Journal of Cardiovascular Disease Research

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

Endodontic flare-ups: A review

Asheesh Sawhny, Richa singh, Saurabh Sharma, Saurav Paul, Pankaj Kumar Priyadarshi, Mukta Bansal,

Rama Dental College Hospital & Research Centre, Rama University, Mandhana, Kanpur,

Uttar Pradesh- India 209217

drasheeshmydentist@yahoo.com

ABSTRACT

Endodontic treatment can stimulate potential symptoms such as pain and swelling during or after the treatment, known as the Endodontic flare-ups, which is a nightmare for both Dentist and Patients. Its incidence can vary from 1.4% to 50%. The multi-causal origin of these flare-ups include the microbial factors, the patient factors and the treatment factors. Among these, conceivably, micro-organisms play a major role. The principal reason for the inter-appointment pain is the development of acute inflammation in the peri-radicular tissue region in response to any irritation extending from the root canal system. Considering these situations, preventive measures and treatment strategies against these flare –ups has been proposed. Having a proficient knowledge about the etiologic factors and the management of these flare –ups can help in reducing the occurrence of this abominable event.

Key words : endodontic treatment, flare-up, inter-appointment pain, microbial causes, root canal infection.

INTRODUCTION

An inter-appointment flare-up is characterized by the development of pain, swelling or both, which commences within few hours or days after the initiation or even completion of root canal treatment1, which requires an unscheduled visit and active treatment. It is an undesirable event to both the clinician and the patient.

An endodontic flare up is defined asan acute exacerbation of an asymptomatic pulpal and /or periradicularpathoses, after initiation or continuation of root canal treatment[2]. Interappointment pain is almost exclusively due to the development of acute inflammation at the periradicular tissues in response to an increase in the intensity of injury coming from the root canal system[3]. The patient experiences varying degrees of pain, which is residual or even exaggerated during and following endodontic treatment[4]. It is of much concern when the patient was previously asymptomatic. Fortunately, the occurrence of flare-ups has no effect on the prognosis of the treatment.

The patients may underestimate the clinician's

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

skills and such an episode also, undermine the patient's confidence in their dentists or patient satisfaction with the treatment[6]. Hence it is desirable to know about the various reasons for an endodontic flare up and also prevent and manage this complication.

Incidence

The incidence of endodontic flare-ups varies according to various studies. It varies from 1.4% to 1.6%[3,7] and upto 50%[7-9] in some researches. The occurrence of flare-ups depends on the pre-operative pulpal and periapical diagnosis, the presence of pre-operative pain and swelling, medications taken, type of instrumentation technique and the number of visits taken to complete a root canal treatment. Its incidence has a direct relationship with the patient's preoperative pathogenesis and signs/symptoms. Lowest frequency is found in patients with vital pulp without periapical pathogenesis and highest frequency among the patients with necrotic pulp and acute apical periodontitis[10].

In a study conducted by Pamboo J et. al in 2014 the following inferences were observed. This study showed a low incidence of flare-ups of 2.35%. Age has no influence on the occurrence of flare-ups[11]. Women experienced more pain compared to men and also had low pain threshold levels. Endodontic flare-ups are more prevalent in females under age of 20 years usually in maxillary lateral incisors, mandibular molars with large periapical lesion and retreatment of previous root canal treatment[12]. Posterior teeth in the mandibular arch experienced more pain because of the presence of more number of canals and bifurcated root canals. The pre-operative pain has a direct influence on the incidence of flare-ups. The incidence of flare ups is more with a necrotic pulp than a vital pulp. Most of the post-operative pain can be controlled by the usage of anti-inflammatory drugs and the judicious use of antibiotics. There was no difference in the incidence of flare ups between single and multiple visits. Most of the studies have found that single visit treatment resulted in less pain compared to multiple visits. The crown down technique with rotary action combined with copious and frequent irrigation resultedin decreased incidence of flare-ups. Intra canal medication is a preventive measure to reduce the incidence of flare-ups[11].

Aetiology and related factors

Mechanical, chemical and/or microbial injuryto the pulp and/or peri-radicular tissues are considered to be the main causative factors of flare-ups[13,14]. It is otherwise called as an Endodontic Inter-Appointment Emergency.The etiological factors can be divided into three main areas. 1) Treatment procedures under the control of the operator, 2) microbial factors related to the contents of the root canal and 3) host factors such as patient demographics, local tissue changes, immunologic changes and psychological factors[15].

Microbial causes

Generally there is balance between the bacterial aggression and the host defence mechanisms. In some situations during endodontic treatment this balance is disrupted, which favours the microbial aggression causing an acute peri-radicular inflammation. These situations could be when there is an apical extrusion of infected debris, changes in the root canal microflora and environmental conditions caused by incomplete chemo-mechanical preparation, secondary intra-radicular infections and an increase in the oxidation-reduction potential within the root canal, all of which favours the growth of facultative bacteria. Specific pathogenic strains, virulent clonal types, the number of cells and microbial interactions are the factors which influence the development of pain associated with endodontic infections[1].

It has been suggested in some reports thatthe presence of certain bacterial species are associated more with particular peri-radicular diseases. Symptomatic peri-radicular lesions including teeth with abscess are associated more with Porphyromonas species[16-19]. Acute clinical symptomsare associated with Prevotella

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

and Peptostreptococcus species[20]. Percussion pain frequently exhibited Peptostreptococcus, Eubacterium, Porphyromonasendodontalis, P.gingivalis and Prevotella species[21]. All these reports is suggestive that Gram- negative anaerobic bacteria are closely associated with the occurrence of symptomatic endodontic infections including acute abscess[16-21].

Apical extrusion of debris

The apical extrusion of infected debris into the peri-radicular tissues is one of the principal causes of post-operative pain[13,22,23]. In asymptomatic cases, there is a balance between the bacterial aggression and the host defence. During the chemo-mechanical preparation, when the infected debris is extruded, this balance is disrupted, for which the host mobilizes an acute inflammation in order to re-establish the equilibrium[1]. Over-instrumentation promotes the apical foramen enlargement, which permits the influx of exudates and blood into the root canal, enhancing the nutrient supply to the remaining bacteria within the root canal, which proliferates causing an acute exacerbation of a chronic peri-apical lesion[24]. Crown- down technique with rotary motion and frequent irrigation usually extrude less infected debris into the periapical area1.

Changes in the endodontic microflora and / of environmental conditions

Normally the root canal bacteria exist in harmony and equilibrium with their environment. Endodontic procedures cause a change in the root canal environment. When the microorganisms are not completely eliminated from the root canal, environmental changes occur, causing the previously inhibited species to overgrow and turn virulent. This damages the peri-radicular tissues leading to an acute exacerbation. Whenthe environmental changes cause a turn on of the virulent genes, previously asymptomatic tooth turns symptomatic. When environmental changes induce a turn-off of the virulent genes, remission of symptoms of the previously symptomatic cases could occur. In order to avoid this, a complete chemo-mechanical preparation should be completed within the same visit whenever possible and intra canal medicament should be placed in cases of multiple visit procedure[1].

Secondary intra-radicular infections

They are caused by microorganisms which were not present in the primary infection. They penetrate the root canal during the treatment, between the appointments or after the completion of the endodontic treatment1. The main source of recontamination could be the remnant plaque, calculus or caries; leakage from rubber dam; contamination of endodontic instruments or irrigating solutions[25]; leakage through breakdown of temporary restoration; fracture of tooth[26] and when the tooth is left open for drainage[27]. Regardless of the time of introduction of microbes, a secondary infection can cause a flare-up, if the microbes are virulent and they multiply to reach a sufficient number to cause an acute inflammation of the peri-apical tissues[1].

Increase in oxidation-reduction potential

When the tooth is opened, the oxygen penetrates the root canal, changing the microbial growth pattern from anaerobic to aerobic. The energy yield is more marked in the presence of oxygen, and there is a faster growth rate causing an acute peri-apical inflammation[28].

Prevention of the microbial causes of flare-ups

Selection of an instrument technique which extrudes less amount of debris apically, completion of the chemo-mechanical preparation in a single visit, placement of an intra canal medicament between multiple visits in cases of infected tooth, not leaving the tooth open for drainage and maintaining an aseptic chain during the endodontic procedures prevent the microbial causes of flare-ups[1].

Patient-related factors

The patient presenting factors associated with an increased risk of developing an endodontic flare-up could be patient demographic(age and gender),

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

systemic conditions, pulpal and periapical diagnosis and pre-operative signs and symptoms[10]. Various studies have shown that female gender, necrotic pulp, acute apical abscess, acute apical periodontitis, large periapical radiolucency and pre-operative pain and swelling have an increased risk of developing an endodontic flare-up[11]. A vital pulp, sinus tract and obturated tooth have reduced chances of developing flare-ups[10].

Treatment factors

These include the factors which are under the control of the dentist. They are the treatment plan and specific treatment approaches that are adopted by the clinician.

Treatment plan

Factors related to the treatment plan include whether single or multiple visits are employed, conventional or retreatment procedures and whether partial or complete debridement is done. The goal is to minimize the post-operative pain whether it is done in a single or multiple visits. Some studies reveal it is better to complete the procedure in a single visit to minimize the post-operative pain. Obturation done in the same visit minimizes the incidence of flare-ups[29]. However in cases of pulpal necrosis with apical periodontitis the incidence of flare ups is more, so multiple visits can be employed. The main goal of the endodontic treatment is to completely debride and disinfect the root canals to get rid of the microbes that cause persistent infection. Inadequate debridement could lead to acute exacerbation. Intra canal placement of steroids or NSAID's could reduce the postoperative pain[10]. Other factors that have an influence on the incidence of flare-ups include over-instrumentation, incorrectly measured working length, periapical extrusion of infected debris, extruded irrigants, overfilling and hyperocclusion[30]. Inadvertant extrusion of irrigants beyond the apical foramen will lead to violent reactions – pain, swelling, haematoma, burning sensation, ulceration, tissue necrosis. Also, excessive pressure during irrigation will cause large amounts of irrigant to come in contact with the periapical tissues[31]. Occlusal reduction as a prophylactic procedure is ineffective, but for teeth with pain on mastication, occlusal reduction reduces the post-operative pain[32].

Therapeutics

Many studies reveal that prophylactic antibiotics are unrelated to the incidence of flare-ups[33,34]. But this depends on the pulpal and periapical diagnosis. Many studies show the pre-treatment administration of analgesics and anti-inflammatory drugs minimize the post-operative pain and reduce the incidence of flare-ups. A combination of the non-steroidal anti-inflammatory agents (NSAID's) and an opiate are effective in reducing the incidence of flare-ups[35].

Treatment of flare-ups

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

Localized treatment measures

These measures include re-instrumentation, relief of occlusion, placement of intra canal medicament and establishment of drainage.

Re-instrumentation

When the working length is short of the apex, it leads to incomplete debridement leaving remnant necrotic pulp tissues uncleaned in the apex which may lead to the development of flare-ups. If the working length is too far beyond the apex, there is extrusion of the infected debris, irrigants and medicaments periapically causing an inflammatory response. Once the patient reports with a flare-up, correct working length is established, followed by complete debridement carefully with frequent and copious irrigation, placement of an intra canal medicament and a temporary restoration[5]. Radiographs should be taken at different angles to rule out the incidence of any missed canals[36].

Relief of occlusion

When an acute abscess develops post-operatively,

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

the tooth gets extruded from the socket, resulting in tenderness on percussion and difficulty in biting. Such teeth should be relieved of occlusion judiciously especially the functional cusps[5]. However some authors suggest a prophylactic occlusal reduction in cases reporting with apical periodontitis[32].

Establishment of drainage

Suppuration usually results in the presence of infections. In such a scenario, drainage of the exudate is the most effective method of reducing the pain and swelling. This is established by removing the temporary dressing from the root canal and the temporary filling of the access opening. In most cases, the accumulated exudates surge through the root canal. In some instances, when there is a blockage of the debris apically, drainage is difficult. In such instances an endodontic instrument is passed through the root canal to re-establish the patency. In exceptional cases, when this also does not provide relief, surgical intervention is necessary. A soft tissue incision or removal of the alveolar bone over the tooth apex to create an artificial sinus tract provides relief. Following the drainage, when the exudation has reduced, a temporary closed dressing can be given. However, some authors prefer to leave the canal open for drainage till the next visit. But this exposes the tooth to the oral microflora and the salivary products leading to an increase in the bacterial growth, introduces new microorganisms into the root canal thereby activating the complement system, leading to an acute exacerbation[5,37].

Intra-canal medicaments

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

Antimicrobial agents

Since the microbes are the major cause of exacerbations, intra canal placement of root canal antiseptics should indirectly reduce the post-operative pain[37]. The anodyne properties of formocresol, eugenol, iodine-potassium iodide, cresatin and camphorated monochlorophenol have been studied[38,39]. None appeared to be effective in reducing the incidence of flare-ups[40].

Irrigating solutions

The type of irrigating solution used has a very little difference in the incidence of post-operative discomfort, provided the irrigating solutions were not forced beyond the apex[37]. Harrison et. al found a higher incidence in post-operative pain in canals either not irrigated or irrigated with normal saline, compared with those irrigated with 5.25% sodium hypochlorite and 3% hydrogen peroxide[41].

Sulfa-compounds

Sulfa compounds when placed inside the root canals, have been reported to reduce the incidence of pain postoperatively[37]. Some studies show that sulphonamides are no better than placebos[42].

Corticosteroids

The anti-inflammatory property of corticosteroids is its ability to retard the release of lysosomes from the cells and inhibit the liberation of free arachidonic acid from phospholipids of the cell membrane by phospholipases. Steroids not only prevent the formation of prostaglandins and thromboxanes but also leukotrienes and other oxygen derivatives. This hormone may cause a hyperpolarization of the nerves in the inflamed area leading to increase in cyclic AMP, which reduces the transmission of nerve impulses[43,-45]. The disadvantage of the usage of steroids in endodontic therapy is that it interferes with phagocytosis and protein synthesis as a result of which the repair gets delayed[46].

Psychological management

The patient presents with fear, anxiety, doubt and often the patient assumes that the treatment has failed and extraction is needed. Hence Reassurance is a critical aspect of treatment. The patient must be explained that flare-ups do occur and are treatable and such instances do not affect the

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

outcome of the treatment. Since fear and anxiety are directly related to the perception, the pain can be successfully managed if there is a reduction in the level of fear and anxiety. The problem must be addressed to the patient and explained about the possible reasons for the pain and swelling. The most important step is to break the pain cycle[5,10].

Pharmacotherapeutics

Local anaesthetics

Sensory nerve blockade is difficult with analgesics, thus demanding the use of long acting local anesthetics[47]. Breaking the pain cycle is important psychologically and neurophysiologically[48].

Antibiotics

Antibiotics are widely used in endodontics, but their use is debatable in patients with pain and swelling. The systemic use of antibiotics should be restricted and prescribed only when there are systemic manifestations like cellulitis, fever, malaise and toxaemia[5,37]. Antibiotics are effective when the cause of fare-ups is microbial. Penicillin is used for most of the dental infections. Because of the poly- microbial cause of dental infections, antibiotics to treat the anaerobic infections are also commonly prescribed[37].

Analgesics

Mild to moderate cases are treated with NSAID's and severe cases or which are unresponsive to NSAID's are treated with opioids and steroids[5]. NSAID's have analgesic with little or no anti-inflammatory properties. Their analgesic and anti-inflammatory property is due to the inhibition of prostaglandin synthesis by cyclo-oxygenase enzyme[49]. They also inhibit phosphodiesterase, leading to increased cyclic AMP production[50]. Narcotic analgesics react with the neurons in the brainstem, spinalcord, thalamus and cerebral cortex[51]. Sharp, localized pain are poorly reliev0ed by opiates, whereas they relieve dull, chronic and less severe pain. However they are capable of increasing the pain threshold by causing relaxation and freedom from anxiety[52].

Systemic corticosteroids have been successfully used to reduce the pain and swelling of dental origin[53-57]. The incidence of post-op pain was less when steroids were administered pre-operatively.

Prevention

Certain guidelines should be followed by the clinician to prevent the occurrence of flare-ups. Access cavities should never be left open during the inter-appoinment period as there are chances for the development of secondary peri-radicular infections. Access cavities should never be dried with compressed air as there are chances for extrusion of debris. To avoid this cotton pellets can be used for this purpose. Instrumentation technique which causes less periapical debris extrusion should be selected. Cases reporting with pain on percussion in the first visit should be relieved occlusally. The entire treatment should be performed under aseptic conditions with frequent irrigation. Single visits are preferred in cases of vital teeth and multiple visits in cases with apical periodontitis. Mechanical debridement should be completed in the same visit. Interappointment dressing with medication is effective in eliminating the microflora[37].

Conclusion

Though the occurrence of endodontic flare-ups does not affect the treatment outcome, it is undesirable to both the patient and the clinician. So it is the responsibility of the clinician to follow proper guidelines and employ proper measures to prevent its occurrence and be able to treat it effectively if it occurs. Having knowledge of its etiopathogenesis, contributing factors and treatment modalities will help to manage the situation effectively.

References

1. Siqueira JF. Microbial causes of endodontic flare-ups. Int Endod J. 2003; 36:453-63.

2. American Association of Endodontists. Glossary of endodontic terms, 7th ed. Chicago, American Association of Endodontists; 2003.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

3. Siqueira Jr JF, Barnett F. Interappointment pain:mechanisms, diagnosis, and treatment. Endodontic Topics 2004, 7, 93–109.

4. Priyanka SR, Veronica DR. Flare-Ups in Endodontics- A Review. IOSR Jour Dental and Material Sciences. 2013;9(4):26-31.

5. Kaur P. Endodontic flare ups: A proposal for etiopathogenesis and psychological management. Int J of Health. 2015;3(2):42-6.

6. Van Wijk J, Hoogstraten J. Reducing fear ofpain associated with endodontic therapy. Int Endod J. 2006;39:384-88.

7. Alves OV. Endodontic flare - ups: a prospective study. Med Oral Patol Oral Cir Bucal2010;110:e68-72.

8. Udoye Ch, Aguwa E. Flare - up incidence and related factors in adults. J Dent Oral Hyg2010; 2:19-22.

9. Ehrmann EH, Messer HH, Adams GG. The relationshipof intracanal medicaments to postoperative pain in endodontics Int Endod J 2003;36:868- 75.

10. Walton RE. Interappointment flare-ups: incidence, related factors, prevention, and management. Endodontic topics 2002:3; 67-76.

11. Pamboo J et al. incidence and factors associated with flare-ups in a post graduate programme in the Indian population. J Clin Exp Dent. 2014;6(5):e514-9.

12. Cohen's pathways of pulp

13. Seltzer S, Naidorf IJ , Flare-ups in endodontics. Part I. Etiological factors. Jour Endodontic 1985: 11, 472-8.

14. Torabinejad M, Kattering JD, McGraw JC, Cummings RR, Dwyer TG, Tobias TS Factors associated with endodontic inter-appoinment emergencies of teeth with necrotic pulps. Jour Endodontics 1988: 14, 261-6.

15. Imura N, Zuolo ML. Factors associated with endodontic flare-ups: a prospective study. Int Endod J. 1995;28:261-5.

16. Sundqvist G Bacteriological Studies of Necrotic Dental Pulps(dissertation). Umea, Sweden: University of Umea, 1976

17. Van Winkelhoff AJ, Carlee AW Graaff Bacteroides endodontalis and other black-pigmented Bacteroides species in odontogenic abscesses. Infection and Immunity 1985: 49,494-8.

18. Haapasalo M, Ranta H, Shah H Black pigmented Bacteroides spp. in human apical periodontitis. Infection and Immunity 1986: 53,149-53.

19. Siqueira JF Jr) Aetiology of endodontic failure: why well-treated teeth can fail. Internat Endodontic Jour 2001a: 34,1-10.

20. Yoshida M, Fukshima H, Yamamoto K, Ogawa K, Toda T, Sasawa H Correlation between clinical symptoms and microorganisms isolated from root canals of teeth with periapical pathosis. Journal of Endodontics 1987: 13, 24-8.

21. Hashioka K, Yamasaki M, Nakane A, Horiba N, Nakamura H (1992). The relationship between clinical symptoms and anaerobic bacteria from infected root canals. Jour Endodontics 18,558-61.

22. Wittgow WC Jr, SabistonCb Jr Microorganisms from pulp chambers of intact teeth with necrotic pulps. Jour Endodontics 1975: 1, 168-71.

23. Siqueira JF Jr Tratamento das Infeccoesendodonticas. Rio de Janeiro, Brazil: Medsi, 1997

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

24. Chavez de Paz Villanueva LE Fusobacterium nucleatum in endodontic flare-ups. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics 2002: 93, 179-83.

25. Siqueira JF Jr, Lima KC Staphylococcuse pidermis and Stapylococcusxylosus in a secondary root canal infection with persistent symptoms: a case report. Austr Endodontic Jour 2002: 28, 61-3.

26. Siqueira JF Jr, Rocs IN, Favieri A, Abad EC, Castro AJR, Gahyva SMM Bacterial leakage in coronally unsealed root canals obturated with three different techniques. Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology and Endodontics 2000a: 90, 587-90.

27. Siqueira JF Jr, Lopes HP, Uzeda M (1998a) Recontmination of coronally unsealed root canals medicated with camphorated paramonochlorophenol or calcium hydroxide pastes after salia challenge. Jour Endodontics 24, 11-4.

28. Matusow RJ Endodontic cellulitis 'flare-up'. Case report. Austr Dental Jour 1995: 40, 36-8.

29. Walton R, Fouad A. Endodontic interappointment flareups.a prospective study of incidence and related factors. J Endod1992: 18: 172–177.

30. Torabinejad M, Kettering J, McGraw J, Cummings R, Dwyer T, Tobias T. Factors associated with endodontic inter appointment emergencies of teeth with necrotic pulps. J Endod1988: 14: 261–266.

31. Hulsmann M, Hahn W, Complications during root canal irrigation – literature review and case reports, Internat Endodontic Jour 2000; 33; 186-193.

32. Rosenberg P, Babick P, Schertzer L, Leung A. Effect of occlusal reduction on pain after instrumentation. J Endod1998:24: 492–496.

33. Walton R, Chiappenelli J. Prophylactic penicillin; effect on post treatment symptoms following root canal treatment of asymptomatic periapical pathosis. J Endod1993: 19: 466–470.

34. Pickenpaugh L, Reader A, Beck M, Meyers W, Peterson L. Effect of prophylactic amoxicillin on endodontic flare-up in asymptomatic, necrotic teeth. J Endod2001: 27: 53–56

35. Dionne R. Preemptive vs. preventive analgesia: which approach improves clinical outcomes? Compend Contin Educ Dent 2000: 21: 51–456.

36. Garg N, Garg A internal anatomy. In Textbook of Endodon-tics 2nd ed. (Garg N & Garg A Eds.), New Delhi, Jaypee 2010: 173.

37. Seltzer S, Irving J, Naidorf I. Flare-ups in endodontics II. Therapeutic measures. J Endod.2004;30,7.

38. Maddox DL, Walton RE, Davis CO. Incidence of posttreatment endodontic pain related to medicaments and other factors. J Endodon 1977;3:447.

39. Kleier DJ, Mullaney TP. Effects of formocresol on posttreatment pain of endodontic origin in vital molars. J Endodon 1980;6:566

40. Harrison JW, Bellizzi R, Osetek EM. The clinical toxicity of endodontic medicaments. J Endodon 1979;5:42.

41. Harrison JW, Baumgartner JC, Svec T. Incidence of pain associated with clinical factors during and after root canal therapy. Part 1. Inter-appointment pain. J Endodon 1983;9:384.

42. 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 1961;14:74.

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

43. Goldstein IM. Pharmacologic manipulation of lysosomal enzyme release from polymorphonuclear leukocytes. J Invest Dermatol 1976;67:622.

44. Vane JR. Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. Nature New Biol 1971;231:232.

45. Kebabian JW, Greengard P. Dopamine-sensitive adenyl cyclase: Possible role in synaptic transmission. Science 1971;174:1346.

46. Smith RG, Patterson SS, El-Kafrawy AH. Histologic study of the effects of hydrocortisone on the apical peridontium of dogs. J Endodon 1976;2:376.

47. Dunsky J & Moore P Long-acting local anesthetics. A comparison of bupivicane and etidocaine in endodontics. J Endod 1984: 10, 457–461.

48. Dunsky J & Moore P Long-acting local anesthetics. A comparison of bupivicane and etidocaine in endodontics. J Endod1984:10, 457–461.

49. Flower RJ. Drugs which inhibit prostaglandin biosynthesis. Pharmacol Rev 1974;26:33.

50. 58. Weiss B, Haitt WN. Selective cyclic nucleotide phosphodiesterase inhibitors as potential therapeutic agents. Ann Rev PharmacolToxicol 1977; 17:441.

51. Miller RR. Clinical effects of pentazocine in hospitalized and medical patients. J Clin Pharmacol 1975;15:198.

52. Schuster CR. Behavioral methods for the study of drug interactions. Interactions of drugs of abuse. Ann NY Acad Sci 1976;281:64.

53. Messer JE, Keller JJ. The use of intraoral dexamethasone after extraction of mandibular

ISSN: 0975-3583, 0976-2833 VOL12, ISSUE 01, 2021

third molars. Oral Surg 1975;40:594.

54. Caci F, Gluck GM. Double-blind study of prednisolone and papase as inhibitors of complications after oral surgery. J Am Dent Assoc 1976;93:325.

55. Greenfield W, Carusso WA. Systemic use of steroids following office oral surgery. NY StateDent J 1976;42:482.

56. Huffman GG. Use of methylprednisolone sodium succinate to reduce post-operative edema after removal of impacted third molars.J Oral Surg 1977;35:198.

57. Williamson LW, Lovson EL, Osborn BB. Hypothalamic-pituitary-adrenal suppression after short-term dexamethasone therapy for oral surgical procedures. J Oral Surg 1980;38:20