

Randomized controlled trial comparing antibiotics to placebo for single simple dental extractions in diabetic patients

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ABSTRACT

Type 2 diabetes mellitus is a prevalent chronic disease in the adult population, and its complications include delayed wound healing. Dentists often have to decide whether to prescribe antibiotics for tooth extractions in these patients. **Aim:** To compare post-surgical variables for single simple dental extractions from controlled type 2 diabetic patients, administering either antibiotic or placebo. **Materials and Method:** The study included controlled type 2 diabetic patients requiring a single dental extraction (tooth non-impacted and without acute infection) from April 2021 to May 2023. They were randomized to amoxicillin or placebo prior to surgery. Extractions were performed without raising flaps or bone removal and took no longer than 45 minutes. Before surgery, blood glucose was measured. Age, gender, tooth to be extracted, surgery time, pain, bleeding, trismus, alveolar osteitis, infection, healing, gastric alterations, and number of analgesics taken were evaluated. Patients were checked by telephone call 2 and 14 days after the procedure, and in person after 7 days during the suture removal visit. The data were analyzed using Chi-square, Fisher's exact or Mann-Whitney U tests, as appropriate ($p < 0.05$, significant). **Results:** The analysis included 56 extractions in 56 patients, aged 41 to 81 years (mean SD = 59 +/- 9). During the telephone call at 2 days, no significant difference was found between groups for pain, trismus, edema, hemorrhage, gastric alterations, or analgesics taken. At the clinical checkup at 7 days, no significant difference was found between groups for pain, edema, trismus, alveolar osteitis, hemorrhage, delayed healing, or gastric alteration; but there was a significant difference in the number of analgesics taken ($p < 0.05$), which was higher in the amoxicillin group. During the second telephone call at 14 days, no significant difference was found between groups for pain, edema, trismus, hemorrhage, or gastric alterations; but there was a difference in the number of analgesics taken ($p < 0.05$). Patients in the amoxicillin group took more pain relievers. No case of alveolar osteitis or local or systemic infection was recorded in either group. No patient required additional treatment or hospitalization. **Conclusion:** No significant difference was found for alveolar osteitis, infection, or healing delay after single simple dental extractions in controlled type 2 diabetics, whether they took amoxicillin or placebo. The data from the present study suggest that antibiotic medication in these cases would not be necessary.

Keywords: diabetes mellitus type 2 - antibiotics - placebo - tooth extraction - bacterial drug resistance.

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Estudio clínico aleatorizado de administración de antibióticos para exodoncias simples en pacientes diabéticos

RESUMEN

La diabetes mellitus tipo 2 es una enfermedad crónica de elevada prevalencia que presenta complicaciones en los procesos cicatrizales. Frecuentemente los odontólogos deben decidir la necesidad de prescripción de antibióticos para exodoncias en estos pacientes. **Objetivo:** Comparar variables post quirúrgicas en extracciones simples unitarias de pacientes diabéticos tipo 2 controlados, administrando antibiótico o placebo. **Materiales y Método:** Se realizaron las exodoncias en pacientes diabéticos tipo 2 controlados que concurrieron al servicio desde abril de 2021 a marzo de 2023, requiriendo la extracción de una pieza dental unitaria, sin retención y sin infección aguda. Se realizó una aleatorización previa de la administración de amoxicilina o placebo. Las exodoncias se realizaron sin la implementación de colgajos ni osteotomías, en tiempos no mayores de 45 minutos de duración. Se evaluaron los siguientes parámetros: edad, género, pieza a extraer, glucemia, tiempo de cirugía, dolor, sangrado, trismus, alveolitis, infección, cicatrización, alteraciones gástricas y cantidad de analgésicos ingeridos. Se realizaron dos controles telefónicos a los 2 y 14 días post-exodoncia y un control presencial a los 7 días post-exodoncia. Los datos obtenidos fueron analizados mediante las pruebas Chi-cuadrado, exacta de Fisher o U de Mann-Whitney, según lo que correspondía ($p < 0.05$, significativo). **Resultados:** la muestra incluyó 56 exodoncias correspondiente en 56 pacientes, edad de entre 41 y 81 años (media y DE = 59 +/- 9). No se encontraron diferencias significativas entre ambos grupos, en el control a los 2 días post-exodoncia, en cuanto a trismus, edema, hemorragia, alteraciones gástricas, analgésicos consumidos, ni dolor. Al control clínico presencial a los 7 días post-exodoncia, no se encontraron diferencias significativas entre ambos grupos, en cuanto a dolor, edema, trismus, alveolitis, hemorragia, retardo cicatrizal, ni alteraciones gástricas; encontrándose diferencia significativa para la cantidad de analgésicos consumidos ($p < 0.05$), siendo mayor el consumo en el grupo amoxicilina. Cuando se realizó el segundo llamado telefónico a los 14 días, no se encontraron diferencias significativas entre ambos grupos, en cuanto a trismus, edema, hemorragia, ni alteraciones gástricas; pero sí hubo diferencias en cuanto a analgésicos consumidos ($p < 0.05$). Los pacientes del grupo amoxicilina consumieron más analgésicos. No se registraron en ambos grupos casos de alveolitis, ni de infecciones locales o sistémicas. No se requirieron terapias alternativas, ni hospitalización en ningún paciente. **Conclusión:** Los datos del presente estudio sugieren que la medicación antibiótica, en pacientes diabéticos tipo 2 controlados, no sería necesaria, ya que no se encontraron diferencias significativas para la alveolitis, infección, retardo cicatrizal al realizar exodoncias unitarias, administrando amoxicilina o placebo.

Palabras Clave: diabetes mellitus tipo 2 - amoxicilina - placebo - exodoncia - farmacoresistencia bacteriana

INTRODUCTION

Diabetes is a chronic hyperglycemic disease estimated to occur in 8.8% of the adult population¹. It is usually classified into two main groups: type 1, also known as childhood-onset diabetes, defined by deficiency in insulin production; and type 2, also called the adult-onset diabetes, characterized by insulin resistance. Type 2 is associated with dietary habits and sedentary lifestyle. It develops slowly, and early diagnosis and management are crucial².

Diabetes has a range of oral manifestations, including xerostomia, increased predisposition to dental caries, periodontal disease, increased tendency for infections, burning mouth syndrome, taste disturbances, and healing disturbances³⁻⁵. After tooth extraction in poorly controlled diabetic patients, especially in the early phases, the overall assessment of alveolar healing is slower than in non-diabetics⁶. Uncontrolled patients with poor dental hygiene have been associated with spreading thoracic infections^{7,8}. Post-extraction dental infections have been related to tooth, age, gender, degree of impaction, and operator experience⁹. When dental infection spreads, poorer outcomes can be predicted based on trismus, dysphagia, dyspnea, trismus, the severity of the infection, the number of spaces involved, and increased white blood cell count¹⁰.

Diabetes was therefore assumed to be associated to the spread of postoperative infections, and antibiotics were sometimes prescribed preventively. In the USA, 1 in 10 antibiotics are estimated to be prescribed by dentists. However, prescribing antibiotics for invasive dental procedures in diabetic patients has recently been called to question¹¹.

The massive administration of antibiotics is one of the current and future concerns of the health system, due to the development of bacterial resistance^{12,13}. Although it has been established that it is not necessary to provide antibiotic regimens for simple extractions in healthy patients, evidence is lacking in diabetic patients¹³⁻¹⁶.

The aim of this study was to compare post-surgical variables in single simple dental extractions in controlled type 2 diabetic patients, administering antibiotics or placebo.

MATERIALS AND METHOD

This was a prospective, randomized, double-blind (patient and operator), parallel group comparison

clinical trial. It was conducted at the Department of Oral and Maxillofacial Surgery I of the School of Dentistry of the University of Buenos Aires (Argentina), from April 2021 to March 2023, on controlled diabetic type 2 patients who required a single simple dental extraction.

Inclusion criteria

The study included type 2 diabetic patients (diagnosed and under medical treatment for at least 6 months), male or female, over 18 years of age, who visited the service for single simple dental extraction of a permanent tooth. A hematological analysis of glycosylated hemoglobin (HbA1c) was requested to evaluate blood glucose levels, and the lower limit was established as 6.5%¹⁷. Participants signed the medical history and the informed consent designed for the present study (CETICA-FOUBA NUM. 008/19).

Exclusion criteria

Patients with any of the following were excluded:

1. Inherent systemic or local contraindications for performing dental surgery: pathologies that affect blood coagulation, chemotherapy treatments, diseases of connective tissue or bone metabolism, heart conditions or vascular diseases, uncontrolled diabetes, chronic kidney disorders, systemic infections, mental disorders, tumors.
2. Blood glucose levels greater than 180 mg/dl before receiving care¹⁸.
3. Multiple extractions (more than one tooth).
4. Teeth with acute infection, or impacted teeth.
5. Smokers.
6. Patients who took antibiotics in the 7 days prior to the intervention.
7. Type I diabetic patients
8. Inability to receive any standardized study medication, e.g., amoxicillin.
9. Pregnant or lactating patients.
10. Patients who refused to participate.

Exclusion from analysis

The following cases were excluded from analysis:

1. Surgeries that lasted more than 45 minutes.
2. Surgeries that as a complementary resource involved lifting a flap, or bone tissue removal.

Subjects were randomized through the generation of random numbers between zero and one in the Microsoft® Excel computer program. Numbers between 0 and 0.5 were assigned to the placebo group, and numbers between 0.5 and 1 were assigned to the amoxicillin group. In the randomization, the number 0.500000000 did not come up. The results were kept in sealed envelopes in ascending order according to the subject's order of entry into the study, and opened prior to surgery.

Study groups:

Group 1: Dental extraction with administration of antibiotics (Amoxicillin 500 mg, Amixen®, Laboratorios Bernabo, Argentina).

Group 2: Dental extraction with administration of placebo.

Surgical protocol

Pertinent clinical, laboratory and imaging studies were performed. Prior to surgery, the patient's blood glucose was measured (FreeStyle Optium Neo®), and was required to be equal to or below 180 mg/dl with at least two hours of fasting (exclusion criteria). Prior to all surgeries, patients were instructed to rinse their mouth with Chlorhexidine 0.12% solution for 1 minute.

The surgeries were performed according to the following clinical steps:

1. Antisepsis with povidone-iodine.
2. Local anesthesia of the area to be operated on (4% articaine hydrochloride with L-Adrenaline 1:100,000, Totalcaina Forte®, Laboratorios Bernabo, Argentina).
3. Intracrevicular incision with scalpel blade number 15.
4. Slight curettage of the periodontal soft tissue.
5. Dislocation with straight Clev-Dent elevator.
6. Extraction with elevator and/or corresponding forceps.
7. Wound toilette.
8. Simple suture.
9. Post-surgical indications.

Group with antibiotic administration

One 500 mg amoxicillin tablet (Amixen®, Laboratorios Bernabo, Argentina) was administered 1 hour before surgery, and continued every 8 hours for 7 days (21 pills altogether)¹⁹.

Group with placebo administration

One placebo 1 tablet (donated by Laboratorios Bernabo, Argentina) was administered 1 hour before surgery, and continued every 8 hours for 7 days (21 pills altogether).

All tablets were packed in identical bottles, each containing 21 pills. Placebo appearance, size, and odor was indistinguishable from amoxicillin tablets.

In the postoperative period, all patients were prescribed Ibuprofen 600 mg according to pain. Special emphasis was placed on asking patients to maintain blood glucose levels below 180 mg/dl during the postoperative period by regulating the intake of hyperglycemic foods, and continuing with the hypoglycemia medication. Researchers' telephone numbers were provided in the informed consent document so that patients could contact them for any questions or problems they might have.

Parameters evaluated:

Age/Gender; tooth to be removed; blood glucose level.

Patients were evaluated or consulted 2, 7 and 14 days after the intervention. Data were recorded in an ad hoc Excel spreadsheet.

Intra-surgical parameters recorded:

Surgery time (min); intra-surgical complications.

Parameters recorded during phone call after 2 days:

Pain: scale with visual analogue scale (VAS); amount of pain relievers taken; gastric alterations: present or absent; hemorrhage: present or absent; trismus: present or absent; edema: present or absent.

Parameters recorded during clinical checkup and suture removal after 7 days:

Pain: VAS scale; amount of pain relievers taken; gastric alterations: present or absent; hemorrhage: present or absent; trismus: present or absent; edema: present or absent; alveolar osteitis: present or absent; infection: present or absent; delayed healing: present or absent.

Parameters recorded during phone call after 14 days:

Amount of pain relievers taken; gastric alterations: present or absent; hemorrhage: present or absent; trismus: present or absent; edema: present or absent.

Statistical analysis

Categorical variables were described by absolute frequencies and percentages with 95% confidence intervals (CI95), estimated using the Wilson method. The description of numerical variables included minimum (Min), maximum (Max), median, first quartile (Q1), third quartile (Q3), mean and standard deviation (SD). To compare frequencies, Pearson's Chi-square or Fisher's exact tests were used, as appropriate. When all expected frequencies were greater than or equal to 5, Chi-square was used; otherwise, Fisher's exact test. To compare two independent sets of numerical observations, the nonparametric Mann-Whitney U test was used. The Student t-test for independent samples was not used because the conditions of normality and homoscedasticity were not met, analyzed using the Shapiro-Wilk tests with the Royston method and F methods, respectively. Any p values lower than 0.05 were considered statistically significant. The analysis was performed using MedCalc v. 22.021 and R v. 4.3.1 with *DescTools* package. The statistical graphs were created with Calc from LibreOffice.

RESULTS

Patient demographics and clinical characteristics

Patients and interventions

Sixty-six controlled type 2 diabetic patients met the inclusion criteria. Four patients refused to be enrolled

in the study, for whom extractions were performed but no data were recorded, and administration of antibiotics was at the discretion of the professional involved in each surgery. Another 6 patients had blood glucose levels higher than 180 mg/dl prior to surgery, so they were excluded from the data analysis. These patients were treated and prescribed antibiotic therapy before and after surgery, and advised to consult the physicians treating their underlying pathology for close follow-up.

The study sample included 56 subjects equally distributed by gender (n=28), age 41 to 81 years (median = 59, Q1-Q3 = 54-65, mean \pm SD = 59 \pm 9. Blood glucose level was between 75 mg/dl and 179 mg/dl (median = 141, Q1-Q3 = 117-168, mean \pm SD = 139 \pm 32). Blood glucose (mg/dl) did not differ significantly (Mann-Whitney U test: U = 377; p = 0.80) between patients on amoxicillin (median = 153, Q1-Q3 = 117-168, mean \pm SD = 141 \pm 31, Min-Max = 75-177) and patients on placebo (median = 135, Q1-Q3 = 115-168, mean \pm SD = 136 \pm 33, Min-Max = 75-179).

There were 28 patients medicated with amoxicillin and another 28 with placebo. Extractions were performed on all types of teeth except lower first premolars (Fig. 1).

Intra-surgical instance

Fifty-six surgeries were performed, which lasted

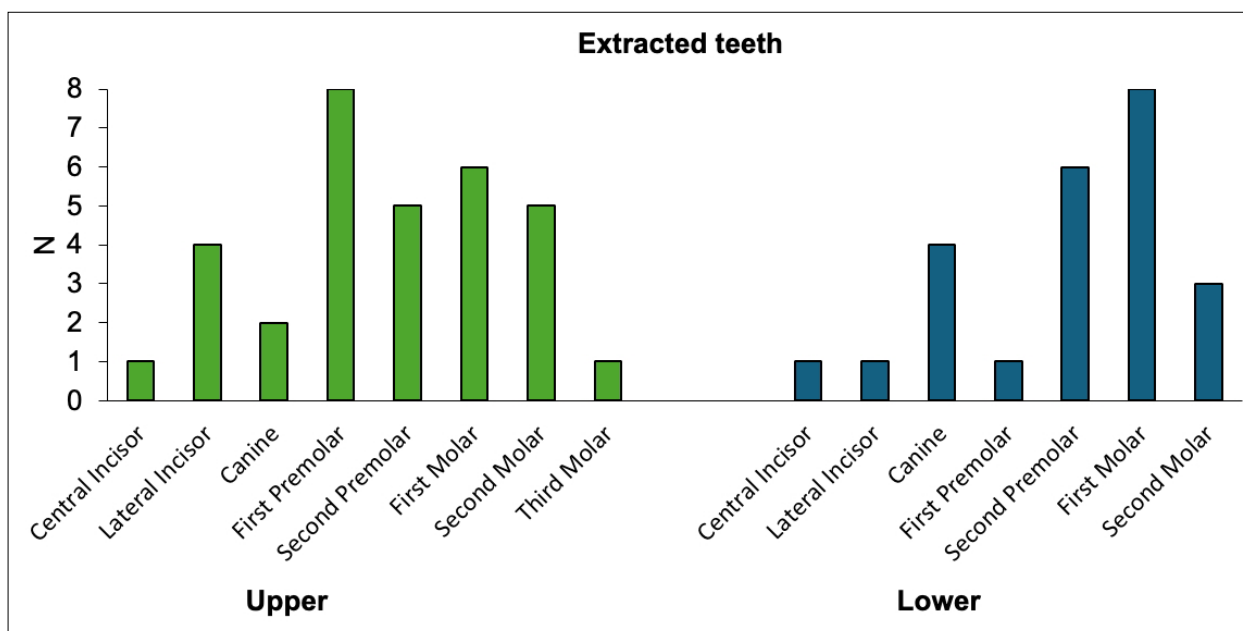


Fig. 1: Number of extractions according to tooth type.

between 5 and 45 minutes (median = 20, Q1-Q3 = 15-25; mean \pm SD = 21 \pm 9). The duration of surgery did not differ significantly (Mann-Whitney U test: $U = 356$; $p = 0.55$) between treatments (amoxicillin, median = 20, Q1-Q3 = 14-23, mean \pm SD = 20 \pm 9, Min-Max = 7-40; placebo, median = 19, Q1-Q3 = 15-27, mean \pm SD = 22 \pm 10, Min-Max = 5-45). No surgery took longer than 45 minutes (exclusion criteria for analysis).

Intraoperative complications

All surgeries were completed without the need to apply osteotomy or raise a mucoperiosteal flap. No relevant intra-surgical complication was observed.

Phone interview 2 days after the intervention

Table 1 summarizes the results obtained by telephone interview two days after the intervention. None of the 56 patients presented trismus (100%; CI95: 94% to 100%). Six patients had edema (11%; CI95: 5% to 21%). Hemorrhage was present in 2 patients (4%; CI95: 1% to 12%) and gastric alterations in 6 (11%; CI95: 5% to 21%). Patients took between 0 and 8 analgesic tablets (median = 2, Q_1 - Q_3 = 1-4, mean \pm SD = 3 \pm 2). The perception of pain assessed on a visual analogue scale (VAS) was between 0 and 6 (median = 3, Q_1 - Q_3 = 1-4, mean \pm SD = 3 \pm 2). There was no significant difference between groups for any of these 6 variables (Table 1).

Clinical checkup 7 days after the intervention

All patients were monitored after a week at the visit at which the suture was removed (Table 2). No patient developed alveolar osteitis (dry socket) or infectious processes associated with tooth extraction. It was not necessary in either group to perform any additional clinical maneuvers at the clinical checkup at 7 days. In 18 surgeries there was delayed healing (32%; CI95: 21% to 45%). Gastric alterations were present in 7 patients (13%; CI95: 6% to 14%). The number of analgesic tablets the patients took was between 0 and 5 (median = 0, Q_1 - Q_3 = 0-2, mean \pm SD = 1 \pm 2). Pain perception on VAS was between 0 and 5 (median = 0, Q_1 - Q_3 = 0-2, mean \pm SD = 1 \pm 1). The number of analgesic tablets taken was the only variable where a significant difference was observed between groups (Mann-Whitney U test: $U = 266$; $p < 0.05$; Fig. 2): the values were higher with amoxicillin

Table 1. Comparison between patients who received amoxicillin or placebo, according to information collected by telephone interview 2 days after the intervention. Categorical variables, N (%; CI95); numerical variables, median (minimum-maximum).

PHONE INTERVIEW 2 DAYS AFTER THE INTERVENTION			
Variable	Medication		
	Amoxicillin	Placebo	p
Trismus			
No	28 (100%, 88 to 100)	28 (100%, 88 to 100)	1*
Yes	0 (0%, 0 to 12)	0 (0%, 0 to 12)	
Edema			
No	26 (93%; 77 to 98)	24 (86%; 69 to 94)	0.67*
Yes	2 (7%; 2 to 23)	4 (14%; 6 to 31)	
Hemorrhage			
No	27 (96%, 82 to 99)	27 (96%, 82 to 99)	1*
Yes	1 (4%, 1 to 18)	1 (4%, 1 to 18)	
Gastric alterations			
No	24 (86%, 69 to 94)	26 (93%, 77 to 98)	0.67*
Yes	4 (14%, 6 to 31)	2 (7%, 2 to 23)	
Analgesic pills	3 (0-7)	2 (0-8)	0.08#
VAS	3 (0-5)	2 (0-6)	0.79#
N total	28	28	
*Fisher's exact test #Mann-Whitney U test			

*Fisher's exact test

#Mann-Whitney U test

(median = 1, Q_1 - Q_3 = 0-3, mean \pm SD = 2 \pm 2) than with placebo (median = 0, Q_1 - Q_3 = 0-2, mean \pm SD = 1 \pm 1).

Phone interview 14 days after the intervention

There was no trismus in any surgery. Two patients suffered edema (4%; CI95: 1% to 12%) and three manifested gastric alterations (5%; CI95: 2% to 15%). The number of analgesic tablets taken was between 0 and 3 (median = 0, Q_1 - Q_3 = 0-0, mean \pm SD = 0.2 \pm 0.7).

As occurred 7 days after the intervention, at 14 days, the use of analgesic tablets also varied significantly between groups (Mann-Whitney U test: $U = 323$; $p < 0.05$; Fig. 3). with higher values for amoxicillin (median = 0, Q_1 - Q_3 = 0-0, mean \pm SD = 0.4 \pm 0.9) than for placebo (median = 0, Q_1 - Q_3 = 0-0,

Table 2. Comparison between patients who received amoxicillin or placebo, according to the checkup 7 days after the intervention. Categorical variables, N (%; CI95); numerical variables, median (minimum-maximum).

CLINICAL CHECKUP 7 DAYS AFTER THE INTERVENTION			
Variable	Medication		
	Amoxicillin	Placebo	p
<i>Delayed healing</i>			
No	20 (71%, 53 to 85)	18 (64%, 46 to 79)	0.57 [§]
Yes	8 (29%, 15 to 47)	10 (36%, 21 to 54)	
<i>Gastric alteration</i>			
No	24 (86%, 69 to 94)	25 (89%, 73 to 96)	1 [*]
Yes	4 (14%, 6 to 31)	3 (11%, 4 to 27)	
<i>Analgesic pills</i>	1 (0-5)	0 (0-4)	<0.05 [#]
VAS	0 (0-5)	0 (0-5)	0.41 [#]
N total	28	28	

[§]Pearson's Chi-square test
^{*}Fisher's exact test
[#]Mann-Whitney U test

mean \pm SD = 0.1 \pm 0.4). For the other 4 variables compared, no significant difference was found between treatments (Table 3).

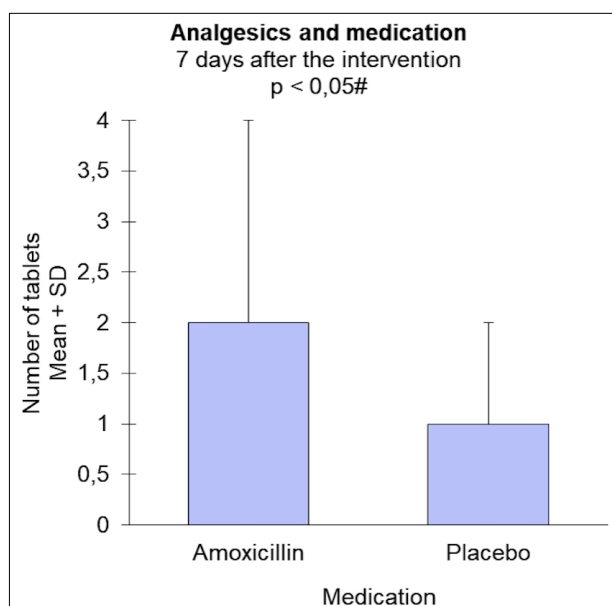


Fig. 2: Analgesics taken (in number of tablets) according to medication, as recorded in the clinical checkup 7 days after the intervention. # Mann-Whitney U test.

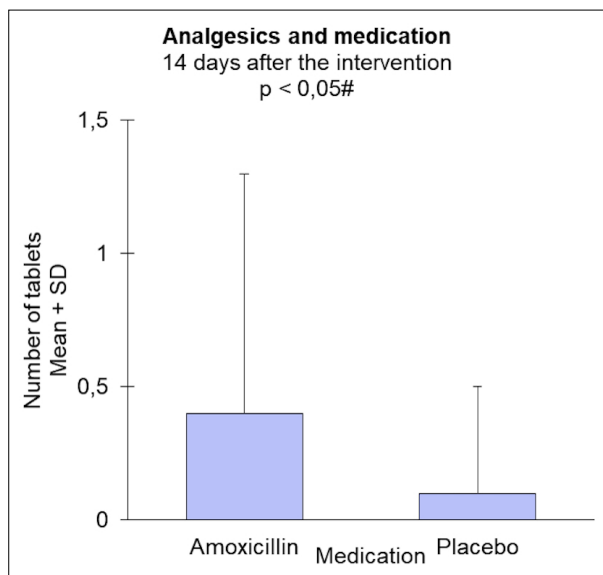


Fig. 3: Analgesics taken (in number of tablets) according to medication, as recorded in a telephone interview 14 days after the intervention. # Mann-Whitney U test.

Table 3. Comparison between patients who received amoxicillin or placebo, according to information collected by telephone interview 14 days after the intervention. Categorical variables, N (%; CI95); numerical variables, median (minimum-maximum).

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PHONE INTERVIEW 14 DAYS AFTER THE INTERVENTION			
Variable	Medication		
	Amoxicillin	Placebo	p
<i>Trismus</i>			
No	28 (100%, 88 to 100)	28 (100%, 88 to 100)	1*
Yes	0 (0%, 0 to 12)	0 (0%, 0 to 12)	
<i>Edema</i>			
No	26 (93%; 77 to 98)	28 (86%; 69 to 94)	0.49*
Yes	2 (7%; 2 to 23)	0 (14%; 6 to 31)	
<i>Hemorrhage</i>			
No	28 (96%, 82 to 99)	28 (96%, 82 to 99)	1*
Yes	0 (4%, 1 to 18)	0 (4%, 1 to 18)	
<i>Gastric alterations</i>			
No	26 (86%, 69 to 94)	27 (93%, 77 to 98)	1*
Yes	2 (14%, 6 to 31)	1 (7%, 2 to 23)	
<i>Analgesic pills</i>	0 (0-3)	0 (0-2)	<0.05*
N total	28	28	

*Fisher's exact test
 #Mann-Whitney U test

None of the patients included in the study (even those medicated with placebo) presented alveolar osteitis or local or systemic infection in the postoperative period. No patient required any additional therapeutic measure, hospitalization, or any other emergency therapeutic measure.

DISCUSSION

Although a 2006 consensus on the use of antibiotics recommended administration for dental extractions in diabetic patients (considered a high-risk group for local and systemic infections)¹¹, more recent studies cast doubt on this recommendation. Reviews argue that there is no evidence for prescribing antibiotics for diabetic patients if their blood glucose is under control^{20,21}. Some studies state that well-controlled diabetic patients do not need antibiotic administration and can be treated as healthy patients^{22, 23}. However, diabetic patients with inadequate control should be prescribed antibiotics if surgery is urgent and their blood glucose cannot be properly leveled. It is also recommended to medicate diabetic patients when there is an active infection, or when surgery is complex or prolonged. This is similar to the treatment of non-diabetic patients^{11, 20, 23}.

Some researchers have compared post-extraction healing in healthy and type 2 diabetic patients. One study that evaluated hematological samples for post-extraction healing in healthy and type 2 diabetic patients found no significant healing difference, and found complications in 10.5% of diabetic patients, and 6.8% of healthy patients. The complications were resolved without need for hospitalization. The authors concluded that it is unnecessary to perform antibiotic prophylaxis for dental extraction in type 2 diabetic patients²⁴. Another study in which extractions were performed in type 2 diabetic and non-diabetic patients found that 5% of type 2 diabetic patients and 7% of healthy patients presented a delay in healing beyond one week. No correlation was found between glycemia and healing in diabetic patients. All patients healed completely within four weeks. The authors concluded that there is no difference in the healing process between groups, and preventive medication is not recommended in these cases²⁵.

The present study provides evidence supporting the premise that antibiotic medication is unnecessary in controlled type 2 diabetic patients. Socket healing after single extractions in diabetic type 2 patients

was satisfactory with or without antibiotics. In this study of simple single extractions, there was no relevant post-surgical complication such as alveolar osteitis, or local or systemic infection. Pain, edema, trismus, alveolar osteitis, infection, hemorrhages, delayed healing, and gastric alterations did not differ statistically between groups. To our knowledge, this is the first trial comparing antibiotics and placebo for dental extractions in diabetic type 2 patients. This study design enabled exploration of post-surgical variables of dental extractions, specifically comparing patients with or without antibiotic administration, which is currently a controversial clinical decision. As the study only included single simple dental extractions performed within a maximum of 45 minutes without raising flaps or bone removal, the sample was reasonably uniform. This trial unexpectedly found significant differences in the intake of analgesic pills (which was higher in the amoxicillin group) at 7 and 14 days after surgery, a characteristic with a non-significant trend at 2 days. This might be because the use of antibiotics such as amoxicillin may be associated with side effects or adverse reactions such as headache, rash, upset stomach, or diarrhea.

Antibiotic prophylaxis in diabetic patients was also observed to be unnecessary in a recent retrospective analysis of diabetic patients. No significant effect was observed on antibiotic prophylaxis with increased odds of post-extraction complication or medical care. The analysis also suggested that it may be necessary to re-evaluate the use of antibiotic prophylaxis in order to minimize unnecessary antibiotic use²⁶.

In another study, cases of serious infections following dental extractions were reported as clinical cases. Generally, the glycemic data reported were high (218 mg, 305 mg, 428 mg, 378 mg), and in some cases, there was no report of glycemia¹¹. These infections spreading to deep anatomical spaces developed in patients with poor glycemic control and poor dental hygiene, and were sometimes associated with other systemic diseases²⁷⁻²⁹.

It is important to highlight the disadvantages of unnecessary administration of antibiotics such as side effects and adverse effects (e.g., diarrhea, vaginitis, anaphylaxis), higher costs, and the silent yet important increase in bacterial resistance to antibiotics⁹. Antibiotic resistance is increasing gradually, with new resistance mechanisms

emerging and spreading worldwide, threatening our ability to treat common infectious diseases. A growing number of infections, such as pneumonia, tuberculosis, septicemia, gonorrhea or foodborne diseases, are becoming increasingly difficult to treat as antibiotics lose effectiveness^{30, 31}.

This trial provides information supporting the premise that antibiotic administration is unnecessary for single simple dental extractions in controlled type 2 diabetic patients. Further studies on larger samples and different clinical situations (e.g., multiple extractions, dental implants¹¹, endodontic

treatment³²) are needed to clarify the advantages and disadvantages of peri-operative administration of antibiotics in these patients.

In conclusion, the analysis of post-surgical variables suggests that single dental extractions can be performed on controlled type 2 diabetic patients, considering them as healthy patients, without the need to administer antibiotics. Patients receiving placebo did not present greater alveolar osteitis, local or systemic infection, delayed healing, trismus, edema, or pain.

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CONFLICT INTERESTS

The authors declare no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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