

# Is prophylactic antibiotic effective in lower third molar surgery?: article analysis

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## **Abstract**

Objective: To justify the use of antibiotic prophylaxis in third molar surgery

Materials and methods: The search through electronic data base restricted to the previous articles published in English focusing on two keywords 'third molar surgery' and 'antibiotic prophylaxis' was performed. Randomized controlled trials complied with the inclusion criteria were reviewed and analyzed descriptively.

Results: There were 37 randomized controlled trials included in this study. The evaluation demonstrated that there were 50% of the previous studies showed statistically significant difference between use and no use of antibiotics on the reduction of post-operative infection complications. The pre-operative prophylactic antibiotic was more effective than post-operative antibiotics administration in decreasing the undesirable post-operative infection.

Conclusion: The antibiotic prophylaxis seems to show effectiveness in reducing post-operative infection by providing pre-operative high-dose antibiotics with two to five days post-operative administration.

Keywords: effectiveness, antibiotic prophylaxis, third molar surgery, review article, pre-operative dose, post-operative dose

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## Introduction

Infection is probably the most common post-operative complications of the surgical procedures.1 It might inevitably occur which sometimes cause severe morbidity to the patients. From the biological point of view; improper patient's immunity, imbalance of biology at surgical site and microorganism imbalance would be the cause of infection in patient undergone surgery,<sup>2</sup> furthermore, 60 to 95% of the oral and maxillofacial infection was the cause of mixed bacteria.3 Oral surgeons do use antibiotics prophylaxis in order to decrease the risk of complications and promote wound healing<sup>4</sup>. According to the nature of surgical procedure, there is an opportunity for the bacteria to contaminate the wound starts from the mucosal opening to wound closure.<sup>2</sup> Timing of antibiotic administration was under consideration since the effectiveness of antibiotics depends on its serum concentration.4,5

Though surgical removal of lower impacted third molar is the most common procedure in oral and maxillofacial surgery, it is considered as clean-contaminated wounds (type II or III). The complications of surgical site infection and alveolar osteitis are also not the uncommon phenomenon.<sup>1,6</sup> Duration of the operation and wound size according to the degree of tooth removal difficulty might be a critical factors influencing the occurrence of complications.<sup>7-9</sup>

The use of antibiotics has been introduced with the hope of prevention and reduction of post-operative infection. 10,11 There is a study showed the routine use of post-operative prophylactic antibiotics in lower third molar surgery involving non-medically compromised patients, particularly partial or full bony impactions. 12 With inappropriate prescription, the antibiotic prophylaxis might result in adverse outcomes. The potential drawbacks of antibiotic overprescribing, including the development of hypersensitivity or allergic reactions, and the emergence of resistant microorganisms, might exceed the risk of infection.<sup>13</sup> Furthermore, with an extreme confidence in the antibiotic efficacy, the reluctance to perform strict sterilization, adequate hemostasis and/or irrigation of wound debris might increase risk of postoperative infection. 13,14

For the past 20 years, highly controversial results on the use of prophylactic antibiotic therapy in lower third molar surgery were reported. The current evidence both supports 12,15,16,17,18,19 and questions<sup>7,20,21,22</sup> the benefits of routine prophylactic antibiotic therapy in reducing risk of post-operative complication (infection). According to the inconclusive results, this study intend to compile and analyze published scientific evidence on the effectiveness of prophylactic antibiotics in third molar surgery whether to justify the consideration of the use of antibiotic prophylaxis in the surgical removal of lower impacted third molar.

## Materials and methods

We search the following databases, MEDLINE, Science Direct, Google, Pubmed and Ovid medline from 1983 to 2013. The keywords used to explore the database including no use antibiotic, third molar surgery and antibiotic prophylaxis. The selected articles were analyzed according to the following inclusion criteria:

- (1) randomized clinical trials (RCTs),
- (2) studies involving the surgical extraction of an impacted mandibular third molar,
- (3) studies including antibiotic prophylaxis as intervention and
- (4) studies including outcomes that are described as postoperative complications cause of discomfort to patients such as surgical site infection (ssi), dry socket (alveolar osteitis), pain, trismus and swelling.

## Results

The above search strategy yielded 48

full-length articles that were further reviewed (Figure 1). After review and data extraction, five studies did not meet the inclusion criteria (Table 1) and another six studies were compiled many studies and conclusions which were excluded from the final analysis. A total of 37 studies were included in this review (Table 2).

The included studies were categorized for further evaluation; effectiveness of antibiotics and timing for antibiotic administration.

## Effectiveness of antibiotics

From 34 recruited articles, there were 11 types of antibiotics (Figure 2) used in evaluated studies namely, amoxicillin, augmentin, clindamycin, metronidazole, ampicillin, azithromycin, minocycline, penicillin, tetracycline, moxifloxacin, cephalexin, and cefditoren pivoxil. Amoxicillin (31.58%), augmentin (23.68%), clindamycin (7.89%) and metronidazole (7.89%) were among the most antibiotics used as prophylactic antibiotic involving lower impacted third molar surgery. The use of antibiotics showed a decrease in complications, including infection, after third molar surgery with 50% (17 articles) of the studies demonstrated significant results.

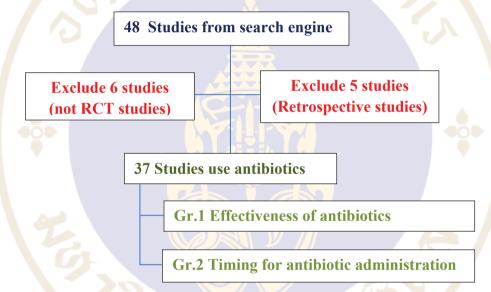


Figure 1 Number of articles which were extracted from the search engine.

Table 1 The excluded studies.

Study	Reason for exclude	Result
Al-Asfour A.13	No systemic antibiotic used in studies.	No significant infection (6/90, 5.5%)
Rui Figueiredo <i>et al.</i> <sup>23</sup>	Retrospective case control study.	Present delayed-onset infection after third molar surgery, take post-operative antibiotic.
Calvo AM et al. <sup>24</sup>	No systemics ATB used in studies.  Record parameter compare pre-operative, peri-operative and post-operative.	No significant increase CRP level. No systemic infections was found after removal of 3 <sup>rd</sup> molar.
Sane VD et al. <sup>25</sup>	No comparative group. Record complication rate from incidence.	No significant infection (1/50, 2%)
Ishihama K <i>et al.</i> <sup>26</sup>	The study design was retrospective, single-center review. No comparative gr. Record complication rate from incidence.	No significant infection (1/45, 2.2%)

Analyzed studies for effectiveness of antibiotics 2 Table

Authors	Sample (Pt)	Age Mean	Route	Timing	Medication	Experimental Group	Control group	Indicates Prophylaxis
Stavropoulos MF et al <sup>2</sup>	123	>18	Topical	Post	Minocycline	Placed in bony defects (n = 63 )	No ATB (n = 60)	Yes
Lacasa JM et al 14	225	> 18	Oral	Pre	Amoxicillin / clavulanate	Gr 1: Pre ATB + Post placebo 5 d (n=75)	Gr 3 : Pre placebo + Post	Yes
					1000/62.5 mg 2 tabs	Gr 2: Pre placebo + Post ATB 5 d (n=75)	placebo 5 d (n=75)	
Monaco G et al 15	59	12 - 19	Oral	Pre	Amoxicillin 2 g	ATB 1 hour before surgery (n=32)	No ATB $(n = 27)$	Yes
Lopez-L-Cedrun J <i>et al</i> <sup>16</sup>	123	22.3	Oral		Amoxicillin	Gr 1: ATB 2 g pre 2 hrs + post placebo TID * 5 d (n=39)	Gr 3 : Placebo pre 2 hrs	Yes
						Gr 2 : Placebo pre 2 hrs + post ATB 500 mg TID $^{\circ}$ 5 d (n=40)	+ post placebo IID * 5 d (n=44)	
Ataoglu H <i>et al</i> <sup>20</sup>	150	22.3	Oral		Amoxicillin 1 g / Clavulanate	Gr 1: Post BID * 5 d (n=50) Gr 2 : Pre BID * 5 d (n=50)	Gr 3 : No ATB (n=50)	2
Siddiai A et al <sup>21</sup>	100		Oral		Amoxicillin	Gr 1: ATB 1 a pre 1 hr (n=48)	Gr 2 : ATB 1 a pre 1 hr (n=47)	2
							+ ATB 500 mg post TID * 2 d	
Foy SP et al 30	116	> 18	≥	Pre	Ampicillin	ATB (n = 56)	No ATB (n = 60)	Yes
Kaziro GN 39	118		Oral	Post	1. Metronidazole 400 mg 2. Arnica	Gr1 ATB BID * 3 d (n=41) Gr2 ATB BID * 3 d (n=39)	Placebo (n=38)	Yes
Krekmanov L & Nordenram A 40	112	19 - 59	Oral	Pre	Phenoxymethyl penicillin	Gr.1 Pre op ATB 1 hr + Post QID * 3 d	Gr. 3 no ATB ( n=36 )	Yes
					0.2% chlohexidine gluconate (CHX)	use syringe rinse gingival pocket + rinse CHX (n=37) Gr. 2 same Gr.1 but no ATB (n=37)		
Mitchell DA 41	20	18 - 30	Oral	Pre	Tinidazole 2 g	Tinidazole (n=25)	Placebo (n=25)	Yes
Happonen RP et al 42	136	24	Oral	Pre 1 hr	Phenoxymethyl penicillin (660 mg)     Tinidazole 500 mg	Gr.1 Continue ATB TID * 5 d (n= 44) Gr.2 Continue ATB TID * 5 d (n=47)	Placebo (n=45)	2
Lyall JB 37	140	22.3	Oral	Pre	Metronidazole 400 mg	ATB pre 2 hrs + continue 2 d ( N=70)	No ATB (n=70)	Yes
Delilbasi C <i>et al <sup>43</sup></i>	177	26.3	Rinse	Post	0.2% chlorhexidine solution (CHX) 500 mg amoxicillin trihydrate, /125 mg	Gr.1 Pre 30 mins CHX (n = 62) Gr. 2 Pre 30 mins CHX & post ATB BID* 5 d (n = 56)	Gr 3 0.09 % sterile saline solution. (n = 59)	Yes
					clavulanic acid			
Bergdahl M & Hedstrom L 36	120	7 - 30	Oral	Pre	Metronidazole 400 mg	ATB before extraction 45 mins $^{*}$ 4 tabs ( n=60)	Placebo (n=60)	Yes
Sanchis MJ <i>et al</i> <sup>28</sup>	200	25.59	Topical	Post	Tetracycline in socket Oral amoxicillin 500 mg	+ Tetracycline (n=100) + Amoxicillin TID *4 d	- Tetracycline (n=100) + Amoxicillin TID *4 d	2
Poeschi PW et al 44	288	14 - 61	Oral	Post	1. Augmentin 1 g 2. Clindamycin 300 mg	Gr1 ATB BID * 5 d Gr2 ATB TID * 5 d	No ATB	2
Arteagoitia I et al 45	490	24.15	Oral	Post	Amoxicillin 500 mg / Clavulanate 125 mg	TID * 4 d (n = 259 )	Placebo (n=231)	Yes
Graziani F <i>et al</i> <sup>46</sup>	30	18- 39	Oral	Pre 3 days	Azithromycin Sublingual piroxicam - FDDF 20 mg (NSAID)	Gr 1 NSAID administered OD (n=10) Gr 2 ATB administered OD (n=9) Gr 3 NSAID + ATB (n=11)		2 Z
Halpern LR & Dodson TB 😕	118	25.3	≥	P er	Penicillin (15,000 units per kg) Or penicillin-allergic subjects, clindamycin (600 mg).	ATB (n=59)	Placebo (n=59) (0.9% normal saline).	Yes
Grossi GB et al 47	213	14 - 67	Oral	Pre	Amoxicillin / clavulanic acid 2 g	ATB 1 hour before surgery (n =119)	No ATB (n =136)	Yes
Calvo AM et al 48	50	>18 (22.8)	Oral	Post	Amoxycillin 500 mg	Osteotomy group TID $*$ 7 d (n = 29)	No osteotomy (n = 20)	S
Bezerra TP et al 49	34	18 - 35	Oral	Pre	Amoxicillin 500 mg * 2	ATB 1 hour before surgery	Placebo	<u>8</u>

O Topical
28.7 Ord Pre 1 hr
18 – 45 Oral Post 1. Amoxicillin 500 mg 2. Clindamycin 300 mg
22.5 Oral Pre Amoxicillin 2 g Dexamethasone 8 mg
15 - Oral Post Cefditoren pivoxil 100 mg 69(28)
>18 Oral Pre 1 hr Amoxicillin 2 g (AMOX) 0.12% chlorhexidine rinse ( CHX )
20-40 (30) Oral Post Amoxicillin trihydrate 500 mg Potassium clavulanate,
19-36 Oral Metronidazole
Oral Lenampicillin ( LAPC) 500mg
23.5 Oral Clindamycin hydrochloride
18-60 Oral Amoxicillin
18 -40 IV Cephradine 1 g (23) Oral Cephalexin 500 mg

Among the thirty four studies, there were three routes of administration; topically, orally and intravenously. Three studies used topical antibiotics post-operatively by applying the medication into the tooth socket. Minocycline were used in two studies<sup>2,27</sup> which showed a significant decrease in post-operative complication (infection). The other study<sup>28</sup>, which tetracycline was used, demonstrated a decrease in postoperative complication but there is no significantly difference. Intravenous administration of penicillin

or ampicillin one hour prior to extraction was reported in two studies which significantly decreased post-operative complications. 29,30 Thirteen studies which used the oral antibiotics showed significantly difference in the elimination of post-operative complications. Though the incidence of post-operative complications in another sixteen studies was also reduced, the result did showed no significantly difference (Figure 2,3).

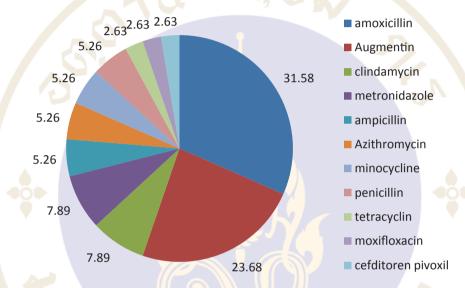


Figure 2 Percentage of type of antibiotics used as prophylactic antibiotic.

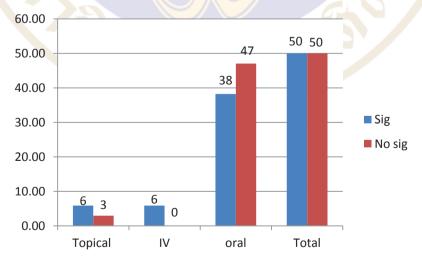


Figure 3 Percentage of studies categorized by the route of administration (comparing significance and non-significance result)

## Timing of antibiotics administration

Among the previous studies showed significant reduction of post-operative complications infection, there were 10 articles of pre-operative antibiotics administration and 7 articles of post-operative antibiotics administration. Antibiotics administration methods of the previous articles are:

- 1) Multiple pre-operative doses regimen in two previous studies did not show significant decrease in post-operative complications infection.
- 2) Single pre-operative dose regimen 30 to 120 minutes before surgery, 48% of the studies showed significant decrease in postoperative complications infection.
- 3) Immediate post-operative doses and continued post-operatively for 2 to 5 days, 35% of the studies showed significant decrease in post-operative complications infection.
- 4) Intraoperative dose by topical antibiotics with post-operative application medication into the tooth socket, there was only one study with this regimen showed significant decrease in post-operative complications infection.

## Discussion

The importance of the patient's discomfort from the surgical removal of third molar impaction is the post-operative complications infection. The antibiotics have been utilized to prevent or reduce the occurrence of those incidences. There were many previous studies showed the concern of the use of antibiotics for prevention and reduction of the postoperative lower third molar removal complications at the surgical site infection and alveolar osteitis. 4 Our analysis from the previous articles supported the antibiotics use and also indicated that amoxicillin did significantly reduce the occurrence of postoperative complications infection. The previous article also showed that 10% of all antibiotics prescriptions of amoxicillinclavulanate related with dental infections.31

The exploit of the most effective effects must be a concern in regimen and time of administration. Our study showed that antibiotics administration involving pre-operative dose could significantly reduce post-operative complications infection but was not found with only postoperative dose in many previous articles.

Single pre-operative dose regimen (30-120 minutes prior to surgery) or combination single pre-operative dose with multiple post-operative doses administration for 3-5 days seemed to be the effective prophylaxis. 32-34

The American academy of Orthopedics quideline of antibiotics administration suggested that there is no benefit from post-operative antibiotics dosage and the antibiotic administration should not be prolonged more than 24 hours.<sup>35</sup> Many previous articles were shown that antibiotics given 60 minutes before surgical procedure could increase antibiotic serum concentration level that might avoid multiplication and spread of bacteria through the surgical injury.34

In order to achieve the optimal antibiotics concentration in serum, many previous articles suggested that the appropriate pre-operative time for the antibiotic administration should be up to two hours orally or up to 1 hours parenterally. 29,30,36,37 These articles were not recommended to use topical antibiotic since it might cause the delay of wound healing. 18 The previous studies suggested that antibiotic should be commonly administered via oral route while the parenteral administration is only indicated when the oral administration is not practical and for the particularly urgent treatment of severe infections. 29,38

Numbers of reports demonstrated that type of lower impacted third molar and duration of the surgery and patient's health condition might be considered as significant risks for occurrence of major complication. Based on previous finding<sup>4</sup>, wound infection after the removal of third molar

could reach 3.5% in erupted tooth and 26.5% in tooth covered by bone when antibiotic has not been administered. Evidence also showed that the removal of lower third molar which located below the occlusal plane could increase the odds of delayed HRQOL recovery.<sup>30</sup> In addition, surgical period of more than two hours showed an association with a significant increase infection rate.34 Furthermore the reduce host defense mechanisms in medically compromised patients, ie. poor controlled diabetes, AIDS, leukemia and other systemic diseases, also indicate antibiotic prophylaxis when performing lower impacted third molar surgery.4 The control of wound contamination, including careful surgical techniques and proper post-operative care, would be significant factor in limiting the risk of post-operative infection.

Except from surgical site infection and alveolar osteitis, it is to note that our study also used several parameters of HRQOL instrument which might imply inflammatory process and infection, ie. pain, oral function in mouth opening (trismus) and facial swelling in the evaluation of the antibiotic efficacy on the reduction of postoperative complications.

In conclusion, this review suggested that antibiotics prophylaxis involving the removal of impacted third molar should be selectively given to patients which expected the effects of therapeutic management of pre-existing infection and prevention of secondary infection in high-risk patients. In case of healthy patients, the prophylaxis is only needed in the removal of bony impacted teeth. Oral administration of amoxicillin is useful and most commonly used for the prevention of post-operative complications. Though single high dose preoperative administration is often sufficient for prophylaxis, it should be combined with 2-5 days post-operative regular dose regimen in high-risk patients.

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# International Abstract

Incidence of Missed Inferior Alveolar Nerve Blocks in Vital Asymptomatic Subjects and in Patients with Symptomatic Irreversible Pulpitis.

Fowler S1, Reader A2, Beck M3.

J Endod. 2015 Mar 11. pii: S0099-2399(15)00096-5. doi: 10.1016/j.joen.2015.01.029.

#### Abstract

#### Introduction:

The purpose of this retrospective study was to determine the incidence of missed inferior alveolar nerve (IAN) blocks by using a 1- or 2-cartridge volume of 2% lidocaine with 1: 100,000 epinephrine in vital asymptomatic teeth and in emergency patients with symptomatic irreversible pulpitis.

#### Methods:

As part of 37 studies, 3169 subjects/patients were evaluated for missed IAN blocks. The study included 2450 asymptomatic subjects and 719 emergency patients presenting with symptomatic irreversible pulpitis. Each subject or patient received either a 1- or 2-cartridge volume of 2% lidocaine with 1:100,000 epinephrine. A missed block was defined as no lip numbness at 15-20 minutes after the IAN block. The effect of anesthetic volume on the incidence of missed blocks was assessed by using mixed models logistic regression with individual studies as a random effect.

#### Results:

The incidence of missed blocks for asymptomatic subjects was 6.3% for the 1-cartridge volume and 3.8% for the 2-cartridge volume. For patients presenting with irreversible pulpitis, the incidence of missed blocks was 7.7% for the 1-cartridge volume and 2.3% for the 2-cartridge volume. In both asymptomatic subjects and patients with irreversible pulpitis, the 2-cartridge volume was significantly (P = .0395) better than the 1-cartridge volume. There were no significant effects for pulpal diagnosis (P = .7523) or the pulpal diagnosis and anesthetic volume interaction (P = .3973).

#### Conclusions:

Concerning missed IAN blocks, we concluded that administration of a 2-cartridge volume was significantly better (P = .0395) than a 1-cartridge volume in both asymptomatic subjects and emergency patients presenting with irreversible pulpitis.

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#### Keywords:

Inferior alveolar nerve block; missed inferior alveolar nerve blocks; symptomatic irreversible pulpitis

Pulp Revascularization after Repositioning of Impacted Incisor with a Dilacerated Root and a Detached Apex.
Plakwicz P1, Kapuścińska A2, Kukuła K3, Czochrowska

J Endod. 2015 Mar 11. pii: S0099-2399(15)00101-6. doi: 10.1016/j.joen.2015.01.034.

#### Abstract

#### Introduction:

Severely impacted and dilacerated incisors are rarely considered for surgical exposure because they may not respond favorably to orthodontic extrusion. These incisors are often extracted, resulting in the need for tooth replacement; however, prosthetic solutions are limited in growing patients. Transalveolar autotransplantation of an impacted incisor may be the only method to preserve the natural tooth and maintain the shape of the alveolus.

#### Methods:

The severely impacted upper central incisor (#9) with a developing root was diagnosed in a 9-year-old girl. The unfavorable tooth position and dilaceration of its root made orthodontic extrusion of the impacted incisor impossible. Initial orthodontic space opening at the recipient site was performed before the surgery. Transalveolar transplantation of the impacted incisor to its normal position was performed to avoid tooth extraction. The incisor was later aligned using fixed orthodontic appliances.

#### Results:

At the 5-year follow-up, the transplanted incisor presented features that were typical of a revascularized tooth (ie, obliteration of root canal but a positive response to vitality tests). Healthy periodontal tissues and continued root development were also noted. However, the root apex, which separated from the transplant at the time of the surgery, continued formation in its initial position.

## Conclusions:

Transalveolar transplantation of an unfavorably impacted upper central incisor with a dilacerated root is a successful treatment, which stands the test of time. The early stage of root development allowed revascularization of the tooth despite dilaceration of the root and detachment of its apex.

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#### Keywords:

Central incisor; impacted tooth; revascularization; root dilaceration; tooth autotransplantation