International Journal Dental and Medical Sciences Research
Volume 6, Issue 2, Mar - Apr 2024 pp 239-247 www.ijdmsrjournal.com ISSN: 2582-6018

Endodontic Flare ups: an Updated Review

Dr Aleena Jose[1], Dr Anulekh Babu[2], Dr Mali G Nair[3], Dr Amrutha S Nath[4]
[1]*Junior Resident, Department of Conservative dentistry & Endodontics, Government Dental College, Thiruvananthapuram*
[2]*Associate Professor,Department of Conservative dentistry & Endodontics, Government Dental College, Alappuzha*
[3]*Professor & Head,Department of Conservative dentistry & Endodontics, Government Dental College, Thiruvananthapuram.*
[4] *Junior Resident, Department of Conservative dentistry & Endodontics, Government Dental College, Thiruvananthapuram*
Corresponding Author:Dr Aleena Jose, Junior Resident, Department of Conservative dentistry & Endodontics, Government Dental College, Thiruvananthapuram

Submitted: 16-03-2024 Accepted: 30-03-2024

ABSTRACT: Endodontic treatment may induce symptoms like pain and swelling, recognized as Endodontic flare-ups, causing challenges for both dentists and patients. Incidence can vary widely between 1.4 to 16%. Causative factors, being multifactorial can be due to microorganisms, chemical or mechanical factors of which microbial factors are common. The major reason behind interappointment pain is found to be the acute inflammation in the periapical tissues in response to irritation in the root canals. In light of these circumstances, preventive measures and treatment strategies have been suggested to address these flare-ups. Acquiring a thorough understanding of the contributing factors and effectively managing these occurrences can contribute to minimizing the likelihood of such undesirable events.
KEYWORDS: Flare up, Post operative pain, Endodontic treatment, Inter-appointment pain, Microbial causes, Root canal infection.

I. INTRODUCTION

Primary aim of endodontic treatment is mechanical and chemical debridement of root canals with a hermetic seal to provide conditions favourable for the periapical tissues to heal to prevent postoperative pain (1). Inter appointment flareups have remained a significant issue over time, despite numerous advances in dentistry. Flareup is a postoperative pain that starts within few hours or days after initiation or even completion of root canal therapeutic procedures which is manifested as pain and/or swelling episodes, requiring unscheduled visit and active treatment(2).

The occurrence of endodontic flareups varies widely, ranging from 1.4 to 16%(3,4) and up to 50% in some studies(5). This variability is influenced by factors such as preoperative pulpal and periapical diagnosis, the presence of pre-operative pain and swelling, medications administered, type of instrumentation and the number of visits taken to complete a root canal treatment(6).

It is widely recognized that endodontic flare-ups are multifactorial which is a combination of mechanical, chemical, host-related, and treatment-related factors, alongside the presence of endodontic infection(7).Understanding the causes of flare-ups is key to preventing them.

CAUSES OF FLARE UPS

Flareup occurs as a result of microorganisms or peri radicular tissue damage caused by instrumentation and irrigants during endodontic treatment. Pulp and periapical destruction may be the result of a shift in the production of IgG over IgA, causing perpetuation and aggravation of the inflammatory process(8). Also, Defensive system of the body fights against this damage resulting in undesirable effects for patient like pain and swelling(9).

Factors that influence the development of the endodontic flare-up are:

a) Mechanical factors
b) Chemical factors
c) Microbial factors

a) Mechanical factors

During endodontic treatment, debris, necrotic pulp masses, irrigation solutions and microorganisms can be pushed from the root canal to the periapical tissues. This can lead to inflammation and postoperative pain that disturbs

healing of peri radicular tissues(10).Prior research indicates that utilizing a combination of the crown-down technique alongside engine-driven nickel titanium (Ni-Ti) systems results in minimal extrusion of debris(2). All these studies concludes that rotary instruments application during endodontic treatment leads to a lower incidence of flare up compared to manual instruments(11).

Working length determination has been an essential element in an endodontic treatment. Any wrong working length can lead to flare up(12). Overestimating the working length (WL) in endodontic procedures can result in extrusion of infected debris and filling material into the surrounding periodontal tissues. This extrusion can cause irritation in the tissues, potentially resulting in a flare-up(9).

It is recommended to maintain apical patency K file instrument (#6, #8, #10) deeper than working length measured to avoid debris accumulation. This will help irrigation solution to access apical third of root canal to facilitate direct contact of intracanal dressing to periapical tissues which finally helps in reducing postoperative pain(13).

Certain other studies showed that this technique may lead to apical extrusion of debris which can cause irritation to apical periodontal tissues leading to post operative pain(14). Also, enlargement of apical foramen seems to be a promoting factor for flare ups as it is linked to higher level of apical extrusion of debris(15).

b) Chemical factors

The substances employed in endodontic procedures, including intracanal medicaments, irrigation solutions, and sealers, can potentially be toxic causing irritation and flare up if they reached the peri radicular tissues(16).Harrison et al discovered a greater occurrence of post-operative pain in canals that were either not irrigated or irrigated with normal saline, in comparison to those irrigated with 5.25% sodium hypochlorite and 3% hydrogen peroxide(17).

c) Microbial factors

Microbial injury caused by microorganisms and their products that egress from root canal system to peri radicular area are the major and most important cause of interappointment flare ups(18). Frequency of flareup is higher in necrotic pulp cases than in cases with vital pulp(19).

In asymptomatic endodontic infections, there is a balance between the bacterial aggression and the host defence mechanism (local adaptation syndrome). This will be disrupted during an endodontic treatment, which favours the microbial aggression causing an acute peri radicular inflammation(2). The intensity of inflammatory response is directly proportional to the intensity of tissue injury in the peri radicular area(20).

Following injury, a myriad of chemical mediators are released or activated which mediate events of inflammation such as vasodilation, increase in vascular permeability and chemotaxis of inflammatory cells. Some mediators cause inflammation by direct stimulation of sensory nerve fibres. But major inflammatory responses are by the increase in the vascular permeability resulting in exudation and oedema formation. An increase in tissue hydrostatic pressure with compression of nerve endings causes pain(20).

In symptomatic endodontic infections, environmental conditions in root canal containing necrotic pulp tissue are conducive to the establishment of strict anaerobes(21).

There are special circumstances in which microorganisms can cause flare ups. They are:

a) Apical extrusion of debris

Apical extrusion of microorganisms and their products during chemo mechanical procedures may induce acute peri radicular inflammation to reestablish the balance between aggression and defence. This is one of the principal causes of postoperative pain. Also, intensity of the inflammation depends on the number and virulence of the extruded organism(2).

b) Changes in the endodontic microbiota or in environmental conditions

The arrangement of microcolonies in the endodontic climax community may be influenced by ecological factors present in different parts of the root canal system. These factors, such as nutrient and oxygen availability, play a crucial role in determining where microcolonies form within the root canal ecosystem(2).The higher prevalence of anaerobic microorganisms in the apical third of the root canal can be attributed to the anaerobic nature of this particular environment(22).
Insufficient chemo mechanical preparation of the root canal can disturb the microbial community balance by allowing previously inhibited species to remain, leading to their overgrowth. If the overgrown species are virulent, it can result in lesion exacerbation and postoperative flareup(21).

c) Secondary intra radicular infections

They are caused by the microorganisms that are not present in primary infections but

penetrate into the root canal during treatment, between appointments or after the conclusion of the endodontic treatment. This can lead to flareup, provided the newly established microbial species are virulent(23).

d) Increase of oxidation-reduction potential

Alteration of oxidation-reduction potential in a root canal can be a cause of exacerbation following root canal procedures. On initiation of endodontic treatment, oxygen penetrates into the root canal, and the microbial growth pattern changes from anaerobic to aerobic. Energy yield of facultative anaerobes being more marked in presence of oxygen, a faster growth is expected which might result in acute peri radicular inflammation(24).

RISK FACTORS CAUSING ENDODONTIC FLARE UP

Development of flare up is caused by 2 group of risk factors: (1) risk factors depending on a patient such as demographics, general state of health, condition of the pulp and apical periodontal tissue, clinical symptoms, treated tooth, (2) risk factors associated with therapeutic procedures that are number of visits, primary endodontic treatment/retreatment and intracanal medicaments(6).

Demographics

The correlation between the incidence of flare-ups and certain demographic criteria, such as age and gender, remains a topic of controversy.Several reports have indicated an absence of correlation between the incidence of flare-ups andthe age and gender of the patients(6,25). While other studies showed that patients older than 50 years had a higher risk of developing flare ups(5,26).A study reported that the efficacy of sodium hypochlorite is influenced by the advancing age of the patient. The findings indicated that it becomes less effective in reducing the count of Enterococcus faecalis in teeth with increased age(27).

Regarding the gender factor, some studies have suggested that women may be more susceptible to developing flare-ups compared to men(6,26,28,29). However, contrasting findings exist, with other reports indicating no significant correlation between gender and pain after such procedures(30).

Also, flare up can be associated with the general health of the patient. It is claimed that individuals diagnosed with diabetes mellitus are prone to encountering flare-ups(31). Immunological response of the patient can also be a contributing factor for flareups(32).

Condition of the pulp and apical periodontal tissue

The correlation between postoperative pain and the status of the pulp (vital tooth or necrotic), is complex and still controversial. Some studies showed that necrotic pulp is positively correlated with postoperative pain. This phenomenon may be attributed to the vital role of microorganisms in triggering inflammation in the peri radicular tissue(2,3,6).

Presence of pre-operative pain

A significant correlation has been observed between preoperative pain and post operative flare up(33,34).The virulent microorganisms within the infected root canal system contribute to the preoperative symptoms. If these microorganisms are inadvertently pushed into the peri radicular area during treatment, they can result in postoperative pain(2).

Treated tooth

Mandibular first molarhas higher chances of postoperative flare up as mandibular arch have thick cortical plates compared to maxilla which results in accumulation of exudates leading to a delay in healing(29,33). While other reports shows that there is no correlation between flare up and tooth type(25,26).

Number of visits during the treatment

In endodontic treatment, the status of the tooth 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. In the case of a necrotic tooth with radiological changes in the peri radicular area, two visits with the use of an interappointment intracanal medicament is recommended, for a maximal disinfection(35). In recent years, single visit was most recommended due to huge advances in endodontic field(36).

While certain studies have found no association between the incidence of flare-ups and the number of treatment visits(26,35,37), contrasting findings suggest a preference for a single-treatment visit for better outcomes regarding flare-ups(25,38). Conversely, alternative research has indicated that flare-ups are more prevalent in cases of single-visit root canal treatment. These conflicting results may be attributed to various factors, such as differences in sample sizes, the

specific endodontic techniques employed, and the status of the treated tooth(39,40).

Irrigation

Irrigation is a main part of the endodontic treatment for disinfection of the root canal systems(41). An extrusion of chemically active solutions beyond the apex , secondary to debris, may cause postoperative pain(9).

In a study, Susila et al. demonstrated that mechanical active irrigation devices offer benefits in terms of reducing postoperative pain and enhancing the cleanliness of canals and isthmuses in endodontic procedures, especially when compared to conventional irrigation methods.(42).

In 2018, Topcuoglu et al. conducted a comparative analysis of four irrigation techniques (needle irrigation without agitation with a side-port needle, sonic agitation, passive ultrasonic irrigation, and manual dynamic agitation) in relation to postoperative pain in endodontic procedures. Their findings indicated that manual dynamic agitation resulted in higher postoperative pain levels following endodontic therapy when compared to the other irrigation techniques(43).

The type of irrigating solution can make very littleinfluence on the incidence of post operative discomfort, provided that the irrigating solution is not forced beyond the apical foramen(32).Studies shows that a higher incidence in post-operative pain was observed in canals either not irrigated or irrigated with normal saline, compared with those irrigated with 5.25% sodium hypochlorite and 3% hydrogen peroxide(17).

Intracanal medicaments

The application of antimicrobial intracanal medication in conjunction with a meticulously performed endodontic treatment results in an improved outcome and reduced postoperative pain(44,45). Singh et al. (2013) demonstrated that the use of chlorhexidine, either alone or in combination with Ca(OH)2, leads to a reduction in postoperative pain(45).

On the contrary, Ledermix has been found to be more effective in reducing postoperative pain compared to Ca(OH)2(44). Corticosteroids suppress the inflammatory response by reducing vessel and polymorphonuclear cell permeability, inhibiting leukocyte activity, impeding phagocytosis, and blocking the synthesis of arachidonic acid. This, in turn, interferes with cyclooxygenase and lipoxygenase pathways, ultimately inhibiting the production of prostaglandins and leukotrienes(32,46).

Intracanal medicaments are not effective in preventing flare ups, which results from extrusion of infected debris through the root apex during the root canal preparation(2).

MANAGEMENT OF ENDODONTIC FLARE UP

The management of endodontic flare-ups involves local treatment measures, psychological management and usage of pharmacotherapeutics.

LOCAL TREATMENT MEASURES

Involves re-instrumentation, relief of occlusion, placement of intracanal medicament, establishment of drainage, cortical trephination.

Re-instrumentation

When the working length falls short of the apex during endodontic procedures, it results in incomplete debridement, leaving residual necrotic pulp tissues in the apex. This incomplete cleaning may lead to the development of flare-ups. Conversely, if the working length extends too far beyond the apex, there is a risk of extruding infected debris, irrigants, and medicaments peri apically, triggering an inflammatory response**.** In cases where a patient presents with a flare-up, working length should be reconfirmed, followed by meticulous debridement with frequent and copious irrigation, the application of an intra-canal medicament, and the provision of a temporary restoration(47).

Also, radiographs should be taken at different angulations to rule out any missed canals(48).

Relief of occlusion

When acute abscess develops postoperatively, the tooth gets extruded out of the socket which may cause pain while biting. Such teeth should be relieved of occlusion(47). Occlusal relief prior to endodontics can be done for the prevention of postoperative endodontic pain in patients with following conditions like(49).

Intracanal medicament

Medicaments that have been shown to provide relief during the acute exacerbation are anti-microbial agents, irrigating solutions, sulfa compounds and steroids.

Antimicrobial agents

As microorganisms play a role in aggravating inflammation, it seems plausible that the use of root canal antiseptics and germicides within the canal should indirectly lessen posttreatment pain(32). The anodyne properties of formocresol, cresatin, eugenol, camphorated monochlorphenol, and iodine-potassium iodide

have been studied(50,51). All these studies showcontradictory results.

Antimicrobial agents like sulpha compounds when placed inside root canals significantly reduced post operative pain(32). While other studies showed that they are no better than placebos(52).

Corticosteroids

The anti-inflammatory activity of corticosteroids is based partly on their ability to retard lysosomal release from cells(53) and inhibition of liberation of free arachidonic acid from the phospholipids of the cell membrane. Steroids not only prevent formation of prostaglandins and thromboxanes, but also leukotrienes unlike NSAIDS(32). Also, these hormones have the potential to induce hyperpolarization of nerves in the inflamed region, resulting in an elevation of cyclic AMP. This, in turn, diminishes the transmission of nerve impulses(32).

Several researchers have documented that the effective placement of corticosteroids into the root canal successfully manages pain(53–55).

The disadvantage of using corticosteroids in endodontic therapy is that it can interfere with phagocytosis and protein synthesis. As a result, infections may become rampant and repair may be delayed(56).

Establishment of drainage

In the presence of suppuration, the most effective approach for alleviating pain and reducing swelling is the drainage of exudate. Drainage is typically achieved by either removing the temporary dressing from the root canal or temporary filling in the access opening. In most cases, the accumulated exudate will surge from the root canal, providing immediate relief. If no exudate is emerging, pass a root canal instrument like file or reamer through the caked material to establish the flow of exudate.

In exceptional cases, where exudate is absent or cannot be evacuated through root canal, surgical intervention is necessary(32).

Cortical trephination

Cortical trephination involves surgically perforating the alveolar bone to eliminate accumulated peri-radicular tissue exudates. Several studies have investigated the efficacy of cortical trephination as a measure to prevent and alleviate postoperative pain(57).

PSYCHOLOGICAL MANAGEMENT

The individual exhibits fear and anxiety, often harbouring concerns that the treatment has been ineffective and that extraction may be necessary. Providing reassurance becomes crucial in managing such patients. It is essential to communicate to the patient that flare-ups can occur, but they are manageable and do not impact the overall treatment outcome. Given the direct connection between fear, anxiety, and perception of pain, successful pain management is achievable through a reduction in these emotional states. The patient should be informed and educated about potential reasons for pain and swelling, addressing the issue at its core. Breaking the pain cycle emerges as a pivotal step in this process(6,47).

PHARMACOTHERAPEUTICS

Local anaesthetics

Achieving sensory nerve blockade with analgesics can be challenging, necessitating the need of long-acting local anaesthetics. Interrupting the pain cycle holds significance both psychologically and neuro physiologically(58).

Antibiotics

Antibiotics have been used, both locally and systemically in endodontic treatment. But their use debatable in patients with pain and swelling. In general, the systemic administration of antibiotics should be limited. However, it seems to be beneficial when the patient displays signs of systemic involvement, such as cellulitis, fever, malaise, and toxaemia(32,47).

Antibiotics prove effective when microbial factors contribute to flare-ups. Penicillin is commonly employed in treating various dental infections. Due to the polymicrobial nature of dental infections, antibiotics targeting anaerobic infections are also prescribed. However, there are no significant studies which show that any specific antibiotic is capable of reducing or eliminating painful exacerbations during endodontic therapy(32).

Analgesics

Mild to moderate instances are managed using NSAIDs, while severe cases, or those not responding to NSAIDs, are addressed with opioids and steroids(47). NSAIDs possess analgesic effects with anti-inflammatory properties. Their analgesic and anti-inflammatory effect is due to the inhibition of prostaglandin synthesis by the cyclo-oxygenase enzyme(59).

Narcotic analgesics interact with neurons in the brainstem, spinal cord, thalamus, and cerebral cortex(60). They are capable of increasing the pain threshold by causing relaxation and freedom from anxiety(61). Systemic corticosteroids

have proven effective in diminishing pain and swelling associated with dental issues. The occurrence of postoperative pain was lower when steroids were administered before the procedure(62,63).

PREVENTION

Certain guidelines should to be followed by the clinician to prevent the occurrence of flare ups. Access cavities should never be left open in between appointments as there are chances of development of secondary peri radicular infections. Occlusal reduction or selective adjustment of cusps is indicated as a palliative measure to prevent flareups. Researchers have found that occlusal reductions largely benefitted patients who initially had preoperative pain, pulp vitality, percussion sensitivity, the absence of a periradicular radiolucency, or a combination of these symptoms(64). Instrumentation technique that causes less peri apical extrusion should be selected.Single visits are recommended for vital teeth, while multiple visits are preferred for cases involving apical periodontitis. Mechanical debridement should be accomplished within the first visit. The use of interappointment dressing with medication has proven effective in eliminating the microflora(32).

II. CONCLUSION

Despite significant advancements in the field of endodontics, flare-ups continue to occur. This phenomenon is multifactorial, involving mechanical, chemical, and microbial triggers. Recent studies have successfully demonstrated the effectiveness of certain actions or guidelines in reducing the incidence of flare-ups. Due to the diverse factors influencing flare-ups, prevention cannot be guaranteed by adhering to a specific treatment protocol. Further research is necessary to establish such procedure

REFERENCES

[1]. Endodontic Practice (Eleventh Edition) by Grossman, Louis I.; Oliet, Seymour; Del Rio, Carlos E.: Very Good Hardcover (1988) Eleventh Edition. | Lotzabooks [Internet]. [cited 2024 Jan 16]. Available from: https://www.abebooks.com/Endodontic-Practice-Eleventh-Edition-Grossman-Louis/21693034764/bd

[2]. Jr JFS. Microbial causes of endodontic flare-ups. International Endodontic Journal. 2003;

[3]. Gotler M, Bar-Gil B, Ashkenazi M. Postoperative Pain after Root Canal Treatment: A Prospective Cohort Study. International Journal of Dentistry.

[4]. Sr SSM, Alfayyadh AY, Alruwaili KK, Almunahi HFF, Alsharari AHL, Magar SP. The Determination of Flare-Up Incidence and Associated Risk Factors During Endodontic Treatment: An Observational Retrospective Study. 2022;

[5]. Azim AA. Prevalence of inter-appointment endodontic flare-ups and host-related factors. Clin Oral Invest. 2017;

[6]. Walton RE. Interappointment flare-ups: incidence, related factors, prevention, and management.

[7]. Dds EGJ. Postoperative Pain after the Application of Two Different Irrigation Devices in a Prospective Randomized Clinical Trial. Clinical Research. 2010;36(8).

[8]. Seltzer S. Pain in endodontics. Journal of Endodontics. 1986 Jan;12(10):505–8.

[9]. Jr JFS, Barnett F. Interappointment pain: mechanisms, diagnosis, and treatment.

[10]. Tinaz AC, Alacam T, Uzun O, Maden M, Kayaoglu G. The effect of disruption of apical constriction on periapical extrusion. J Endod. 2005 Jul;31(7):533–5.

[11]. Afzalifar D. Original Article. J Dent.

[12]. Iqbal M, Kurtz E, Kohli M. Incidence and factors related to flare-ups in a graduate endodontic programme. International Endodontic Journal. 2009;

[13]. Yaylali IE. Maintaining Apical Patency Does Not Increase Postoperative Pain in Molars with Necrotic Pulp and Apical Periodontitis: A Randomized Controlled Trial. 2017;

[14]. Goldberg F, Massone EJ. Patency File and Apical Transportation: An In Vitro Study.

[15]. Influence of foraminal enlargement on the apical extrusion of filling material: Volumetric analysis using micro- computed tomography. 2020;

[16]. 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). [cited 2023 Oct 31]; Available from:

https://acrjournals.onlinelibrary.wiley.com /doi/10.1002/acr.20543

[17]. Harrison JW, Baumgartner JC, Svec TA. Incidence of Pain Associated with Clinical Factors During and After Root Canal Therapy. Part 2. Postobturation Pain. Journal of Endodontics. 1983;9(10).

[18]. Seltzer S, Naidorf IJ. Flare-ups in endodontics: II. Therapeutic measures. J Endod. 1985 Dec;11(12):559–67.

[19]. Walton R, Fouad A. Endodontic interappointment flare-ups: a prospective study of incidence and related factors. J Endod. 1992 Apr;18(4):172–7.

[20]. Inflammation by Henry O. Trowbridge, Robert C. Emling - Ebook | Everand [Internet]. [cited 2023 Nov 8]. Available from: https://www.everand.com/book/428409643/Inflammation-A-Review-of-the-Process

[21]. Sundqvist G. Ecology of the root canal flora. J Endod. 1992 Sep;18(9):427–30.

[22]. Fabricius L, Dahlén G, Ohman AE, Möller AJ. Predominant indigenous oral bacteria isolated from infected root canals after varied times of closure. Scand J Dent Res. 1982 Apr;90(2):134–44.

[23]. Recontamination of coronally unsealed root canals medicated with camphorated paramonochlorophenol or calcium hydroxide pastes after saliva challenge - PubMed [Internet]. [cited 2023 Nov 9]. Available from: https://pubmed.ncbi.nlm.nih.gov/9487858/

[24]. Matusow RJ. Endodontic cellulitis "flare-up". Case report. Aust Dent J. 1995 Feb;40(1):36–8.

[25]. Onay EO. The evaluation of endodontic flare-ups and their relationship to various risk factors. 2015;

[26]. Nair M, Rahul J, Devadathan A, Mathew J. Incidence of Endodontic Flare-ups and Its Related Factors: A Retrospective Study. J Int Soc Prev Community Dent. 2017;7(4):175–9.

[27]. Ozdemir HO, Buzoglu HD, Calt S, Stabholz A, Steinberg D. Effect of ethylenediaminetetraacetic acid and sodium hypochlorite irrigation on Enterococcus faecalis biofilm colonization in young and old human root canal dentin: in vitro study. J Endod. 2010 May;36(5):842–6.

[28]. Hj N, Np C. Temporization for endodontics. International endodontic journal [Internet]. 2002 Dec [cited 2023 Nov 11];35(12). Available from: https://pubmed.ncbi.nlm.nih.gov/12653314/

[29]. Influence of preoperative pain intensity on postoperative pain after root canal treatment: A prospective clinical study - PubMed [Internet]. [cited 2023 Nov 11]. Available from: https://pubmed.ncbi.nlm.nih.gov/26678517/

[30]. Ng YL, Glennon JP, Setchell DJ, Gulabivala K. Prevalence of and factors affecting post-obturation pain in patients undergoing root canal treatment. Int Endod J. 2004 Jun;37(6):381–91.

[31]. Comparative evaluation of interappointment flare-ups in diabetic and in non-diabetic patients | International Journal of Current Research [Internet]. [cited 2023 Nov 11]. Available from: https://journalcra.com/article/comparative-evaluation-interappointment-flare-ups-diabetic-and-non-diabetic-patients

[32]. Seltzer S, Naidorf IJ. Flare-ups in Endodontics: II. Therapeutic Measures. Journal of Endodontics. 2004;30(7).

[33]. Shresha R, Shrestha D, Kayastha R. Post-Operative Pain and Associated Factors in Patients Undergoing Single Visit Root Canal Treatment on Teeth with Vital Pulp. Kathmandu Univ Med J (KUMJ). 2018;16(62):220–3.

[34]. Aoun C, El Osta N, Naaman A, Zogheib C, Khalil I. 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. 2019 Sep 1;20(9):1033–40.

[35]. Figini L, Lodi G, Gorni F, Gagliani M. Single versus multiple visits for endodontic treatment of permanent teeth: a Cochrane systematic review. J Endod. 2008 Sep;34(9):1041–7.

[36]. Preclinical endodontology: an international comparison - Qualtrough - 1999 - International Endodontic Journal - Wiley Online Library [Internet]. [cited 2023 Nov 12]. Available from: https://onlinelibrary.wiley.com/doi/abs/10.1046/j.1365-2591.1999.00253.x

[37]. Incidence of Postoperative Pain after Single- and Multi-Visit Endodontic Treatment in Teeth with Vital and Non-Vital Pulp - PMC [Internet]. [cited 2023 Nov 12]. Available from:

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2761157/

[38]. Mohammadi Z, Farhad A, Tabrizizadeh M. One-visit versus multiple-visit endodontic therapy--a review. Int Dent J. 2006 Oct;56(5):289–93.

[39]. Yoldas O, Topuz A, Isçi AS, Oztunc H. Postoperative pain after endodontic retreatment: single- versus two-visit treatment. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2004 Oct;98(4):483–7.

[40]. Ghoddusi J, Javidi M, Zarrabi MH, Bagheri H. Flare-ups incidence and severity after using calcium hydroxide as intracanal dressing. N Y State Dent J. 2006;72(4):24–8.

[41]. Haapasalo M, Shen Y, Wang Z, Gao Y. Irrigation in endodontics. Br Dent J. 2014 Mar;216(6):299–303.

[42]. Susila A, Minu J. Activated Irrigation vs. Conventional non-activated Irrigation in Endodontics - A Systematic Review. Eur Endod J. 2019;4(3):96–110.

[43]. Topçuoğlu HS, Topçuoğlu G, Arslan H. The Effect of Different Irrigation Agitation Techniques on Postoperative Pain in Mandibular Molar Teeth with Symptomatic Irreversible Pulpitis: A Randomized Clinical Trial. J Endod. 2018 Oct;44(10):1451–6.

[44]. Ehrmann EH, Messer HH, Adams GG. The relationship of intracanal medicaments to postoperative pain in endodontics. Int Endod J. 2003 Dec;36(12):868–75.

[45]. Singh RD, Khatter R, Bal RK, Bal CS. Intracanal Medications versus Placebo in Reducing Postoperative Endodontic Pain - A Double- Blind Randomized Clinical Trial. Braz Dent J. 2013;

[46]. Effect of supraperiosteal injection of dexamethasone on postoperative pain - PubMed [Internet]. [cited 2023 Nov 12]. Available from: https://pubmed.ncbi.nlm.nih.gov/18352900/

[47]. Kaur P. Endodontic flare ups: A proposal for etiopathogenesis and psychological management. International Journal of Health.

[48]. Textbook of Endodontics, 2nd Edition | PDF | Human Tooth | Tooth Enamel [Internet]. [cited 2023 Nov 13]. Available from: https://www.scribd.com/doc/132311000/Textbook-of-Endodontics-2nd-Edition

[49]. Cohen's pathways of the pulp - Colorado State University [Internet]. [cited 2023 Nov 15]. Available from: https://colostate.primo.exlibrisgroup.com/discovery/fulldisplay/alma991001114209703361/01COLSU_INST:01COLSU

[50]. Kleier DJ, Mullaney TP. Effects of formocresol on posttreatment pain of endodontic origin in vital molars. J Endod. 1980 May;6(5):566–9.

[51]. Incidence of posttreatment endodontic pain related to medicaments and other factors - PubMed [Internet]. [cited 2023 Nov 15]. Available from: https://pubmed.ncbi.nlm.nih.gov/27529893/

[52]. Seltzer S, Bender IB, Ehrenreich J. Incidence and duration of pain following endodontic therapy. Relationship to treatment with sulfonamides and to other factors. Oral Surg Oral Med Oral Pathol. 1961 Jan; 14:74–82.

[53]. Goldstein I, Hoffstein S, Gallin J, Weissmann G. Mechanisms of Lysosomal Enzyme Release from Human Leukocytes: Microtubule Assembly and Membrane Fusion Induced by a Component of Complement. Proc Natl Acad Sci U S A. 1973 Oct;70(10):2916–20.

[54]. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs - PubMed [Internet]. [cited 2023 Nov 15]. Available from: https://pubmed.ncbi.nlm.nih.gov/5284360/

[55]. Kebabian JW, Greengard P. Dopamine-sensitive adenyl cyclase: possible role in synaptic transmission. Science. 1971 Dec 24;174(4016):1346–9.

[56]. Smith RG, Patterson SS, El-Kafrawy AH. Histologic study of the effects of hydrocortisone on the apical periodontium of dogs. J Endod. 1976 Dec;2(12):376–80.

[57]. Tomer DAK, Saini DN, Jain DS, Sabharwal DG, Guin DA. Endodontic postoperative flare up: A review. International Journal of Applied Dental Sciences.

[58]. Long-acting local anesthetics: a comparison of bupivacaine and etidocaine in endodontics - PubMed [Internet]. [cited 2023 Nov 18]. Available from: https://pubmed.ncbi.nlm.nih.gov/6387029/

[59]. Flower RJ. Drugs which inhibit prostaglandin biosynthesis. Pharmacol Rev. 1974 Mar;26(1):33–67.
[60]. Miller RR. Clinical effects of pentazocine in hospitalized medical patients. J Clin Pharmacol. 1975;15(2–3):198–205.
[61]. Schuster CR. Behavioral methods for the study of drug interactions. Ann N Y Acad Sci. 1976;281:64–73.
[62]. Messer EJ, Keller JJ. The use of intraoral dexamethasone after extraction of mandibular third molars. Oral Surg Oral Med Oral Pathol. 1975 Nov;40(5):594–8.
[63]. Caci F, Gluck GM. Double-blind study of prednisolone and papase as inhibitors of complications after oral surgery. J Am Dent Assoc. 1976 Aug;93(2):325–7.
[64]. Rosenberg PA, Babick PJ, Schertzer L, Leung A. The effect of occlusal reduction on pain after endodontic instrumentation. J Endod. 1998 Jul;24(7):492–6.