

## Systemic antibiotics: Are they necessary in the prevention of wound healing issues following intra-alveolar tooth extractions?

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### Abstract

A considerable majority of maxillofacial surgery procedures involve the extraction of asymptomatic teeth. The need for prescribing antibiotics indiscriminately before and after tooth extraction in such instances is a topic of debate. The current study sought to assess the role of systemic antibiotics in the prevention of wound healing issues following asymptomatic intra-alveolar excision of a tooth. A double-blinded randomised control study was conducted on a total of 800 patients, divided into two groups namely Group A (n=400; prescribed without antibiotics and only with analgesics) and Group B (n= 400; prescribed both antibiotics and analgesics). The subjects underwent standard tooth extractions and, they were assessed on the 7<sup>th</sup> day for the parameters of clinical healing (normal healing alveolus, dry socket, acutely inflamed socket, or acutely infected socket) for the primary outcome. Secondary outcome assessed was pain with the aid of a visual analog scale. The incidence of normal healing [group A= 95.1% (368) vs. group B= 95.3% (368)], dry sockets [group A= 1.55% (6) vs. group B= 1.29% (5)], inflamed sockets [group A= 1.55% (6) vs. group B= 1.29% (5)] and, Infected sockets [group A= 1.29% (5) vs. group B= 0.77% (3)] did not show significant differences when compared between groups without and with antibiotics. The pain scores did show a significant intergroup difference (p=0.0005) but not the pain grades (p=0.255). The use of antibiotics did not considerably aid in improving clinically detectable wound healing, nor decreased the incidence of dry sockets, inflamed sockets and infected sockets. A judicious use of antibiotics is recommended in asymptomatic cases needing intra-alveolar extractions.

**Keywords:** Antibiotics, extraction, healing, wound

### Full-length article

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### 1. Introduction

Antibiotics are one of the commonly prescribed drugs in dental practice more so in cases of exodontia. These drugs are given often without clinical, bacteriological, epidemiological or immune status determination or ideal judgement [1]. They were historically prescribed on the basis those antibiotics when used, in addition to appropriate treatment (such as extraction of offending tooth) may aid in boosting the host defenses apart from the elimination of persisting bacteria. Ideally, evidence of clinical sign or involvement of odontogenic spaces with possibility of spread of infection dictates use of antibiotics. Also, special situations may demand a need for antibiotic prophylaxis such as high-risk infective endocarditis, organ transplanted cases, or with a poorly controlled diabetes [1].

Tooth extractions are the procedure with a high rate of antibiotic prescription [2-4]. Now, in exodontia cases with a very low risk of infection (simple tooth extraction in

a healthy patient without systemic disease, or asymptomatic orthodontic extraction) are highly questionable [4,5]. The concern here is antibiotic resistance that could develop due to indiscriminate prescription of antibiotics to any given patients, tagged as 'antibiotic misuse' [2,4,5].

Penicillins (Amoxicillin), penicillins with beta-lactamase inhibitors, clindamycin (a broad-spectrum antibiotic), Metronidazole, cephalosporins (2nd -4th generation), Quinolones, Macrolides, and Tetracyclines were prescribed in varying fashion in dental settings in Korea, USA and Germany [6-8]. Amoxicillin (with or without beta-lactamase inhibitors) seems to be used drug in this regard [4,7,8]. The use of antibiotics such as amoxicillin was more that of the use in medical clinics, which raises a question for the need for use in all exodontia cases [8]. The existing studies stated that antibiotics are 'not required' after simple extractions when not medically comprised. Also,

study highlighted that they have no role in preventing postoperative complications [9,10]. The evidence is of poor quality and deemed insufficient to assess the effects of systemic antibiotics on symptomatic apical periodontitis or acute apical abscess [11]. These points for understating of antibiotics are needed for asymptomatic exodontia cases. Clinical trials in this regard are minimal and those conducted did specify their need for patients undergoing contaminated, long-duration third molar extraction surgery, and not all cases of extraction [12]. Given the gaps in understating for asymptomatic tooth extraction cases, and low-quality evidence for the role of antibiotics in symptomatic cases, we conducted a randomised control trail. The current study aims to assess the need for systemic antibiotics in the prevention of wound healing issues following intra-alveolar excision of an asymptomatic tooth.

## 2. Materials and Methodology

### 2.1. Study settings

A double blinded randomised control trail was conducted at the Department of Oral and Maxillofacial surgery, Mahatma Gandhi Post Graduate Institute of Dental Sciences, Government of Puducherry Institution. The institutional Ethics committee (IEC reference number) accepted the study with Ref No: I-98/MGPGIDS/IEC/2020/MDS/No.20-2020; dated: 04/03/2020) and was conducted in accordance with the CONSORT guidelines 2010 [13].

### 2.2. Sample size

The research was done on a sample of 800, which was calculated by convenient sampling. The sample was randomised in 1:1 fashion into either group A or Group B by computer generated sequencing.

### 2.3. Inclusion criteria

Healthy male and female participants aged between 20 – 50 years, who required a routine asymptomatic intra-alveolar extraction were included in the study. Those patients who had taken antibiotics before one week of planned extraction, patients undergoing surgical extractions; patients with deciduous teeth or that age group; patients with impacted mandibular third molars; those undergoing extractions of endodontically treated teeth; patients with acute oral infection at site, those who are immuno-compromised, pregnant/lactating women, those with acute complications that contraindicate or delay extraction (with acute space infection, bleeding/ clotting disorders etc.), patients receiving chemotherapy/radiotherapy, those needing total extraction due to severe periodontitis, patients with known adversities/ previous documented reactions to any of the study drugs or their prototypes, and those who were uncooperative/ unwilling for participation were excluded from the study. The symptomatic cases of extraction (with pain or untreatable caries disease, impactions etc.) those deemed for extensive surgical extraction with anticipated soft tissue / flap manipulations were also excluded from the study.

### 2.4. Subjects

The research was conducted on a total of 800 patients, categorized into two groups namely Group A

(n=400; without prescribed antibiotics with analgesics) and Group B (n= 400; prescribed both antibiotics and analgesics). The group A participants were given T. Ibuprofen: 400 mg (every 8 hours for 3 days), and T. Famotidine 20mg (every 12 hours for 3 days) for control of pain. The group B participants were given antibiotics [i.e., Cap. Amoxicillin 500mg (every 8 hours for 3 days), T. Metronidazole 400mg (every 8 hours for 3 days)] apart from the stated analgesics given for group A. A common dose was given to all participants irrespective of the age/ weight.

### 2.5. Intervention

For all recruited patients, the extraction will be performed, with as little trauma as possible to the surrounding soft tissues. The procedure was completed under LA and method of extraction followed was as per standards. Following extraction, all patients were given the same post- extraction instructions.

### 2.6. Outcome

All the patients will be reviewed on day seven (7th day). The outcomes assessed were healing and pain. The healing (primary outcome) was determined by the clinical evaluation of the extraction sockets, and graded for incidence of normal healing alveolus, dry sockets, acutely inflamed socket, and acutely infected socket. The secondary parameters i.e. pain was assessed using a visual analog scale (VAS) and the incidence of pain grade (moderate or severe) were reported for both the groups. The data obtained for primary and secondary outcomes was compared by statistical tests. Patients were refrained from any other medication (additional prototype/ similar drugs/ those with known interactions with study drugs) during the period.

### 2.7. Statistical methods

The data was analysed using SPSS v 24. The continuous variables were represented as mean± standard deviation (SD). The difference between variable was evaluated using Chi square test and independent t tests keeping  $p < 0.05$  for significance in all instances.

## 3. Results

The study looked at the role of systemic antibiotics in the prevention of wound healing problems following asymptomatic intra-alveolar extraction. This was achieved by comparing the parameters of clinical healing (normal healing alveolus, acutely inflamed socket, dry socket, or acutely infected socket) and scores of pain between groups with and without prescription of antibiotics for extractions. The study started with screening of 800 patients as per set eligibility criteria. Those who did not meet eligibility [not fitting in criteria (n=23); not willing due to participate without routine prescription (n=4)] are shown in figure 1. The sample randomized and considered for analysis in the study was 773 with mean age of  $37.57 \pm 7.68$  in group A and mean age of  $40.79 \pm 6.38$  in group B. The gender distribution in the group A was 51.4% (n=198) and 48.3% (n= 187) for males and females respectively. Likewise, group was represented by 56.7% (n=219) males and 43.7% (n=169) females respectively.

**Table 1:** Incidence of occurrence of various healing outcomes between groups

Parameter	Incidence	Group A(n=387)	Group B (n=386)	Chi-square	Sig.
Normal healing	Normal	95.1% (368)	95.3% (368)	0.936	0.333
	Abnormal	4.39% (17)	3.1%(12)		
Dry socket	Absent	97.9% (379)	99.2% (383)	0.100	0.752
	Present	1.55%(6)	1.29% (5)		
Acutely Inflamed	Absent	97.9% (379)	99.2% (383)	0.100	0.75
	Present	1.55%(6)	1.29% (5)		
Acutely infected	Absent	98.1% (380)	99.7% (385)	0.521	0.470
	Present	1.29%(5)	0.77% (3)		

*n, sample size; Sig, significance*

**Table 2:** Comparison of pain scores between groups

Parameter	Groups	n	Mean±SD	Sig
Pain Scores (VAS)	Group A	385	2.01±0.98	0.0005*
	Group B	386	1.56±0.79	
Pain Grade (mild)	Group A	367	1.297	0.255
	Group B	376		
Pain Grade (moderate – severe )	Group A	18		
	Group B	12		

*n, sample size; SS, standard deviation; Sig, significance*

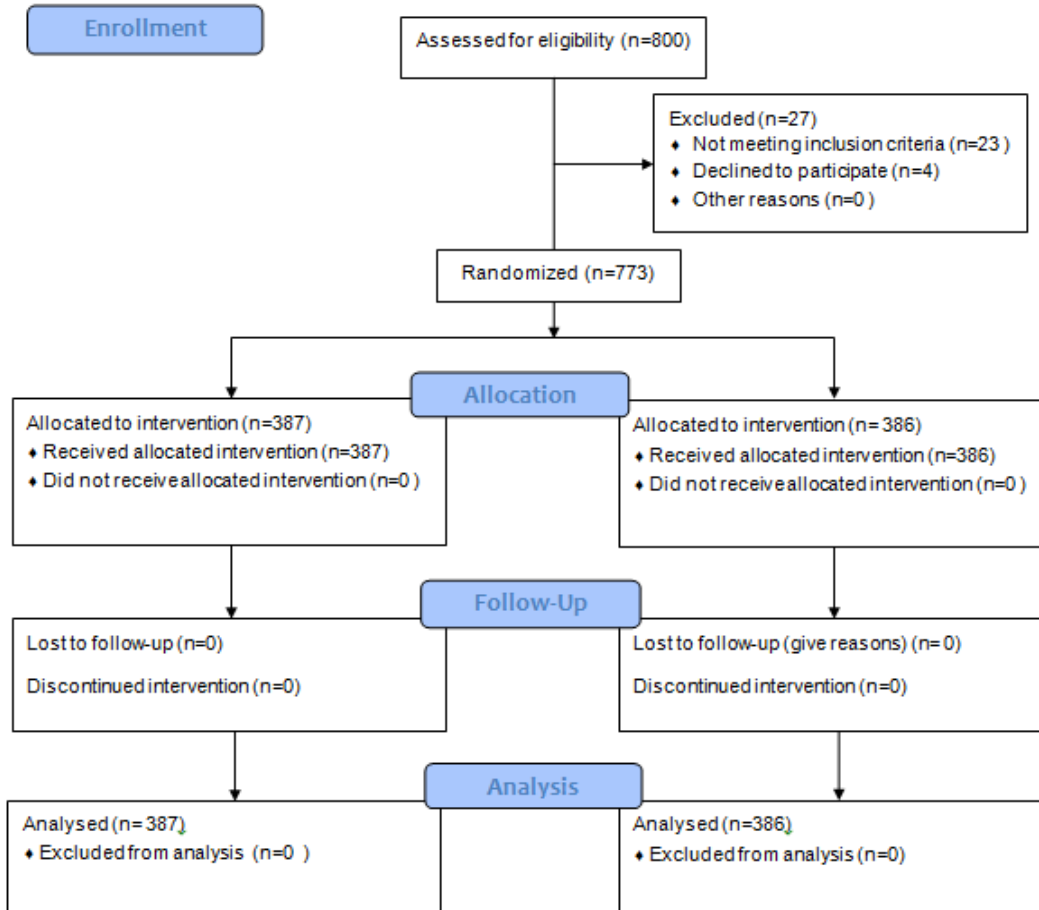


Figure 1: CONSORT flow diagram

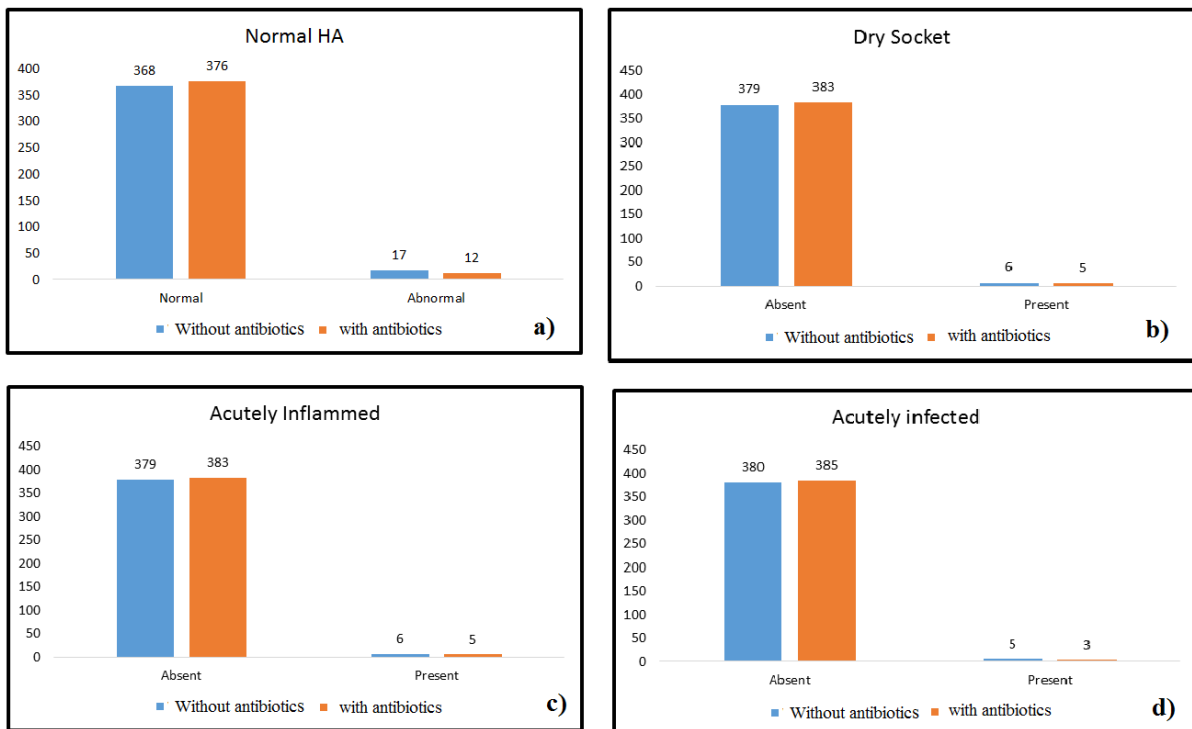
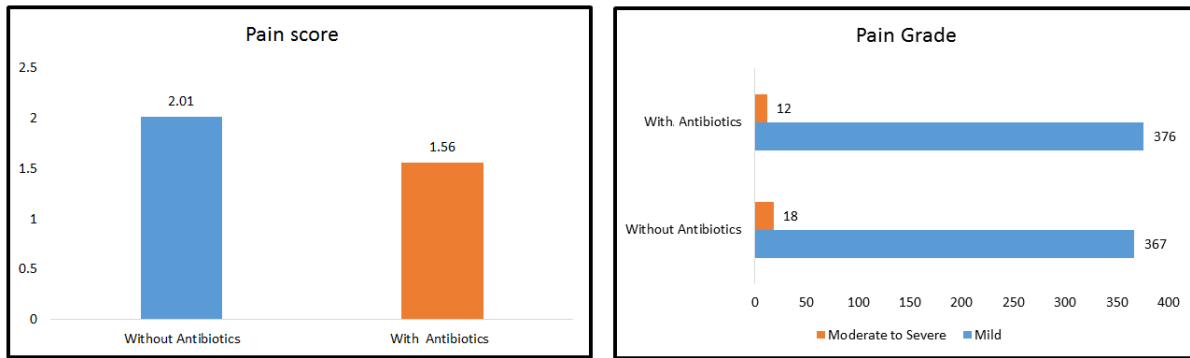


Figure 2: Comparison of healing outcomes between groups a) normal healing; b) dry socket c) inflamed socket d) infected socket



**Figure 3: a)** Intergroup comparison of pain scores: Group A (without antibiotics) showed a higher mean pain score than group B (with antibiotics) **b)** Intergroup comparison of pain grades showing no significant differences between group

The primary outcomes measured were healing outcomes. There was no considerable differences ( $p > 0.05$ ) among groups considering these parameters. Normal healing occurred in 95.1% ( $n = 368$ ) when antibiotics were not given and in 97.4% ( $n = 376$ ) when given with antibiotics. The occurrence of dry socket inflamed or infected socket followed similar pattern. (See Table 1/ figure 2). The secondary outcome assessed in the study was the pain (scores on the VAS). The pain scores among groups showed considerable variation ( $p < 0.001$ ) when compared between scores. See table 2/ Figure 3.

#### 4. Discussion

The study looked at the role of systemic antibiotics in the prevention of wound healing issues after intra-alveolar excision of an asymptomatic tooth. Tooth extraction cases with a very low risk of infection such as simple extraction in a healthy patient without systemic disease, or asymptomatic orthodontic extraction is not recommended as per recent reports [4,5]. The antibiotic misuse may lead to resistance, which was a concern in some studies [2,4,5] while other just argue that there is no quality evidence for the need of antibiotics for all extraction cases [9,10, 12]. The current study thus had identified the presence of normal healing alveolus, acutely inflamed socket, dry socket, or acutely infected socket as a qualitative assessment of wound healing. Also, the pain scores along with the wound healing were compared between groups with and without prescription of antibiotics for extractions. The mean age of participants in the current study was  $37.57 \pm 7.68$  (group A) /  $40.79 \pm 6.38$  (group B), with a mild male predominance in either group. The similar studies reported previously employed samples of 146- 490 subjects [9,11]. In the current study, normal healing occurred in 95.1% when antibiotics were not given and in 95.3% when given only along with antibiotics. The occurrence of dry socket inflamed or infected socket followed similar pattern. This is in line with the existing study that reported that 91.8% presented with no postoperative complications, of which only 1 patient (0.7%) had infection of the extraction socket in the non-antibiotic group, as opposed to none in antibiotic group [9].

Considering the dry socket there was insignificant differences i.e., occurrence was nearly the same 1.55% vs. 1.29% in group without and with antibiotics respectively. Previous research found no difference between the test and control groups in terms of erythema, dehiscence, edoema, discomfort, trismus, and infection depending on microbial load. However, the data for alveolar osteitis/dry sockets were statistically significant, with the occurrence of alveolar osteitis (14.58%) in the placebo group [12]. This may be taken as a paradoxical observation as study group in the current study had 'asymptomatic patients only' unlike the previous study. Taking the inflammatory and infected sockets, the study showed no significant differences between groups. This is in line with previous reports [2,4,7]; yet a study showed antibiotics do have a role in inflammation control as per one study [11]. The observations for pain scores did differ significantly between groups in the current study, which is paradoxical observation when contrasted with existing evidence [3,14]. As systematic review had summarized that compared to placebo, antibiotics may decrease the risk of postsurgical infectious complications in patients undergoing third molar extractions by approximately 66% (RR 0.34, 95% CI 0.19-0.64) but with low-certainty evidence. Likewise, antibiotics may reduce the risk of dry socket by 34% (RR 0.66, 95% CI 0.45-0.97) again with low-certainty evidence. Now, neither of these applies to be contrasted with current report as these were evaluated for extraction following impacted wisdom teeth, and not an 'asymptomatic teeth' [3]. The evidence remains same that antibiotics have no role in case of those given as prophylaxis regime [15]. The use of antibiotics is cautioned not just for extractions but post periodontal surgeries and implants, where there is unrequired repeated use post operatively [16]. A similar randomised control trail with same patient group (routine intra-alveolar extractions in healthy patients) having likewise objectives had shown that no significant differences with respect to pain ( $\chi^2 = 4.939, p = 0.552$ ), swelling ( $\chi^2 = 10.048, p = 0.347$ ), or post extraction complications, which is in line with the current study. [17]. Another comprehensive review stated that further clinical research are needed to provide specific criteria, and until then, oral surgeons should consider patients' local/general health status before recommending

any novel medicine [18]. The recent high quality evinced suggested that the development of microbial drug resistance and the risk of allergic reactions are to be underscored factors before use of multiple antibiotic prescriptions for routine extractions [19,20]. The strengths of the study lie in the concept of addressing 'asymptomatic extractions' and not limiting only to 'molar extractions', while limitations lie in sample size. Studies that assessed larger patient cohorts from multiple centers add more value to this subject of debate.

## 5. Conclusion

The use of antibiotics did not considerably aid in improving clinically detectable wound healing, nor decreased the incidence of dry sockets, inflamed sockets and infected sockets. The pain scores but not grades of pain however did show a mild difference between groups. A judicious use of antibiotics is recommended in asymptomatic cases needing intra-alveolar extractions.

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