However, in 2010, one study showed that the use of 5.25% sodium hypochlorite for irrigation was related to higher incidence of pain when compared to the use of 2% chlorhexidine solution (Bashetty and Hegde, 2010). Lately, Riaz et al. compared the same solutions with the same concentrations and observed no difference concerning postoperative pain (Riaz et al., 2018). In 2012, Fedorowicz et al., compared different solutions of irrigation (5.25% NaOCl, 5.25% NaOCl combined with 3% hydrogen peroxide and 5% of NaOCl used alone or in combination with proteolytic enzyme) and showed that postoperative pain after root canal treatment is not influenced by irrigant solutions (Fedorowicz et al., 2012). Another study showed that 5.25% NaOCl was associated with significantly lower postoperative pain compared to 2.5% NaOCl (Farzaneh et al., 2018). Recently, in 2020, 1.3% NaOCl has been shown to be associated with less intense and less frequent post-endodontic pain when compared to 5.25% NaOCl (Mostafa et al., 2020). These results, didn't match with those found by Verma et al. when they compared 2 different concentrations of sodium hypochlorite (1% and 5%) and did not find a significant difference in the clinical outcome concerning postoperative pain (Verma et al., 2019).

3. Risk factors causing flare-up after endodontic treatment

Risk factors that may lead to flare ups after endodontic treatment can be divided into two groups. The first group includes those related to the patient (demographics, general state of health, condition of the pulp and apical periodontal tissue, clinical symptoms and tooth which is being treated). The second group includes factors related to the therapeutic procedures (number of visits, retreatment and intracanal medicaments) (Walton, 2002).

3.1. Demographics

The correlation between incidence of flare ups and some demographic criteria like age and gender are still controversial. While different reports showed absence of correlation between the incidence of flare ups and age and gender of the patient (Walton, 2002; Onay et al., 2015), a report from El Mubarak et al. (2010) showed that post-operative pain often occur among patients with age ranging between 18 and 33 years old (Naoum and Chandler, 2002). Moreover, Azim et al.

(2017) stated that age is a strong predictor for flare ups, especially in patients older than 50 years (Azim et al., 2017). This result correlates with the one obtained by Nair et al. (2017) showing that patients in the age group of 40–60 years had a higher risk of developing flare-ups (Nair et al., 2017).

Concerning the gender factor, while some studies showed that women are more susceptible to develop flare ups than men (Naoum and Chandler, 2002; Walton, 2002; Ali et al., 2016; Nair et al., 2017; Garcia-Font et al., 2018; Shresha et al., 2018), other reports showed no correlation between gender and pain after endodontic treatment (Ng et al., 2004) (Table 1).

It is proclaimed that patients with diabetes mellitus are prone to flare-up (Armada-Dias et al., 2006). Recently Kaur et al. (2020) revealed that Interappointment Flare-ups in patients with Diabetes is higher than in patients without Diabetes (Kaur et al., 2020).

3.2. Condition of the pulp and apical periodontal tissue

The correlation between postoperative pain and the pulpal status (vital tooth or necrotic), is complex and still controversial where some reports identified a significant relation between these two factors (Segura-Egea et al., 2009; Gotler et al., 2012), others didn't (Ince et al., 2009; Ali et al., 2012; Pasqualini et al., 2012; Sevekar and Gowda, 2017) (Table 2). Moreover, some studies showed that necrotic pulp is positively correlated with postoperative pain (Walton, 2002; Siqueira, 2003; Tinaz et al., 2005; Gotler et al., 2012; Azim et al., 2017). This could be explained by the fact that microorganisms are essential for inflammation induction in the periradicular tissue, so it is logical that treatment of necrotic tooth will be related to a higher level of flare ups than in the case of vital tooth. However, different studies showed that a higher incidence of flare ups is related to vital tooth (Gotler et al., 2012).

Visible "Bone destruction" in dental radiograph was also considered to be a risk factor of post-operative pain and flare-up (Naoum and Chandler, 2002; Walton, 2002). It raises the chance of a flare in 9.64 times when detected (Iqbal et al., 2009). Genet et al. (1987) defined the relation between the size of the bone destruction area and post-operative pain: bone destruction of 5 mm and more is said to increase the probability of pain occurrence (Genet et al., 1987). In contrast, one study showed that teeth with a periapical lesion larger than 3 mm was significantly associated with less post-obturation pain than teeth with a smaller lesion (Ng et al., 2004).

3.3. Presence of pre-operative pain

A strong correlation found between existence of pain before the treatment and the incidence of pain after treatment (Shresha et al., 2018; Aoun et al., 2019). In 2018, Vieyra et al. showed a significant association between postoperative pain with previously symptomatic teeth and apical periodontitis (Vieyra et al., 2018). These findings are in agreement with the study done by Aoun et al. in 2019, they showed that pre-operative symptoms is a significant factor, that influence flare-up occurrence (Aoun et al., 2019). The virulent microorganisms in the infected root canal system causes the preoperative symptoms and if extruded during treatment into the periradicular area, they will lead to postoperative pain

Table 2 Studies findings regarding correlation of pulp condition and flare-ups.

Study	Finding
(Segura-Egea et al., 2009; Gotler et al., 2012)	There is correlation between postoperative pain and the pulpal status (vital tooth or necrotic)
(Ince et al., 2009; Ali et al., 2012; Pasqualini et al., 2012; Sevekar and Gowda, 2017)	No correlation between postoperative pain and the pulpal status (vital tooth or necrotic)

(Siqueira, 2003). Furthermore, a post operative pain will increase the level of stress of the patient, and this will negatively affect the immune system, thus increasing the possibility of developing a flare up (Walton, 2002). Torabinejad et al. (1994) observed a significant correlation between preoperative fear and the incidence of post-operative pain (Torabinejad et al., 1994).

3.4. Treated tooth

Endodontically treated-Mandibular molar are related to a high incidence of post operative pain (Segura-Egea et al., 2009; Ali et al., 2016; Shresha et al., 2018). This can be attributed to the fact that the mandibular arch have a cortically thicker plate compared to maxilla, especially at the level of molars. This, in turn, results in the accumulation of exudates in addition to a lower blood circulation, that will lead to a delayed healing (Ali et al., 2012). On the contrary, other reports showed no significant association between the tooth type and the incidence of flare ups after endodontic treatment (Onay et al., 2015; Nair et al., 2017).

3.5. Number of visits during the treatment

In endodontic treatment, the tooth status is considered as the main determinant if the treatment will be accomplished in one or more visits. When the tooth is vital or retreated with no clinical symptoms, one visit is recommended (Figini et al., 2008). In the case of a necrotic tooth with radiological changes in the periradicular area, two visits are recommended with the use of an interappointments intracanal medicament, for a maximal disinfection (Figini et al., 2008). However, in the last decades, a single visit of treatment was the most recommended (Qualtrough et al., 1999). This is feasible due to the huge advances in the endodontic field, such as NiTi rotary instruments, reciprocating instruments, apex locators, digital radiography, biocompatible sealer, microscopic endodontics and developed irrigation technique (Kishen et al., 2016).

While some studies showed no correlation between incidence of flare-ups and number of visits (Figini et al., 2008; Ince et al., 2009; Ali et al., 2012; Nair et al., 2017; Sevekar and Gowda, 2017; Riaz et al., 2018), others revealed the preference of a single treatment visit for a better outcome concerning flare-ups (Mohammadi et al., 2006; Onay et al., 2015). Oppositely, different studies showed that flare-ups are more common for single visit root canal treatment (Alomaym et al., 2019). These controversial results could be attributed to many factors including the sample size, endodontic technique used and tooth status (Table 3).

3.6. Intracanal medicaments

Antimicrobial intracanal medication with a well done endodontic treatment leads to a better outcome and less post-operative pain (Ehrmann et al., 2003; Singh et al., 2013; Samir Abouelenien et al., 2018). However, some studies showed no correlation between the use of the intracanal medication and the occurrence of postoperative flare-ups (Siqueira, 2003). Despite its effectiveness against microorganisms (Georgopoulou et al., 1993), calcium hydroxide Ca(OH)₂ effect was found to be limited on postoperative pain

Table 3 Summary of studies comparing post operative pain and number of visits during treatment.

Study	Finding
(Riaz et al., 2018); (Ali et al., 2012); (Ince et al., 2009); (Sevekar and Gowda, 2017); (Figini et al., 2008);	No correlation between incidence of flare-ups and number of visits
(Onay et al., 2015); (Erdem Hepsenoglu et al., 2018); (Fonzar et al., 2017)	Single visit treatment is related to a lower incidence of flare-ups
(Alomaym et al., 2019)	Flare-ups are more common for single visit root canal treatment

(Anjaneyulu and Nivedhitha, 2014). Singh et al. (2013) demonstrated that usage of chlorhexidine with or without Ca(OH)₂ reduces postoperative pain (Singh et al., 2013). In 2017, Sinhal et al. showed that 2% chlorhexidine gel and triple antibiotic paste reduce the interappointment flare-up and postoperative symptoms in diabetic patients, when compared to calcium hydroxide paste (Sinhal et al., 2017). These results are in agreement with those obtained by Swathi et al. in 2014, where Triple antibiotic paste was found to be more effective than calcium hydroxide in preventing the occurrence of flare-up (Pai et al., 2014). On the other hand, Ledermix is more effective in reducing postoperative pain when compared to Ca(OH)₂ (Ehrmann et al., 2003).

3.7. Irrigation

Irrigation is a main part of the endodontic treatment. Its major function is disinfection of the root canal systems (Haapasalo et al., 2014). It can be performed with either conventional manual syringe irrigation technique with needle or with different delivery and agitation techniques. An extrusion beyond the apex of chemically active solutions, secondary to debris, causes postoperative pain (Siqueira and Barnett, 2004).

A new study by Topçuoğlu et al., comparing two types of irrigation needles, showed that the use of double side-vented needles is more useful in decreasing postoperative pain when compared to conventional open-ended needle (Topçuoğlu, et al. 2020). Whereas Tavares et al., found no influence of the depth of insertion of the irrigation needle into the canal on the occurrence of pain after endodontic treatment (Tavares et al., 2020).

In the recent decades, new techniques were introduced to enhance the irrigation efficacy. Recently Susila et al. showed that mechanical active irrigation devices are beneficial in reducing post-operative pain and improving canal and isthmus cleanliness during Endodontics when compared to conventional irrigation (Susila and Minu, 2019). Irrigant activation using EndoActivator demonstrated effectiveness in reducing postoperative pain (Ramamoorthi et al., 2015; Yilmaz et al., 2019). Moreover, Ramamoorthi et al. observed that EndoActivator usage can be an effective method to reduce postoperative pain when compared to endodontic irrigating needle (Ramamoorthi et al., 2015). Further, the Application of EndoVac reduces significantly postoperative pain if compared to the conventional needle irrigation. (Gondim et al., 2010; Topcuoglu et al., 2018). Consistently, the continuous ultra-

sonic irrigation was found more useful than the conventional endodontic syringe irrigation in reducing the postoperative pain (Middha et al., 2017). In 2018, Topçuoğlu et al. compared four techniques of irrigation (needle irrigation without agitation with a side-port needle, sonic agitation, passive ultrasonic irrigation and manual dynamic agitation) regarding the endodontic postoperative pain; They showed that manual dynamic agitation causes greater postoperative pain after endodontic therapy (Topçuoğlu et al., 2018). Moreover, the Low Level Laser showed a good efficiency in decreasing postoperative pain (Metin et al., 2018; Nabi et al., 2018). The use of diode laser also reduces the post-operative pain after endodontic treatment (Genc Sen and Kaya, 2019). The addition of cryotherapy to the endodontic treatment can reduce the incidence of postoperative pain (Alharthi et al., 2019; Vieyra et al., 2019).

In a recent simulation study, many risk factors were compared in order to establish their relation to endodontic flare-ups and rank them in order of their importance. “Periapical lesion” and “preoperative pain” were found as the most important risk factors that showed the strongest impacts on endodontic flare-up, followed by the factor “number of visits”. Whereas, the least sensitive risk factors for endodontic flare-up were “retreatment,” “female gender,” “necrotic teeth,” and “analgesics.” (Aksoy et al., 2020)

4. Preoperative medicine intake for postoperative pain management

Preoperative intake of some medicines seems to be effective in decreasing post-endodontic pain. Such medications include a single dose of piroxicam, dexamethasone or deflazacort who showed an equal effect in controlling pain after endodontic treatment (Konagala et al., 2019). Ibuprofen, dexamethasone or diclofenac sodium if administered prior to treatment can help too, and the dexamethasone and tramadol submucosal injections can significantly reduce postoperative pain (Jorge-Araujo et al., 2018; Aksoy and Ege, 2020). A single dose of prednisolone can reduce pain in patients with symptomatic irreversible pulpitis (Praveen, et al. 2017; Veitz-Keenan and Ferraiolo, 2018). Kaladi et al. (2019) showed that a preoperative dose of ibuprofen (400 mg) or ketorolac (20 mg) in patients with irreversible pulpitis reduces pain after treatment with preference for ketorolac (Kaladi et al., 2019). Likewise, a buccal infiltration of ketorolac in similar cases can also have a pain-suppressive effect (Akhlaghi et al., 2019). Acupuncture was reported to be beneficial in pain suppression if administered prior to treatment in teeth with symptomatic apical periodontitis (Arslan et al., 2019). A very recent systematic review and meta-analysis, showed that a prophylactic administration of antibiotics has no superiority in preventing postoperative endodontic symptoms in patients with necrotic teeth (Shamszadeh et al., 2020).

5. Postoperative medicine intake for postoperative pain management

Corticosteroids seem to be effective in reducing postoperative pain after endodontic treatment (Shamszadeh et al., 2018; Suneelkumar, et al. 2018). Administration of Nonsteroidal

anti-inflammatory drugs (NSAIDs) and/or paracetamol can help to manage postoperative pain (Stamos et al., 2019). Fuller et al. (2018) showed that a postoperative administration of Oral methylprednisolone, did not significantly reduce pain in patients with necrotic or symptomatic tooth (Fuller et al., 2018). Occlusal reduction can be done too, for the purpose of reducing post endodontic treatment pain (Balevi, 2019; Emara et al., 2019). Interestingly, application of Photobiomodulation therapy after endodontic treatment caused a significant decrease in postoperative pain incidence (Lopes et al., 2019).

6. Prevention

Due to the fact that flare-up is a multi-etiological process, a prevention strategy should be taken into consideration. However, till date, no prevention strategy is scientifically approved and adopted by the endodontic community. Yet, some instructions are recommended during treatment, which could help to decrease the incidence of flare-up. This include:

- Asepsis: is the key of success of any endodontic treatment, and dentists should ensure the accomplishment of the endodontic treatment in aseptic conditions, avoiding any contamination. The use of rubber dam during treatment is one of these conditions (Siqueira, 2003).
- Adopting a chemico-mechanical procedure producing the less amount of debris extrusion in the periradicular area, and ensuring the debridement of the totality of the root canal system. On example is the combination of crown-down technique with engine-driven Ni-Ti Systems and an appropriate irrigation (Siqueira, 2003). The use of apex locator and radiology is essential for precising the working length WL. Some devices could be used to enhance the irrigation efficacy.
- The use of preoperative medicines such as: Ibuprofen, dexamethasone, diclofenac sodium, piroxicam, deflazacort, ketrolac or prednisolone, especially in cases with symptomatic irreversible pulpitis (Praveen et al., 2017; Jorge-Araujo et al., 2018; Veitz-Keenan and Ferraiolo, 2018; Konagala et al., 2019; Aksoy and Ege, 2020).
- Accomplishment of the endodontic treatment during one visit if possible, and use of intracanal medications between sessions for infected teeth (Ehrmann et al., 2003; Singh et al., 2013). In addition, prescription of postoperative medicine is efficient in controlling pain, like Corticosteroids, NSAIDs or paracetamol (Shamszadeh et al., 2018; Suneelkumar et al., 2018; Stamos et al., 2019).

7. Conclusion

Despite the huge development in the endodontic field, flare-ups still occur. It is a multifactorial phenomenon triggered by mechanical, chemical and microbial factors. Recent studies succeeded proved the efficiency of some actions or guidelines in reducing its incidence. Since many factors influence the incidence of flare-ups, prevention cannot be guaranteed by following a specific treatment protocol. Further studies are required to establish such procedure.

8. Ethics approval and consent to participate

Not applicable.

CRedit authorship contribution statement

Sanaa Bassam: Conceptualization, Investigation, Writing - original draft, Writing - review & editing, Visualization, Supervision. **Rima El-Ahmar:** Investigation, Writing - original draft, Writing - review & editing. **Sara Salloum:** Investigation, Writing - original draft, Writing - review & editing. **Sara Ayoub:** Investigation, Writing - original draft, Writing - review & editing, Supervision.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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A financial affiliation does not exist.

Authors' contributions

SB and SS did substantial contributions to the conception and design of the work.

SB, RA; SA and SS did substantial contributions to the collection of data for the work.

SB, RA; SA and SS drafted, revised and approved the version for publication.

References

- Akhlaghi, N., Azarshab, M., Akhoundi, N., Meraji, N., 2019. The effect of ketorolac buccal infiltration on postoperative endodontic pain: a prospective, double-blind, randomized, controlled clinical trial. *Quintessence Int.* 50, 540–546.
- Aksoy, F., Ege, B., 2020. The effect of pretreatment submucosal injections of tramadol and dexamethasone on post-endodontic pain in mandibular molar teeth with symptomatic irreversible pulpitis: a randomized controlled clinical trial. *Int. Endod. J.* 53, 176–185.
- Aksoy, U., Pehlivan, S., Buhara, O., 2020. The top risk factors for endodontic flare-up: a Monte Carlo simulation. *Clin. Oral. Investig.*, 00
- Albuquerque, P.P., Hungaro Duarte, M.A., Pelegrine, R.A., Kato, A. S., Stringheta, C.P., Duque, J.A., Bueno, C., 2020. Influence of foraminal enlargement on the apical extrusion of filling material: Volumetric analysis using micro-computed tomography. *Aust. Endod. J.*
- Alharthi, A.A., Aljoudi, M.H., Almaliki, M.N., Almalki, M.A., Sunbul, M.A., 2019. Effect of intra-canal cryotherapy on post-endodontic pain in single-visit RCT: A randomized controlled trial. *Saudi Dent. J.* 31, 330–335.
- Ali, A., Olivieri, J.G., Duran-Sindreu, F., Abella, F., Roig, M., Garcia-Font, M., 2016. Influence of preoperative pain intensity on postoperative pain after root canal treatment: A prospective clinical study. *J. Dent.* 45, 39–42.
- Ali, S.G., Mulay, S., Palekar, A., Sejpal, D., Joshi, A., Gufran, H., 2012. Prevalence of and factors affecting post-obturation pain following single visit root canal treatment in Indian population: A prospective, randomized clinical trial. *Contemp. Clin. Dent.* 3, 459–463.
- Alomaym, M.A.A., Aldohan, M.F.M., Alharbi, M.J., Alharbi, N.A., 2019. Single versus Multiple Sitting Endodontic Treatment: Incidence of Postoperative Pain - A Randomized Controlled Trial. *J. Int. Soc. Prev. Commun. Dent.* 9, 172–177.
- Anjaneyulu, K., Nivedhitha, M.S., 2014. Influence of calcium hydroxide on the post-treatment pain in Endodontics: A systematic review. *J. Conserv. Dent.* 17, 200–207.
- Aoun, C., El Osta, N., Naaman, A., Zogheib, C., Khalil, I., 2019. Post-endodontic Flare-ups after a Single-visit Treatment Using the FUI Scoring Method and Associated Factors: A Clinical Prospective Study. *J. Contemp. Dent. Pract.* 20, 1033–1040.
- Armada-Dias, L., Breda, J., Provenzano, J.C., Breitenbach, M., Rôças, I., Gahyva, S.M., Siqueira Jr., J.F., 2006. Development of periradicular lesions in normal and diabetic rats. *J. Appl. Oral. Sci.* 14, 371–375.
- Arslan, H., Ahmed, H.M.A., Yildiz, E.D., Gundogdu, E.C., Seckin, F., Arslan, S., 2019. Acupuncture reduces the postoperative pain in teeth with symptomatic apical periodontitis: a preliminary randomized placebo-controlled prospective clinical trial. *Quintessence Int.* 50, 270–277.
- Arslan, H., Guven, Y., Karatas, E., Doganay, E., 2017. Effect of the Simultaneous Working Length Control during Root Canal Preparation on Postoperative Pain. *J. Endod.* 43, 1422–1427.
- Azim, A.A., Azim, K.A., Abbott, P.V., 2017. Prevalence of inter-appointment endodontic flare-ups and host-related factors. *Clin. Oral. Investig.* 21, 889–894.
- Balevi, B., 2019. Managing post endodontic treatment pain by eliminating occlusal contacts. *Evid. Based Dent.* 20, 109–110.
- Bashetty, K., Hegde, J., 2010. Comparison of 2% chlorhexidine and 5.25% sodium hypochlorite irrigating solutions on postoperative pain: a randomized clinical trial. *Indian J. Dent. Res.* 21, 523–527.
- Borges Silva, E.A., Guimaraes, L.S., Kuchler, E.C., Antunes, L.A.A., Antunes, L.S., 2017. Evaluation of Effect of Foraminal Enlargement of Necrotic Teeth on Postoperative Symptoms: A Systematic Review and Meta-analysis. *J. Endod.* 43, 1969–1977.
- Ehrmann, E.H., Messer, H.H., Adams, G.G., 2003. The relationship of intracanal medicaments to postoperative pain in endodontics. *Int. Endod. J.* 36, 868–875.
- Emara, R.S., Abou El Nasr, H.M., El Boghdadi, R.M., 2019. Evaluation of postoperative pain intensity following occlusal reduction in teeth associated with symptomatic irreversible pulpitis and symptomatic apical periodontitis: a randomized clinical study. *Int. Endod. J.* 52, 288–296.
- Erdem Hepsenoglu, Y., Eyuboglu, T.F., Ozcan, M., 2018. Postoperative Pain Intensity after Single- versus Two-visit Nonsurgical Endodontic Retreatment: A Randomized Clinical Trial. *J. Endod.* 44, 1339–1346.
- Eyuboglu, T.F., Ozcan, M., 2019. Postoperative pain intensity associated with the use of different nickel-titanium shaping systems during single-appointment endodontic retreatment: a randomized clinical trial. *Quintessence Int.* 50, 624–634.
- Farzaneh, S., Parirokh, M., Nakhaee, N., Abbott, P.V., 2018. Effect of two different concentrations of sodium hypochlorite on postoperative pain following single-visit root canal treatment: a triple-blind randomized clinical trial. *Int. Endod. J.* 51 (Suppl 1), e2–e11.
- Fedorowicz, Z., Nasser, M., Sequeira-Byron, P., de Souza, R.F., Carter, B., Heft, M., 2012. Irrigants for non-surgical root canal treatment in mature permanent teeth. *Cochrane Database Syst. Rev.*, Cd008948
- Figini, L., Lodi, G., Gorni, F., Gagliani, M., 2008. Single versus multiple visits for endodontic treatment of permanent teeth: a Cochrane systematic review. *J. Endod.* 34, 1041–1047.
- Fonzar, F., Mollo, A., Venturi, M., Pini, P., Fabian Fonzar, R., Trullenque-Eriksson, A., Esposito, M., 2017. Single versus two visits with 1-week intracanal calcium hydroxide medication for endodontic treatment: One-year post-treatment results from a

- multicentre randomised controlled trial. *Eur. J. Oral. Implantol.* 10, 29–41.
- Fuller, M., Younkin, K., Drum, M., Reader, A., Nusstein, J., Fowler, S., 2018. Postoperative Pain Management with Oral Methylprednisolone in Symptomatic Patients with a Pulpal Diagnosis of Necrosis: A Prospective Randomized, Double-blind Study. *J. Endod.* 44, 1457–1461.
- Garcia-Font, M., Duran-Sindreu, F., Morello, S., Irazusta, S., Abella, F., Roig, M., Olivieri, J.G., 2018. Postoperative pain after removal of gutta-percha from root canals in endodontic retreatment using rotary or reciprocating instruments: a prospective clinical study. *Clin. Oral. Investig.* 22, 2623–2631.
- Garg, N., Sharma, S., Chhabra, A., Dogra, A., Bhatia, R., Thakur, S., 2017. Clinical evaluation of maintenance of apical patency in postendodontic pain: An *in vivo* study. *Endodontology* 29, 115–119.
- Genc Sen, O., Kaya, M., 2019. Effect of Root Canal Disinfection with a Diode Laser on Postoperative Pain After Endodontic Retreatment. *Photobiomodul. Photomed. Laser Surg.* 37, 85–90.
- Genet, J.M., Hart, A.A., Wesselink, P.R., Thoden van Velzen, S.K., 1987. Preoperative and operative factors associated with pain after the first endodontic visit. *Int. Endod. J.* 20, 53–64.
- Georgopoulou, M., Kontakiotis, E., Nakou, M., 1993. In vitro evaluation of the effectiveness of calcium hydroxide and para-mono-chlorophenol on anaerobic bacteria from the root canal. *Endod. Dent. Traumatol.* 9, 249–253.
- Goldberg, F., Massone, E.J., 2002. Patency file and apical transportation: an *in vitro* study. *J. Endod.* 28, 510–511.
- Gondim Jr., E., Setzer, F.C., Dos Carmo, C.B., Kim, S., 2010. Postoperative pain after the application of two different irrigation devices in a prospective randomized clinical trial. *J. Endod.* 36, 1295–1301.
- Gotler, M., Bar-Gil, B., Ashkenazi, M., 2012. Postoperative Pain after Root Canal Treatment: A Prospective Cohort Study. *Int. J. Dent.* 2012.
- Haapasalo, M., Shen, Y., Wang, Z., Gao, Y., 2014. Irrigation in endodontics. *Br. Dent. J.* 216, 299–303.
- Hawker, G.A., Mian, S., Kendzerska, T., French, M., 2011. Measures of adult pain: Visual Analog Scale for Pain (VAS Pain), Numeric Rating Scale for Pain (NRS Pain), McGill Pain Questionnaire (MPQ), Short-Form McGill Pain Questionnaire (SF-MPQ), Chronic Pain Grade Scale (CPGS), Short Form-36 Bodily Pain Scale (SF-36 BPS), and Measure of Intermittent and Constant Osteoarthritis Pain (ICOAP). *Arthritis Care Res. (Hoboken)* 63 (Suppl 1), S240–S252.
- Ince, B., Ercan, E., Dalli, M., Dulgergil, C.T., Zorba, Y.O., Colak, H., 2009. Incidence of postoperative pain after single- and multi-visit endodontic treatment in teeth with vital and non-vital pulp. *Eur. J. Dent.* 3, 273–279.
- Iqbal, M., Kurtz, E., Kohli, M., 2009. Incidence and factors related to flare-ups in a graduate endodontic programme. *Int. Endod. J.* 42, 99–104.
- Jorge-Araujo, A.C.A., Bortoluzzi, M.C., Baratto-Filho, F., Santos, F. A., Pochapski, M.T., 2018. Effect of Premedication with Anti-inflammatory Drugs on Post-Endodontic Pain: A Randomized Clinical Trial. *Braz Dent. J.* 29, 254–260.
- Vieyra, J.P., Acosta, F.O., Osuna, S.K., 2018. Incidence of Flare-Ups and Apical Healing after Single-Visit or Two Visits Treatment of Teeth with Necrotic Pulp and Apical Periodontitis after a Two-Year Control Period. A Randomized Clinical Trial. *J. Dent. Oral Health* 4.
- Kaladi, S.R., Tegginmani, V., Manoosha, M., Mitta, S., Chigadani, P., Viswanadhan, A., 2019. Effectiveness Of Pre-operative Oral Medication of Ibuprofen and Ketorolac on Anesthetic Efficacy of Inferior Alveolar Nerve Block with Irreversible Pulpitis: Randomized Controlled Trial. *Cureus* 11, e6346.
- Kashefinejad, M., Harandi, A., Eram, S., Bijani, A., 2016. Comparison of Single Visit Post Endodontic Pain Using Mtwo Rotary and Hand K-File Instruments: A Randomized Clinical Trial. *J. Dent. (Tehran)* 13, 10–17.
- Kishen, A., Peters, O., Zehnder, M., Diogenes, A., Nair, M., 2016. Advances in endodontics: Potential applications in clinical practice. *J. Conserv. Dent.* 19, 199–206.
- Konagala, R.K., Mandava, J., Pabbati, R.K., Anupreeta, A., Borugadda, R., Ravi, R., 2019. Effect of pretreatment medication on postendodontic pain: A double-blind, placebo-controlled study. *J. Conserv. Dent.* 22, 54–58.
- Lopes, L.P.B., Herkrath, F.J., Vianna, E.C.B., Gualberto Junior, E.C., Marques, A.A.F., Sponchiado Junior, E.C., 2019. Effect of photobiomodulation therapy on postoperative pain after endodontic treatment: a randomized, controlled, clinical study. *Clin. Oral. Investig.* 23, 285–292.
- Kaur, Maj Summerdeep, Awasthi, Maj Pankaj, Mahajan, Akshita., 2020. Comparative evaluation of interappointment flare-ups in diabetic and in non-diabetic patients. *Int. J. Curr. Res.* 12(01), 9301–9304.
- Metin, R., Tatli, U., Evlice, B., 2018. Effects of low-level laser therapy on soft and hard tissue healing after endodontic surgery. *Lasers Med. Sci.* 33, 1699–1706.
- Middha, M., Sangwan, P., Tewari, S., Duhan, J., 2017. Effect of continuous ultrasonic irrigation on postoperative pain in mandibular molars with nonvital pulps: a randomized clinical trial. *Int. Endod. J.* 50, 522–530.
- Mohammadi, Z., Farhad, A., Tabrizzadeh, M., 2006. One-visit versus multiple-visit endodontic therapy — a review. *Int. Dent. J.* 56, 289–293.
- Moline, S.A., 2006. Retreatment of resorcinol-formalin past root fillings: studies on dissolving properties of various solutions. SoDM Masters theses. Paper 1.
- Mostafa, M., El-Shrief, Y.A.I., Anous, W.I.O., Hassan, M.W., Salamah, F.T.A., El Boghdadi, R.M., El-Bayoumi, M.A.A., Seyam, R.M., Abd-El-Kader, K.G., Amin, S.A.W., 2020. Postoperative pain following endodontic irrigation using 1.3% versus 5.25% sodium hypochlorite in mandibular molars with necrotic pulps: a randomized double-blind clinical trial. *Int. Endod. J.* 53, 154–166.
- Nabi, S., Amin, K., Masoodi, A., Farooq, R., Purra, A.R., Ahangar, F.A., 2018. Effect of preoperative ibuprofen in controlling postendodontic pain with and without low-level laser therapy in single visit endodontics: A randomized clinical study. *Indian J. Dent. Res.* 29, 46–50.
- Nair, M., Rahul, J., Devadathan, A., Mathew, J., 2017. Incidence of Endodontic Flare-ups and Its Related Factors: A Retrospective Study. *J. Int. Soc. Prev. Commun. Dent.* 7, 175–179.
- Naoum, H.J., Chandler, N.P., 2002. Temporization for endodontics. *Int. Endod. J.* 35, 964–978.
- Ng, Y.L., Glennon, J.P., Setchell, D.J., Gulabivala, K., 2004. Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. *Int. Endod. J.* 37, 381–391.
- Onay, E.O., Ungor, M., Yazici, A.C., 2015. The evaluation of endodontic flare-ups and their relationship to various risk factors. *BMC Oral Health* 15.
- Pai, S., Vivekananda Pai, A., Thomas, M., Bhat, V., 2014. Effect of calcium hydroxide and triple antibiotic paste as intracanal medications on the incidence of inter-appointment flare-up in diabetic patients: An *in vivo* study. *J. Conserv. Dent.* 17, 208–211.
- Pasqualini, D., Mollo, L., Scotti, N., Cantatore, G., Castellucci, A., Migliaretti, G., Berutti, E., 2012. Postoperative pain after manual and mechanical glide path: a randomized clinical trial. *J. Endod.* 38, 32–36.
- Praveen, R., Thakur, S., Kirthiga, M., 2017. Comparative Evaluation of Premedication with Ketorolac and Prednisolone on Postendodontic Pain: A Double-blind Randomized Controlled Trial. *J. Endod.* 43, 667–673.

- Qualtrough, A.J., Whitworth, J.M., Dummer, P.M., 1999. Preclinical endodontology: an international comparison. *Int. Endod. J.* 32, 406–414.
- Ramamoorthi, S., Nivedhitha, M.S., Divyanand, M.J., 2015. Comparative evaluation of postoperative pain after using endodontic needle and EndoActivator during root canal irrigation: A randomized controlled trial. *Australian Endod. J.* 41, 78–87.
- Riaz, A., Maxood, A., Abdullah, S., Saba, K., Din, S.U., Zahid, S., 2018. Comparison of frequency of post-obturation pain of single versus multiple visit root canal treatment of necrotic teeth with infected root canals. A Randomized Controlled Trial. *J. Pak. Med. Assoc.* 68, 1429–1433.
- Ruddle, C., 2002. Cleaning and shaping root canal systems. In: Loui, S. (Ed.), *Pathways of the Pulp*, eighth ed., pp. 231–291.
- Samir Abouelenien, S., Mohamed Ibrahim, S., Gameel Shaker, O., Mohamed, Ahmed G., 2018. Evaluation of postoperative pain in infected root canals after using double antibiotic paste versus calcium hydroxide as intra-canal medication: A randomized controlled trial. *F1000Res.* 7, 1768.
- Segura-Egea, J.J., Cisneros-Cabello, R., Llamas-Carreras, J.M., Velasco-Ortega, E., 2009. Pain associated with root canal treatment. *Int. Endod. J.* 42, 614–620.
- Sevekar, S.A., Gowda, S.H.N., 2017. Postoperative Pain and Flare-Ups: Comparison of Incidence Between Single and Multiple Visit Pulpotomy in Primary Molars. *J. Clin. Diagn Res.* 11.
- Shamszadeh, S., Asgary, S., Shirvani, A., Eghbal, M.J., 2020. Effects of antibiotic administration on post-operative endodontic symptoms in patients with pulpal necrosis: A systematic review and meta-analysis. *J. Oral. Rehabil.*
- Shamszadeh, S., Shirvani, A., Eghbal, M.J., Asgary, S., 2018. Efficacy of Corticosteroids on Postoperative Endodontic Pain: A Systematic Review and Meta-analysis. *J. Endod.* 44, 1057–1065.
- Shresha, R., Shrestha, D., Kayastha, R., 2018. Post-Operative Pain and Associated Factors in Patients Undergoing Single Visit Root Canal Treatment on Teeth with Vital Pulp. *Kathmandu Univ. Med. J. (KUMJ)* 16, 220–223.
- Singh, R.D., Khatter, R., Bal, R.K., Bal, C.S., 2013. Intracanal medications versus placebo in reducing postoperative endodontic pain a double blind randomized clinical trial. *Braz. Dent. J.* 24, 25–29.
- Sinhal, T., Shah, R.R., Shah, N., Jais, P., Hadwani, K., 2017. GFJGJJFH ** interappointment flare-up in diabetic patients: A randomized double-blinded clinical study. *Endod.ontology* 29, 136–141.
- Siqueira Jr., J.F., 2003. Microbial causes of endodontic flare-ups. *Int. Endod. J.* 36, 453–463.
- Siqueira Jr., J.F., Rocas, I.N., Souto, R., Uzeda, M., Colombo, A.P., 2001. Microbiological evaluation of acute periradicular abscesses by DNA-DNA hybridization. *Oral. Surg. Oral. Med. Oral. Pathol. Oral. Radiol. Endod.* 92, 451–457.
- Siqueira Jr, J.F., Barnett, F., 2004. Interappointment pain: mechanisms, diagnosis, and treatment. *Endod. Top.* 7, 93–109.
- Stamos, A., Drum, M., Reader, A., Nusstein, J., Fowler, S., Beck, M., 2019. An Evaluation of Ibuprofen Versus Ibuprofen/Acetaminophen for Postoperative Endodontic Pain in Patients With Symptomatic Irreversible Pulpitis and Symptomatic Apical Periodontitis. *Anesth. Prog.* 66, 192–201.
- Suneelkumar, C., Subha, A., Gogala, D., 2018. Effect of Preoperative Corticosteroids in Patients with Symptomatic Pulpitis on Postoperative Pain after Single-visit Root Canal Treatment: A Systematic Review and Meta-analysis. *J. Endod.* 44, 1347–1354.
- Susila, A., Minu, J., 2019. Activated Irrigation vs. Conventional non-activated Irrigation in Endodontics - A Systematic Review. *Eur. Endod. J* 4, 96–110.
- Tavares, S.G., Fontana, C.E., Martin, A.S., Pinheiro, S.L., Pelegrine, R.A., Rocha, D.G.P., 2020. In Vivo Evaluation of Painful Symptomatology after Endodontic Treatment Performed Using Two Different Irrigation Needle Insertion Depths. *Eur. J. Dent.* 14, 274–280.
- Tinaz, A.C., Alacam, T., Uzun, O., Maden, M., Kayaoglu, G., 2005. The effect of disruption of apical constriction on periapical extrusion. *J. Endod.* 31, 533–535.
- Topçuoğlu, G., Topçuoğlu, H.S., Delikan, E., Çalışkan, S., 2020. The effect of two different irrigation needles on post-operative pain after pulpectomy in primary molar teeth: A randomized clinical study. *Int J. Paediatr Dent.*
- Topcuoglu, H.S., Topcuoglu, G., Arslan, H., 2018. The Effect of Apical Positive and Negative Pressure Irrigation Methods on Postoperative Pain in Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis: A Randomized Clinical Trial. *J. Endod.* 44, 1210–1215.
- Topçuoğlu, H.S., Topçuoğlu, G., Arslan, H., 2018. The Effect of Different Irrigation Agitation Techniques on Postoperative Pain in Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis: A Randomized Clinical Trial. *J. Endod.* 44, 1451–1456.
- Torabinejad, M., Cymerman, J.J., Frankson, M., Lemon, R.R., Maggio, J.D., Schilder, H., 1994. Effectiveness of various medications on postoperative pain following complete instrumentation. *J. Endod.* 20, 345–354.
- Udoye Ch, A.E., 2010. Flare- up incidence and related factors in adults. *J. Dent. Oral Hyg.* 2010 (2), 19–22.
- Veitz-Keenan, A., Ferraiolo, D.M., 2018. Single dose oral prednisolone and post-operative endodontic pain. *Evid. Based Dent.* 19, 10–11.
- Verma, N., Sangwan, P., Tewari, S., Duhan, J., 2019. Effect of Different Concentrations of Sodium Hypochlorite on Outcome of Primary Root Canal Treatment: A Randomized Controlled Trial. *J. Endod.* 45, 357–363.
- Vieyra, J.P., Enriquez, F.J.J., Acosta, F.O., Guardado, J.A., 2019. Reduction of postendodontic pain after one-visit root canal treatment using three irrigating regimens with different temperature. *Niger J. Clin. Pract.* 22, 34–40.
- Walton, R.E., 2002. Interappointment flare-ups: incidence, related factors, prevention, and management. *Endod.ontic Topics* 3, 67–76.
- Yaylali, I.E., Kurnaz, S., Tunca, Y.M., 2018. Maintaining Apical Patency Does Not Increase Postoperative Pain in Molars with Necrotic Pulp and Apical Periodontitis: A Randomized Controlled Trial. *J. Endod.* 44, 335–340.
- Yilmaz, K., Tufenkci, P., Adiguzel, M., 2019. The effects of QMix and EndoActivator on postoperative pain in mandibular molars with nonvital pulps: a randomized clinical trial. *Clin. Oral. Investig.* 23, 4173–4180.