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Original Article / Оригинални рад

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Influence of different forms of calcium hydroxide and chlorhexidine intracanal medicaments on outcome of endodontic treatment of teeth with chronic apical periodontitis

Утицај различитих облика калцијум-хидроксида и хлорхексидина као интерсеансних медикамената на исход ендодонтског лечења зуба са хроничним периапексним лезијама

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Утицај различитих облика калцијум хидроксида и хлорхексидина као интерсеансних медикамената на исход ендодонтског лечења зуба са хроничним периапексним лезијама

SUMMARY

Introduction/Objective This study determined the 12 months clinical and radiographic periapical healing of teeth with apical periodontitis treating with different formulations of calcium hydroxide (CH): paste (CH-paste) and gutta-percha points (CH-GP), and chlorhexidine (CHX): gel (CHX-gel) and gutta-percha points (CHX-GP).

Methods Eighty patients with chronic apical periodontitis were randomly allocated to 4 different treatment groups according to the intracanal medicament used: CH-paste, CH-GP, CHX-gel and CHX-GP group. Seventy eight patients were analyzed clinically and radiographically 12-month postoperatively. The Periapical index (PAI) was used for radiographic evaluation of treatment success.

Results Overall outcome was classified according to radiographic evaluation only, because in all patients clinical success was observed. In all groups significant reduction in PAI scores were observed ($p < 0.001$). The proportions of healed teeth (PAI ≤ 2) were 73.7%, 60.0%, 68.4% and 65.0% in CH-paste, CH-GP, CHX-gel and CHX-GP group, respectively, with no significant differences between the groups.

Conclusion The results suggested that there are no differences between investigated CH- and CHX-delivery systems regarding treatment outcome of teeth with apical periodontitis.

Keywords: calcium hydroxide; chlorhexidine; periapical diseases, root canal therapy, treatment outcome

САЖЕТАК

Увод/Циљ Циљ овог истраживања је био да се испита клинички и радиографски исход лечења зуба са апексним периодонтитисом 12 месеци након завршене терапије и примене различитих облика калцијум-хидроксида (КХ): паста (КХ-паста) и гутаперка поени (КХ-ГП) и хлорхексидина (ХХ): гел (ХХ-гел) и гутаперка поени (ХХ-ГП).

Методе Рандомизовано је 80 испитаника са хроничним периапексним лезијама су у четири групе на основу врсте коришћеног интерсеансног медикамента: КХ-паста, КХ-ГП, ХХ-гел и ХХ-ГП. Дванаест месеци после завршеног лечења прегледано је 78 испитаника и урађени су ретроалвеоларни снимци. За процену радиографског успеха лечења коришћен је периапикални индекс (ПИ).

Резултати Исход лечења је класификован на основу радиолошког налаза јер је код свих испитаника забележен клинички успех лечења. У свим испитиваним групама је забележено значајно смањење вредности ПИ индекса ($p < 0,001$). Излечење (ПИ ≤ 2) је уочено код 73,3% зуба у групи КХ-паста, 60% у КХ-ГП групи, 68,4% у групи ХХ-гел и код 65% зуба у групи ХХ-ГП, при чему разлике између група нису биле статистички значајне.

Закључак Резултати овог истраживања показују да не постоји разлика у исходу лечења зуба са апексним периодонтитисом након примене испитиваних облика калцијум-хидроксида и хлорхексидина.

Кључне речи: калцијум хидроксид, хлорхексидин, периапексно оболење, ендодонтски третман, исход лечења

INTRODUCTION

Microorganisms play a definite role in the development and persistence of apical periodontitis [1] and the successful endodontic therapy depends on their reduction. Mechanical instrumentation and irrigation significantly reduce, but not completely eliminate microbiota present in the root canal. Therefore, the use of an interappointment intracanal dressing has been recommended to supplement the antibacterial effects of chemomechanical procedures and maximize bacterial reduction [2].

Calcium hydroxide (CH) is one of the most effective antibacterial dressing during endodontic therapy due to its antimicrobial activity, tissue-dissolving ability, detoxification of lipopolysaccharides, and induction of repair by formation of hard tissue [3]. Despite the favourable properties of CH,

other substances, such as chlorhexidine (CHX) has been proposed with the aim of targeting bacteria resistant to CH [4].

Effectiveness of intracanal medicament depends not only on its antibacterial effect but also on its bioavailability directly influenced by delivery system. CH is commonly mixed with aqueous, viscous or oily vehicles, while CHX has been used in form of liquid or gel. Another delivery method for intracanal dressing is the use of gutta-percha points impregnated with medicament, either CH or CHX. According to the manufacturer, these points are easy to insert and remove from the canal, and they have the ability to release large quantities of medicament from their surface in a time-dependent fashion. So far almost all research about medicated gutta-percha points considered only their *in vitro* antibacterial activity, with contrasting results [5-11]. More recently, antibacterial effect of medicated gutta-percha points were evaluated in clinical settings [12,13]. Investigations found no difference of CH gutta-percha points (CH-GP) compared to CH paste [12,13] or CHX gutta-percha points (CHX-GP) [13]. Regardless of the reported antibacterial efficacy of medicated gutta-percha points from some *in vitro* [5-11] and *in vivo* [12,13] studies clinical decision making should be based on outcome of clinical research, because antibacterial efficacy and successful therapeutic treatment might not always coincide with each other. Long-term effectiveness of CH-GP as intracanal medicament was investigated only in few, mainly case report studies. CH-GP were showed to be successful in the treatment of different type of periapical lesions [14], root resorption [14,15], and for apexification treatment [16].

Thus, the aim of this study was to determine the 12 months clinical and radiographic periapical healing of teeth with apical periodontitis treated with different formulations of CH (paste and gutta-percha points) and CHX (gel and gutta-percha points). The null hypothesis tested was that the type of intracanal medicament (CH vs. CHX) or its formulation (paste and gel vs. gutta-percha points) had no influence on the clinical and radiographic healing of teeth with apical periodontitis.

METHODS

Patients selection

The study was approved by the Ethical Committee of the Faculty of Medicine and conformed to the principles embodied in the Declaration of Helsinki. A sample was selected from patients referred to Endodontic Department at the Faculty for nonsurgical root canal treatment between 2011 and 2013.

The inclusion criteria for the study were: 1) Healthy subjects age 18 years and older, both sexes; 2) Single-rooted and single-canalled teeth with nonvital pulps which was confirmed by negative response to sensitivity pulp test (cold and electric stimulation tester); 3) Presence of periapical radiolucencies (minimum size ≥ 2.0 x 2.0 mm); 4) No previous endodontic therapy of the involved tooth; 5) Absence of tooth or root fracture of the involved tooth; 6) Absence of periodontal pocket (> 4 mm) of the involved tooth.

The exclusion criteria were: 1) Absence of enough tooth structure for rubber dam isolation, 2) Patients with contributory medical history; 3) Patients who received antibiotic therapy during previous 6 months.

Once eligibility was confirmed and after written and verbal informed consent was obtained, the patient was randomly assigned to one of following four groups according to the intracanal medicament used: CH-paste (Calxyl-blue, OCO Products GMBH, Dirnstein, Germany), CH-GP (Roeko Calcium hydroxide Plus Points, Coltene/Whaledent, Langenau, Germany), CHX-gel (Consepsis V, Ultradent, South Jordan, Utah, USA) and CHX-GP (Roeko Active Points, Coltene/Whaledent, Langenau, Germany). The sample was randomized using a computer-generated random numbers by a person who did not belong to the research group. The group assignment was passed on the clinician, endodontic specialist, only at the time of treatment. Operator blinding could not be performed due to different colour and form of used medicaments.

The minimum sample size per group was determined with the method described by Zhong [17]. Sixteen teeth per group were calculated to be required to obtain a power of 80% at 5% level of significance, with minimal clinically significant mean difference between groups of 0.5 units (standard deviation±0.5 unit) using the Periapical index scale (PAI) [18]. Assuming possible losses of 20% during 12-month follow-up period, the number of teeth per group was adjusted to 20.

Clinical procedures

Each tooth was polished with pumice and isolated from the oral cavity with a rubber dam. Antisepsis of the crown and operative field was conducted according to a previously described decontamination protocol [19]. All subsequent procedures were performed aseptically. Caries lesion and/or leaking restoration were removed and a standard access cavity was prepared. The canal working length was established using the apex locator (Raypex® 5, VDW, GmbH, Munich, Germany) and confirmed radiographically. Canal instrumentation was performed using step-back technique with K-type files (0.02 taper ISO) and Gates-Glidden drills (both from Dentsply/Maillefer, Ballaigues, Switzerland) to the apical size of at least #35 depending on both the initial size of the root canal and root anatomy. Canal was irrigated with 2 mL of 1% sodium hypochlorite after each file size. When instrumentation was completed, canal was flushed with 5 mL 17% ethylenediaminetetraacetic acid followed by 5 mL of 1% sodium hypochlorite. After drying the canal with sterile paper points, intracanal medicament was placed in the root canal. For teeth assigned to CH-paste group, a lentulo spiral was used to fill canal with a paste. In CHX-gel group, gel was placed into the root canals by means of the syringe and needle. Teeth in CH-GP and CHX-GP were dressed by using medicated gutta-percha point inserted to full working length into the canal with a drop of sterile water, according to the manufacturer's instructions. The access cavity was sealed with temporary filling (Cavit, 3M ESPE AG, Seefeld, Germany) and glass ionomer cement (Fuji IX, GC, Tokyo, Japan). After 15 days with intracanal medication, root canal was obturated with gutta-percha and AH Plus sealer (Dentsply,

DeTrey, GmbH, Konstanz, Germany) using cold lateral compaction technique. Definitive restoration was obtained within one month after completion of treatment.

Assessment of treatment outcome

The comparisons of clinical and radiographic findings at 12-month follow-up with that documented at preoperative examination were used for assessment of outcome of endodontic therapy. One investigator, uninvolved in the treatment of the subjects, performed all follow-up examinations.

Clinical outcome measures were the evaluation of presence of pain, percussion and palpation sensitivity, soft tissue status, tooth mobility, marginal bone level at 12 month. Absence of spontaneous pain and percussion or palpation sensitivity, absence of sinus tract, absence of soft-tissue swelling, absence of tooth mobility and no increase in periodontal probing depth compared with baseline were used as clinical criteria for treatment success (healing).

Radiographic outcome measure was the change in periapical radiolucencies at 12-month follow-up. The radiograph at follow-up was made by using the individual patient's bite registration and the same exposure settings used for the preoperative image. PAI index was used for radiographic evaluation of treatment success [18]. Index consists of five categories numbered 1–5 as follows: 1, normal periapical structures; 2, small changes in bone structure; 3, changes in bone structure with some mineral loss; 4, periodontitis with well-defined radiolucent area; 5, severe periodontitis with exacerbating features, where scores 3 or higher represent disease.

All radiographic films obtained preoperatively and at follow-up were coded blind and organized in random order. To improve calibration and inter-examiner agreement, two experienced endodontists who had not been involved in the treatment or follow-up appointments analyzed a series of radiographs (not related to the study samples) representing a wide range of periapical bone densities, before study evaluation. After that, they independently analyzed the study radiographs under moderate illumination at a light table. In cases of disagreement, joint re-evaluation and consensus were made. After 1 month, the examiners repeated the entire analysis of study radiographs. Inter-and intra-examiner agreement produced a Cohen kappa above 0.71 and 0.81, respectively.

At 12-month follow-up, tooth was classified as healed if presented no clinical signs or symptoms and had PAI ≤ 2, or as unhealed if clinical signs or symptoms were presented and/or had PAI ≥ 3.

Statistical analysis

SPSS 19.0 for Windows (IBM Corp., Armonk, NY, USA) was used for statistical analysis. The distribution of the variables: gender, dental arch involved and tooth type was evaluated using chi-square test, while age was analyzed using ANOVA. The Kruskal-Wallis followed by Mann-Whitney U test and Wilcoxon signed rank test were used for intergroup and intragroup comparison of PAI scores, at baseline and 12-month follow-up, respectively. To determine difference in proportion of

healed teeth between the groups and to identify variables that may influence treatment outcome chi-square was used. A level of $p < 0.05$ was chosen for statistical significance.

RESULTS

Demographic data

At the start of the treatment 80 healthy persons (29 males) were recruited. The mean age was 37.58 (range 18–76) years. From each patient only one tooth was included; 20 teeth per each group. Two of the 80 teeth included in the study were lost at the 12-month follow-up (one in CH-paste and one in CHX-gel group).

Comparisons between the groups showed no statistical difference in the distribution of age, gender, tooth type or dental arch involved (Table 1).

Table 1. Demographic characteristics of study population, tooth type and dental arch by group.

Intracanal medicament form	n	Age mean ± SD	Man n (%)	Women n (%)	Tooth type			Dental arch	
					incisor n (%)	canine n (%)	premolar n (%)	maxilla n (%)	mandible n (%)
CH-paste	19	39.58±10.96	7 (36.8)	12 (63.2)	9 (47.4)	4 (21.0)	6 (31.6)	12 (63.2)	7 (36.8)
CH-GP	20	37.55±17.86	5 (25.0)	15 (75.0)	13 (65.0)	2 (10.0)	5 (25.0)	10 (50.0)	10 (50.0)
CHX-gel	19	39.53±17.32	6 (31.6)	13 (68.4)	10 (52.6)	3 (15.8)	6 (31.6)	14 (73.7)	5 (26.3)
CHX-GP	20	34.65±11.12	9 (45)	11 (55)	9 (45.0)	2 (10.0)	9 (45.0)	14 (70.0)	6 (30.0)
Total	**78**	**37.78±14.56**	**27 (34.6)**	**51 (65.4)**	**41 (52.6)**	**11 (14.1)**	**26 (33.3)**	**50 (64.1)**	**28 (35.9)**
p		0.692	0.596		0.765			0.424	

n- number of teeth; CH-paste-calcium hydroxide paste; CH-GP- calcium hydroxide gutta-percha points; CHX-gel-chlorhexidine gel; CHX-GP- chlorhexidine gutta-percha points.

Treatment outcome

At 12-months examination none of patients had any clinical symptoms and/or abnormal findings. The PAI scores at baseline and 12-month follow-up for CH-paste, CH-GP, CHX-gel and CHX-GP are presented in table 2. No significant differences between the groups were observed for both baseline examination and 12-month control. Intragroup analysis revealed that in all treatment protocols PAI score decreased significantly ($p<0.001$). An improvement in the PAI score was found in all patients except three cases (15%) in CH-GP group.Successful healing (PAI≤ 2) was observed in 73.7%, 60.0%, 68.4% and 65.0% of cases in groups CH-paste, CH-GP, CHX-gel and CHX-GP, respectively ($p=0.832$).

Table 2. Periapical status according to Periapical index (PAI) before and after 12 month follow-up for each group.

Periapical index (PAI)	Before treatment				12-month control				*p*
	CH-paste n=20	CH-GP n=20	CHX-gel n=20	CHX-GP n=20	CH-paste n=19	CH-GP n=20	CHX-gel n=19	CHX-GP n=20	
PAI 1	0	0	0	0	12	8	10	10	<0.001
PAI 2	0	0	0	0	2	4	3	3	<0.001
PAI 3	3	2	4	5	5	4	5	7	<0.001
PAI 4	13	12	10	11	0	3	1	0	<0.001
PAI 5	4	6	6	4	0	1	0	0	<0.001
p	0.681				0.434				

n- number of teeth; CH-paste-calcium hydroxide paste; CH-GP- calcium hydroxide gutta-percha points; CHX-gel- chlorhexidine gel; CHX-GP- chlorhexidine gutta-percha points.

Table 3. Bivariate association between selected variables and success rate (PAI ≤ 2) in total sample.

Variables	n	Success n (%)	*p*
Age			
<38 y	46	30 (65.2)	0.810
≥38 y	32	22 (68.8)	
Gender			
Women	51	33 (64.7)	0.801
Men	27	19 (70.4)	
Tooth type			
Anteriors	52	32 (61.5)	0.210
Premolars	26	20 (76.9)	
Tooth location			
Maxilla	50	30 (60.0)	0.134
Mandible	28	22 (78.6)	
Size of lesion			
< 5mm	62	47 (77.0)	0.001
≥5mm	26	14 (23.0)	
Root-filling*			
Acceptable	64	46 (71.9)	0.058
Unacceptable	14	6 (42.9)	

n- number of teeth; *Acceptable filling- the filling ends 0–2 mm short of the radiographic apex with no voids visible within the material or between the material and the root canal walls; Unacceptable filling-the filing material ends more than 2 mm from the radiographic apex or extruded beyond the apex and/or visible voids within or between the material and the root canal walls.

Influence of other selected variables on treatment outcome in the total material is presented in table 3. Only factor that showed a positive favourable influence on radiographic healing was existence of preoperative periapical lesion smaller than 5 mm (p=0.001).

DISCUSSION

In this study clinical and radiographic parameters of apical periodontitis healing were evaluated concerning different form of intracanal medicaments, paste and gutta-percha points for CH, and gel and gutta-percha points for CHX. To the best of our knowledge, this is the first clinical study assessing the effect of these points on periapical healing. All type of medicaments resulted in similar periapical healing patterns.

In the present study patients were randomly assigned to treatment groups and no significant difference was found between them in terms of preoperative factors (age, sex, tooth type, dental arch and PAI score at baseline). Root canal treatment was performed according to a standardized protocol by one experienced endodontist, representing specialty practice settings. Since in all patients clinical success of treatment was observed, overall outcome was classified according to radiographic evaluation. Limited diagnostic ability of periapical radiography has been well reported on. It has been shown that cone-beam computed tomographic (CBCT) imaging is more accurate than radiography for identifying periapical lesions. However, periapical radiography has been used almost in all endodontic outcome studies so far and has been adopted as a standard of practice. In addition, CBCT is not recommended for routine diagnosis of periapical pathosis and the assessment of the root canal treatment outcome [20]. The applied criteria for treatment outcome were based on those suggested by Ørstavik et al. [18] accepted as a valid and reliable tool for measuring radiographic changes in apical bone density. The variability in radiographic reading is well recognized due to subjectivity of radiographic assessment. To overcome this shortcoming radiographic evaluation in our study was performed by two examiners with a substantial level of intra- and inter-examiner agreement. One year observation period for radiological outcome in this study was chosen as the most of the teeth with preoperative apical periodontitis heal during the first year after treatment [21,22].

All treatment protocols led to significant decrease in PAI scores. About 73.7% of teeth could be judged as healed in CH-paste group, 60% in CH-GP, 68.4% in CHX-gel, and 64% in CHX-GP group. The healing rate observed in CH-paste group is corroborating the results of previous studies in which the calcium hydroxide has been used for intracanal medication of teeth with apical periodontitis [21-23]. Concerning CHX, only available clinical report showed the healing rate of 94% 2–4 years of follow-up after treatment with 2% CHX in form of liquid [24], a rate much higher than for CHX in our study. Disagreement with our findings may be due to difference in chemomechanical preparation, delivery system used for medication and the time frame for outcome observation. However, if decrease in PAI score was used as favourable outcome in our study number of healed teeth would concur well with that obtained by mentioned study [24].

Calcium hydroxide was used as a dressing material in most studies dealing with treatment outcome, with very few exceptions [23]. There are only few studies which demonstrated that the type of intracanal medicaments significantly influence the outcome. The use of calcium hydroxide medicament resulted in better treatment outcome than no dressing [20] or one containing corticosteroid [25]. In the present study, outcome of endodontic therapy of teeth with apical periodontitis did not significantly differ between the groups. Thus, from clinical point of view, healing pattern seems largely unrelated to type and delivery system of intracanal medicament used, suggesting that both CH- and CHX- based medicaments can be used in therapy of primary chronic apical periodontitis. However, there was tendency toward more favourable outcome in teeth medicated with CH-paste (75%) in comparison with CH-GP (60%). Considering the facts that both CH formulations placed in root canal for 15 days showed similar efficacy in periapical healing, and that CH-GP contain more than two times as much CH than CH-paste (58% vs. 23%) it can be assumed that bioavailability of CH in CH-GP is lower. Accordingly, release kinetics of calcium and hydroxyl ions from CH-GP was lower than that of other form of CH [12,26,27]. In addition, CH-GP presented short-term alkalinity [28] and minor antimicrobial activity in comparison to CH-paste [9-11]. In contrast to CH, CHX by itself possess significant pharmacokinetics characteristic, adsorption on oral mucosa and the microbial cell wall (antimicrobial substantivity), permitting it long-lasting antibacterial effect. Some authors found that CHX gel seemed to be more effective than CHX-GP in the reduction of bacterial counts *in situ* [5] and in the inhibition of bacterial colonization of the dentin *in vitro* [29]. Comparing mentioned *in vitro* and *in situ* findings considering only bacterial effectiveness, with our results concerning outcomes obtained from clinical settings gel of 2% CHX and gutta-percha points of 5% CHX showing similar rate of periapical healing, it could be suggested that in clinical situation there are no differences between investigated CHX delivery systems in their bioavailability. Considering influence of medicated gutta-percha points on periapical tissue healing, there is only data about CH-GP, mainly from clinical case series showing CH-GP to be very successful in treating teeth with persistent periapical inflammation [14]. Moreover, Bezgin et al. [16] found acceptable results in apexification treatment using CH-GP and recomended these points as apexification agent in cases

where CH apexification is indicated. However, direct comparison of present with above mentioned studies concerning heling outcome is difficult to make due to differences in study population, diagnosis, and treatment protocol. Further studies, including larger sample size are needed to elucidate clinical effectiveness of medicated gutta-percha points on periapical healing.

In this study we also analyzed possible influence of other variables on treatment outcome. For the total material, only size of periapical lesion had significant impact. Teeth with a preoperative lesion greater than 5 mm had lower healing rate than teeth with smaller lesion. Having in mind that healing process is a function of time, a favourable outcome of smaller sized lesion should be applicable to larger sized lesion, if sufficient time was allowed for healing to take place [30].

CONCLUSION

Under the conditions of this study, there are no differences between investigated CH- and CHX-delivery systems regarding treatment outcome of teeth with apical periodontitis. Definitive conclusions about influence of the type of intracanal medicament on periapical healing cannot be drawn and further randomized controlled trials to identify the most appropriate medication regime (type and method) are needed to carry.

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