

Original Article

Effect of Propolis Extract in Combination with Eugenol-Free Dressing (Coe-Pak™) on Pain and Wound Healing after Crown-Lengthening: A Randomized Clinical Trial

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KEY WORDS

Propolis;

Dressing;

Crown lengthening;

ABSTRACT

Statement of the Problem: Researchers have long been in search of products to enhance healing and patient comfort postoperatively.

Purpose: This study aimed to assess the efficacy of propolis extract in combination with Coe-Pak™ dressing for pain relief and wound healing after crown lengthening surgery.

Materials and Method: This randomized clinical trial was performed on 36 patients who were randomly divided into two groups of Coe-Pak™ dressing with (trial group) and without (control group) propolis extract. Pain and burning sensation by use of visual analog scale (VAS) and number of analgesics taken were asked from patients. Gingival color and consistency, bleeding on probing (BOP) and presence of infection were studied 7 days after dressing removal.

Results: Although a large number of patients in the trial group did not have burning sensation, this difference was not significant between the two groups ($p > 0.05$). In both groups, the majority of patients experienced moderate and mild pain and there was no pain in the trial group after three days. No significant difference was noted between the two groups in pain score and number of analgesics taken ($p > 0.05$). The two groups were not significantly different in terms of inflammation and healing process (BOP, gingival consistency and color), after 7 days ($p > 0.05$).

Conclusion: The study results showed no difference in use of Coe-Pak™ dressing with and without propolis extract in terms of postoperative pain and healing process following the crown lengthening surgery. More studies are required to confirm these results.

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Received June 2016;
Received in revised form August 2016;
Accepted November 2016;

Cite this article as: Askari M., Saffarpour A., Purhashemi J., Beyki A. Effect of Propolis Extract in Combination with Eugenol-Free Dressing (Coe-Pak™) on Pain and Wound Healing after Crown-Lengthening: A Randomized Clinical Trial. *J Dent Shiraz Univ Med Sci.*, 2017 September; 18(3): 173-180.

Introduction

Periodontal dressings were introduced for the first time in 1923 when Ward used a paste obtained from eugenol for wound protection. [1] There are different types of dressing materials for coverage and protection of wound surface after periodontal surgery. [2] The conventional periodontal dressings provide a neutral mechanical bar-

rier. Dressings do not affect cellular behaviors or biological events that occur during the healing phase. [3] An ideal dressing should be soft with sufficient flexibility for easy application. It should have adequate setting time and optimal stability. It should be non-allergic as well. [4] In the recent years, researchers have been in search of safe natural compounds with tissue healing

properties, easy application, low cost and antibacterial effects. [5] Propolis is a non-toxic resin material in the form of paste with a pleasant smell and a color changing from green to dark brown. [6-7] Antimicrobial activity of propolis is its most important biological property. Evidence shows that propolis is effective on a wide range of Gram-positive and Gram-negative bacteria, fungi and viruses. Although the properties of propolis depend on the source of extracts used by each hive, all types show considerable antibacterial activity. [8] Propolis is a strong antioxidant and this property is related to the high concentration of phenolic compounds in its composition. [9] Moreover, it increases antibody production and activates the T and B-lymphocytes. This property is seen in all propolis types. [10] Propolis can serve as an anti-inflammatory agent since it contains flavonoids and cinnamic acid derivatives, which regulate prostaglandin and leukotriene production and activity of myeloperoxidase, NADPH-oxidase, ornithine decarboxylase, tyrosine-kinase and hyaluronidase. [11-12] It has been reported that propolis extract can be used in dentistry as a topical anesthetic with low absorbance. [13] Propolis has some properties that can be effective for wound healing. [14-17] It decreases the activity of free radicals and enhances the healing of wound matrix. [17-19] Propolis has positive effects on collagen metabolism during the healing phase and increases the tissue content of collagen types 1 and 3, which play a role in regeneration of cellular matrix and formation of granulation tissue. [16] Coe-Pak™ is a commonly used dressing in periodontal surgery. Its mechanism of action is based on the reaction of metal oxide and fatty acids. [17] It serves as a protective barrier for wound. Aside from its mild antibacterial activity, it has no other effect on wound healing. [18-19] Considering the optimal biological properties of propolis, this study aimed to assess the efficacy of application of propolis extract in combination with eugenol-free dressing (Coe-Pak™) for enhancement of wound healing after crown lengthening surgery.

Materials and Method

Preparation of 20% propolis hydroalcoholic solution

Propolis was frozen at -20°C and was then ground in a precooled mortar and pestle. The ground material was mixed with 99.8% (v/v) ethanol in a hermetically-sealed

glass container at a ratio of 1 g of propolis powder to 3 mL of ethanol. Containers were incubated for one week at room temperature in the dark, with continuous stirring. The resulting ethanolic solution was centrifuged at 7000 g for 60 s and then the supernatant was collected and filtered by #4 Whatman filter paper. Ethanol-soluble components were collected by evaporation to dryness under vacuum. Next, 20% (w/v) propolis hydroalcoholic solution was obtained by re-dissolving the extract in pure ethanol. The final solution was kept in hermetically-sealed brown-glass bottles at room temperature. [20-21] It has been shown that propolis extract is stable for 6 months, maintaining its antimicrobial activity during this period. [22] In this study, propolis hydroalcoholic solution was produced by a biotechnology company (Suren Tec. Tus, Mashhad, Iran).

Study design and subjects

This randomized clinical trial was performed on patients referred to the Department of Periodontology, in Dental College of Tehran University, 2014-2015. The study was approved by the ethics committee of this university (IR.TUMS.REC.1394.1943). All patients were briefed about the procedure and written informed consent was obtained from all patients.

Inclusion criteria

The inclusion criteria were 1-2 mm of bone removal during crown lengthening surgery, 90-115 minutes duration of surgery, use of chisel and bur, minimum age of 18 years, no systemic disease, no history of periodontal disease at the surgical site, no contraindication for surgery, not requiring antibiotic prophylaxis and no use of corticosteroids or hormones in the past two months.

Exclusion criteria

The exclusion criteria were not showing up for the follow up visit, patients with incomplete files, occurrence of pulpitis in the operated tooth after the procedure, loss of part or all of the periodontal dressing, smoking and allergic reaction to the dressing.

Surgical procedure

The patients rinsed their mouth before surgery with 0.12% chlorhexidine for 30 seconds. Local anesthesia was administered by injecting 2% lidocaine with 1:100,000 epinephrine (Septodont, France). A flap was elevated and granulation tissue was removed. Osteotomy was performed using 13K/TG Kirkland periodontal chisel (Hu-Friedy Dental Instruments, Chicago, USA)

and carbide burs (JOTA AG Rotary Instruments; Ruzh, Switzerland) under saline irrigation until 3mm distance was achieved from the bone crest to the most cervical part of the pocket measured with a Williams periodontal probe (Neumar®). At the end of the procedure, a simple suture was made with a silk thread (Supa, Iran). The operation time from the first incision to the final stitch for all patients ranged from 90 to 115 minutes. After surgery, the patients were randomly divided into two groups of trial and control. The trial group received propolis extract combined with Coe-Pak™ dressing while the control group only received the Coe-Pak™ dressing. Randomization was performed using 10 opaque envelopes containing five cards reading, “propolis extract combined with Coe-Pak™” and envelopes containing five cards reading “Coe-Pak™ dressing”. Each card was randomly allocated to one patient. After the first 10 surgeries, the randomization process was continued until both groups were completed. The examiner was blinded to the group allocation of patients. Before the study, all the procedures and instructions were standardized by an expert. The same materials were used for all patients. In the control group, the dressing was mixed with a sterile spatula on a sterile glass slab according to the manufacturer’s instructions. Dressing was formed on the wound. The same dressing was used in the trial group except that per each 5 mm length of dressing paste, 0.1 mm of 20% propolis hydroalcoholic

solution was added and applied on the wound after mixing. This amount of propolis extract did not have any effect on the final consistency. All patients were instructed to control plaque by rinsing 0.12% chlorhexidine every 12 hours for 7 days. In addition, 400 mg ibuprofen was prescribed every 6 hours for use in case of pain. The amount and the time of first analgesic taken were also recorded. All patients received written and verbal postoperative instructions. Some objective and subjective criteria were used to assess the healing process (Figure 1).

Subjective assessment

Postoperative pain and burning sensation in patients were determined on the first, second, third, fourth, fifth, sixth and seventh days using a visual analog scale (VAS). All patients were contacted between 5-7 P.M. VAS score was as follows:

Pain scale: zero (without pain), 10 (severe pain); scores 1, 2 and 3 showed mild pain, scores 4, 5 and 6 showed moderate pain and scores 8, 9 and 10 showed severe pain.

Burning sensation scale: 0 (no burning sensation), 1 (presence of burning sensation).

Objective assessment

Consistency of gingiva

Gingival consistency was assessed on the seventh day by palpation with a blunt instrument and was scored as soft or firm.

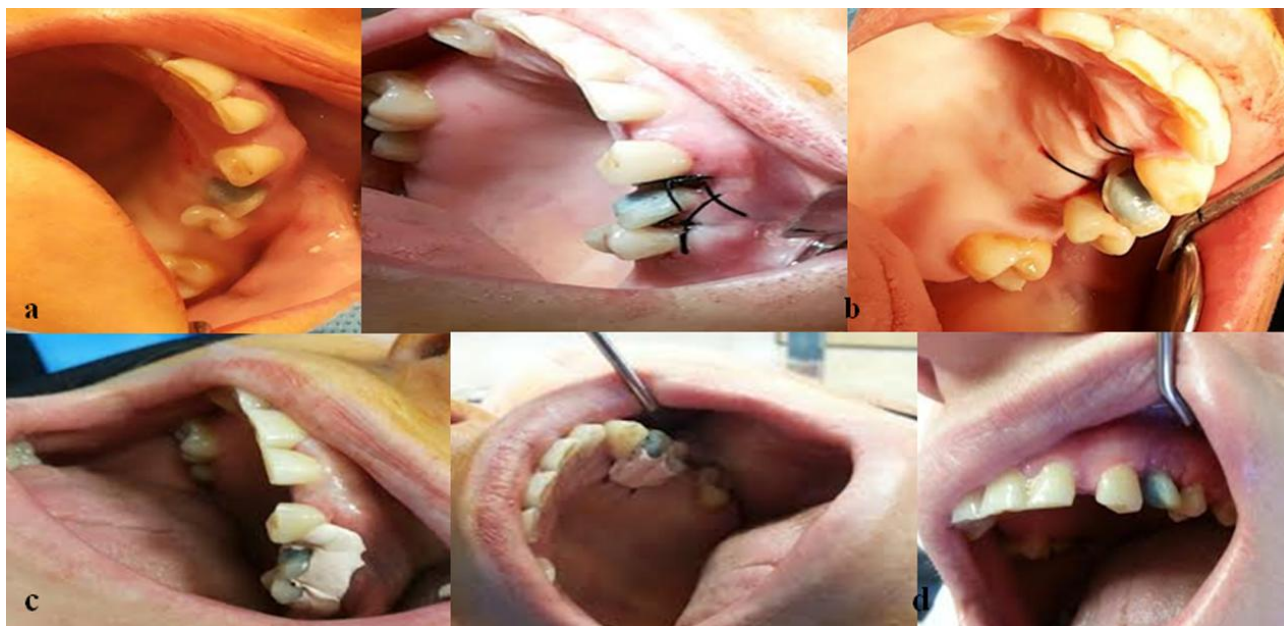


Figure 1a: Before surgery (maxillary left second premolar); **b:** After surgery, **c:** After placement of periodontal dressing (Coe Pak™ and propolis extract), **d:** After 7 days

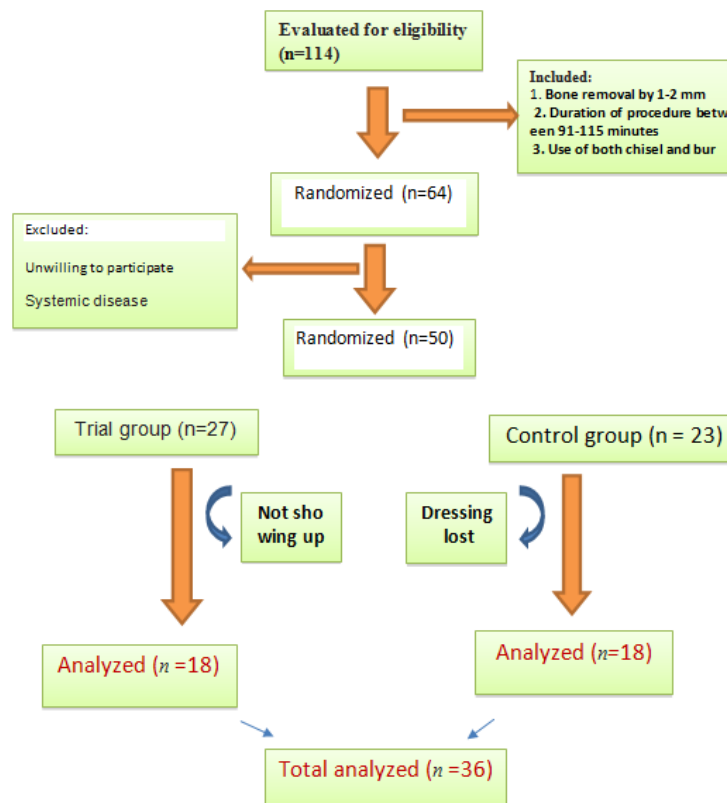


Figure 2: The study flowchart

Color match

Gingival color match of the surgical site with the adjacent gingiva was evaluated using VAS on the seventh day. Score zero indicated no color match while score 10 showed perfect color match with the adjacent gingiva. Scores 1, 2 and 3 showed poor color match, scores 4, 5 and 6 showed moderate color match and scores 8, 9 and 10 showed good color match.

Infection

Presence/absence of infection was assessed on the second and seventh days and scored as zero (without infection) or 1 (with infection).

Bleeding on probing was assessed on the seventh day and scored as zero (without bleeding) or 1 (with bleeding).

Data collection

Sample size was calculated to be 18 patients in each group considering $\alpha=5\%$ and $\beta=0.2$. Sampling method was random.

Statistical analysis

The data were analyzed using SPSS software. The Mann-Whitney test was used for pairwise comparisons. Type one error was considered as $\alpha=5\%$ and $p<0.05$ was considered statistically significant.

Results

Figure 2 shows the study flowchart. From 114 patients that needed crown lengthening surgery, after incorporating three inclusion criteria namely bone removal by 1-2 mm, duration of surgery between 90-115 minutes and use of chisel and bur, only 64 patients remained in the study. After integrating the remaining criteria, 50 patients were qualified to participate in this study. From the mentioned patients, 14 patients were excluded since they lost their dressing earlier than 7 days or did not show up for removal of dressing on the seventh day. Thus, statistical analysis was performed for 36 patients. Table 1 shows the participants' demographics in this study. The number of females was more than males in both groups.

Table 1: Distribution of demographic factors in the two groups

Groups		Control	Trial
Gender	Female	12	12
	Male	6	6
Age (years)	Number	18	18
	Minimum	19	25
	Maximum	54	54
	Mean	36.11	38.67
	Std. deviation	11.504	9.016

Most patients did not report any burning sensation

Table 3: Distribution of pain score in the two groups

Pain during 7 days		0	1	2	3	4	5	6	7	8	9	10	p
First day	Control	2	0	0	2	5	5	0	2	1	1	0	0.460
	Trial	4	0	0	3	4	2	1	2	2	0	0	
Second day	Control	5	1	0	5	3	1	1	1	0	1	0	0.835
	Trial	4	1	4	3	1	1	3	0	1	0	0	
Third day	Control	7	1	1	5	1	1	0	1	0	1	0	0.961
	Trial	6	2	3	1	3	2	1	0	0	0	0	
Fourth day	Control	9	1	4	1	1	1	1	0	0	0	0	0.823
	Trial	10	1	3	0	2	1	1	0	0	0	0	
Fifth day	Control	13	0	2	1	0	2	0	0	0	0	0	0.610
	Trial	11	2	1	2	1	1	0	0	0	0	0	
Sixth day	Control	12	2	1	1	0	1	0	0	0	0	0	0.837
	Trial	12	0	2	2	0	1	0	0	0	0	0	
Seventh day	Control	15	1	0	1	0	0	1	0	0	0	0	0.981
	Trial	15	0	0	2	0	1	0	0	0	0	0	

since the first day in both groups. None of the patients in the trial group had burning sensation from the third day on. Most patients had no burning sensation in the trial group; the difference in this respect was not significant between the two groups ($p > 0.05$; Table 2).

Table 2: Distribution of burning sensation in the two groups during 7 days

Groups	Control		Trial		p Value
	Absence	Presence	Absence	Presence	
First day	14	4	14	4	1.000
Second day	15	3	17	1	0.296
Third day	16	2	18	0	0.151
Fourth day	16	2	18	0	0.151
Fifth day	17	1	18	0	0.317
Sixth day	18	0	18	0	1.000
Seventh day	18	0	18	0	1.000

In both groups, only two patients had severe pain on the first day and the others experienced moderate or mild pain. From the second day on, most patients did not have any pain nor had mild pain.

No severe pain was reported by patients in the trial group from the third day on, but the difference in this respect was not significant between the two groups ($p > 0.05$; Table 3).

Only two patients in the control group did not take any analgesics. Other patients reported taking analgesics since the first postoperative day. In both groups, the patients did not receive analgesics after the third day. The difference in this respect was not significant between the two groups ($p > 0.05$; Table 4).

Table 4: Distribution of analgesic use in the two groups

Group	Number of analgesics taken										p
	Control	0	1	2	3	4	6	8	9	12	
Control	2	2	3	2	1	3	3	1	1	1	0.148
Trial	3	6	2	3	1	1	0	0	2		

Table 5 shows that most patients did not have bleeding on probing after 7 days and following removal of the dressing but the difference in this respect was not significant between the two groups ($p > 0.05$). No infection was noted in any group. After removing the dressing, gingival consistency was soft in patients of both groups and only one patient in each group had firm gingival consistency; the difference in this respect was not significant between the two groups ($p > 0.05$).

Table 5: Distribution of bleeding on probing, infection, gingival color and gingival consistency in the two groups

Groups	Control	Trial	p Value	
Bleeding on probing	With	4	3	0.678
	Without	14	15	
Infection	With	0	0	0.317
	Without	18	18	
Gingival consistency	Soft	17	17	1.000
	Firm	1	1	
	Poor	1	0	
Color match	Moderate	7	6	0.871
	Excellent	10	12	

The color match was good after removing the dressing in patients of both groups and no significant difference was noted between the two groups ($p > 0.05$).

Discussion

Considering the optimal biological effects of propolis, the aim of this study was to compare the efficacy of propolis extract combined with Coe-Pak™ dressing compared to Coe-Pak™ alone for pain relief and wound healing after the crown lengthening surgery. Periodontal dressings are produced from several materials; each constituent is added to serve a purpose. Coe-Pak™ is a commonly used dressing in periodontal surgery. It is supplied in the form of two pastes: the first paste con-

sists of zinc oxide, which contains oil (for plasticity), resin (for tenacity), lorotidol (a fungicide), coconut fatty acids thickened with colophony resin and chlorothymol (a bacteriostatic agent). [23-25]

Biological dressings are used aiming to enhance healing and shorten the recovery period by their impact on cellular behavior. [26-27] The results of the current study showed that most patients in the two groups had no burning sensation since the first day, which is probably due to the protective effect of dressing ($p > 0.05$). However, the benefit of propolis for this purpose was not proven. The results showed that from the second day on, number of patients with no burning sensation in the trial group was more than that in the control group and this number on the third day reached zero. The difference in this respect was not significant between the two groups and should be tested on more patients. A large number of patients had moderate to severe pain from the first day with Coe-Pak™ dressing alone and propolis extract combined with Coe-Pak™. However, pain score was low in many patients on the second day. Evaluation of pain score was the main objective of this research and although the criteria used in this study for this purpose were subjective, these criteria are commonly used for this purpose and have been proven to yield reliable results for pain assessment. [28] Pain after using periodontal dressing following periodontal flap surgery has been reported in some studies; in some cases, severe pain has been reported in the first 48 hours after surgery following the use of periodontal dressing. [29-31] In contrast, some other studies reported the same level of pain in patients who underwent periodontal flap surgery with and without placement of dressing. [32-33] Although in the current study a high number of patients in the trial group had mild pain on the first postoperative day, this difference was not significant with the control group ($p > 0.05$). It seems that adding propolis extract to Coe-Pak™ dressing paste did not have any efficacy for pain relief. Comparison of the analgesic effect of ethanolic extract of propolis with some of its constituents in a previous study revealed that the analgesic effect of 5, 7- dihydroxy flavanone (Pinocembrin), 5 hydroxy-7 methoxyflavone (Pinostrobin) and caffeic acid esters was 3 times higher than that of propolis. [34] We did not notice the analgesic effect of propolis in this study, which may be due to the small amount of propolis add-

ed to Coe-Pak™ dressing since we did not want to have an adverse effect on the consistency of the paste. Addition of the afore-mentioned constituents in their pure form to Coe-Pak™ may yield results that are more favorable.

Resolution of inflammation and enhanced healing, determined by assessment of BOP and gingival color and consistency following dressing removal, were not significantly different between the two groups of Co-Pak™ dressing alone and with propolis at 7 days.

In the present study, gingival swelling subsequent to dressing removal was seen, which has been reported in a previous study as well. [31]

Fatty acids, steroids, Terpenoids, vitamins and mineral present in the composition of propolis play a role in its healing properties. [30] However, these compounds are not well in contact with the connective tissue at the surgical site in periodontal flap surgery. Addition of propolis at a higher concentration or its constituents in pure form to Coe-Pak™ may more effectively decrease pain and inflammation and enhance healing. No significant difference was detected between two groups in our study, which may also be due to the limited surgical site in periodontal flap surgery. The efficacy of addition of propolis to Coe-Pak™ should be evaluated in healing of open wounds secondary to periodontal surgery for example graft procurement from the palate, which has a more complex healing course and enables further contact of connective tissue with the constituents of propolis to cast a judgment regarding the efficacy of propolis for this purpose.

Infection did not occur in any patient and the antimicrobial effects of addition of propolis to Coe-Pak™ could not be determined. It appears that the antimicrobial agents present in the composition of Coe-Pak™ have been effective enough for prevention of microbial infection at the surgical site of periodontal flap surgery under the dressing.

In this study, we used eugenol-free Coe-Pak™ dressing since it causes less inflammation and has more tenacity. [35-37] It yields favorable clinical results due to its optimal physical properties [38] and is commonly used in periodontal studies. [33, 39-41]

Conclusion

The results of this study showed no difference in pain

score and healing process after the crown lengthening surgery between the use of Coe-Pak™ dressing alone or in combination with propolis extract. Future studies with larger sample size are required to confirm these results. The same results were obtained in the trial and control groups in our study. Future studies must include a dressing-free control group or have a split-mouth design to obtain results that are more reliable. Moreover, similar studies are required on open wounds secondary to periodontal surgery since they can better reveal the efficacy of compounds present in the composition of propolis. Methods enabling addition of higher concentrations of propolis to Coe-Pak™ or industrial production of propolis as an oral dressing may result in higher effective dose of propolis at the surgical site and its subsequently higher efficacy.

Acknowledgments

This study was derived from a thesis submitted to Tehran University of Medical Sciences, International Campus.

Conflict of Interest

The authors declare that they have no conflict of interest regarding this study.

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