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THE EFFECTS OF A NEW DECONTAMINANT SOLUTION ON ROOT CANAL BLEEDING DURING ENDODONTIC TREATMENT: A RANDOMIZED CONTROLLED STUDY

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Blood contamination of the canal during preparation and obturation can be a problem in Endodontics; this may result in apical microleakage. The purpose of this investigation was to observe and evaluate the hemostatic properties of biofilm decontaminant material (sulfonic/sulphuric acid solution, HybenX, EPIEN Medical) used in teeth with necrotic pulp and unstoppable bleeding after root canal shaping. A prospective study was designed with 2 randomized parallel groups: decontaminant material (experimental group) and sodium hypochlorite 5% (control group). The analysis of the root canal bleeding was evaluated by the clinician before and after the application of the sulfonic/sulphuric solution or sodium hypochlorite 5%, by measuring the millimeters of blood on a sterile paper point introduced in the root canal. Sixty patients with necrotic pulp and unstoppable bleeding were enrolled in this study and randomly divided into 2 groups: decontaminant material in 30 patients (experimental group) or sodium hypochlorite 5% in 30 patients (control group). *T*-test showed that the percentage change in millimeters of blood detected in the root canal was statistically greater for experimental group [mean difference: 0.74 (IC: 0.66-0.82); p<0.0001]. The hemostatic properties were better in the experimental group than in the sodium hypochlorite 5% group (control). Further research may be needed to confirm the results of this study.

The necessity to dry the root canal before proceeding to its filling, in order to increase adherence of the filling material to the root canal's walls, is agreed by everyone as a matter of fact (1-3). Indeed, humidity can alter the cement hardening properties, increasing or decreasing the working time (4-6) and inhibit its penetration into the dentinal tubules (7). Blood and/or other exudates represent a state of humidity in the canal: during the performance of a root treatment, pathologic situations can induce a bleeding in the canal that can sometimes be difficult to control, prevent an adequate drying of the canal and lead to the necessity to finish the treatment in more than one session.

Blood presence can inhibit effectiveness of irrigant solutions (sodium hypochlorite), due to a high concentration of albumin (8). The most frequent cause of bleeding is irreversible pulpitis; in this case, the blood comes from the canal system and often needs a prolonged rinsing and waiting time to stop. Other causes of bleeding can be due to iatrogenic factors (over instrumentation, dentinal chips extrusion, irrigation beyond the apex, perforations, stripping) or anatomical factors, such as minor or ignored canals still containing bleeding pulp. Sometimes, bleeding can be connected to the presence of exudate from an acute or chronic apical lesion.

Key words: calcium hydroxide, endodontic treatment, root canal bleeding, root canal exudation

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DISCLOSURE: ALL AUTHORS REPORT NO CONFLICTS OF INTEREST RELEVANT TO THIS ARTICLE.

In most cases, the bleeding stops after canal cleaning and shaping; in all other situations (apical periodontitis, long and over instrumentation, dentinal chips extrusion irrigation past the apex, perforations and stripping) drying the canal may be difficult. Besides, a higher risk of bleeding can be found in patients affected by congenital coagulopathies (coagulation factors deficit) acquired coagulopathies or drug induced (antiplatelet, warfarin or new generation anticoagulants).

To prevent bleeding in patients with coagulation problems, it is necessary to comply with protocols coded for each disease, while no coded procedures are reported in literature for local causes of bleeding. From a clinical point of view, the problem is not worthy of interest and only practical, not experimental, suggestions can be found, mainly about hemostatic drugs generally used in dentistry (pulpotomy, surgical endodontics): lidocaine 1:50.000, ferric sulfate, calcium hydroxide, sodium hypochlorite. There are no coded protocols yet to control root canal bleeding with sure and predictable results.

A new device (HYBENX®, EPIEN Medical, Saint Paul, MN, USA) has been developed with the purpose of destroying dental biofilm. The material is a mixture of hydroxybenzenesulfonic acid (37%) and hydroxymethoxybenzene acids (23%), sulphuric acid (28%), and water (12%). The product is currently marketed by the producer both for use in Periodontics (HybenX Oral Tissue Decontaminant) and for Endodontics (HybenX Root Canal Cleanser). The two forms of the product, which have the same chemical composition but differ in consistency, viscous gel for periodontal use and liquid gel for endodontic use.

This device has been successfully used in periodontology. Recent studies (9, 10) have demonstrated the effectiveness of the oral tissue decontaminant material in the treatment of clinical cases showing acute periodontal abscess without the use of systemic or local antibiotics. Similar favorable effects were obtained in the treatment of peri-implant mucositis and peri-implantitis (11, 12). In addition, a randomized controlled trial (RCT) also demonstrated the beneficial effects of the material in the treatment of oral aphthae (13).

Based on this scientific information, a clinical and microbiological study was planned, using the decontaminant device in cases of teeth with necrotic pulp with the aim to destroy the dental biofilm of root canals. The ability of the decontaminant device to stop bleeding immediately after canal instrumentation was discovered accidentally during the procedures of this still unpublished trial.

Due to this surprising evidence, the authors were interested in evaluating the coagulation property of the decontaminant material. The purpose of this study was to test the reduction of root canal bleeding in terms of significant percentage change for millimeters of blood in the canal at 2 different time points (before and after treatment).

MATERIAL AND METHODS

A single center, participants and biostatistician blind, two-arm, randomized, placebo controlled clinical trial study was performed following the CONSORT statement (14) in the Endodontics Department, University Hospital Florence Careggi, Florence, Italy.

Study population

The study population consisted of patients that were treated between April 2017 and December 2017 at the Endodontics Department of the University Hospital of Florence Careggi, Italy. Subject inclusion criteria were: patients aged between 20 and 60 years, able and willing to sign a consent form, single-rooted teeth with necrotic pulp confirmed by electric vitality test, associated with healthy periodontium, physiologic sulcus depth (<3 mm), and absence of bleeding on the probing of the involved teeth.

Exclusion criteria were: patients with systemic diseases, using anticoagulants, antibiotics, or anti-inflammatory therapies in the last 30 days, patients with an allergy to sulphur in any form and pregnancy. All subjects were informed of the nature and potential risks and benefits of their participation in the study. They also received information on the duration of the procedure and the possible intraoperative and postoperative complications.

The study protocol was submitted and approved by the Ethics Committee of the University Hospital

of Florence (SPE16.302 University Hospital of Florence). Patients provided written and signed informed consent in accordance with the Helsinki Declaration of 1975, as revised in 2000, 2008 and 2013. Each recruited patient was examined, and routine preoperative information with respect to the number of appointments, duration of the procedure, and possible intraoperative and postoperative complications was given.

Treatment

The root canal therapy procedure was standardized and limited to one experienced endodontist (R.P.). Treatments were performed at the Endodontics Departments of the University Hospital of Florence Careggi, Italy, under local anesthesia using 1.8 mL mepivacaine hydrochloride with 1:200000 epinephrine (Optocaine; Molteni Dental SRL, Scandicci, Italy), and the teeth were isolated with rubber dams. After preparing the access cavity, the working length was determined with an electronic apex locator (Propex II Dentsply Maillefer Instruments, Ballaigues, Switzerland) with a size 10 k-file and confirmed taking a periapical radiograph with the 10 k-file inserted in the root canal. Root canals were shaped using ProTaper Universal NiTi files (Dentsply Maillefer Instruments, Ballaigues, Switzerland) in the following sequence: S1, S2, F1, F2, and F3 until each instrument reached the working length.

After each instrument, the root canals were rinsed with NaClO (Niclor 5, Ogna, Italy) using a syringe with a side-vented 30 G needle. ProTaper NiTi instruments were driven with an endodontic motor (XSmart Endo Motor, Dentsply Maillefer Instruments, Ballaigues, Switzerland) with a 16:1 contrangle set up as suggested by the manufacturer.

After the root canal shaping was performed, the root canal was dried with 4 sterile paper points. Quantifying root canal bleeding with paper points can be challenging, since the size of the paper point (if smaller than the apical constriction), will pass the foramen and draw blood or fluid from the periapical area. To avoid this inconvenience, a fifth 30 size-sterile paper point was introduced in the root canal, up to the working length, for 10 seconds to detect blood presence. With a caliber on the sterile paper point, the millimeters of blood present within the root canal were measured.

Only the teeth that at this point showed 1 or more millimeters of blood within the root canal were included in the present study and randomized to the 2 experimental groups to reach the estimated *a priori* sample size. In the patients excluded from the study, the ordinary endodontic treatment was carried out.

Before further treatment, the teeth were allocated to an experimental (HybenX) or a control group (sodium hypochlorite 5%) according to an uneven block randomization designed by the statistician (A.N.). For each tooth, closed envelopes were opened in a consecutive order, assigning the tooth to either the experimental or the control group.

HybenX was approved as a Class I CE medical device by the Italian Ministry of Health (no. 483768) on February 7, 2012.

Experimental Group

The decontaminant material was introduced inside the root canal using the pre-dosed syringe, and activated for 20 sec, with a sterile paper point, with an up and down movement up to the working length. Finally, the canal was rinsed with sterile water using a syringe with a side-vented 30 G needle 1 mm shorter than the working length.

The root canal was then dried with 4 sterile paper points. Finally, a fifth 30 size-sterile paper point was introduced in the root canal, up to the working length, for 10 seconds to detect the presence of blood. The millimeters of blood inside the root canal were measured again according the previous criteria.

Control Group

The root canal was irrigated with 5% sodium hypochlorite with a syringe and a side-vented 30G needle, activated for 20 sec with a sterile paper point with an up and down movement up to the working length to ensure a flow of irrigant solution throughout the canal.

Finally, the canal was rinsed with sterile water using a syringe with a side-vented 30 G needle 1 mm shorter than the working length. The root canal was then dried with four sterile paper points. Finally, a fifth sterile paper point was introduced in the root

canal, up to the working length, for 10 seconds to detect the presence of blood; the millimeters of blood inside the root canal were measured again according the previous criteria.

Sample Size Estimation

A total number of 60 patients (30 patients per group) were evaluated to reject the null hypothesis of equality between the two experimental groups in terms of root canal bleeding based on the following assumptions:

- Power of approximately 90% in rejecting the null hypothesis of equality
- Expected means at the baseline of 4 mm for both of the two groups
- Expected means gain after using the decontaminant material 2.5 mm (reduction of 40%) and 4 mm after using 5% sodium hypochlorite (no reduction)
- Standard deviation of 1.7 mm in both the experimental group
- Overall significance level = 5% two-sided.

Statistical Analysis

Data were analyzed using SAS Version 9.3 software (SAS Institute, Inc., Cary, NC). A preliminary Levene's test was performed to verify the homogeneity of variance for the percentage change in the two groups. A t-test was performed to verify the null hypothesis by using a type I error equal to 0.05. In order to confirm the firmness of the results a Wilcoxon non-parametric test was also carried out.

RESULTS

The initial study sample consisted in 72 consecutive patients with necrotic pulp. After the root canal instrumentation, 12 patients were excluded because they did not present root canal bleeding. Sixty patients (26 women and 34 men) with a mean age of 37.6 years (standard deviation, 10.1 years) (Table I) with a tooth with necrotic pulp and unstoppable root canal bleeding after instrumentation were enrolled in this study, and randomly divided into two groups according to the intervention used in order to control the bleeding:

1. Experimental Group: 30 teeth (14 mandibular teeth, 16 maxillary teeth)

2. Control Group: 30 teeth (11 mandibular teeth, 19 maxillary teeth)

All the efficacy analyses have been performed on the intention to treat (ITT) population. Any deviation from the predetermined randomization list occurred.

Descriptive statistical analysis of millimeters of blood detected in the root canal at baseline and after the treatment in both groups is shown in Table II. No relevant differences in terms of root canal bleeding at the baseline were detected between experimental and control group. Levene's test assessed the equality of variances for the measured variable calculated for the two groups. T-test showed that the percentage change in millimeters of blood detected in the root canal was statistically significant greater for experimental group (Table III). Wilcoxon test, performed to support the

Table I. *Demographic and baseline characteristics.*

	Total	HybenX	Control
Gender			
Men	34	18	16
Women	26	12	14
Age	37.6±10.1	40.1±9.9	35.2±10.2
Smoking habit			
Smokers	41	22	19
Non-smokers	19	8	11
Arch			
Maxillary	35	16	19
Mandible	25	14	11
Position			
Incisive	21	12	9
Canine	18	8	10
Premolar	21	10	11

result of the t-test, confirmed that experimental group was statistically significantly better than control group in percentage change of millimeters of blood in the root canal ($p<0.001$).

DISCUSSION

The results of the present study show the effect of a decontaminat device on the ability to dry the root canal in the presence of serum-hematic blood or exudates.

In case of root canal treatment, more frequently in case of over-instrumentation, a serosanguineous exudate is seen when a sterile paper point is placed into the apical extent of the canal. The persistence of this exudate may significantly affect final sealing with the persistence of microleakage.

Optimum sealing conditions were obtained when totally dry canals were filled with a single gutta-percha cone and a ZOE- based sealer. When Methacrylate-based Endodontic Sealers are used, the root canal walls must have a slight degree of humidity to promote adhesion to the root canal walls, but all materials exhibited some evidence of dye penetration. Root canals that remained totally wet (flooded), showed a higher degree of leakage. In these cases, liquids (irrigant solution, blood, and exudate) cannot be displaced completely in spite of the hydrophilic properties of the sealers. Liquids permeation during the polymerization process might result in the entrapment of water droplets within the sealer-dentin interface. This might result in bond disruption and further increased leakage (15). Furthermore, inflammatory exudate and blood itself are rich in proteins such as albumin, which can partially inactivate the antibacterial activity of commonly used disinfectant in root canal treatment (16).

There are no clinical studies that analyze how the problematic exudate can be controlled during ordinary endodontic treatment; in Literature, most of the studies concern the bleeding in case of pulpotomy. In cases of bleeding from the pulp calcium hydroxide, anesthetic solution with 1:50.000 epinephrine or ferric sulphate placed on a sterile paper point, are recognized as effective hemostatic agents (17-21).

It is generally believed that calcium ions play a key role in the regulation of platelet function (22). Furthermore, the use of calcium hydroxide as a root canal dressing can help to promote platelet aggregation probably because calcium binds to the phospholipids that appear secondary to the platelet activation and provides a surface for assembly of various coagulation factors (23).

According to Mohammadi (24), in a "weeping canal" condition, the most successful way of stopping the exudate is by drying the canal with sterile paper points and placing calcium hydroxide paste in the canal. It is the basic pH of calcium hydroxide that modifies the acidic pH of periapical tissues and changes it into a more basic condition that is responsible for this process. Other theories have been proposed:

a) Ca(OH)2 has a caustic action which can cauterize chronically inflamed tissue (25);

Table II. *Descriptive statistics.*

Group	Variable	N	Mean
1 Experimental	Baseline (mm)	30	3.40
	After treatment (mm)	30	0.26
	% Change	30	0.95
2 Control	Baseline (mm)	30	3.73
	After treatment (mm)	30	3.03
	% Change	30	0.21

b) Ca(OH)2 has an antibacterial effect may have an ability to inactivate toxins (26).

None of the methods with files and conventional irrigant solution (NaOCl 3%-EDTA 17%-Saline solution) used were efficient in removing the entire dressing from the canal walls, leaving 25 to 45% of the surface of the walls covered with the calcium hydroxide dressing, although the instrumentation of root canals allowed irrigation needles to reach most areas (27).

The study revealed that considerable amounts of calcium hydroxide remain at canal walls, and apical regions may interfere with the sealing efficiency from a mechanical point of view; it has also been shown to interact with zinc oxide-eugenol based sealers, influencing the setting reaction of the sealer and blocking the gutta-percha entrance, along with placement up to the working length and in to dentinal tubules. ZnOE cements, when in contact with calcium hydroxide, are completely disorganized as the zinc oxide-eugenol reaction is compensated for the preferential interaction of calcium hydroxide with eugenol. The presence of such remnants at critical areas, like the apical region, may adversely affect the clinical performance of the sealer and possibly the long-term prognosis of root canal therapy (28).

During a still unpublished clinical and microbiological study, using a decontaminant device (sulfonic/sulphuric acid solution) in order to destroy the dental biofilm of root canals, the authors were surprised to verify the immediate cessation of bleeding after using the material. Therefore, due to this outcome, the authors were interested in evaluating the coagulation properties of the decontaminant material during endodontic treatment.

Based on clinical observations, the sulfonic/sulphuric acid solution is able to stop bleeding in the root canal completely and permanently after rinsing it for 20 sec. The sulfonic/sulfuric acid solution is an aqueous solution, and thus it can be removed easily from the root canal with sterile water irrigation. In addition to this, since the device is purple in color, it allows the operator to verify its complete removal from the canal lumen in the drying phase with absorbent paper points. This enables the practitioner to proceed to root canal filling without the use of calcium hydroxide dressings.

Thus, the procedure can be concluded in a single visit. The importance of proceeding with treatment in a single appointment has always been a controversial aspect in Literature. In a review by Morerira et al. all the factors interacting in the endodontic success are evaluated between therapies in a single visit *vs* multiple visits. This review article stated that although there is no statistically significant difference between the two methods, a trend of superiority of the single visit therapy is observed in patients with periapical periodontitis in terms of incidence of postoperative complications and treatment efficacy (29). For this reason, having a device capable of stopping the bleeding that may be present inside the root canal at the end of the shaping and cleaning phase could represent an important tool in everyday endodontic practice.

This solution generates a final effect due both to

Table III. *T-Test on percentage change as (baseline - after treatment) x 100/baseline.*

Group	%Change estimates [95%IC]	H0:LSMean1=LSMean2 Pr > |t|
1 Experimental	0.95 [0.90 – 1,00]	<.0001
2 Sterile Saline Water	0.21 [0.15 – 0.27]	

		Difference Between Means	95% Confidence Limits for LSMean(i)-LSMean(j)	
		0.74	0.66	0.82

the keratolytic effect of hydroxybenzenes and the hygroscopic and denaturing ability of the sulfonate group and sulfuric acid (30). The final effect is associated with the interaction between the sulphate group and water molecules, since the sulphate group shows internal polar structure, while oxygen atoms display a strong charge on negative surface on the outside surface. The combination between large negative surfaces of the sulphate group with the positive surfaces of water molecules creates an electrostatic interaction, known as a hydrogen bond, where the positive charge of hydrogen atoms on the surface of the water molecule is attracted to the negative charge of the oxygen atoms surface (30-36). A possible explanation for the reduction of intracanal bleeding is that it is based upon the rapid desiccation of debris at the damaged vascular bed interface within the root canal. The product's sulphate groups molecularly remove bound water from the detritus at this interface causing instant denaturation of the tissue debris. This could lead to coagulation in the vascular bed and subsequent hemostasis. The effect is probably not tied to conventional blood factor hemostasis chemistry.

This chemical property also produces the denaturation of biofilm, with rapid subtraction of water from the matrix by sulfonic and sulfuric acids, leading to the detachment of biofilm materials from the root surface and facilitating root instrumentation and disinfection (37-51).

One possible limitation of this study was that there was no clinician blinding. Another limitation could be represented by the fact that, even though the measurement of the millimeters of blood in this study has been made with paper point with the same size of the latest instrument used to shape the canal (size 30), the bleeding registered with the sterile paper point could come totally or partly from the periapical inflamed tissues. On the other hand, the authors cannot completely ruled out that the haemostatic action of the material is a consequence of the leakage of minimal quantities of product into the periapical tissues. Further studies with larger patient samples are needed to confirm the findings of the present study.

Within the limits of the present study, the results show that the decontaminant material administered in teeth with necrotic pulp, dry the root canal significantly in the presence of serum-hematic blood or exudates**.**

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This study is registered on clinicaltrials.gov with number NCT03336853.

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