

Are systemic antibiotics necessary in the prevention of wound healing complications after intra-alveolar dental extraction?

**O. M. Gbotolorun,
I. M. Dipo-Fagbemi, A. O. Olojede,
S. Ebigwei, J. O. Adetoye**
Oral Surgery Unit, Randle General Hospital,
Lagos, Nigeria

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Abstract. This double-blind, randomized controlled study was done to assess the necessity of systemic antibiotics in the prevention of wound healing complications after intra-alveolar dental extraction. A consecutive recruitment method was used to allocate participants to two treatment groups. Subjects in group A (antibiotics group, $n = 75$) received amoxicillin and metronidazole for 5 days postoperatively, while those in group B (placebo group, $n = 75$) were given identical-looking placebo drugs in place of the antibiotics. Postoperative socket healing complications, pain, and compliance with postoperative instructions were assessed postoperatively. Healing was uneventful in 129 patients (86%). Twenty-one patients (14%) developed wound healing complications. Dry socket was the most common complication in the antibiotics group (six subjects), while acutely inflamed sockets was the most common in the placebo group (five subjects). Non-adherence to postoperative instructions and postoperative pain were found to be significantly associated with the development of wound healing complications. The prescription of antibiotics after routine intra-alveolar dental extraction in healthy patients may not play any significant role in preventing wound healing complications. However, non-compliance with postoperative instructions might be associated with increased wound healing complications.

Key words: antibiotics use; intra-alveolar dental extraction.

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Tooth extraction is the most common procedure in oral surgical practice.¹ In an ideal situation, it entails the painless removal of the whole tooth or its root, with

minimal trauma to the surrounding soft tissues.² Successful tooth extractions are based on an understanding of the basic surgical principles of the procedure.³ In

spite of this understanding, complications still arise, although their frequency is reported to have reduced following advancements in knowledge and

techniques.⁴ In clinical practice, antibiotics are sometimes prescribed post-extraction to prevent these complications. This practice is, however, controversial. The prescription of antibiotics post-extraction is supported by those who believe that extraction wounds require antibiotics to heal unevenly.⁵ Others hold a dissenting view and claim that the risk of developing infectious complications following tooth extraction is too small to warrant antibiotic use, even with surgical extractions.⁴⁻⁷ This latter group further argues that the defence mechanisms of the body enable the healing process to ensue without the need for antibiotics.^{4,6}

Guidelines for the use of antibiotics are generally available for most surgical procedures. These principles are well established and are related to the procedure being performed, the type of wound, and the health of the patient.⁶ However, they are reportedly not always followed.^{6,7} Statistics even show that approximately half of the total antibiotic prescriptions in many hospitals across the globe are administered with neither signs nor symptoms of an ongoing infection, and a proportion of this misuse is attributed to prescription by dental experts.⁷ In addition, the literature also reveals that antibiotics are sometimes used as 'drugs of fear' to cover negligence and errors committed during surgical procedures.⁷

Justification for the use of antibiotics, especially after dental extractions, comes from the vast information in text books, dental school instructions, and even continuing education lectures.⁷ This justification, coupled with anecdotal evidence that patients tend to get better whenever antibiotic drugs are prescribed, has resulted in their continual use. The worry is that this trend, if unabated, could culminate in multiple microbial resistance, thus reducing the effectiveness of antibiotics, which to date remain the most powerful tools available in combating microbial attacks.⁸⁻¹⁰

This double-blind, randomized controlled study aimed to determine the role of postoperative antibiotic medication in the prevention of infectious complications following routine intra-alveolar dental extractions in a hospital in Lagos, Nigeria.

Materials and methods

This study was conducted in the dental outpatient department of a general hospital in Lagos, Nigeria. All consecutive patients who met the inclusion criteria and agreed to participate were included in the study. Inclusion criteria encompassed male and

female subjects, aged between 20 and 50 years, who required a routine intra-alveolar extraction. Patients with chronic oral infections, immune-compromised patients, and pregnant and lactating women were excluded from the study. Also excluded were patients receiving chemotherapy or radiation therapy, patients already on antibiotics before seeking care at the hospital, patients needing total extraction or with severe periodontitis, and patients who had any other oral pathology. Ethical clearance was obtained for the study and written informed consent was also obtained from each patient after they were assured of the confidentiality of the findings of the study.

A consecutive recruitment method was used to enrol patients in the study. After their dental extraction, eligible patients were allocated randomly to the antibiotics or placebo group by picking tallies in a box that was pre-marked A or B. The letter picked by the patient determined the treatment group the patient was assigned to. Neither the patient nor the postoperative assessor knew the treatment assigned to the group they had picked. The grouping was known only to the chief pharmacist of the hospital, through whom the drugs for the study were supplied. The antibiotics and placebo drugs were identical in appearance and were supplied by the same company (Emzor Pharmaceutical Industries Ltd, Lagos, Nigeria).

For all recruited patients, the extraction was performed with dental forceps and/or elevators by surgeons of a similar level of experience, with as little trauma as possible to the surrounding soft tissues. A preoperative oral rinse with 0.12% chlorhexidine mouthwash was done 1-2 min prior to the commencement of each procedure. The dental extractions were done after injection of lidocaine (2%) with adrenaline (1:80,000). Following the extraction, the socket was packed with gauze and the patient was asked to bite hard on it, to apply pressure to the socket wound; the socket was checked for haemostasis after about 20 min.

All patients were given the same post-extraction instructions, both verbally and in written form, as follows: (1) do not rinse vigorously, suck on straws, for 24 h; (2) do not smoke or drink alcohol for 72 h; (3) commence warm saline mouth wash/bath after 24 h, six times daily for 1 week; (4) commence the use of analgesics and antibiotics immediately after removal of the pack from the mouth, as directed.

Patients in the antibiotic group (group A) received the following drugs from the pharmacy: amoxicillin 500 mg every 8 h for 5 days, metronidazole 400 mg every

8 h for 5 days, paracetamol 1000 mg every 8 h for 3 days, and vitamin C 100 mg every 8 h for 2 weeks. Patients in the placebo group (group B) were given placebo tablets in place of amoxicillin and metronidazole for the same durations, paracetamol 1000 mg every 8 h for 3 days, and vitamin C 100 mg every 8 h for 2 weeks.

To promote patient compliance and eliminate bias, both groups were given drugs directly from the hospital pharmacy. All patients were reviewed on days 1, 3, and 7 postoperatively for the assessment of socket wounds and compliance with both the postoperative instructions and use of medications. All postoperative assessments were done by one of the investigators (IMD) to prevent inter-examiner variability.

Patients who did not show up for review and those who took any other medication during the period of assessment apart from the drugs prescribed were withdrawn from the study. Patients who developed socket healing complications were also withdrawn from the study and transferred to the oral surgery department for management of the complications; however, their data were included in the analysis. Patients were also instructed to report any case of increased persistent pain or other unusual experience.

Clinical evaluation of the extraction sockets was done based on the following criteria⁷: (1) normal healing alveolus: a healing alveolus with decreasing pain or without pain, with evidence of gradual or complete socket closure. (2) Dry socket: persistent or increased postoperative pain in and around the extraction site, accompanied by a partially or totally disintegrated blood clot or an empty socket, with or without halitosis; the diagnosis is confirmed when extremely sensitive bare bone is encountered when passing a small curette into the extraction wound. (3) Acutely inflamed socket: painful socket with inflamed tissue, but without pus or systemic fever. (4) Acutely infected socket: painful socket with suppuration, erythema, and oedema, with or without systemic fever.

Pain was assessed using a four-point verbal rating scale (VRS) and categorized as follows: 1 = no pain (no pain experienced); 2 = mild pain (pain almost unnoticeable); 3 = moderate pain (noticeable pain, but does not disturb daily activities); 4 = severe pain (very noticeable pain that disturbs daily activities).

Patients were questioned regarding compliance with both antibiotic use and the postoperative instructions, and their

Table 1. Socio-demographic characteristics of the study subjects in each treatment group.

Variable	Group A Antibiotics <i>n</i> = 75 (100%)	Group B No antibiotics <i>n</i> = 75 (100%)	χ^2	<i>P</i> -value
Age group, years			0.113	0.945
<30	36 (48)	34 (45.3)		
30–39	26 (34.7)	27 (36)		
≥40	13 (17.3)	14 (18.7)		
Mean age	30.1 ± 9.1	31.8 ± 9.4		
Sex			0.108	0.743
Male	35 (46.7)	33 (44)		
Female	40 (53.3)	42 (56)		
Ethnic group			1.52	0.461
Yoruba	41 (54.7)	34 (45.3)		
Igbo	25 (33.3)	28 (37.3)		
Other	9 (12)	13 (17.3)		
Cigarette smoker			0.000	1.000
Yes	3 (4)	3 (4)		
No	72 (96)	72 (96)		
Alcohol drinker			0.074	0.785
Yes	8 (10.7)	7 (9.3)		
No	67 (89.3)	68 (90.7)		
Tooth extracted			1.798	0.407
Anterior	4 (5.3)	8 (10.7)		
Premolar	15 (20)	17 (22.7)		
Molar	56 (74.7)	50 (66.7)		
Location of extracted tooth			0.96	0.327
Maxilla	35 (46.7)	41 (54.7)		
Mandible	40 (53.3)	34 (45.3)		
Indication for tooth extraction			0.07	0.797
Caries	67 (89.3)	69 (92)		
Other	8 (10.7)	6 (8)		
Preoperative pain			0.03	0.864
Mild/moderate	27 (36)	26 (34.7)		
Severe	48 (64)	49 (65.3)		

responses were recorded as either 'followed instructions' or 'did not follow instructions'.

Data were recorded and analyzed using SPSS version 17.0 software (SPSS Inc., Chicago, IL, USA). Percentages and mean and standard deviations of numerical variables were determined. The χ^2 test or Fisher's exact test (as appropriate) was used to compare categorical variables, while the Student *t*-test was used to compare numerical variables. The confidence interval was set at 95% for all statistical tests.

Results

A total of 171 patients were enrolled in the study. Twenty-one patients – 11 in group A and 10 in group B – were lost to follow-up and were thus excluded from the analysis. This gave a response rate of 87.7%. The recruited patients ranged in age from 20 to 50 years (mean age 30.6 ± 9.3 years). The majority of the subjects (46.7%) were in the age group 20–29 years (Table 1). There were 68 males and 82 females (male-to-female ratio 1:1.2).

Dental caries (90.7%) and their sequelae were the most common indication for extraction. The majority of the patients

had a single tooth extracted (*n* = 145, 96.7%), and about 52% of teeth were extracted from the maxilla, 59.3% were on the right side, and 70.7% were located posteriorly. Only a small proportion of the patients smoked or consumed alcohol: six smoked (4%) and 15 consumed alcohol (10%), with five of these patients (3.3%) doing both. The χ^2 test was used to compare preoperative variables between the two groups, as shown in Table 1. There was no statistically significant difference between the groups for any of the variables compared (*P* > 0.05).

Healing complications

Healing was uneventful in 129 patients (86%). Twenty patients (14%) developed complications on or before day 3 postoperative, while one additional patient had

developed complications by day 7. Complications recorded in the study included 10 (6.7%) with dry socket, 10 (6.7%) with an acutely inflamed socket, and one (0.7%) with an acutely infected socket.

In group A (antibiotics group), all complications developed on or before day 3 postoperative. There were 12 cases of postoperative complications in this group. Dry socket was the most common complication, affecting six cases, and there were also five cases of acutely inflamed socket and one case of acutely infected socket. In group B (placebo group), there were nine cases of postoperative complications, with eight occurring on or before day 3 postoperative and the last one occurring before day 7. There were five cases of acutely inflamed socket and four cases of dry socket. All cases of acutely inflamed socket occurred on or before day 3 postoperative,

Table 2. Comparison of wound healing complications between the treatment groups.^a

	Group A Antibiotics <i>n</i> = 75 (100%)	Group B No antibiotics <i>n</i> = 75 (100%)
No complication	63 (84)	66 (88)
Complication	12 (16)	9 (12)

^a $\chi^2 = 0.92$; *P* = 0.337.

Table 3. Mean pain score (verbal rating scale) of patients in the two treatment groups, preoperatively and on the first, third, and seventh day postoperative.

Time point	Group A Antibiotics	Group B No antibiotics	<i>t</i>	<i>P</i> -value
Preoperative	3.59 ± 0.62	3.63 ± 0.56	0.414	0.679
Postoperative day 1	1.80 ± 0.82	1.89 ± 0.82	0.698	0.486
Postoperative day 3	1.61 ± 0.88	1.52 ± 0.70	0.715	0.476
Postoperative day 7	1.03 ± 0.18	1.12 ± 0.33	1.886	0.062

whilst the one case of dry socket occurred after day 3.

The comparison of the development of wound healing complications between the two treatment groups is shown in Table 2; there was no statistically significant difference between the groups ($P > 0.05$).

Pain experience

Pain decreased in both groups from day 1 to day 7, with 88 subjects (58.7%) having no pain on the VRS scale on day 3 postoperative compared to 120 (80%) on day 7. Six (4%) subjects had severe pain on

day 3 and none had severe pain on day 7. The comparison of pain experienced between the two treatment groups is shown in Table 3. There was no significant difference in mean pain score between the two groups on postoperative day 1, 3, or 7 ($P > 0.05$).

Table 4. Comparison of clinical variables between patients experiencing wound healing complications and those not experiencing these complications.

Variables	Wound healing		χ^2	<i>P</i> -value
	Complications <i>n</i> = 21 (100%)	Normal <i>n</i> = 129 (100%)		
Age group, years			0.14	0.706 ^a
<30	9 (12.9)	61 (87.1)		
≥30	12 (15)	68 (85)		
Sex			0.516	0.472 ^a
Male	8 (11.8)	60 (88.2)		
Female	13 (15.9)	69 (84.1)		
Number of teeth to be extracted			0.155	0.694 ^a
1	20 (13.8)	125 (86.2)		
2	1 (20)	4 (80)		
Number of cartridges used			0.08	1.000 ^a
1	19 (14.3)	114 (85.7)		
>1	2 (11.8)	15 (88.2)		
Tooth extracted			0.74	0.689
Anterior	2 (16.7)	10 (83.3)		
Premolar	3 (9.4)	29 (90.6)		
Molar	16 (15.1)	90 (84.9)		
Location of extracted tooth			0.41	0.524 ^a
Maxilla	12 (15.8)	64 (84.2)		
Mandible	9 (12.2)	65 (87.8)		
Duration of surgery			1.828	0.253 ^a
<1 min	7 (21.2)	26 (78.8)		
≥1 min	14 (12.0)	103 (88.0)		
Intraoperative fracture			0.538	0.614 ^a
Yes	2 (22.2)	7 (77.8)		
No	19 (13.5)	122 (86.5)		
Postoperative instructions			31.932	<0.001 ^b
Followed appropriately	0 (0)	85 (100)		
Not followed appropriately	21 (32.3)	44 (67.7)		
Postoperative medication			39.84	<0.001 ^b
Taken appropriately	0 (0)	93 (100)		
Not taken appropriately	21 (36.8)	36 (63.2)		
Smoked cigarettes			1.02	0.596 ^a
Yes	0 (0)	6 (100)		
No	21 (14.6)	123 (85.4)		
Drank alcohol			0.74	0.695 ^a
Yes	1 (6.7)	14 (93.3)		
No	20 (14.8)	115 (85.2)		
Indication for extraction			2.72	0.111 ^a
Caries	17 (12.5)	119 (87.5)		
Other	4 (28.6)	10 (71.4)		
Extent of caries	<i>n</i> = 17	<i>n</i> = 119	0.02	1.000 ^a
Moderate	12 (12.2)	86 (87.8)		
Gross/retained tooth	5 (13.2)	33 (86.8)		

^a Fisher's exact test.

^b Statistically significant value.

Wound healing complications and other demographic variables

The comparison of other variables between patients with wound healing complications and those with normal wound healing is shown in Table 4. Although more complications were observed in patients aged >30 years, in females, for extracted molars, and for extracted maxillary teeth, these relationships were not statistically significant. The two factors significantly associated with wound healing complications were non-adherence to postoperative medications and non-adherence to postoperative instructions (both $P < 0.001$).

Discussion

The goal during tooth extraction is to make the procedure painless, with minimal trauma to the surrounding soft tissues, so that healing is uneventful and postoperative prosthetic challenges are prevented.¹¹ The majority of extraction sites in this study (86%) showed uncomplicated healing of the socket wound. This is comparable to the findings of other studies from Nigeria (89%),¹² China (87.5%),¹³ and Iraq (89.3%).¹⁴ In line with reports published in the literature, the reason for this may be that proper wound healing depends to a large extent on the patient's ability to resist infection, to provide essential nutrients for use as building materials, and to carry out reparative cellular activity.^{15,16}

In this study, dental caries (90.7%) was the most common reason for extraction, followed by periodontitis (4.7%). This is consistent with the literature, in which dental caries is also reported as the most common reason for extraction.^{12,17,18} The wide margin in the proportions of the two indications in this study may be due to the exclusion of the older age groups, in which periodontitis is reportedly prevalent. Also, although Jaafar et al. stated in their article that there may likely be a trend towards a reversal of the proportions of these indications, with periodontitis as an indication increasing above caries,¹⁷ this reversal has not been documented in most studies in Nigeria.^{12,18,19} Poor awareness on the availability of improved and varied treatment options, as suggested by an earlier researcher, may be the reason for this trend.¹⁸

In this study, three different types of post-extraction socket wound healing complication were identified: dry socket, acutely inflamed socket, and acutely infected socket. Dry socket and acute

inflammation occurred in equal proportions (6.7%), while acute infection presented in only one case (0.6%). The literature is divided on the most common complication after tooth extraction. While many researchers have reported dry socket (also termed alveolar osteitis, localized osteitis, and fibrinolytic alveolitis^{13,16,20}) as the most common complication of extraction socket wound healing,^{19,20} others have reported acute inflammation as the most frequent complication of tooth extraction.^{13,21}

Surprisingly, the proportion of socket healing complications in this study was observed to be higher in the group of patients who received postoperative antibiotics (16%) than in the group of patients who received placebo (13.2%). A similar trend was reported by Murali et al., who reported pain and possible healing complications for 24% in the antibiotics group and 6% in the placebo group, although the complications were not specified.²² In contrast, Akinbami and Osagbemi reported 6.2% in the antibiotics group and 8% in the non-antibiotics group, although the complications assessed were not the same as those in the present study.²³

The very similar proportions of observed complications in the treatment and control groups seen in this study and in the other studies mentioned above is suggestive of the fact that antibiotic medication is of little or no value in the prevention of post-extraction wound healing complications. The use of antibiotics after routine extractions might therefore not only be of little value, but might also be injurious, particularly in connection with their misuse/abuse and the potential subsequent development of drug-resistant microbial strains. This is especially true in communities such as that from which the subjects in the present study were recruited, where self-medication is rife due to inadequate enforcement of drug purchase policies.²⁴

Pain after dental surgery is normal and is due to high-intensity stimuli commonly associated with tissue injury.²⁵ It was observed in this study that postoperative pain reduced from day 1 through days 3–7 in both treatment groups; 59.7% of subjects in the antibiotic group and 62.7% in the placebo group experienced pain up until 24 h after surgery, with the proportion decreasing with the increasing number of postoperative days. The percentage of patients experiencing pain postoperatively after simple dental extractions varies widely in the literature, from as high as 81.8% reported by Al-Khateeb and

Alnahr,²⁶ to as low as 37.7% reported by Bortoluzzi et al.²⁵ There was no statistically significant difference in pain experienced between the antibiotics group and the placebo group in this study ($P > 0.05$). A significant association was, however, observed between pain and the development of complications, especially by postoperative day 3. This is in agreement with earlier studies that have reported the development of socket healing complications to be associated with prolonged and/or severe pain.^{13,19,22,25,26}

Adherence to postoperative instructions and compliance with medications were found to be significantly associated with the development of wound healing complications in both the antibiotic and placebo group in this study (both $P < 0.001$). Also, it was observed that all 21 patients with complications in this study reported non-compliance with both postoperative instructions and postoperative medications (both antibiotics and placebo) (Table 4). Although the use of postoperative antibiotics has been reported both in earlier studies and this present one not to increase statistically wound healing complications. Non-compliance with the post-extraction regimen, namely immediate postoperative irrigation, alcohol intake, smoking, and a lack of or improper use of saline rinse after dental extractions, has been reported to increase the incidence of postoperative complications.^{27–29} Only six patients (4%) had a smoking habit and 15 (10%) had a habit of alcohol intake prior to their extraction in this study. Also, only one of these patients (0.6%) was non-compliant with the postoperative instructions. It is therefore believed that immediate postoperative smoking and alcohol intake might not have had a very significant part in the findings of this study.

In a previous study, immediate postoperative irrigation/rinsing was implicated in an increased incidence of dry socket postoperatively.²⁸ It was postulated in the study that post-extraction socket bleeding is very important for proper uncomplicated socket healing and that a normal blood clot is more likely to form if the blood is not washed away immediately postoperatively; therefore, post-extraction socket bleeding can potentially lead to uncomplicated socket healing without the development of alveolar osteitis. They further suggested that socket bleeding at the extraction site creates a favourable environment for the formation of a blood clot – a protective dressing – necessary for favourable osseous healing of the socket.²⁸ Rinsing of the socket area within 24 h of

extraction could have played a role in the development of postoperative complications in the present study.

Nevertheless, postoperative saline mouth rinsing has been documented in the literature to significantly reduce the incidence of localized alveolar osteitis.^{29–31} The benefits of its use are attributed to the hypertonicity of the solution; this hypertonicity is said to have a bacteriostatic effect via plasmolysis and to cause vasodilatation, which improves the migration of phagocytes to the surgery site.³² Akpata et al., in a study performed at two centres in Nigeria (Ile Ife and Benin City), found that compliance with warm saline mouth rinse alone was the most effective method for the prevention of alveolar osteitis following dental extraction when compared with other regimens, namely warm saline rinse plus antibiotics plus analgesic, warm saline rinse plus analgesic, and antibiotics plus analgesic.³⁰ They also found that a relatively higher incidence of the complication was observed among patients who were non-compliant with the post-extraction regimen, irrespective of the regimen.

Another study from Lagos, Nigeria also reported the effectiveness of warm saline mouth rinse in preventing wound healing complications; in addition they concluded that there was no significant difference between patients who gargled twice or six times daily, and that patients found the twice-daily regimen convenient and thus were more compliant with it.³² Patients in the present study were instructed to gargle six times daily and this could have contributed to the non-compliance recorded.

The proportion of subjects with complications in both treatment groups was observed to be higher in those aged ≥ 30 years; this is in agreement with other studies.^{14,19} Researchers have attributed this finding to suggestions that age influences healing in an inverse relationship.¹⁶ The relationship between the two entities in this study was, however, not statistically significant. Also, the proportion of females with complications in this study was higher than the proportion of males, in consonance with other studies reported in the literature.¹⁴ However, this relationship was also not statistically significant. Posterior teeth (molars then premolars) constituted the majority of teeth affected by socket healing complications in this study. This is consistent with other reports in the literature, all of which found an increased proportion of socket healing complications among patients undergoing the extraction of these teeth.^{30,33} No explanation has been given for this, but it may be due

to the fact that these are the teeth most often extracted. Neither the degree of trauma during extraction nor cigarette smoking was significantly associated with increased wound healing complications in this series.^{13,14,16} The reason for this is not very clear, but it is believed that this might be related to the small sample size of the study.

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Competing interests

None.

Ethical approval

Health Research Ethics Committee (HREC) of Lagos State University Teaching Hospital (Ref. No. LREC/10/06/372).

Patient consent

Not required.

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Address:

Olalekan Micah Gbotolorun
Oral and Maxillofacial Surgery Department
Faculty of Dental Sciences
College of Medicine
University of Lagos
Lagos
Nigeria
Tel: +234 802 3097188
E-mail: lekangbotol@gmail.com