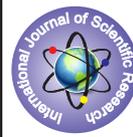


An in vivo comparative pain evaluation on using *Azadirachta indica* as an intracanal medicament



Dental Science

KEYWORDS: *Azadirachta indica*, intracanal medicament, Neem, pain

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ABSTRACT

Herbal products are renewable resources having advantages of easy availability, cost effectiveness, increased shelf life, low toxicity and lack of reported microbial resistance. While in vivo observations of herbal products appear promising, clinical trials are needed to evaluate the biocompatibility and safety factor before they can conclusively be recommended as intracanal medicaments and irrigants. Products made from *Azadirachta indica* have been used in India since two millennia. As a root canal irrigant, *Azadirachta indica* extract has exhibited better antimicrobial properties than Sodium hypochlorite.

Objective: To clinically evaluate pain on using *Azadirachta indica* as an intracanal medicament in comparison with standard intracanal medicaments

Materials and methods: Fifteen patients with chief complaint of pain were evaluated prior to endodontic treatment using the Heft-Parker visual analogue scale. The patients were divided randomly into three different groups as follows: Group A- 5 patients receiving Calcium hydroxide and Chlorhexidine as intracanal medicament, Group B- 5 patients receiving Calcium hydroxide and saline and Group C- 5 patients receiving *Azadirachta indica* (Neem) powder and saline. This was followed by access cavity preparation, working length determination and intracanal medicament placement. At the third evaluation, after one week, obturation was undertaken if the patient was asymptomatic.

Results: Calcium hydroxide with Chlorhexidine reduced pain significantly better than *Azadirachta indica* extract.

Clinical significance: As an intracanal medicament, *Azadirachta indica* extract is less efficacious than Calcium hydroxide combinations in reducing interappointment pain. This study does not negate the beneficial effects of *Azadirachta indica*, but Neem when used in a dried leaf powder form with saline does not have a strong analgesic property

Introduction

The basic biological rationale for achieving success with root canal treatment consists primarily of eliminating microorganisms from the entire root canal system and creating an environment that is most favourable for healing. [1] One approach is to restrict the recolonisation of bacteria in the root canal by the usage of intracanal medicaments, which also decrease the pain experience of the patient. Plant-derived medicines have been a part of health care and oral care since hundreds of years. In endodontics, because of the cytotoxic reactions of most of the commercial intracanal medicaments used and their inability to eliminate bacteria from dentinal tubules, the recent trend is biologic medication extracted from natural plants.[2,3] Prior to broadly recommending the usage of herbal derivatives in all areas of endodontics, these phytomedicines need to be evaluated in vivo to compare their efficacy with standard potent medicaments.

Aim: to evaluate pain on using *Azadirachta indica* as an intracanal medicament in comparison with two other standard intracanal medicaments

Materials and methods:

From amongst the patients reporting to the out-patient department of Endodontics, fifteen patients with the chief complaint of moderate to severe pain in single rooted teeth that were scheduled for root canal treatment were included in the study. Prior to commencement

of the in vivo study, ethical clearance was obtained from the institutional ethical board. Every patient was explained in detail in the local language regarding the proposed study and written consent obtained for participation in the study. Pain of the patient was evaluated at the commencement of endodontic treatment, prior to administration of local anesthetic using the Heft-Parker visual analogue scale (VAS). Patients were instructed to place a mark on the horizontal scale to represent the intensity of pain experience; furthermore, they were asked to use the verbal descriptors as a guide. Patients recorded their pre-operative pain level by using a VAS in the presence of a clinician to ensure that they understood the instructions. The standard procedure for all groups at the first visit included local anaesthesia, rubber dam isolation, pulp extirpation and standard access preparation. The patients were randomly distributed by another blinded operator into three different groups for placement of intracanal medication.

Group A: Calcium hydroxide [Calcium hydroxide Safe plus, Neelkanth healthcare, Jodhpur, India] and 0.1% Chlorhexidine [Chlorhexidine gluconate solution Safe plus, Neelkanth healthcare, Jodhpur, India]

Group B: Calcium hydroxide and saline [Sodium chloride irrigating solution IP, Parenteral drugs, India]

Group C: *Azadirachta indica* powder [Arishtha powder, Ashruth

laboratories, Goa, India] and saline

After placement of the respective intracanal medicaments, the patients were recalled 3 days later for the completion of chemo-mechanical preparation. Patients recorded their pain level by using the VAS prior to commencement of treatment in the second appointment. Intracanal medicament was placed on completion of chemo-mechanical preparation with standard stepback technique. The patients were recalled after one week for obturation with lateral gutta percha compaction and pain was evaluated using the VAS.

The data thus obtained was submitted for statistical analysis done using SPSS version 14. A p-value of <0.05 was considered statistically significant. Comparison of mean VAS scores was done using ANOVA with post-hoc Tukey's test (Table 1)

Results:

Group A: Patients experienced moderate to severe pain in teeth at the pre-operative VAS assessment. They exhibited the least pain after chemo-mechanical preparation and no significant pain was noted at the third appointment.

Group B: Patients experienced moderate to severe pain in tooth at the pre-operative VAS assessment, reduced pain at the second sitting after placement of the medicament and minimal pain was noted at the obturation appointment.

Group C: Patients experienced moderate to severe pain at the pre-operative VAS assessment. A transiently severe pain was noted after placement of Neem. The pain was moderately high at the appointment scheduled for obturation and two patients reported swelling. Therefore, obturation was rescheduled and completed only when the patient was asymptomatic. [Graph 1]

Discussion

Owing to the cytotoxic reactions of many of the commercially available intracanal medicaments, their difficulty in eliminating bacteria completely from dentinal tubules as well as their overuse and misuse, medication extracted from natural plants (phytomedicines) are being increasingly researched for use. [4] Herbal products are renewable resources having advantages of easy availability, cost effectiveness, increased shelf life, low toxicity and lack of reported microbial resistance. The in vitro observations of herbal products appear promising but preclinical and clinical trials are needed to evaluate the biocompatibility and safety factor before they can conclusively be recommended as intracanal irrigating solutions and medicaments.

The current intracanal medicament of choice is calcium hydroxide. Studies have shown Calcium hydroxide to be an effective antimicrobial agent and an efficacious interappointment dressing over several weeks.[5] It is the 'gold standard' against which any new intracanal medicament can be compared and evaluated. Hence it was chosen for comparison with *Azadirachta indica* extract.

A preliminary study in 1993 by the National Institutes of Health reported positive results in in vitro tests where Neem bark extracts killed the AIDS virus.[6] Scientific studies agree with the anecdotal evidence and thousands of years of traditional use of Neem.[7] According to the University of Michigan Health system, Neem leaf products can be used to treat and prevent dental health ailments.[8]

Bohora et al state that the antioxidant and antimicrobial properties make Neem a potential agent for root canal irrigation as an alternative to sodium hypochlorite.[9] In addition to antibacterial, antifungal, antiviral, anti-inflammatory, antipyretic, anti-oxidant, analgesic and immunostimulant properties, Neem also has anti-adherence activity by altering the bacterial adhesion and ability of the microbe to colonise.[10] The active components of Neem are nimbin, niimbinol, nimbanene, 6-desacetylnimbinene, nimbandiol, nimboldide, ascorbic acid, n-hexacosanol, aminoacid, 7-desacetyl-7-

benzoylazadiradion, 7-desacetyl-7-benzoylgedunie and 17-hydroxyazadiradione.[11]

Candida albicans and *Enterococcus faecalis* are the most predominant microorganisms recovered from root canals of teeth. Several in vitro studies have shown that *Azadirachta indica* (Neem) leaf is a viable medicament against *C. albicans*, *E. Faecalis* and even their mixed state. [9,12]

In the present study, Calcium hydroxide in combination with Chlorhexidine reduced pain significantly better than *Azadirachta indica* extract. As an intracanal medicament, *Azadirachta indica* extract was less efficacious than combinations of Calcium hydroxide in reducing inter-appointment pain. Two patients of Group C reported pain and swelling at the third recall. The probable causes may be that a dried form of neem leaf may be inactive as an analgesic. The vehicle (saline) may not allow proper condensation of Neem into the root canal. The percolation property of saline may be inadequate in Neem in powder form. The powder form of Neem may not be active on periapical tissues. Further study and clinical research regarding the form of Neem and the vehicle to be used and its effect on the endodontic system as a whole are required.

As the global scenario is now changing towards the use of non-toxic plant products that have traditional medicinal usage- Ethnomedicine- extensive research and developmental work therefore should be undertaken on Neem and its products for their better economic and therapeutic utilization. Simultaneously, a thorough analysis regarding their usage must be conducted before these herbal medicines replace the currently established medicaments. This study does not negate the beneficial effects of *Azadirachta indica*, but it emphasizes the fact that Neem when used in a dried leaf powder form with saline does not have a strong analgesic property.

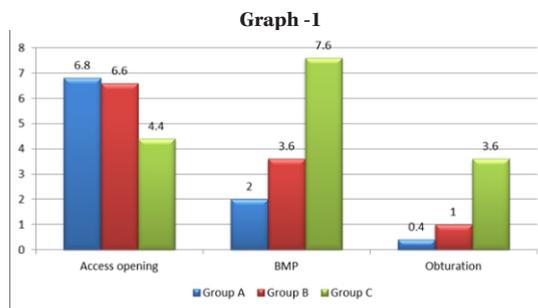


Table 1

| | group | | | | | | p-value | Post-hoc test |
|----------------|-------|------|------|------|------|------|-------------|---------------|
| | A | | B | | C | | | |
| | Mean | SD | Mean | SD | Mean | SD | | |
| Access opening | 6.80 | 1.92 | 6.60 | 2.41 | 4.40 | 2.70 | 0.245; NS | - |
| BMP | 2.00 | 1.22 | 3.60 | 1.67 | 7.60 | 1.95 | <0.001; Sig | C>A,B |
| Obturation | .40 | .55 | 1.00 | 1.22 | 3.60 | 2.70 | 0.102; NS | - |

References

1. Singh S, Garg A. Incidence of post-operative pain after single visit and multiple visit root canal treatment: A randomized controlled trial. J Conserv Dent 2012;15:323-7
2. Palombo EA. Traditional medicinal plant extracts and natural products with activity against oral bacteria: potential application in the prevention and treatment of oral diseases. Evidence-based Complementary and Alternative Medicine.2011
3. Kamat S, Rajeev K, Saraf P. Role of herbs in endodontics: An update. Endodontology. 2011;23:96-100
4. Neelakantan P, Jagannathan N, Nazar N. Ethnopharmacological approach in endodontic treatment: A focused review. International Journal of Drug Development and Research. 2011
5. Badr AE, Omar N, Badria FA. A laboratory evaluation of the antibacterial and cytotoxic effect of Liquorice when used as root canal medicament. International Endodontic Journal. 2011, Jan 1;44(1):51-8
6. Anyaehie UB. Medicinal properties of fractionated acetone/water neem (*Azadirachta indica*) leaf extract from Nigeria: A review. Nigerian Journal of Physiological Sciences 2009;24 (2): 157 -159
7. Chatterjee A, Saluja M, Singh N, Kandwal A. To evaluate the antigingivitis and antiplaque effect of *Azadirachta indica* (neem) mouthrinse on plaque induced gingivitis: A double-blind, randomized, controlled trial. J Indian Soc Periodontol 2011;15:398-401

8. Pai MR, Acharya LD, Udupa N. The effect of two different dental gels and a mouthwash on plaque and gingival scores: a six-week clinical study. *Int Dent J* 2004;54:219-23.
9. Bohora A, Hegde V, Kokate S. Comparison of antibacterial efficacy of neem leaf extract and 2% sodium hypochlorite against *E. faecalis*, *C. albicans* and mixed culture- an in vitro study. *Endodontology* 2010;22:8-12
10. Vinoth B, Manivasagaperumal R, Rajaravindran M. Phytochemical analysis and antibacterial activity of *Azadirachta indica* A. Juss. *Int J Res Plant Sci* 2012;2(3):50-5
11. Kaushik A, Tanwar R, Kaushik M. Ethnomedicine: Applications of Neem (*Azadirachta indica*) in dentistry. *Dental hypothesis*. 2012, volume 3, issue 3, page 112-114
12. Hegde V, Kesaria DP. Comparative evaluation of antimicrobial activity of neem, propolis, turmeric, liquorice and sodium hypochlorite as root canal irrigants against *E. faecalis* and *C. albicans*- An in vitro study. *Endodontology*. 2013 Dec;25(2):38-45