

Efficacy of Antibiotics Treatment in Preventing Postoperative Complications after Tooth Extraction Surgery: A Prospective, Randomized, Double-Blind Controlled Study

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Despite evidence that antibiotics abuse is related to unknown pathogen infection, antibiotics are badly overused in China, as common people can easily buy antibiotics in pharmacy stores, even without prescriptions from doctors. The necessity and feasibility of antibiotics treatment after tooth extraction surgery, among the most common surgical operations, remain unclear. We examined the clinical significance of necessity of antibiotics treatment after tooth extraction using 103 patients treated with amoxicillin and metronidazole and 104 subjects treated with vitamin C as control. A randomized, double-blind, placebo-controlled, clinical trial design was performed. Univariate analyses for general characteristics of the study population were performed and there were no significant differences in gender, age, extraction position between the two groups before operation. The operation time was also not significantly different between the two groups. The postoperative complications were evaluated regarding pain, swelling, opening degree and alveolitis. The statistical analysis revealed that postoperative amoxicillin and metronidazole treatment did not produce statistically significant better results than placebo with regard to pain, swelling, opening degree and alveolitis. These findings extend our understanding of antibiotics using after tooth extraction surgery and suggest that this therapeutic strategy does not seem to impose additional benefits to Chinese population.

Key words: Infection, tooth extraction, antibiotics, postoperative complications

Tooth extraction is a very common surgical procedure and is often followed by pain, swelling, trismus, alveolar osteitis, and infections of the wound, prebuccal site and anterior isthmus of the fauces^[1]. The most common is alveolar osteitis, which affects 25 %-30 % of patients^[2]. Infection of the wound is also common, ranging from 2 % to 12 %^[3,4]. Antibiotics are frequently prescribed with nonsteroidal anti-inflammatory drugs in dental clinics to prevent infections that may occur after invasive surgical treatment^[5]. The rate of antibiotic prescription after tooth extractions is high^[6]. Among all antibiotic prescriptions, the proportion of prescriptions from dental clinics was approximately 10 %^[7,8]. The efficacy of antibiotic prophylaxis in preventing complications after tooth extraction has long been controversial. Some studies have reported lower rates of infection^[4,9,10] and others have reported greater rates^[11-14]. Misuse of antibiotics may cause antibiotic resistance to the extent that a warning was announced by the World Health Organization^[15]. Infection with

antibiotic-resistant bacteria may kill 10 million people each year until 2050^[16]. Better evidence is needed about the use of antibiotic prophylaxis in patients undergoing tooth extraction in order to determine appropriate use. The main goal of the present prospective, randomized, double blind controlled study was to evaluate and compare the effectiveness of amoxicillin and metronidazole vs. placebo on the postoperative complications of tooth extraction surgery in a Chinese population sample. In the present study, inclusion criteria were set as patients above 18 y old and exclusion criteria were set as patients who did not prefer the participation after the publication of this study^[17]. A total of 207 patients undergoing tooth extraction 18 y to 45 y old, including 92 women and 115 men, were recruited to participate in the present study from November 2020 to June 2021. The study was approved by The Affiliated Stomatological Hospital of Nanjing Medical University and then written consent was obtained from participants. A randomized, double-

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blind, placebo-controlled, clinical trial design was performed. Two experimental groups were established according to the antibiotic treatment regimen used. Group A (treatment group), amoxicillin and metronidazole administered postoperatively; group B, (placebo group), equivalent dose of vitamin tablets. By the use of computer generated random numbers, the patients were assigned to group A (odd number) or group B (even number) at their first appointment. Patients in the treatment group took amoxicillin 0.5 g 1 h and metronidazole 0.2 g 1 h postoperatively (3 times/d). Patients in the placebo group took a placebo with the same shape and dose on the same times. Surgery was performed by the same team on all patients and a standardized technique was used. Postoperative data were collected from all patients after 7 d and were evaluated regarding pain, swelling, opening degree and alveolitis. Severity of pain after extraction was measured on Visual Analogue Scales (VAS). Swelling was measured as the difference between the distance (mm) between the lower earlobe and the mesentum on the extraction side. Mouth opening degree was measured as the distance between upper and lower incisors (mm). The scores of pain, swelling and opening degree range from 0 ("no pain/no swelling/no difficulty of mouth opening") to 3 ("severe"). The data collected were analyzed statistically with the Statistical Package for the Social Sciences (SPSS) 17.0 program. The chi square test and the parametric Student's t-test were used to compare the proportions of alveolitis and age mean between the groups. The Wilcoxon signed rank test was used to compare the scores of pain, swelling and mouth opening between the groups. Bilateral tests were used for comparisons, with the level of significance set at $\alpha=0.05$. $p<0.05$ was considered significant. The general characteristics of the study population in the two groups were shown in Table 1. The chi square test and the parametric Student's t-test indicated that there were no significant differences in gender, age, extraction position and operation time between the two groups. Fig. 1 and Table 2 show the postoperative complications in the two groups. The chi square test in fig. 1 revealed there was no significant difference in pain ($\chi^2=0.072$, $p=0.788$), in swelling ($\chi^2=0.252$, $p=0.615$), in opening degree ($\chi^2=0.138$, $p=0.710$) and alveolitis (continuity correction $\chi^2=2.265$, $p=0.132$) between the two groups. Furthermore, the scores of pain, swelling and mouth opening were compared using Wilcoxon signed rank test (Table 2). The results also indicated no significant difference in these scores between the two groups. Despite the use of different treatment protocols,

including different antibiotics, administration regimens (pre and/or postoperatively) and administration routes (oral vs. intravenous), the usefulness of antibiotic therapy in patients undergoing tooth extraction surgery has remained a matter of debate. Penicillin has long been the antibiotic of choice, because it is highly effective against the bacterial spectrum normally found in these patients and is nontoxic and bactericidal. Amoxicillin is a useful antibiotic for the treatment of oral infections and has been previously evaluated in several clinical trials of tooth extraction surgery^[18,19]. Sekhar *et al.* study indicated that antimicrobial prophylaxis did not seem to reduce morbidity after removal of lower third molars and metronidazole was active only against anaerobic bacteria^[20]. However, the comparison of the regimen of amoxicillin and metronidazole administered postoperatively vs. placebo has never been investigated in a Chinese group of patients. The present study attempted to assess the clinical advantages of amoxicillin and metronidazole treatment after tooth extraction surgery. Because this was a randomized study, the possibility of selection bias was virtually eliminated, giving validity to the obtained results. Furthermore, the study was conducted in a double-blind fashion, an independent research assistant evaluated the results and the clinical procedures were performed in the same surgical room. These factors significantly minimized the effect of preconceived ideas or prejudgments of the surgeon concerning the potential benefits of antibiotics. Our results showed that the postoperative amoxicillin and metronidazole treatment did not produce statistically significant better results than placebo with regard to pain, swelling, opening degree and alveolitis. This was consistent with Monaco *et al.* results which did not find statistically significant differences in postoperative sequelae when comparing postoperative amoxicillin to control, although the dose of amoxicillin used in their study (2 g/d) was greater than in our study^[21]. This was inconsistent with Head *et al.* results which proved that the use of penicillin V and metronidazole in combination might be effective in the prevention of the sequelae of postextraction bacteremias^[22]. None of the patients included in the treatment group met the definition for alveolitis. Only 4 patients had been diagnosed as alveolitis. These data are consistent with the results of a previous study that included 118 patients undergoing third molar surgery in which alveolitis was not observed in the group treated with antibiotics compared with placebo^[23]. The rate reported in our study was much lower than that reported in other studies, in which the

rate of alveolitis in the treated patients was 3.23 % and 14.81 % in the untreated patients^[10,24] and 6.2 % to 14.4 % in a recent review^[25]. Pain and swelling are the most invalidating complications produced after tooth extraction surgery and perhaps the main cause for the loss of working hours. In our study, a statistically significant pain or swelling reduction was not observed after 7 d postoperatively in patients treated with amoxicillin and metronidazole. In summary, we

compared the amoxicillin and metronidazole treatment in patients undergoing tooth extraction surgery in a randomized, double-blind, placebo-controlled fashion. The results showed that amoxicillin and metronidazole did not have a statistically significant beneficial effect in the postoperative recovery of patients undergoing tooth extraction surgery. Thus, this therapeutic strategy does not seem to impose additional benefits to Chinese population.

TABLE 1: DISTRIBUTIONS OF CHARACTERISTICS OF THE STUDY POPULATION

	Treatment group n (%)	Placebo group n (%)	χ^2 or t-value	p
Gender				
Male	55 (53.4)	60 (57.7)	0.386	0.53
Female	48 (46.6)	44 (42.3)		
Age (years, mean \pm SD)	24.37 \pm 4.722	24.31 \pm 4.750	0.091	0.93
Extraction position				
Lower jaw	46 (44.7)	47 (45.2)	0.006	0.94
Upper jaw	57 (55.3)	57 (54.8)		
Operation time				
<10 min	54 (52.4)	66 (63.5)	4.881	0.09
10-30 min	36 (35.0)	33 (31.7)		
>30 min	13 (12.6)	5 (4.8)		

Note: p<0.05 indicates significance

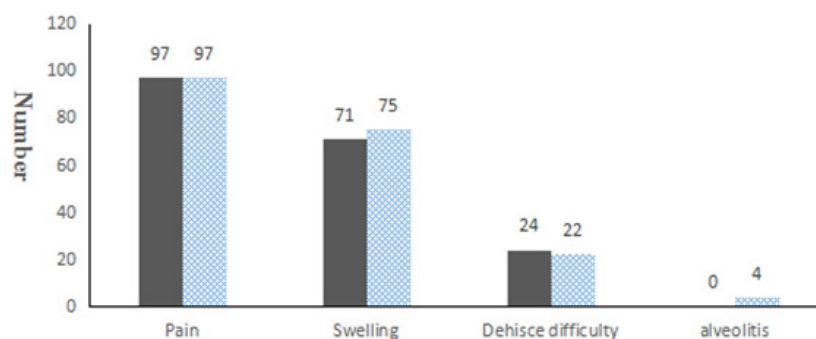


Fig. 1: Postoperative complications including pain, swelling, opening degree and alveolitis in 217 cases (Group A 103 cases and Group B 104 cases), (■) treatment group and (▨) placebo group

TABLE 2: THE SCORES OF POSTOPERATIVE COMPLICATIONS

Variable	Z	p value
Pain	-0.24	0.81
Swelling	-0.342	0.732
Mouth opening degree	-0.5	0.617

Note: Wilcoxon signed rank test was performed, p<0.05 indicates significance

Conflict of interests:

The authors declared no conflict of interest.

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