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ORIGINAL ARTICLE

Effectiveness of Carisolv compared with sodium hypochlorite and calcium hydroxide

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Abstract
The aim of this study was to compare the effectiveness of Carisolv with that of two other alkaline substances: NaOCl and $Ca(OH)_2$. Sixty extracted teeth were randomly divided into three groups and split down the center of a carious lesion. In group I, one half of the cavity was excavated with NaOCl (0.5%, pH 11.7), the corresponding half with $Ca(OH)_2$ (pH 12.4); in group II with NaOCl and Carisolv; and in group III with $Ca(OH)_2$ and Carisolv ($n = 20$ in each case). Carisolv hand instruments were used. Histological specimens were subsequently produced from all cavities and analyzed with a light-microscope following Mallory-Azan staining. The thickness of the remaining caries was measured (<1 mm or >1 mm) and the locations were recorded. The data were statistically evaluated using the chi-square test. In group I, 50.5% of the specimens treated with NaOCl and 48.7% treated with $Ca(OH)_2$ were evaluated to be caries-free. The results in group II were NaOCl 61.5% and Carisolv 75.4% caries-free, and in group III $Ca(OH)_2$ 61.2% and Carisolv 73.9%. No statistically significant differences were found between NaOCl and $Ca(OH)_2$ excavation (group I: $p = 0.89$). Compared to NaOCl and $Ca(OH)_2$, Carisolv produced significantly better results for chemo-mechanical caries removal (groups II + III: $p < 0.05$). In the NaOCl and $Ca(OH)_2$ treated specimens, carious layers with a thickness >1 mm were found significantly more often than in the Carisolv-treated specimens (groups II + III: $p < 0.05$), whereas there were no differences between NaOCl and $Ca(OH)_2$ excavation ($p = 0.06$). There were no statistically significant differences in the location of the remaining caries in any of the groups ($p > 0.05$).

Key Words: *Caries excavation, chemo-mechanical caries removal*

Introduction

Carisolv (MediTeam, Göteborg, Sweden) is a viscous substance for the chemo-mechanical removal of caries. Two liquids are mixed before application: liquid 1 contains mainly three amino acids (leucine, lysine, and glutaminic acid); liquid 2 is sodium hypochlorite (NaOCl) (Table I). Although one problem with chemo-mechanical caries removal using Carisolv is its prolonged time of excavation compared to rotary instruments [1–3], Carisolv can decompose degenerated collagen. Degenerated collagen shows higher solubility than intact fibres, whereas solubility depends on the concentration of NaOCl [4]. Hence, it can be speculated that the main effect of chemo-mechanical caries removal depends on the alkaline pH which dissolves the degenerated collagen as a result of the carious lesion. The application of sodium hypochlorite softened the sound dentin and the inner layer of carious dentin more than Carisolv [5]. In evaluating the effectiveness of Carisolv, Hannig [6] treated fractured dentinal surfaces with phosphoric acid or lactic acid and collagenase, respectively, and exposed them to Carisolv or NaOCl (0.25%) for 20 min without mechanical action. In contrast to Carisolv, NaOCl completely dissolved the demineralized and denatured dentin layer within 20 min. NaOCl is more reactive than Carisolv, because the amino acids are likely to react with the sodium hypochlorite, thus reducing the organic tissue-solving properties of the NaOCl in Carisolv [6].

NaOCl alone is more effective in dissolving altered collagen than Carisolv because the amino acids may

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Table I. Composition of Carisolv (MediTeam, Göteborg, Sweden) LOT 03-008 according to the manufacturer's information

Carisolv	Ingredients	g/l
Syringe I	Glutaminic acid	2.5
	Leucine	2.5
	Lysine	2.5
	NaCl	5.8
	NaOH	17.5
	Carmellose (Na-CMC 1300–2200 mPas)	25.0
Syringe II	NaOCl (0.95%)	195.0

inhibit NaOCl. Therefore, the hypothesis of this study was that two alkaline substances used in dentistry for many years—NaOCl and $Ca(OH)_2$—might be effective in chemo-mechanical caries removal as well.

Material and methods

Sixty carious human teeth (10 incisors, 12 premolars, and 38 molars) were selected and stored in PBS buffer (pH 7.2) immediately after extraction. All the teeth had an occlusal and/or cervical carious lesion at dentin level. The 60 teeth were randomly divided into 3 groups ($n=20$). Using a diamond saw (Modell 1600; Leitz, Wetzlar, Germany), the teeth were split down the center of a carious lesion under permanent cooling with water spray. Two corresponding halves were obtained from each tooth (120 specimens, 40 per group).

In group I, one half of the cavity was treated with NaOCl (0.5%), the corresponding half with $Ca(OH)_2$, in group II with NaOCl and Carisolv (MediTeam, Göteborg, Sweden), and in group III with $Ca(OH)_2$ and Carisolv, respectively, and excavated using Carisolv hand instruments (MediTeam, Göteborg, Sweden). Twenty specimens were treated in each case and group. The ingredients of Carisolv are given in Table I.

A pilot study had revealed that the 0.5% NaOCl solution was too liquid for chemo-mechanical caries excavation. In concordance with Carisolv, the NaOCl solution was mixed with Carmellose to increase the viscosity and a more gel-like material was obtained (Table II). It was necessary to use the NaOCl gel directly after mixing because a decrease in the pH value was observed during storage due to the fact that the NaOCl reacted with the organic Carmellose. The NaOCl gel was therefore freshly prepared with a pH value of 11.7 for every specimen treated.

Table II. Composition of NaOCl gel per serving

Ingredients	g
NaOCl 0.5%	20.00
Carmellose	1.0
NaOH	0.25

Table III. Composition of 10 g "Calxyl rot" according to the manufacturer's information (OCO, Dirmstein, Germany), LOT 000106

Ingredients	g
$Ca(OH)_2$	2.3
H_2O	7.7

"Calxyl rot" (OCO, Dirmstein, Germany), pH 12.4, was used to assess the efficiency of $Ca(OH)_2$ in removing dentinal caries (Table III).

In each group, 20 teeth halves were treated with Carisolv, NaOCl, or $Ca(OH)_2$, respectively. Each cavity was filled with one of the medicaments. After 30 s affecting time, the caries was removed with Carisolv hand instruments (MediTeam, Göteborg, Sweden). The affecting time was chosen in accordance with the instructions of the manufacturer of the Carisolv. The procedure was repeated for each substance until no more carious dentin could be removed with the hand instruments. The aim was to excavate the dentin until it appeared to be caries-free according to the following parameters: hard on probing, dentin coloration, and "cri dentaire". It was not always possible to remove all caries, so caries remained in some cavities. Excavation and clinical evaluation of the specimens were undertaken by an experienced dentist.

All teeth were embedded in epoxy resin (Paladur farblos; Heraeus-Kulzer, Wehrheim, Germany) for histological examination after excavation. Longitudinal serial sections (200 µm thick) were obtained by cutting throughout the complete extent of the cavities parallel to the first sectional plane; a diamond saw was used (Modell 1600; Leitz, Wetzlar, Germany). The first sectional plane was produced by splitting the teeth in half. As many sections as possible were produced (5 to 11, 722 in total) to include the complete cavity as well as the adjoining dentin for evaluation. The amount of the obtained sections depended on the size of the cavity. Every section was pasted on to an object plate (Thermanox Plastic Coverslips 174985; Nunc, Rochester, USA). Subsequently, the sections were stained with Mallory-Azan. All teeth were stained separately. The sections were first stained for 15 min with acid fuchsin (0.25%) and, after removing surplus with filter paper, a second staining with 2C 084 Aniline Blue-Orange Mallory (0.5 g Aniline blue, 2 g orange, 1 g phosphowolfram acid in 100 ml Aqua dest) (Chroma-Gesellschaft mbH & Co., Münster, Germany) was performed. Finally, the sections were rinsed in ethanol (90%). After drying with filter paper the sections were histologically evaluated with a microscope (Orthoplan; Leitz, Wetzlar, Germany) at 32-fold magnification by a blinded examiner unaware of how the specimens had been treated. The remaining caries was stained red and recorded for every section (yes/no decision). The thickness of the remaining caries was measured

Table IV. Comparison of the excavation of NaOCl, $Ca(OH)_2$, and Carisolv. Carisolv was more effective ($p<0.05$). (Significant differences marked with an asterisk)

	Group I		Group II		Group III	
Excavation	Caries-free	Caries	Caries-free	Caries	Caries-free	Caries
NaOCl	50.5%	49.5%	61.5%*	38.5%*	–	–
$Ca(OH)_2$	48.7%	51.3%	–	–	61.2%*	38.8%*
Carisolv	–	–	75.4%*	24.6%*	73.9%*	26.1%*

(category I: less than 1 mm; category II: more than 1 mm) and the location of the remaining caries was recorded. The following three locations were determined: central half of the cavity, outer half of the cavity, complete cavity, and stained red. All results were statistically evaluated using the chi-square test.

Results

Results of the caries excavation

Group I: NaOCl vs. $Ca(OH)_2$: 50.5% of the sections (53 out of 105) excavated with NaOCl and 48.5% (56 out of 115) in the $Ca(OH)_2$ group were caries-free (Table IV).

Group II: NaOCl vs. Carisolv: 61.5% of the sections (72 out of 117) were evaluated to be caries-free after NaOCl excavation and 75.4% (95 out of 126) after excavation with Carisolv. The difference was statistically significant ($p<0.05$) (Table IV).

Group III: $Ca(OH)_2$ vs. Carisolv: 61.2% (74 out of 121) of the sections after $Ca(OH)_2$ excavation and 73.9% (102 out of 138) after Carisolv excavation were evaluated to be caries-free. The difference was statistically significant ($p<0.05$) (Table IV).

Evaluation of the thickness of the remaining caries

Group I: NaOCl vs. $Ca(OH)_2$: After NaOCl treatment, 2% (1 out of 52 sections), and after $Ca(OH)_2$ treatment, 13.6% (8 out of 59), of the specimens with remaining caries showed a caries layer with a thickness of >1 mm (category II). The difference was not statistically significant ($p=0.06$) (Table V).

Group II: NaOCl vs. Carisolv: In this group, 45 sections showed remaining caries after NaOCl excavation. In 20% (9 sections) of these cases the caries layer was thicker than 1 mm (category II), whereas after Carisolv excavation the layer did not exceed 1 mm in any of the 31 sections with caries. The difference was statistically significant ($p<0.05$) (Table V).

Group III: $Ca(OH)_2$ vs. Carisolv: After $Ca(OH)_2$ excavation, 47 of the sections remained carious; in 14.9% (7 sections) of these cases the caries layer was thicker than 1 mm (category II). In none of the specimens treated with Carisolv (36 sections) was the layer thicker than 1 mm. The difference was statistically significant ($p<0.05$) (Table V).

Evaluation of the location of the remaining caries

There were no statistically significant differences in the location of the remaining caries in any of the groups ($p>0.05$).

Discussion

The teeth, extracted for various reasons, were stored in PBS buffer solution because PBS buffer does not alter carious dentin. Storage media such as alcohol, formalin, or glutaraldehyde may react with the collagen structure of dentin and lead to a hardening of dentin caries. In contrast, PBS buffer possesses a slight antibacterial effect without changing the collagen structure of dentin or denaturated proteins (Ericson D., pers. comm., 2003).

It is important to note that the excavation was performed at room temperature (21°C), and it is possible that at mouth temperature the rate of caries-free specimens might be higher because the chemical reactions are more rapid at higher temperatures. But considering the overall objective of the present investigation (to compare the effectiveness of different alkaline substances in chemo-mechanical caries removal), excavation at room temperature seems justifiable.

Standardization of carious lesions is difficult. By randomly dividing the teeth into three groups, excavating corresponding cavity halves and evaluating the sections ($n=722$) to increase the number of specimens, the influence of factors such as extension, depth, localization, structure, etc., the excavation results can be minimized.

A control group with the dentin excavated using only hand instruments was not performed because a similar study showed no statistically significant differences

Table V. Comparing the thickness of remaining caries after NaOCl, $Ca(OH)_2$, and Carisolv excavation. Remaining caries with a thickness <1 mm (category I) was found significantly more often after Carisolv treatment ($p<0.05$). (Significant differences marked with an asterisk)

	Group I		Group II		Group III	
Excavation	Caries < 1 mm (cat. I)	Caries > 1 mm (cat. II)	Caries < 1 mm (cat. I)	Caries > 1 mm (cat. II)	Caries < 1 mm (cat. I)	Caries > 1 mm (cat. II)
NaOCl	98.0%	2.0%	80.0%*	20.0%*	–	–
$Ca(OH)_2$	86.4%	13.6%	–	–	85.1%*	14.9%*
Carisolv	–	–	100.0%*	0.0%*	100.0%*	0.0%*

between excavation with Carisolv and hand instruments only [2].

Only one dentist performed the excavation so that treatment and classification of the excavation were identical for all groups. The histological evaluation was carried out by one examiner who was unaware of the different treatment groups. The histological sections were evaluated without it being known how the specimens were treated.

A caries diagnosis using clinical criteria such as surface hardness and dentin color can be made in a scientific examination only with restrictions, because the examiner is strongly influenced by subjective experience. A histological examination was needed to obtain reproducible results [7]. It has to be kept in mind for histological staining that dentin caries can be divided into two distinct layers. The outer layer is contaminated by bacteria causing a non-remineralizable necrotic collagen matrix. In the inner layer, bacteria are much less frequently observed and the collagen has been reversibly denaturated but retains the cross-banded ultrastructure. The inner layer can potentially remineralize if the acid influence is removed [8]. It is possible to stain the exact boundaries between these two layers with Mallory-Azan staining [9]. Healthy, non-altered collagen is stained blue, whereas affected carious dentin appears red [10]. Ohgushi & Fusayama showed that the first layer of dentin caries with degenerated collagen is fuchsin-stainable, and that this staining is identical to results of electron microscopic evaluation [8]. Mallory-Azan staining is therefore a large-scale method which delivers exact results [9]. This reliable method has also been used in similar studies [2,7].

Because the number of sections was not identical in the three groups, the statistical evaluation was undertaken using the chi-square test to eliminate the influence of different specimen numbers.

Carisolv (pH 11) contains NaOCl (0.5%). Hence, the present study compared the effect of Carisolv with NaOCl (0.5%) and $Ca(OH)_2$ (i.e. "Calxyl rot"), two other alkaline substances commonly used in dentistry. Whereas chemo-mechanical caries removal with NaOCl and $Ca(OH)_2$, respectively, showed 50–60% caries-free specimens, Carisolv excavation resulted in 75% caries-free sections. This difference was statistically significant. Within the limitations of this *in vitro* study, Carisolv was more effective in chemo-mechanical caries removal than NaOCl or $Ca(OH)_2$.

The chemo-mechanical caries removal is based on the destruction of altered collagen molecules [11]. It is assumed that a chlorination of the functional groups takes place which is responsible for the secondary and quaternary collagen structure. In addition, a transformation of the hydroxyproline to pyrrol-2-carboxyl acid and an attack of the fibrillary structure of collagen were observed [12–14]. However, the exact mechanism of action of Carisolv is not clear, despite these explanations. As a consequence, the question that crops up is why Carisolv is more effective than NaOCl alone or $Ca(OH)_2$. Wakabayashi et al. [15] explained the limitation of $Ca(OH)_2$ to dissolve soft tissue as follows: The solubility of $Ca(OH)_2$ powder to water is very low (0.16 g/100 g water at 20°C), and the number of dissociated hydroxyl ions is little, although the mixture of $Ca(OH)_2$ powder to water exhibits a pH of 12 and higher. As soon as the $Ca(OH)_2$ dissolves the soft tissues, the hydroxyl ions are consumed during the reaction [15].

The tissue-dissolving effect of NaOCl is well proven in the dental literature [16]. NaOCl has a considerable capacity to disintegrate carious dentin when applied in large amounts (more than the volume of a cavity), higher concentration (up to 5.25%), or prolonged incubation (up to 24 h) [17]. Whereas predentin appeared to be labile to NaOCl, calcified dentin does not seem to be significantly altered [18].

The amino acids play an unclear part in chemo-mechanical caries removal with Carisolv. The three amino acids are electrically differently charged (lysine = positive, glutamic acid = negative, and leucine = neutral), which leads to different interaction with the denaturated collagen in combination with NaOCl [19]. On mixing the two Carisolv solutions, relatively stable monochlorinated forms of the three amino acids are produced. The chlorine atom of NaOCl is transferred to the amino group of each amino acid [20]. The structure of all proteins, including that of carious collagen, is made up of hydrophilic (positively or negatively charged and non-charged positive or negative polar) and hydrophobic sections resulting from the distribution of amino acids within the primary structure [21].

By using three chloroamino acids in Carisolv with fundamentally different side chain properties, positively and negatively charged and hydrophobic, it is ensured that they will electrostatically attract all three possible protein sections, effectively bringing reactive power to the carious target. NaOCl may not be strong enough to break covalent peptide bonds in proteins. Neither the bi- nor the tri-dentate type covalent collagen cross-links are broken by NaOCl [20].

The combination of three different amino acids with three different charges (positive, negative, neutral) as a vehicle for the NaOCl leads to three different effects between the substrate (denaturated collagen) and the chlorinated amino acids. In addition to a simple diffusion into the tissue it comes to an electrostatic effect on the components of the altered collagen and the chlorinated amino acids [19]. The high pH causes a swelling of the organic tissue which may facilitate penetration of the chloramines into the demineralized dentin [22]. The chloramines are unstable and the loose bounded chlorine ions of this molecule therefore react with the carious altered collagen in the dentin [12].

The results of the present study and the cited literature show that Carisolv is more effective in chemo-mechanical caries removal than alkaline substances such as $Ca(OH)_2$ or NaOCl. This observation may be explained by the amino acids in the Carisolv gel which increase the solubility of carious collagen to NaOCl. While on the one hand the amino acids in Carisolv decrease the aggressive effect of NaOCl on sound dentin and the inner layer of carious dentin, on the other hand they may enhance the disruption of degenerated collagen in the outer layer of carious dentin [5]. As previously shown, the proteolytic effects of $Ca(OH)_2$ seem to be too weak to dissolve collagen completely [15].

To clarify the results of this preliminary study, an additional biochemical examination should be made to analyze the collagen degradation or cross-linking to evaluate differences in the method of action between the three agents used.

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