Performance of herbal mouth rinse in the prevention of oral infections

Desempenho de um enxaguante bucal fitoterápico na prevenção de infecções orais
Desempeño del enjuague bucal herbal en la prevención de infecciones orales

Anne Caroline Gercina
ORCID: 0000-0002-0381-9543
Doutoranda em Odontologia pela Universidade Estadual de Campinas, Brasil
E-mail: annegerc@gmail.com

Klinger de Souza Amorim
ORCID: 0000-0003-4693-1356
Doutor em Odontologia pela Universidade Estadual de Campinas, Brasil
E-mail: klinger.amorim@outlook.com

Bruna Haidê de Souza Menezes
ORCID: 0009-0000-8366-0298
Cirurgiã-dentista pela Universidade Federal de Sergipe, Brasil
E-mail: brunahaidesm@hotmail.com

Gustavo Marques Sobral dos Santos
ORCID: 0009-0001-9873-4026
Mestre em Odontologia pela Universidade Federal de Sergipe, Brasil
E-mail: gmsobral@hotmail.com

Rangel Cyrilo Lima de Melo
ORCID: 0000-0002-8556-0546
Mestre em Odontologia pela Universidade Federal de Sergipe, Brasil
E-mail: rangelrcl@hotmail.com

Liane Maciel de Almeida Souza
ORCID: 0000-0003-0651-5470
Professora associada na Universidade Federal de Sergipe, Brasil
E-mail: odontoliu@gmail.com

Francisco Carlos Groppo
ORCID: 0000-0002-8513-773X
Doutor em Odontologia pela Universidade Estadual de Campinas, Brasil
E-mail: fcgroppo@unicamp.br

RESUMO

Objetivo: Avaliar a performance de uma solução fitoterápica Elixir Sanativo® no pós-operatório de extrações dentárias. **Material e método**: Trata-se de um ensaio clínico randomizado e cruzado, realizado em 30 voluntários que necessitavam de exodontia simples em lados opostos. Após a cirurgia os pacientes receberam 150 mL de digluconato de clorexidina a 0,12% e uma solução de Elixir Sanativo para usar na região operada durante sete dias. Para avaliar o efeito analgésico de ambos os protocolos, utilizamos una escala analógica visual (EAV) de 10 cm o consumo de analgésicos no pós-operatório. Para avaliar a prevalência de complicações pós-operatórias examinamos a presença de sangramento, hiperemia e necrose após sete dias da cirurgia. **Resultados**: Não houve diferença estatística significante (Wilcoxon, p> 0.05) entre os tratamentos a respeito da escala EVA no período de 24 horas ou 7 dias depois da cirurgia, nem com relação ao consumo de analgésicos (Wilcoxon, p=0.5536). No período de 7 dias, houve uma diminuição na pontuação da escala EVA em ambos os grupos. No entanto, somente a clorexidina apresentou diferença estatisticamente significativa (Wilcoxon, p= 0.0178). Não houve diferença entre os tratamentos quanto as complicações pós-operatórias (sangramento, hiperemia e necrose) (exato de Fisher, p= 0.9656). **Conclusão**: O elixir Sanativo® apresentou uma eficácia igual a da clorexidina e demonstrou ser uma valiosa opção para a prevenção de complicações pós-operatórias. **Palavras-chave:** Clorexidina; Extração dentária; Medicina herbal.

ABSTRACT

Objectives: To evaluate the performance of an herbal Sanative® solution in the postoperative of tooth extractions. **Methods:** This randomized, crossover, clinical trial was conducted in 30 patients who presented an indication for simple tooth extractions on opposite sides. After surgery, patients received 150 mL of chlorhexidine digluconate 0.12% and an herbal Sanative® for use in the region for seven days after oral surgery. To evaluate the analgesic effect of both protocols, we used a 10 cm visual analog scale (VAS) and postoperative analgesic consumption. To assess the prevalence of postoperative complications, we examined the presence of bleeding, hyperemia, or necrosis seven days after oral surgery. **Results:** No difference (Wilcoxon test, p> 0.05) was found between the treatments regarding VAS score in the period of 24 hours or 7 days after surgery or regarding postoperative analgesic consumption (Wilcoxon test, p=0.5536). In the period of 7 days, there was a decrease in the VAS score of both groups. However, only chlorhexidine showed difference (Wilcoxon, p= 0.0178). There

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was no difference between treatments considering bleeding, hyperemia, and necrosis (Fisher's exact test, p= 0.9656). **Conclusion:** Sanative® presented equal efficacy to chlorhexidine. and demonstrated to be a valuable option for the prevention of postoperative complications. **Keywords:** Chlorhexidine; Tooth Extraction; Herbal medicines

RESUMEN

Objetivo: Evaluar el rendimiento de una solución herbal Sanative® en el postoperatorio de extracciones dentales. **Métodos**: Este ensayo clínico aleatorizado y cruzado se llevó a cabo en 30 pacientes que presentaban indicación de extracciones dentales simples en lados opuestos. Después de la cirugía, los pacientes recibieron 150 mL de digluconato de clorhexidina al 0.12% y una solución herbal Sanative® para usar en la región durante siete días después de la cirugía oral. Para evaluar el efecto analgésico en ambos protocolos, utilizamos una escala analógica visual (EAV) de 10 cm y el consumo de analgésicos en el postoperatorio. Para evaluar la prevalencia de complicaciones postoperatorias, examinamos la presencia de sangrado, hiperemia o necrosis siete días después de la cirugía oral. **Resultados**: No se encontraron diferencias (prueba de Wilcoxon, p> 0.05) entre los tratamientos con respecto a la puntuación de la EAV en el período de 24 horas o 7 días después de la cirugía, ni en el consumo de analgésicos en el postoperatorio (prueba de Wilcoxon, p=0.5536). En el período de 7 días, hubo una disminución en la puntuación de la EAV en ambos grupos. Sin embargo, solo la clorhexidina mostró diferencia (Wilcoxon, p= 0.0178). No hubo diferencia entre los tratamientos en cuanto a sangrado, hiperemia y necrosis (prueba exacta de Fisher, p= 0.9656). **Conclusión**: Sanative® presentó una eficacia igual a la de la clorhexidina y demostró ser una opción valiosa para la prevención de complicaciones postoperatorias. **Palabras clave:** Clorexidina; Extração dentária; Medicina herbal.

INTRODUCTION

The oral microbial habitat is composed of a wide variety of species, which play a significant role in maintaining the well-being of the oral cavity. Changes in oral environmental conditions may disrupt the normal symbiotic relationship between the host and its resident microbes and resulting in an increased risk of disease[1]. Thereby, oral microbiome imbalance may affect the alveolar healing process and provides alveolar osteitis (AO)[2].

Alveolar osteitis, commonly known as dry socket, is a frequent postoperative complication. The precise occurrence of AO is uncertain, but it has been reported to range from 0.5% to 5% for routine dental extractions[3]. As AO is a condition characterized by intense pain, several studies have been conducted over the years to discover the most effective method for its prevention[4, 5].

Oral rinsing using chlorhexidine is extensively used in dentistry for preventing oral infections. Nevertheless, prolonged utilization of chlorhexidine is linked to side effects including taste alteration, tooth staining, increased calculus formation, and oral mucosa irritation[6]. For this reason, there is a seeking for new protocols of postoperative prevention of infections[6, 7, 8, 9].

At the same time, the interest in herbal medicines in dentistry is increasing. Herbal medicines have been used in dentistry as anti-inflammatory agents, antimicrobials, and sedatives[10]. Among the herbal antimicrobials, the Sanative® herbal rinse (Laperli Laboratory, Recife, Pernambuco, Brazil) is a hydroalcoholic extract of native plants (20% of *Piptadenia colubrina, Benth*, 20% of *Schinus terebinthifolius*, *Raddi*, 1.7% of *Physalis angulata*, *Linné*, and 1.7% of *Cereus peruvianus, Miller)*[11,12] from the Northeast region of Brazil.

Despite the promising properties of Sanative®, there is a lack of studies that explored the use of this herbal medicine in dentistry. Therefore, the aim of this study was to compare the use of Chlorhexidine and Sanative® solutions in the postoperative tooth extractions.

METHODS

This randomized, crossover, single-blind clinical trial was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee (protocol CAAE number: 43224315.1.0000.5546) and registered by the Brazilian Clinical Trials Registration (ReBEC) (REQ-9914).

The inclusion criteria were healthy patients aged between 18 and 60 years old, absence of systemic disease (ASA I) presenting an indication of tooth extractions on opposite sides presenting similar surgical positions, similar difficulties, and that did not require osteotomy.

All participants were informed of both the risks and benefits of the study before signing an informed consent form. The exclusion criteria were as follows: history of pericoronitis or other inflammatory/infectious diseases at the time of surgery; any medication used within seven days of study

initiation; history of hypersensitivity to drugs, substances, or any materials used in this experiment; and pregnancy or lactation. After anamnesis and an initial clinical examination, the patients were allocated to two groups for intervention (Chlorhexidine and Sanative®).

Patients received 150 mL of the randomized solution (Chlorhexidine Digluconate 0.12% or Sanative®) for use in the region for 7 days after oral surgery. A total of three investigators participated with well-defined roles in the study, and no exchanges were allowed. Randomization was conducted by a collaborator who was not involved in surgical procedures or assessments through the Random Number Generator Pro 2.15 software. An investigator conducted the anamnesis, clinical, and radiographic examinations and provided postoperative guidance. All surgeries were performed by a single operator to standardize the surgical technique used. The operator did not know which protocol (Chlorhexidine or Sanative®) would be employed.

Each patient underwent two surgical procedures, separated by a minimum interval of one month. Tooth extractions were performed following antisepsis, and local anesthesia was induced using 2 cartridges of 2% lidocaine with epinephrine 1:100,000. Patients were instructed regarding postoperative care, feeding, cleaning of the operated region and restriction of physical effort. The volunteers were also provided with dipyrone tablets (500 mg) and instructed to take one tablet every 6 hours only whether they experienced pain.

An investigator contacted all patients on a daily basis via phone calls to provide consistent reminders regarding oral hygiene care and the utilization of solutions (Chlorhexidine or Sanative®). They were instructed to rinse the operated region using gauze three times a day for 7 days following the surgical procedure.

The analgesic efficacy was assessed using a visual analog scale (VAS) ranging from 0 to 10 cm, where zero indicated "no pain" and ten indicated "unbearable pain". All volunteers were instructed to evaluate their pain levels at two specific time intervals: 24 hours and 7 days after surgery. Additionally, they were requested to record the number of tablets they consumed. Parameters such as the presence of bleeding, hyperemia, or necrosis were evaluated during suture removal i.e.7 days after surgery.

This study had postoperative pain as one of its objectives. Considering the results with 10 patients of the previous pilot study for postoperative pain in 24 hours, mean ± standard deviation of Chlorhexidine group (11.69 ± 10.58) and Sanative® group (4.82 ± 2.37) in millimeter on the VAS, 30 subjects would be needed to achieve a 95% test power with a significance level of 5%, since this is a crossover study with an equal proportion for both samples (t test paired BioEstat 5.0).

Fisher's exact, chi-square, Mann–Whitney, and Wilcoxon tests were performed to analyze the data in this study. For all tests, the level of significance was set at 5%. GraphPad 8.0 and BioEstat 5.0 were used to perform the analysis.

RESULTS

A total of 40 volunteers were assessed for eligibility whose 8 did not meet the inclusion criteria, and 2 declined to participate in the study. Thus, 30 participants were included in this study: 20 women aged 32.0 ± 13.0 years (mean ± standard deviation) and 10 men aged 26.6 ± 8.5 years (mean age ± standard deviation). There were no differences between age and sex (Mann–Whitney, p=0.44).

Table 1 indicated no differences in treatments in terms of the types of extracted teeth (Fisher's exact test, p= 0.42) and their arch position (Chi-square, p= 0.61). Figure 1 demonstrated that there was no difference (Wilcoxon test, p> 0.05) between the treatments regarding VAS scores after 24 hours or after 7 days. Furthermore, both groups showed a decrease in the VAS scores over the 7-day period. However, a significant difference in VAS scores between 24 hours and 7 days was observed only in the chlorhexidine group. (Wilcoxon, p= 0.0178), in which, the mean VAS score of the chlorhexidine group decreased from 1.150 to 0.4150.

Table 2 indicated no differences between treatments (Figure 2) regarding analgesic consumption (Wilcoxon test, p=0.5536) and considering bleeding, hyperemia, and necrosis (Fisher's exact test, p= 0.9656). Besides, no signs of infection were observed in any of the cases.

Table 1 - Distribution of extracted teeth according to the position in the arch.

Variables	Chlorhexidine	Sanative	P
Teeth (%) ¥			
Incisors	1 (3.3%)	1 (3.3%)	0.42
Premolars	4 (13.3%)	1 (3.3%)	
Molars	25 (83.3%)	28 (93.3%)	
Mouth position (%) ǂ			
Upper	13 (46.3%)	16 (53.3%)	0.61
Lower	17 (53.7%)	14 (46.7%)	
Fisher exact test ¥ Chi-square test ǂ			

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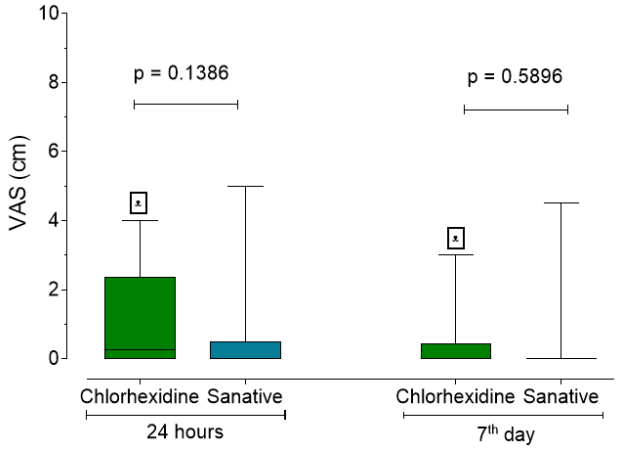

Figure 1 - Visual analog scale score median (±interquartile range) according to postoperative time intervals. The symbols represent statistically significant differences between periods, considering the same group (Wilcoxon, p= 0.0178).

Table 2 indicated no differences between treatments (Figure 2) regarding analgesic consumption (Wilcoxon test, p=0.5536) and considering bleeding, hyperemia, and necrosis (Fisher's exact test, p= 0.9656). Besides, no signs of infection were observed in any of the cases.

Table 2 - Relative distribution of bleeding, hyperemia and necrosis observed in treatments

Variables		Chlorhexidine	Sanative	P
Bleeding	yes	5 (16.7%)	3 (10%)	ns
	no	25 (83.3%)	27 (90%)	
Redness	yes	9 (30%)	9 (30%)	ns
	no	21 (70%)	21 (70%)	
Necrosis	yes	0 (0%)	0 (0%)	ns
	no	30 (100%)	30 (100%)	
Fisher Exact test				

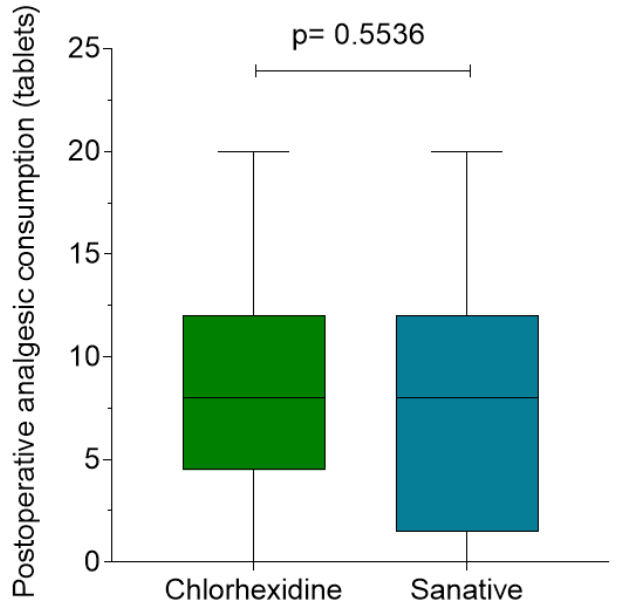

Figure 2 - Postoperative analgesic consumption of chlorhexidine and sanative over a period of 7 days (Wilcoxon test).

DISCUSSION

Inflammatory complications such as pain, swelling, trismus, infection, and AO harm the quality of life of patients after tooth extractions. Several strategies may be applied to reduce the occurrence of these complications[6]. Mouthrinses have been used preoperatively and postoperatively to prevent infectious complications[13]. The benefit of mouthwashes is the capacity of acting locally at the surgical site, also providing mechanical debridement. In addition, they are cheap options and exhibit fewer side effects compared to oral antibiotics[6].

Chlorhexidine, the gold standard antiseptic to reduce plaque, has an antimicrobial activity[6] since it acts by disintegrating the bacterial plasma membrane.[14] Several studies demonstrated the benefit of mouth rinse 0.12% chlorhexidine rinsing preoperatively and 7 days postoperatively for preventing AO[3,6].

Sanative®, an herbal mouthrinse, is composed of alcohol, aqua, and extracts from Physalis angulata, Schinus terbinthifolius, Piptadenia colubrina, and Cereus peruvianus[11,12]. Physalis angulata has demonstrated diverse biological activities, including anticancer, anti-inflammatory, antimicrobial, immunoregulatory, trypanocidal, and leishmanicidal properties[15]. Schinus terebinthifolius is associated with antinociceptive and anti-inflammatory effects[16,17]. Piptadenia colubrine, known for its high tannin content, is commonly used for treating diarrhea, hypertension, rheumatism, hemorrhage, stomach and kidney disorders, as well as inflammatory conditions[16]. Finally, Cereus jamacaru is linked to various effects, including antioxidant, antimicrobial, prebiotic, healing, antiulcer, anti-inflammatory and anti-hyperlipidemic effects[18].

In this study, the postoperative pain assessment analyzed by VAS and postoperative analgesic consumption was compatible with what is expected in a tooth extraction without the presence of complications. As no differences were found between the Chlorhexidine and Sanative® groups concerning pain, bleeding, hyperemia, and necrosis we assume that Sanative® was as efficient as chlorhexidine in prevention of postoperative oral infections.

Despite promising results, some questions require to be answered. In this study, we opted to analyze the performance of Sanative® after simple tooth extraction instead of complex surgical extractions, such as impacted third molar removal. As mild pain is expected in this type of procedure, the full potential analgesic of sanative may not have been explored. The analgesic property of Sanative® could be better explored, for instance, in complex surgeries or infected teeth. Therefore, further stud-

ies should be conducted to explore the full potential of Sanative® since it can be an option for patients who have a preference for herbal medicines or for those unable to use chlorhexidine due to its side effects.

CONCLUSION

Sanative® presented equal efficacy to chlorhexidine and demonstrated to be a valuable option for the prevention of postoperative infections.

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