USE OF A BIOADHESIVE GEL ON SUTURES IN ORAL TISSUES UNDERGOING EXTRACTIVE SURGICAL PROCEDURES

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Introduction

In oral extractive surgical therapy, an appropriate soft tissue suturing technique allows adequate healing to be obtained, eluding a possible post-surgical infection. Nevertheless, the same sutures can retain bacterial biofilms, which, precisely through their path, then have the possibility of translocating deeply, with possible local or general, even significant infectious consequences (1, 2). The type of suture performed, both in terms of the material used (3) and the technique of making and removal, are determining factors for bacterial adherence to the surgical site (4).

A super-infection, within the treated area, can induce sequelae in the healing process, the main one being the lack of healing by "first intention" of the flaps

(5). Healing by "second intention", therefore, could be considered as inappropriate, increasing the risk of tissue deiescence.

The post-surgical risk of infection can be reduced, thanks to some pre-surgical procedures ranging from strict compliance with asepsis in the setting up of the operating room and the materials used (6), to the preliminary decontamination of the patients' oral cavity. Summers et al. (7) demonstrated a substantial decrease in aerobic and anaerobic bacterial load after intra-oral preparation for surgery with iodinated povidione solution. Kosutic et al. (8) obtained similar results thanks to the use of 1% solution of cetrimide. Johnson et al. (9) described a numerical reduction of bacterial colonies in the oral cavity of pre-surgical patients, thanks to irrigations with 0.2% chlorhexidine.

Greater doubts are highlighted, however, in the literature on the real effectiveness of various active ingredients, applied topically in the post-extraction sites of the oral cavity, both in relation to the prevention of infectious complications, and as a function of the healing process and its complications, first of all post-extraction dry alveolitis. This inflammatory disease in which the alveolar cavity appears empty and dry, without granulation tissue and with shiny bone walls, induces localized and lasting pain, sometimes resistant to drugs, halitosis and lymphadenopathy. In such patients, the preliminary clot tends to break down and is associated with insufficient granulation tissue formation. The indicated therapy is substantially local. A maneuver of cautious curettage and alveolar washing should be followed by daily applications of active ingredients. Given the inflammatory nature of the disease, systemic antibiotic therapy does not improve its prognosis.

The use of chlorhexidine for local application has been repeatedly proposed, both in the prevention of post-extraction dry alveolitis, and in the therapy of other post-surgical extractive infectious sequelae, due to the well-known antiseptic characteristic of the molecule.

In this regard, it has recently been shown that mouthwashes based on chlorhexidine gluconate 0.2%, used for a week, can significantly prevent the occurrence of "dry socket" pathologies (10). Richards (11), however, in an extensive review of the literature, considers that he cannot confirm this hypothesis. In the treatment of dry alveolitis, Haraji et al. (12, 13) showed a good result in pain relief, if chlorhexidine is placed in situ thanks to gelatin sponges saturated with active ingredient, especially in elderly subjects and provided that the surgical gesture was not traumatic.

Furthermore, the efficacy of chlorhexidine in mouthwash does not seem to change in the prevention of post-extraction alveolar osteitis, at the two concentrations: 0.12% and 0.20% (14, 15).

Rodriguez-Perez (16) showed a reduction in post-operative alveolar osteitis with the use of chlorhexidine gel at both 0.2% and 1% concentrations. The antibacterial action of a chlorhexidine-based gel is also demonstrated when it impregnates the sutures used, provided that the gel includes a slow-release system, for example represented by specific fatty acids (17).
The use of chlorhexidine, however, is often associated with the onset of undesirable side effects: some of which have been known for some time, while others are more recently identified (cytotoxicity on odontoblasts, unilateral and bilateral parotid irritations, accentuated mineral precipitation with the formation of tartar deposits, negative immunological reactions). The variety of side effects and the ascertained, limited or absent, healing action of chlorhexidine promote the search for therapeutic alternatives to this active ingredient.
Syrjanen (18), using penghawar fibers and eugenol ("Alveogyl") had not found any significant therapeutic effects in terms of healing, apart from a good coagulating action. More recently, Kaya et al.(19) compared the effect of Alveogyl to that of SaliCept compresses or laser therapy in the treatment of alveolar osteitis, noting a more important therapeutic role attributable to the use of low-intensity laser. Possible alternatives to chlorhexidine in post-extraction oral surgery seem to be represented by sutures impregnated with a copolymer of glycolic acid and lactic acid ("Vicryl") or by the use of ozonated oil ("Ozoral"). Speaking of oils, more recently some essential oils applied topically on sutures made in extraction sites have been tested. Faria et al. (20), using calendula officinalis and camellia sinensis found an antimicrobial activity towards bacteria on sutures, but not comparable to that obtained with chlorhexidine. Cruz et al. (21) also showed an excellent reduction in bacterial colonization along braided silk sutures, following the application of an ointment composed of 15.5% iodoform and 5% calendula oil.

Scope of work

The present controlled, randomized and "blinded" clinical research aims to detect, preliminarily, the levels of overall and specific bacterial growth within the suture threads, used in the practice of oral extraction surgery in the short period following dental extractions.
We then wanted to verify whether the application of an innovative bioadhesive gel (Hobagel Plus, Hobama srl) was able to control bacterial contamination along the applied sutures, compared to a chlorhexidine-based gel or the simple mechanical removal of biofilms.
The third objective of the research was to clinically evaluate the quality of scarring processes in the soft tissues surrounding the sutured extraction site.

Material and method

Twenty-one adult patients of both sexes, about to perform single or multiple extractions of dental elements, irretrievable with conservative therapy, were enrolled in the present research procedure. The selected cases met the following inclusive criteria: absence of evident ongoing infectious processes, good general health, acceptable home hygiene. Patients in whom there were ascertained metabolic-degenerative diseases, the need for the administration of anti-inflammatory drugs/antibiotics, ascertained allergies to the active ingredients used were excluded from the group of cases. The included cases were divided into three groups:
1. test group A: cases on which, after extraction, a 1% chlorhexidine gel has been applied;
2. test group B: cases in which the innovative bioadhesive gel was applied instead;
3. test group C: cases in which the sutures, after application, have not been decontaminated with any gel, but only mechanically cleansed with saline.

The investigation procedure included, after prior informed consent from the included subjects, an occupational hygiene session, as needed, carried out one week before the extraction. In the surgical session, any biofilms still present were preliminarily removed with ultrasound or polishing or, possibly, with sterile gauze and saline solution ("Digital Brush Baby" – Enacare, Micerium, Avegno (Ge) Italy). Local anesthesia and extraction surgery were then performed, with the least traumatic procedure possible. The suturing phase of the site with silk thread was carried out with the following steps.
A first sutural thread was exclusively passed through the mucosa surrounding the surgical site and then immediately cut and placed in a sterile container to be sent to the laboratory for bacterial evaluation. This sampling was considered to be the initial assessment time (T0). The appropriate sutures suitable for each case treated were then applied, taking care to create a

additional suture to be removed and sent for microbiological evaluation one week after surgery (T1). At the end of the operation (Figs. 1 and 2) the sutures and the surrounding soft tissues were covered with gel ("Hobagel Plus" - Hobama srl or "Curasept 1%" - Curadent Healthcare spa), except in the cases of the group in which only mechanical cleansing was carried out.

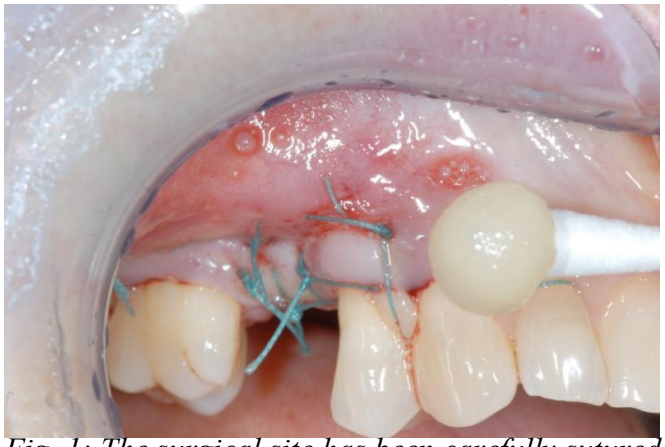

Fig. 1: The surgical site has been carefully sutured and the operator is about to place the Hobagel Plus bioadhesive gel on the threads and tissues

Fig 2: After application, the Hobagel Plus bioadhesive gel soaks the treated area tenaciously

Before the patients were discharged, they were provided with instructions and materials suitable for the antibacterial control of the treated sites, to be continued for the expected period. Patients belonging to group A (chlorhexidine) were advised to be treated at home with an extra-soft toothbrush ("post-operation") and chlorhexidine-based toothpaste 0.2% ("Curasept 0.2%")
- Curadent Healthcare spa). Patients in group B (innovative bioadhesive gel "Hobagel Plus") were prescribed a similar protocol to be carried out, however, with toothpaste based on essential oils/cytylpyridiniochloride ("Hobagel" – Hobama srl). The cases of group C were limited to the mechanical removal of biofilms with the aid of gauze soaked in saline solution ("Digital Brush Baby" – Enacare, Micerium, Avegno (Ge) Italy). None of the subjects included in the research used mouthwash or post-extraction antibiotic therapy. The reinforcement of the motivation for home hygiene pertinent to the case took place on the occasion of the suture samples which, as mentioned, were carried out at the same time as the extraction (T0) and 1 week later (T1).
The gel used in the research ("Hobagel Plus") owes its bio-adhesiveness to a complex original system of natural rubbers and resins (Ca/Na PVM – Ma copolymer). It contains antibacterial substances (cetyl-pyridinium-chloride and essential oils of Manuka and Melaleuca) and re-epithelializing substances (the same essential oils, hyaluronic acid at different molecular weights including the oligomers of the molecule, and the PVP/hydrogen peroxide complex). Soothing substances such as allantoin, bisabolol, vitamin E complete the picture.
The sutures taken were placed in a sterile tube, labeled with the patient's code of

reference for the "blind" assessment. The samples, stored in the refrigerator, were then sent to the laboratory for the examination of the overall and specific bacterial count. The microbiological evaluation was carried out with the "Polymerase Chain Reaction" (PCR) technique which involves three reactions for each sample. The first of these quantifies the total amount of bacteria, while the second identifies and quantifies the bacteria of the "red complex" (P. Gengivalis, T. Forsythia, T. Denticola). Finally, the third reaction highlights the presence of Aggregatibacter Actynomicete-comitans, Fusobacterium Nucleatum, Campylobacter Rectus.
At T0 and after one week, a Plaque Index (PI according to Mombelli) and a bleeding evaluation on the survey (B.O.P. according to Van der Weijden) were performed. With the same timing, some clinical evaluations were also carried out to highlight the presence or absence of pain at post-extraction contact, the level of overall discomfort complained of by the treated patients and the objective observation of a healing process for the 1st or 2nd intention.
All these data were subjected to statistical evaluations suitable for identifying any significant differences in the three groups of patients examined.

Results

The results of the research are summarized in the tables and tables presented below.
Tables 1, 2 and 3 show that during the course of the survey the parameters relating to the total bacterial load and that of the specific bacterial types did not undergo, despite the tendency of their decrease, statistically significant variations in the three groups of cases taken into consideration. The same tables show that even the overall Plaque Index carried out in the three groups does not show significant changes. Tables 4 and 5 show the behaviour of the parameter "bleeding at probing" (BOP) in the comparison, both between cases treated with the new bio-adhesive gel ("Hobagel Plus") and both in those treated with chlorhexidine gel 1% (Table 4) and in the comparison between cases treated with "Hobagel Plus" and those in which it was limited to a mechanical removal of the biofilms at the surgical site (Table 5). Also in this case, no statistically significant variation can be highlighted, not even taking into consideration some sub-variables such as sex, mandibular or maxillary location of the extracted tooth, or the fact that this was a monoradicular or a multi-radicular.
A significant variation, of a purely clinical nature, is instead highlighted by tables 1, 2 and 3 which describe the trend of three specific clinical parameters (pain, patient comfort and type of healing) in the short term (one week after surgery).
Table 1, in fact, shows that the pain on contact, complained of by patients, is still present at one week, in 87% of cases treated with chlorhexidine or with purely mechanical cleansing of the site. The percentage is reduced to 46% in cases where the bioadhesive gel "Hobagel Plus" has been used. Mild overall discomfort is described at one week (table 2) in 100% of cases with cleansing alone, compared to 87% of cases "chlorhexidine group" and 46% of cases "Hobagel Plus group". As for the healing process by "1st intention" (table 3), it can be seen in 71% of cases "Hobagel Plus group", in 54% of cases "chlorhexidine group" and only in 28% of cases of cleansing alone.

HOBAGEL	MEAN	STD. DEVIATION	STD. ERROR MEAN	95% CONFIDENCE INTERVAL OF DIFFERENCES		t	df	Sig. (2-tailed)
				lower	upper			
CBT1-CBT2	-3,3E+07	5,9E+07	2,4E+07	-9,5E+07	2,8E+07	-1,389	5	,223
CR1-CR2	-76718,5	186416,9	76104,36	-272351	118914	-1,008	5	,360
FN1-FN2	-353371	425920,3	173881,2	-800347	93605,27	-2,032	5	,098
P1-P2	-12,4667	19,7901	8,0793	-33,2351	8,3017	-1,543	5	,183
PG1-PG2	-1154,33	3202,1813	1307,2850	-4514,82	2206,1498	-,883	5	,418
TD1-TD2	3089,8333	7640,2381	3045,6294	-4739,21	10918,87	1,015	5	,357
TF1-TF2	659,1667	1614,6220	659,1667	-1035,28	2353,6085	1,000	5	,363

Tavola 1: Risultati riferiti al gruppo pazienti trattato con Hobagel Plus

CLOREX	MEAN	STD. DEVIATION	STD. ERROR MEAN	95% CONFIDENCE INTERVAL OF DIFFERENCES		t	df	Sig. (2-tailed)
				lower	upper			
AA1-AA2	-236,4000	528,6065	236,4000	-892,7516	419,9516	-1,000	4	,374
CBT1-CBT2	-2,2E+07	2,1E+07	9257461	-4,8E+07	3831132	-2,363	4	,077
CR1-CR2	-103184	162235,8	72554,03	-304627	98257,89	-1,422	4	,228
FN1-FN2	-1452593	1527091	682936,1	-3348727	443541,7	-2,127	4	,101
P1-P2	-20,2000	31,7994	14,2211	-59,6841	19,2841	-1,420	4	,229
PG1-PG2	-309,2000	1558,2223	696,8582	-2243,99	1625,5885	-,444	4	,680
TD1-TD2	-9997,20	16906,58	7560,8544	-30989,5	10995,10	-1,322	4	,257
TF1-TF2	-227,2000	335,7450	150,1497	-644,0825	189,6825	-1,513	4	,205

Tavola 2: Risultati riferiti al gruppo pazienti trattato con gel di Clorexidina 1%

DIGITAL BRUSH	MEAN	STD. DEVIATION	STD. ERROR MEAN	95% CONFIDENCE INTERVAL OF DIFFERENCES		t		Sig. (2-tailed)
				lower	upper			
AA1-AA2	-295,0000	645,6867	322,8434	-1322,43	732,4316	-,914		,438
CBT1-CBT2	-2,6E+07	4,7E+07	2,4E+07	1,0E+07	4,9E+07	-1,122		,343
CR1-CR2	-203458	372019,4	186009,7	-795424	388507,7	-1,094		,354
FN1-FN2	-1917265	3678734	1839367	-7770951	3936421	-1,042		,374
P1-P2	-26,1750	30,762	15,4881	-75,4650	23,1150	-1,690		,190
PG1-PG2	44,7500	106,3810	53,1905	-124,5259	214,0259	,841		,462
TD1-TD2	-4763,00	9536,1244	4768,0622	-19937,1	10411,10	-,999		,391
TF1-TF2	-56,0000	158,3267	79,1633	- 307,9331	195,9331	-,707		,530

Tavola 3 : Risultati riferiti al gruppo pazienti trattato con esclusiva rimozione meccanica di biofilm (tramite “Digital Brush”)

CONFRONTO HOBAGEL - CLOREXIDINA	VALUE	df	ASYMP. SIG. (2-slided)	EXACT SIG. (2-slided)	EXACT SIG. (1-slided)
Pearson Chi-square	,749	1	,387		
Continuity correction	,034	1	,853		
Likelihood ratio	,754	1	,385		
Fisher’s exact test				,545	,424
Linear-by-linear association	,681	1	,409		

Tavola 4 : Variazione di comportamento del B.O.P. nel confronto tra i casi trattati con Hobagel Plus e quelli con Gel Clorexidina 1%

CONFRONTO HOBAGEL – DIGITAL BRUSH	VALUE	df	ASYMP. SIG. (2-slided)	EXACT SIG. (2-slided)	EXACT SIG. (1-slided)
Pearson Chi-square	,741	1	,389		
Continuity correction	,000	1	1,000		
Likelihood ratio	1,095	1	,295		
Fisher's exact test				1,000	,600
Linear-by-linear association	,667	1	,414		

Tavola 5 : Variazioni di comportamento del B.O.P. nel confronto tra i casi trattati con Hobagel Plus e quelli in cui si è rimosso il biofilm con procedura esclusivamente meccanica (tramite "Digital Brush")

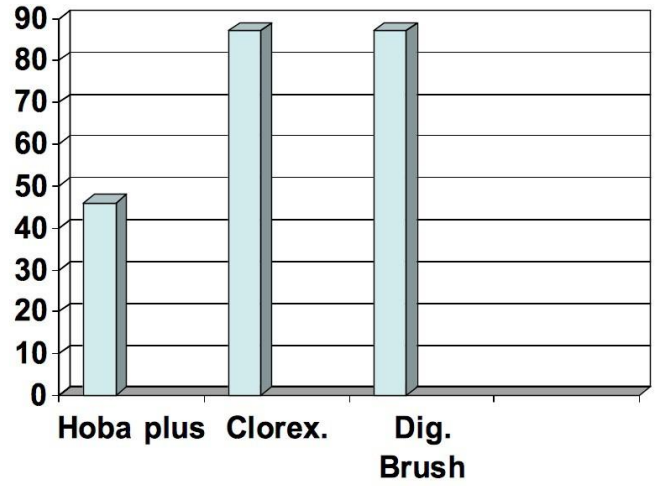

Tabella 1: Diminuzione del parametro "dolore al contatto" dopo 1 settimana dall'estrazione dentale nei tre gruppi di pazienti trattati

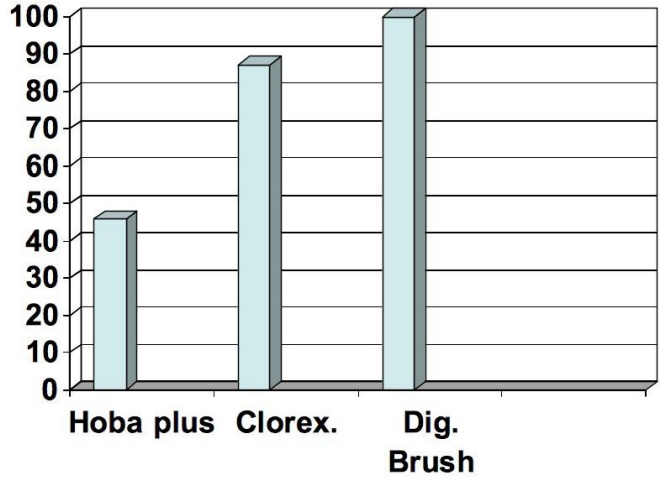

Tabella 2 : Presenza di disagio complessivo di grado "lieve" dopo 1 settimana dall'estrazione dentale nei tre gruppi di pazienti trattati

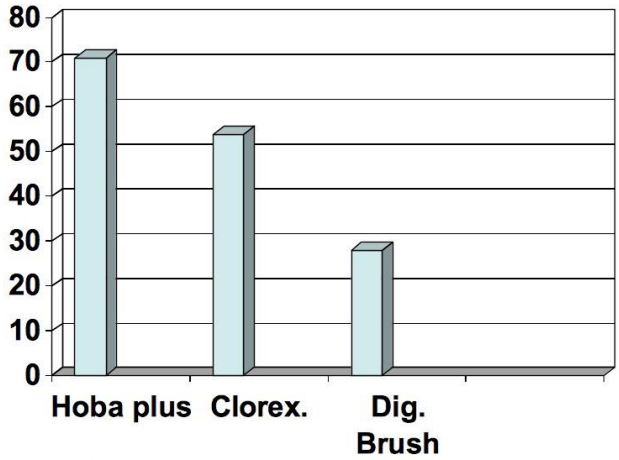

Tabella 3 : Guarigione per “1° intenzione” dopo 1 settimana dalla estrazione dentale nei tre gruppi di pazienti trattati

Discussion and conclusions

The adhesion of bacterial biofilms in the context of sutures is a known clinical evidence, also observed in the present investigation. This contamination is potentially able to induce odontogenic infections within the sutured tissues, with important consequences, especially in subjects at risk. The absorption potential of the different types of sutures towards bacteria can be partly controlled by the correct home cleansing carried out by the patient in the oral cavity and, in particular, on the sutured tissues. However, the local use of active ingredients with antiseptic properties has been repeatedly invoked and proposed, in an attempt to promote adequate tissue healing and prevent complications.

In the present research, two different gels were used, respectively applied to two groups of patients: in the first group, sutures and tissues were impregnated with a 1% chlorhexidine gel; in a second group, however, the procedure was carried out with the innovative bio-adhesive gel ("Hobagel Plus") previously described. With both methods, there is a tendency to a reduction in total and specific bacterial loads, as well as in the overall plaque and bleeding indices of patients, in the short observation period (1 week), with overlapping results, however in the absence of statistical significance. These results are referable not only to the "chlorhexidine/bioadhesive gel" comparison, but also by comparing the two groups of patients treated, with the group of cases in which the removal of biofilms took place with an exclusively mechanical technique. It could be hypothesized that this trend is justified by the absence of covalent bonds between the gels applied and the silk thread sutures that have been impregnated with them. From the point of view of antibacterial control, therefore, these results confirm previous research which, by comparing the effects of chlorhexidine with those of some essential oils, was not able to highlight particular advantages attributable to chlorhexidine, at least on most of the bacterial species examined (22,23). It should be noted, however, that in these researches the active ingredients were provided in the liquid form of mouthwash, while in the present research they are formulated in gel, certainly more retentive than the traditional rinse. However, the antiseptic effect does not reach levels of statistical significance.

On the other hand, the clinical observation relating to the initial healing process of the sutured tissues was of a different tenor, which takes place, both from an objective and subjective point of view, in a significant way in patients who used the new "Hobagel Plus", both with respect to those who used chlorhexidine, and with respect to the other control cases (simple wound cleansing). In fact, an interference attributable to chlorhexidine on the healing process, independent of its undoubted antibacterial activity, has been described by some authors (24, 25), who hypothesize an inhibitory activity on the proliferation of fibroblasts and keratinocytes.

Despite the limited sample observed, in fact, 71% of patients treated with "Hobagel Plus" had a healing process by first intention and only 46% of cases, one week after extraction, still complained of pain on contact or discomfort in normal oral functions. The same could not be observed, however, in patients in whom chlorhexidine was used or in

Controls.
The clinical results obtained must be interpreted on the basis of the formulation of the new gel which includes a mix of various substances. The intense bioadhesiveness of the product is determined not only by the lipophilic substrate of many components, but above all by the original mix of rubbers and resins (mixed Na/Ca salt of the methyl-vinyl-ether copolymer and Ma carboxy-methyl-cellulose). The antiseptic activity is obtained with the insertion of cityl-pyridinium-chloride 0.05% and two essential oils (tea tree and manuka) active on various oral bacteria. These essential oils are extracted from the leaves of medicinal plants of the myrtaceae family. They are easily absorbed and particularly rich in terpenes and triketones. The effect of re-epithelialization of the tissues is instead obtained from the peculiarities of other substances including, in the foreground, hyaluronic acid at different molecular weights. The low weight of the oligomers of the substance favors tissue penetration, cell migration and the synthesis of native hyaluronate; The high-weight component, on the other hand, moisturizes and stabilizes the cells in the tissue. In addition, the "PVP-hydrogen peroxide 0.1%" complex cleanses and sanitizes the surgical area, while the presence of allantoin, bisabolol and vitamin E guarantee the gel a soothing, anti-irritative and anti-oxidant capacity.

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