THE SAAD ESSAY PRIZE

# DISCUSS HOW PAIN IS CONTROLLED IN ENDODONTIC THERAPY

**Rhodri Thomas** 

2014

#### This Is Going to Hurt Just a Bit

One thing I like less than most things is sitting in a dentist chair with my mouth wide open,

And that I will never have to do it again is a hope that I am against hope hopin'.

Because some tortures are physical and some are mental, but the one that is both is dental.

## Introduction

It has been over half a century since the American poet Ogden Nash offered his satire towards the dental profession and yet today's dental practioners still continue to be challenged. The terms pain and root canal are often thought of as one by the public<sup>[1]</sup> and clinicians must frequently deal with this misguided preconception. Managing this pain is an integral part of the field of endodontics, often considered a sign of clinical excellence; it requires a thorough understanding of the pain system and the mechanisms by which drugs and therapies offer relief.

Dental pain may arise before, during or after endodontic therapy and the method for management of this pain is different in each case. This paper aims to explain the mechanisms responsible for this pain and then address its management in relation to stages of treatment.

#### Where does this pain arise from?

Pain can be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage." <sup>[2]</sup> The perception of this pain is subjective, varying greatly between patients and their individual backgrounds. <sup>[3]</sup>

The nociceptors responsible for dental pain are the A beta and A delta nerve fibres which transmit sharp stabbing pain and the C delta nerve fibers which transmit slow dull pain. The principal fibres concerned with inflammatory pain from the dental pulp and periradicular tissues are thought to be the unmyelinated C fibres. This is attributed to C

fibres comprising 70-90% of the innervation to the pulp along with their responsiveness to inflammatory mediators and the dull ache commonly associated to C fibres that accompanies pulpitis.<sup>[1]</sup>

Fig.1 represents a diagram explaining two mechanisms, the hydrodynamic theory and inflammation, which are responsible for the stimulation of these nociceptive nerve fibres in both the dental pulp and the periradicular tissues.

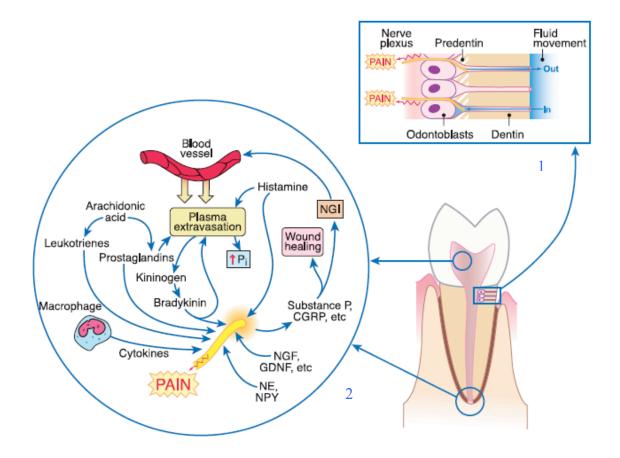


Fig.1-The mechanisms responsible for dental pain:

- 1. Acute dentinal pain: According to the hydrodynamic theory, stimuli that cause fluid movement in exposed dentinal tubules result in the stimulation of nociceptive nerve fibers.
- 2. Pain with inflammation: Inflammation is associated with the synthesis or release of mediators, including prostaglandins, bradykinin, substance P, and histamine. The interrelationships of these inflammatory mediators form a positive feedback loop, allowing inflammation to persist far beyond cessation of the dental procedure.

From Hargreaves K. M.<sup>[6]</sup>

# **Pain Management**

A sensible and effective approach to the management of endodontic pain is first to diagnose the cause of pain, and then offer definite treatment with the use of drugs and other therapies if appropriate.

#### Diagnosis

When presenting with pain, a patients symptoms often do not correlate to their histological findings, <sup>[7,8]</sup> despite this challenge, it is essential that before the management of pain can begin an accurate diagnosis is made. A patient who presents with pain from a tooth may be suffering from a vast range of problems such as periapical disease, pain of non odontogenic origin, a fractured tooth, referred pain, dentine hypersensitivity, irreversible pulpitis, reversible pulpitis or even an abscess to name but a few. Treatments for each of these diagnoses are different and hence effective pain management and treatment hinges upon a correct diagnosis.

# **Definitive Treatment**

It is worth noting that frequently dental treatment itself can be used to manage pain. In instances where an abscess has formed, incision and drainage may be indicated, or the pulpectomy of an irreversibly inflamed pulp, both of these procedures reduce pain by reducing concentrations of mediators and lowering tissue pressure.<sup>[9]</sup> Therefore, an accurate diagnosis and effective treatment can be used before other therapies are needed.

# Drugs Pre Treatment

The management of pain particularly during the initial phases of endodontic treatment is fundamental to put the patient at ease not only in that moment but also for the remainder of

treatment. It allows the patient to gain confidence in the dentist and the dentist to proceed with his clinical work without worry.

# **Nonnarcotic Analgesics**

A major class of drugs that can be used before treatment begins is the nonnarcotic analgesics; this includes both the nonsteroidal antiinflammatory drugs (NSAIDs) and paracetamol.

Before treatment begins the administration of an NSAID has been shown to produce a significant benefit for the patient to reduce post treatment pain.<sup>[10]</sup> The rationale behind this approach is to reduce the input from peripheral nociceptors while also acting upon the CNS.<sup>[11]</sup> Even those who cannot take NSAIDS have been shown to benefit from pre treatment administration of paracetamol.<sup>[12]</sup>

There is very limited evidence against this approach<sup>[13]</sup> and when combined with other therapies to be discussed later, it would seem this is a valuable step for placing the patient at ease.

Despite a wide range of NSAIDs available (See Table 1) there are unfortunately few comprehensive studies comparing the efficacy and safety of each when used for endodontic pain. Therefore only suggestions can be made to dental practitioners.

Analgesic	Dose Range (mg)	Daily Dose (mg)
Paracetemol	325-1000	4000
Aspirin	325-1000	4000
Diclofenac Potassium	50-100	150-200
Ibuprofen	200-800	24000
Naproxen	250-500	1500
Ketoprofen	25-75	300
Fenoprofen	200	1200

Table 1. A summary of Selected Nonnarcotic Analgesics. Adapted from Hargreaves<sup>[1]</sup>

Ibuprofen is the most commonly used of these drugs, due to its efficacy and well documented safety <sup>[14]</sup> even though Ketoprofen may be more a powerful analgesic. <sup>[15]</sup> Therefore it is advised that patients can be pretreated 30 minutes before the procedure with either an NSAID (e.g. ibuprofen 400 mg) or with paracetamol 1000 mg.

The first systematic reviewing comparing NSAIDs and their use in endodontics to reduce post endodontic pain concluded that both pre treatment and post treatment with NSAIDs provides effective pain relief.<sup>[16]</sup> However, the clinician should be aware of limitations and drug interactions when considering the use of NSAIDs for managing endodontic pain.<sup>[17]</sup>

# **During Treatment**

#### Local Anaesthesia

It is important to achieve profound anaesthesia prior to commencing treatment. It is also vital to ensure this is of adequate duration. However, achieving sufficient anaesthesia in teeth with an inflamed pulp is often a challenge for dental practitioners. Several theories surround this medical challenge, it is thought infection lowers the pH, which prevents anaesthetic penetrating the nerve membrane as the anaesthetic molecule does not dissociate, remaining in its ionised form. <sup>[18]</sup> Others suggest that inflammation alters resting potentials, leading to the inability of local anaesthetics to prevent impulse transmission <sup>[19,20]</sup> or simply that nervous patients have a lowered pain threshold. <sup>[20]</sup> For these reasons, supplementary techniques and therapies are often advised to be used alongside local anaesthetics.

A valuable pharmacological approach for pain management is the use of long-acting local anaesthetics. Bupivacaine has consistently been shown to eliminate pain during the endodontic therapy and reduce both post treatment pain and the need for analgesics after treatment has completed. <sup>[21,22]</sup> Case selection is important with such anaesthetics as some patients may not like the long lasting sensation and children must take care after an ID nerve block to not unintentionally injure their lips, cheeks or tongue.

# **Supplemental Intra-osseous injection**

Intra-osseous injections placed distal to the target tooth are useful to allow direct access to cancellous bone and overcome the challenges of anaesthetic penetrating the cortical plate. The Stabident system, used on posterior teeth within the mandible has high success rates of 89%. <sup>[23]</sup> The X-Tip system offers similarly high success rates at 82%. <sup>[24]</sup> The use of articaine as oppose to lidocaine in these instances also achieves comparable success results of 86%. <sup>[25]</sup>

#### **Intrapulpal injection**

When pain continues to persist when the pulp is entered intrapulpal injections may be considered as a last option, working by raising the pressure within the pulp to an extent that the nerves depolarize once and then remain unresponsive. The main disadvantage here is the potentially painful administration of the injection. <sup>[26]</sup> However it can be highly successful (94%) when given under backpressure as oppose to passively depositing the solution. <sup>[26]</sup>

#### Corticosteroids

The use of cotricosteroids to prevent postoperative pain has been increasingly investigated in the last decade. <sup>[27]</sup> During shaping of a canal system, the periradicular tissues may become unintentionally irritated by bacterial products, irrigants, bacteria or necrotic tissue. This will cause the release of inflammatory mediators, increased vascular permeability and tissue pressure, leading to stimulation of pain fibres. <sup>[28]</sup> Corticosteroids aim to prevent this pathway from occurring.

#### Intracanal

Intracanal administration is one method. One study indicated the use of dexamethasone solution reduces pain at 24 hrs but not in the days following. <sup>[29]</sup> A further study showed the use of a steroid solution reduced post op pain when the pulp was vital but offered no relief when the pulp was necrotic. <sup>[30]</sup> Additional studies did not manage to show significant differences or effectiveness to reduce pain with the use of ledermix, calcium hydroxide or formocresol. <sup>[31]</sup> Although another study did provide evidence ledermix reduced post treatment pain compared to calcium hydroxide or no dressing at all. <sup>[32]</sup> Despite mixed reviews it can be concluded that while other pain control methods may be more effective, intracanal use of steroids may reduce post treatment pain in the short term and when the pulp is vital.

## Systemic

Intramuscular injections of dexamethasone have been shown in several studies to reduce pain at 4-8 hours post treatment but no longer. <sup>[33, 34]</sup> Oral administration of dexamethosone achieved similar results with 8-24 hours being the maximum times post treatment pain was controlled. <sup>[35]</sup> The most compelling evidence for the use of systemic corticosteroids comes from an intra osseous injection of methylprednisalone, which sustained significant pain reduction in teeth with irreversible pulpitis for 7 days. <sup>[36]</sup>

Despite this, the overall efficacy and safety of these drugs means they are rarely used and other methods of pain control should be used before corticosteroids are considered.

#### **Post Treatment**

Pain following treatment is a crucial aspect of endodontic therapy that must be managed. This pain is usually most severe within the first 12 hours <sup>[37]</sup> and as shown by a cochrane systematic review, may be more common after single visit treatments. <sup>[38]</sup> However, its prevalence appears to vary greatly, especially between stages of treatment, recently reported by Ince *et al.* <sup>[39]</sup> to be at 70% out of 306 patients following canal preparation

while Ng *et al.* <sup>[40]</sup> reports 40% of 415 patients report pain following canal obturation. Yet an even more recent systematic review by Nixdorf *et al.* <sup>[41]</sup> revealed post treatment pain to occur in 5.3% of cases, even lower than previously reported by Fox *et al.* at 10%. <sup>[42]</sup> The discrepancy in reports may be attributed to the skill of the dentists, patient selection and actions taken after treatment was complete. Despite the variation in occurrence of post treatment pain, it can still be successfully managed with the correct therapies.

# **Opioid analgesics.**

Opioids are a group of analgesics that can be used for the relief of this pain, commonly in combination with ibuprofen or paracetamol (See Table 2). They inhibit both signals from the trigeminal nucleus to higher centers in the brain and act on peripheral opioid receptors in the dental pulp.<sup>[42]</sup> It is also worth noting, that besides opioids often being used in tablet form, when morphine is administered as an intraligamentary injection it has been shown to notably reduce endodontic pain.<sup>[44, 45]</sup>

Analgesic	Dose (mg)
Codeine	60
Dihydrocodeine	60
Hydrocodone	10
Tramadol	50

Table 2. A summary of Selected Opioid Analgesics. Adapted from Troullos et al. [46]

Clinicians should however be aware that the side effects of opioids do limit their use, such as nausea, drowsiness and dizziness. A commonly advised strategy to manage post treatment pain does include the use of opioids, but in combination with other drugs, this is known as a flexible plan.

# Flexible Plan.

To minimise post treatment pain and side effects a flexible plan for the administration of drugs can be used (Fig.2). The hope is that a patient can receive sufficient pain relief by use of timed NSAIDS taken as per the specific drugs instructions and if needed the addition of paracetamol or parecatemol-opioid combination.

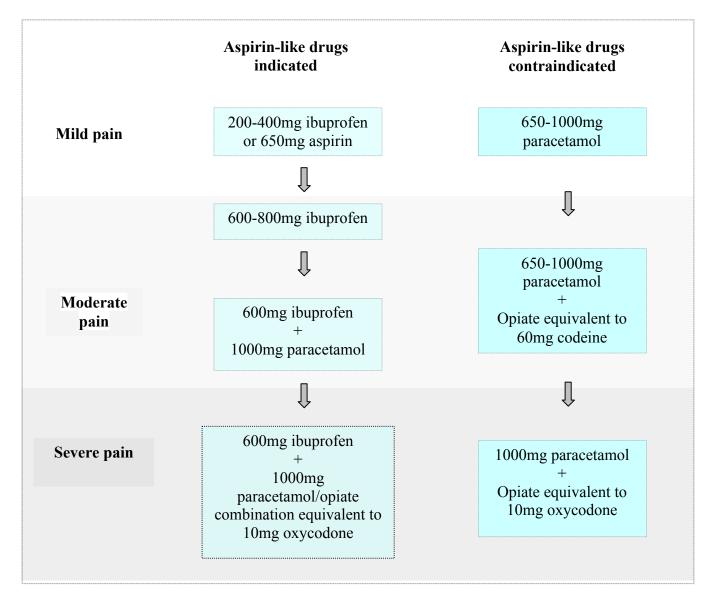


Fig. 2- A flexible analgesic plan. Adapted from Hargreaves<sup>[1]</sup>

Several studies have indicated that ibuprofen combined with paracetamol or a paracetamolopioid combination is significantly more effective than ibuprofen alone (See Fig.3).<sup>[47, 48]</sup>

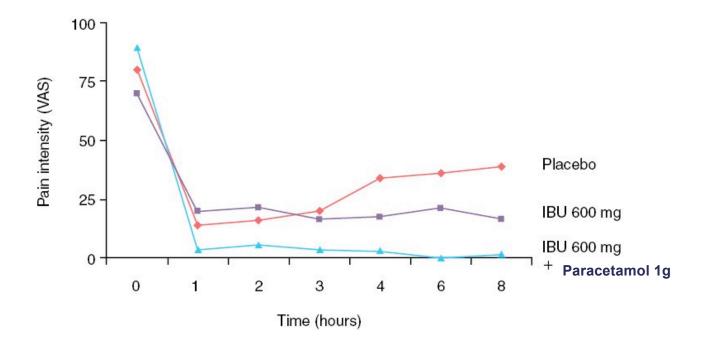


Fig. 3- Comparison of ibuprofen 600 mg with paracetamol 1g to ibuprofen alone or to placebo treatment in postendodontic pain patients. *From Menhinick et al.* <sup>[48]</sup>

As apparent in this graph, a combination approach achieves minimal pain intensity not only initially, but also consistently for the entire duration of the drugs effects when compared to ibuprofen alone. Therefore this method of pain control following treatment is highly effective and simple to put in place.

# Antibiotics.

Antibiotics are indicated to manage infection of endodontic origin, when there are systemic signs of infection or swelling. And in these cases they are effective in reducing bacterial counts and relieving patient pain. However the prophylactic administration of antibiotics to attempt to reduce post treatment pain is controversial for well-known reasons of bacterial resistance and patient sensitisation.<sup>[49]</sup> A recent cochrane systematic review concluded antibiotics offer no pain relief where irreversible pulpitis is concerned.<sup>[50]</sup> Furthermore, two randomised, prospective, clinical studies have shown the prophylactic use of antibiotics offers no reduction in post treatment pain or flare-ups.<sup>[51, 52]</sup> This information should be recognised by clinicians to appreciate the correct circumstances to administer antibiotics to achieve pain relief.

#### **Further techniques**

## Sedation

Inhalation or intravenous sedation are both viable options for reducing patient anxiety and placing the patient more at ease. While sedation does directly reduce pain, it has been shown that high levels of anxiety reduce pain tolerance. <sup>[53]</sup> Therefore, as sedation reduces patient anxiety, pain tolerance also increases and the patient is able to undergo endodontic treatment in a more comfortable manner.

# Hypnotherapy

Deep breathing combined with muscle relaxation is an effective way of reducing anxiety and stress in patients. <sup>[54, 55]</sup> Practicing this method has been shown to quickly and effectively help the patient to enter a relaxed state. <sup>[56]</sup>

Guided imagery is another technique that can be used to relax an anxious patient.<sup>[57]</sup> Focussing on a place that is comfortable and safe to the patient will help to manage pain during procedures,<sup>[58, 59]</sup> especially when combined with relaxation techniques.<sup>[60]</sup> Recent research has reinforced findings that these techniques can be used to manage pain and anxiety in the dental environment.<sup>[61]</sup>

# Acupuncture

Evidence from two systematic reviews would suggest that acupuncture is effective in managing pain during and after dental procedures. <sup>[62, 63]</sup> However, further research is required on this topic to define the optimal technique and draw comparisons to other methods of pain control but this alternative treatment may be one to consider for the future.

#### Conclusion

The management of pain in endodontic therapy is a demanding but critical area of dentistry. Understanding the neurophysiology responsible in addition to the possible variation in diagnoses is vital to establishing the correct approach to alleviate pain. An effective method for the successful management of endodontic pain involves tailoring methods of pain control for each individual patient and the use of appropriate therapies at each stage throughout treatment.

Pre treatment administration of NSAIDS, followed by effective local anaesthetics or long acting anaesthetics and lastly a flexible pharmacological plan that includes opioids is a basic structure for dental practioners to use. Alternative methods can easily be integrated to this framework, as should careful clinical techniques and effective patient communication.

As a final word, we must remember what Ogden Nash said, "*some tortures are physical and some are mental, but the one that is both is dental.*" An empathetic approach, ensuring the patient is at ease and is reassured before the management of the physiological pain itself begins is essential to a dental practioners success.

#### Bibliography

Hargreaves K M and Cohen S. Cohen's Pathways of the pulp. 10th ed. Mosby Elsevier.
2010. pp 671-690.

2. International association for the study of pain Sub-Committee on Taxonomy. Pain Terms: a list with definitions and notes on usage, recommended by the IASP Sub-Committee on Taxonomy. *Pain*. 1979. 6:249-252.

3. Dorner TE, Muckenhuber J, Stronegger WJ, Rasky E, Gustorff B, Freidl W. The impact of socio-economic status on pain and the perception of disability due to pain. *European Journal of Pain*. 2011. 15:103–9.

4. Johnsen D, Johns S. Quantitation of nerve fibres in the primary and permanent canine and incisor teeth in man. *Arch Oral Biol.* 1978. 23(9):825–829.

5. Nair PN. Neural elements in dental pulp and dentine. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1995. 80(6):710–719.

6. Hargreaves K. M. Seltzer and Bender's Dental Pulp. Second Edition. Edited by K.M. Hargreaves, H.E. Goodis and F.R. Tay. Quintessence Publishing Co., Chicago. 2012.

7. Seltzer S, Bender IB, Ziontz M. The dynamics of pulp inflammation: correlations between diagnostic data and actual histological findings in the pulp. Part I. *Oral Surg Oral Med Oral Pathol.* 1963. 16:846.

8. Seltzer S, Bender IB, Ziontz M. The dynamics of pulp inflammation: correlations between diagnostic data and actual histological findings in the pulp. Part II. *Oral Surg Oral Med Oral Pathol.* 1963. 16:969-77.

9. Hasselgren G, Reit C: Emergency pulpotomy: pain relieving effect with and without the use of sedative dressings, *J Endod. 1989.* 15:254.

 Jackson DL, Moore PA, Hargreaves KM. Preoperative nonsteroidal anti-inflammatory medication for the prevention of postoperative dental pain. *J Am Dent Assoc.* 1989.
119:641-647.

11. Svensson CI, Yaksh T L. The spinal phospholipase cyclooxygenase-prostanoid cascade in nociceptive processing. *Annu Rev Pharmacol Toxicol*. 2002. 42:553-583.

12. Moore PA, Werther JR, Seldin EB, Stevens CM. Analgesic regimens for third molar surgery: pharmacologic and behavioral considerations, *J Am Dent Assoc.* 1986. 113:739-744.

13. Attar S, Bowles WR, Baisden MK, Hodges JS, McClanahan SB. Evaluation of pretreatment analgesia and endodontic treatment for postoperative endodontic pain. *J Endod*. 2008. 34: 652-655.

14. Dionne R. Suppression of dental pain by the preoperative administration of flubiprofen. *Am J Med Sci.* 1986. 80:41

15. Cooper S, Berrie R, Cohn P. The analgesic efficacy of ketoprofen compared to ibuprofen and placebo. *Adv Ther.* 1988. 5:43

16. Holstein A, Hargreaves KM, Niederman R. Evaluation of NSAIDs for treating Post endodontic pain. *Endod Topics*. 2002. 3:3-13.

17. Byrne B. Drug interactions: a review and update. Endod Topics. 2004. 4:9-21.

18. Malamed SF. Handbook of Local Anesthesia. 4th ed. St. Louis; Mosby. 1997.

19. Byers MR, Taylor PE, Khayat BG, Kimberly CL. Effects of injury and inflammation on pulpal and periapical nerves. *J Endod*. 1990. 16:78-84.

20. Gutmann JL, Dumsha T. Problem solving in endodontics. In: Gutmann JL, Dumsha TC, Lovdahl PE, Hovland EG. Problems in Managing Endodontic emergencies St. Louis;C.V. Mosby, 1997.

21. More TJ, Dunsky JL. Bupivacaine anaesthesia – a clinical trial for endodontic therapy. *Oral Surg Oral Med Oral Pathol.* 1983. 55:176.

22. Parirokh M, Yosefi MH, Nakhaee N, Manochehrifar H, Abbott PV, Reza Forghani F. Effect of bupivacaine on postoperative pain for inferior alveolar nerve block anesthesia after single-visit root canal treatment in teeth with irreversible pulpitis. *J Endod*. 2012. 38(8):1035-9.

23 - Parente SA, Anderson RW, Herman WW, Kimbrough FW, Weller NR. Anaesthetic efficacy of the supplemental intraosseous injection for teeth with irreversible pulpitis. *J Endod.* 1998. 24(12):826-828.

24. Nusstein J, Kennedy S, Reader A, Beck M, Weaver J. Anesthetic Efficacy of the Supplemental X-tip Intraosseous Injection in Patients with Irreversible Pulpitis. *J Endod*. 2003. 29(11):724-728.

 Bigby J, Reader A, Nusstein J, Beck M, Weaver J. Articaine for Supplemental Intraosseous Anesthesia in Patients With Irreversible Pulpitis. *J Endod*. 2006. 32(11):1044-1047.

26. VanGheluwe J, Walton R. Intrapulpal injection: Factors related to effectiveness. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997. 83(1):38-40.

27. Marshall G. Consideration of steroids for endodontic pain. *Endod Topics*. 2002. 3:41-51.

28.Heyerass KJ, Berggreen E. Interstitial fluid pressure in normal and inflamed pulp. *Crit Rev Oral Biol Med.* 1999. 10(3):328-36.

29. Moskow A, Morse DR, Krasner P, Furst ML. Intra canal use of corticosteroid solution as an endodontic anodyne. *Oral surg Oral med Oral Pathol*. 1984. 58(5):600-604.

30. Chance K, Lin L, Shovlin F, Skribner J. Clinicial trial of intracanal corticosteroid in root canal therapy. *J Endod*. 1987. 13(9):466-468.

31. Trope M.. Relationship of intracnal medicaments to endodontic flare ups. *Endod Dent Traumatol.* 1990. 6(5):226-269.

32. Hermann EH, Messer HH, Adams GG. The relationship of intracanal medicaments to postoperative pain in endodontics. *Int Endod J.* 2003. 36(12):868-875.

33. Marshall J, Walton R. The effect of intramasucular ijection of steroid on posttreatment endodontic pain. *J Endod*. 1985. 10(12):584-588.

34. Leisinger A, Marshall F. Effect of variable doses of dexamethasone on posttreatment endodontic pain. *J Endod*. 1993. 19(1):35-39.

35. Krasner P, Jackson E. Management of postteatrment endodontic pain with oral dexamethosine: a double blind study. *Oral Surg Oral Med Oral Path*. 1986. 62(2):187-190.

36. Gallatin E, Reader A, Nist R, Beck M. Pain reduction in untreated irreversible pulpitis using an intraosseous injection of Depo-Mendrol. *J Endod*. 2000. 26(11):633-638.

37. Seymour RA, Blair GS, Wyatt FAR. Postoperative dental pain and analgesics efficacy. Part I. *Br J Oral Surg.* 1983. 21:290–297.

38- 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. 34(9):1041-1047.

39. Ince B, Ercan E, Dalli M, Dulgergil CT, Zorba YO, Colak H. Incidence of postoperative pain after singleand multi-visit endodontic treatment in teeth with vital and non-vital pulp. *Eur J Dent*. 2009. 3(4):273–279.

40. 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. 37(6):381–391.

41. Nixdorf DR, Moana-Filho EJ, Law AS, McGuire LA, Hodges JS, John MT. Frequency of persistent tooth pain after root canal therapy: a systematic review and metaanalysis. *J Endod*. 2010. 36(2):224–230.

42. Fox J, Atkinson JS, Dinin AP. Incidence of pain following one-visit endodontic treatment. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1970. 30:123–30.

43. Fehrenbacher J, Sun XX, Locke E, Henry M, Hargreaves KM. Capsaicin-evoked iCGRP release from the human dental pulp: a model system for the study of peripheral neuropeptide secretion in normal healthy tissue. *Pain*. 2009. 144(3):253-261.

44. Hargreaves KM, Joris J. The peripheral analgesic effects of opioids. *J Am Pain Soc.* 1993. 2:51.

45. Hargreaves KM, Keating K, Gathers S, Dionne RA. Analgesic effects of morphine after PDL injection in endodontic patients. *J Dent.* 1991. 70:445.

46. Troullos E, Freeman R, Dionne RA. The scientific basis for analgesic use in detnsirty. *Anaesth Prog.* 1986. 33(3):123-138.

47. Breivik E, Barkvoll P, Skovlun E. Combining Diclofenac with acetaminophen or actemominophen-codeine after oral surgery: a randomized, double blind, single oral dose study. *Clin Pharmacol Ther*. 1999. 66(6):625-635

48. Menhinick K, Gutmann J, Regan J, Taylor SE, Buschang PH. The efficacy of pain control following non surgical root canal treatment using ibuprofen or a combinatin of ibuprofenand acetaminophen in a randomized double blind, placebo-controlled study. *Int Endod J.* 2003. 37(8):531-541.

49- Fouad A. Are antibiotics effective for endodontic pain? An evidence based review. *Endod Topics*. 2002. 3(1):52-66.

50. Keenan JV, Farman AG, Fedorowicz Z, Newton JT. A cochrane systematic review finds no evidence to support the use of antibiotics for pain relief in irreversible pulpitis. *J Endod.* 2006. 32(2):87-92.

51. Walton R Chiappinelli J. Prophylactic penicillin: effect on posttreatment symptoms following root canal treatment of asymptomatic periapical pathosis. *J Endod*. 1993. 19(9):466-470.

52. Fouad A, Rivera E, Walton R. Penicillin as a supplement in resolving the localised acute periapical abscess. *Oral Surg Oral Med Oral Pathol.* 1996. 81(5):590-595.

53. Rhudy JL, Meagher MW. Fear and anxiety: divergent effects on human pain thresholds. *Pain.* 2000. 84(1):65-75.

54. Corah NL, Gale EN, Illig SJ. The use of relaxation and distraction to reduce psychological stress during dental procedures. *J Am Dent Assoc.* 1979. 98(3):390-394.

55. Corah NL, Gale EN, Pace LF, Seyrek SK. Relaxation and musical programming as means of reducing psychological stress during dental procedures. *J Am Dent Assoc.* 1981. 103(2):232-234.

56. Milgrom P, Weinstein P, Getz T: The problem of fear in dentistry. In: Milgrom P,Weinstein P, Getz T, ed. Treating fearing dental patients: a patient management handbook,2nd ed. Seattle, WA: University of Washington, Continuing Dental Education. 1995.

57. Bills IG. The use of hypnosis in the management of dental phobia. *Aust J Clin Experimental Hypnosis*. 1993. 21:13.

58. Fick LJ, Lang EV, Logan HL, Lutgendorf S, Benotsch EG. Imagery contact during nonpharmacologic analgesia in the procedure site: where your patients would rather be. *Acad Radiol.* 1999. 6:457.

59. Lang EV, Lutgendorf S, Logan H. Nonpharmacologic analgesia and anxiolysis for interventional radiological procedures. *Semin Interv Radiol.* 1999. 16:113.

60. Shaw AJ, Niven N. Theoretical concepts and practical application of hypnosis in the treatment of children and adolescents with dental fear and anxiety. *British Dental Journal*. 1996. 180(1):11-6

61. Lang EV, Benotsch EG, Fick LJ. Adjunctive non-pharmacological analgesia for invasive medical procedures: a randomised trial. *Lancet*. 2000. 355(9214):1486-1490.

62. Ernst E, Pittler MH. The effectiveness of acupuncture in treating acute dental pain: a systematic review. *Br Dent J.* 1998. 184(9)443-437.

63. Rosted P. The use of acupuncture in dentistry: a review of the scientific validity of published papers. *Oral Dis.* 4(2):100-104.