

## Uses and Misuses of Antibiotic in Dental Practice. A Review

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### الخلاصة

المضادات الحيوية هي من الأدوية التي توصف بكثرة والتي يساء استخدامها في طب الأسنان . وفي طب الاسنان وصفات المضادات الحيوية تكون إما علاجية أو وقائية. فهي فعالة في علاج الالتهابات بسبب سميتها الانتقائية ؛ أي أن لديهم القدرة على إيذاء أو قتل الكائنات الحية الدقيقة دون الإضرار بخلايا المضيف. تم تركيز الكثير من الاهتمام على القضاء على سوء استخدام المضادات الحيوية لأن هذا الاختيار للعامل المضاد للميكروبات الأكثر ملائمة يتطلب معرفة جيدة بقابلية الكائنات الحية الدقيقة لمضادات حيوية معينة ، وموقع الإصابة والعوامل المتعلقة بالمريض كل ذلك يحتاج الى الفهم الكامل لدور طبيب الأسنان في هذه القضية الصحية العالمية و التعرف على أسباب الاستخدام الوقائي والعلاجي للمضادات الحيوية في طب الأسنان. بالنظر إلى خطورة مقاومة المضادات الحيوية ، تسلط هذه الدراسة الضوء على الاتجاهات في ممارسات وصف المضادات الحيوية ، وتميز العوامل التي تساهم في استخدام المضادات الحيوية وإساءة استخدامها في طب الأسنان ، وتوفر نظرة ثاقبة على أهمية تأثير المضادات الحيوية في بيئة صحة الفم ، وتشجع أطباء الأسنان على التفكير في ممارسات وصف المضادات الحيوية.

### ABSTRACT

Dental antibiotics are commonly used and abused drugs. In dentistry, antibiotic prescriptions are either therapeutic or prophylactic. They are effective against infections owing to their selective toxicity; that is, they can hurt or eradicate microorganism with no harm on the host cells. Much attention has been focused on eliminating the misuse of antibiotics since though appropriate selection of antimicrobial agent and having good knowledge about the susceptibility of the microorganism to a specific antibiotic, the position of the infection and factors related to patients . Full understanding of the dentist responsibility in this global health problem needs to identify the causes of the antibiotics usage in dentistry. This study highlights strategy of antibiotic prescription, recognize aspects attributed to the uses and misuses of them by dental patients, and providing insights into the significance of antibiotic indications in the dental field, and promote dental practitioners to review their prescriptions of antibiotics.

**Key words:** Antibiotic, infection, dental, use, misuse.

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### INTRODUCTION

Antibiotics are commonly used in dental practice. About 10% of all antibiotic prescriptions are extended to infections of dental origin. Their indication in dentistry for the treatment of odontogenic infection, non-odontogenics oral infection, as a prophylactic

measure against local infection, in addition to spread to adjacent tissues and organs.<sup>(1)</sup> Misuse of antibiotics is a growing problem since it is considered as the main cause of antibiotic resistance. Therefore, the decision of antibiotic prescription is essential, and the advantages must be weighed against the disadvantages.<sup>(2)</sup>

Also considering that antibiotics can produce reversible minor to debilitating severe adverse drug reactions or even fatal.<sup>(3)</sup>

Dentists usually prescribe antibiotics as prophylactic or therapeutic.<sup>(4)</sup> Prophylactic antibiotics for prevention of infection are classified as either primary "prevention of an initial infection, such as antibiotics administered to prevent surgical site infections" or secondary "prevention of infection at a distant site".<sup>(5)</sup> On the other hand, therapy by antibiotics is applied for the treatment of infections & can be divided as primary "first-line treatment for an infection and is rare in dentistry" or adjunctive "given in conjunction with a surgical intervention, together with oral health treatment".<sup>(6)</sup> Studies suggested that unsuitable antibiotic applications by dentists may be common & there is evidence about both inappropriate prescriptions for dental infections<sup>(7,8)</sup>. This review attempts to examine the practice of antibiotic prescription by dentists during the management of their patients and to explain antibiotic prescribing behaviors in dentistry.

Dentists prescribe several categories of medications to manage a variety of oral diseases and conditions. Among these conditions are bacterial, fungal, and viral infections. Antibiotics continue to be the most commonly prescribed drugs in children and adults<sup>9</sup>. Most antibiotics are given to patients who had no signs or symptoms of any infection, mostly to "prevent" infections & to make sure that "everything was done". Dentists usually depend

on five groups of antibiotics to treat oral & dental infections. These are "beta-lactams (mainly Phenoxymethyl penicillin, amoxicillin, and co-amoxiclav), macrolides, lincosamides, tetracyclines, & metronidazole"<sup>(8,10)</sup>. Different patterns in dental diseases including susceptibility and resistance profile of oral microorganisms will determine differences in prescription writing in different geographical areas to deal with dental and oral infections<sup>8</sup>. Amoxicillin was considered as the basic drug in dental management. It is the first choice for periodontists & oral surgeons alone & in combination with clavulanic acid and metronidazole for acute apical abscess or apical periodontitis<sup>11</sup>. The British National Formulary underlined either "Amoxicillin 500 mg every 8 h in adults for 5 days" or "Metronidazole 400 mg every 8 hourly in adults for 3–7 days".<sup>8,12</sup>

#### **Prophylactic and therapeutic antibiotics:**

Oral diseases are mostly presented as both inflammatory and painful conditions. Dental pain mainly comes from pulp infections, which are usually managed by operative care interventions, rather than antibiotics.<sup>13</sup> Pulpitis, dry socket, acute periapical infections & chronic inflammation of periodontium are clinical cases that need no antibiotic use.<sup>14</sup> Systemically, antimicrobial agents used in acute periodontal diseases where drainage and debridement is unfeasible, during the local spread of the infections or where the systemic distribution has occurred.<sup>15</sup> Unfortunately, dentists still prescribe antibiotics for common dental

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infections affecting pulp & periodontium, which require only operative measures.<sup>12</sup> Also some of them still depend on antibiotics for treatment of viral infections "like herpes simplex virus-1 infections".<sup>16</sup>

Clinical dental cases that need antibiotic treatment are frequently limited. They usually involve infections associated with fever & signs of systemic involvement like lymphadenopathy and trismus.<sup>3,17</sup> A serious disease like facial cellulitis, with or without dysphagia, must be controlled by antibiotics rapidly because of the possible spread of infection by systemic circulations, in association with septicemia. Another indication of antibiotic use is a number of a localized oral lesion like acute necrotizing ulcerative gingivitis, periodontal abscess and pericoronitis.<sup>12,14</sup>

Amoxicillin and clindamycin are used in the prevention of bacteremia following dental treatment "mainly tooth extraction", it is usually transient in its nature & associated with small number of the bacteria.<sup>18</sup> It was suggested that the use of antibiotic prophylaxis in such conditions should be limited. Since there are no proofs about the usefulness of antibiotic use for the prevention of bacteremia in patients "at risk".<sup>19,20</sup> So, it becomes necessary to ask if the routine use of antibiotics is mandatory & if the need of guidelines updating should be discussed.<sup>21</sup> The prescription of antibiotics for patients at risk dental procedures is a widely accepted practice.<sup>22</sup>

The endodontic treatment failure is related mainly to the root canal & periradicular tissue invasions by microorganisms. Such root canal system infection is polymicrobial, holding mixed bacteria "anaerobic & aerobic". which end in intracanal infection &, accordingly, periapical infection, leading failure of root canal healing. So, intracanal medicaments represent an important step to achieve total bacterial eradication.<sup>23</sup>

In practical dentistry, antibiotics are commonly prescribed together with mechanical therapy & surgery to care for periodontal disease & acute and chronic periapical infections. Also, a lot of dentists depend on antibiotics to help patients just for pain as the only complain of the patient.<sup>12,24</sup>

Dentists were expected to provide antibiotics prescription for patients who were not under complete final recommended surgical treatment as an offer choice.<sup>25</sup>

Antibiotic prophylaxis prior to dental treatment is a common practice. This term indicates the prescription of antibiotics before surgical and non-surgical procedures in order to prevent local & systemic infective complications. The primary prophylaxis is commonly used for both healthy persons and those subjected to risk of infection, like undergoing invasive measures like surgical endodontic therapy or apicectomy, nonsurgical endodontic therapy & extractions, especially surgical tooth extractions "for example, impacted third-molar extractions".

Secondary antibiotics prophylaxis was used in particular to those with specific heart problems or artificial joint prosthesis who were underwent oral health procedures. Dentists, mainly prefer to use prophylactic antibiotics with patients having cardiac problems because they are an infective endocarditis risk group. For non invasive procedures such as intraoral radiography, orthodontic treatment, shedding of primary teeth, fluoride topical application therapy, & supragingival restorations there is no need for antibiotics .<sup>12,24, 22,26</sup>

The oral cavity is one of the most contaminated regions of the human body, with a

microflora including hundreds of different microbial species, many of them are able to infect distant sites . The rationale for antibiotics prophylaxis in dentistry is to protect patients with a certain specific risk from local microbial contamination or systemic spread of oral bacteria during various dental procedures which induce bleeding & transient bacteraemia. Recently it was reported that prophylactic uses of antibiotics in dentistry is often not necessary & not adequately supported by scientific evidence, especially in healthy subjects various dental procedures.<sup>27,28</sup>(Table 1 & 2)

**Table (1):** Indications for prophylactic antibiotic use in dentistry

<b>Indication</b>	<b>Regimen</b>
<b>Implant Placement with High Infection risks.</b>	Amoxicillin: " 1-2 grams, 1 hour preoperatively with or without 500 mg postoperatively, tid or qid, 2-3 days" oral (OR)
<b>Infective Endocarditis</b>	1. No penicillin allergy "Amoxicillin:2grams,30minutes to1h preoperatively Ampicillin:" 2 grams, IM or IV, 30 min to 1 h preoperatively (unable to take orally)" , Cefazolen: "50 mg/ml" , ceftriaxone: "1000 mg /day" 2. Penicillin allergy" Cephalexin: "2 gram, 30 min to 1 h preoperatively" Clindamycin: "600 mg (oral, IM, or IV), 30 min to 1 h preoperatively" Azithromycin: "500 mg, 30 min to 1 h preoperatively " Clarithromycin: "500 mg, 30 min to 1 h Preoperatively"
<b>Medical Compromization</b>	1. No penicillin allergy Amoxicillin: "2 grams, 30 min to 1 h preoperatively" Ampicillin: "2 grams, IM or IV, 30 min to 1 h" preoperatively ( unable to take orally) 2. Penicillin allergy Cephalexin: "2 grams, 30 min to 1 h preoperatively" Clindamycin: "600 mg (oral, IM, or IV), 30 min to 1 h preoperatively" Azithromycin: 500 mg, 30 min to 1 h Preoperatively Clarithromycin: "500 mg, 30 min to 1 h preoperatively."

	Cefazolin: "1 grams, IM or IV, 30 min to 1 h preoperatively"
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**Table (2):** Indications for therapeutic antibiotic use in dentistry

Indication	Regimen
<b>Odontogenic infections</b>	1. No penicillin allergy Amoxicillin: "500 milligrams, tid, with or without loading dose of 1,000 mg, 3-7 days" Amoxicillin/clavulanic acid: 500/125 mg, tid, 5 days" Penicillin V potassium: "500-600 mg, qid, 5-7 days" 2. Penicillin allergy Metronidazole: "500 mg, bid or 200 mg, tid, 3-7 days" Erythromycin: "250-500 mg, tid or qid, 3-7 days" Clindamycin: "300-450 mg, qid or loading dose of 600 mg followed by 300 mg qid12 or 150 mg, qid, 3-7 days" Cephalexin: "500 mg, qid, 7 days" Clarithromycin: "250 mg, bid, 7 days"
<b>Pericoronitis</b>	Metronidazole: "200 mg, tid, 3 days" , Amoxicillin: "500 mg, tid, 7 days"
<b>Sinusitis</b>	Amoxicillin: "500 mg, tid, 7 days" Doxycycline: "Loading dose of 200 mg, followed by 100 mg, once daily"
<b>Acute necrotizing ulcerative gingivitis</b>	Metronidazole: "200-500 mg, bid or tid, 3-7 days" Amoxicillin: 500 mg, tid, 3 d
<b>Chronic or aggressive periodontitis</b>	Amoxicillin (with or without clavulanic acid): "250-500 mg, tid, 8 days" Tetracycline: "250 mg, qid, 6-30 days" Minocycline: "100 mg, once daily or bid, 21 days" Doxycycline:"100 mg immediately, followed by 100 mg qd or bid or 50 mg bid or tid 21 days" Metronidazole (with or without amoxicillin): "250-500 mg, bid or tid, 7-8 days" Clindamycin: "300 mg, bid, tid, or qid, 8 d or 150 mg, qid, 10 days" Ciprofloxacin: "500 mg, bid, 8days"

**Factors affecting the Antibiotic Prescription by dentists**

Bacterial infections are familiar in clinical dental practice; therefore, antibiotic use is also frequent.<sup>1</sup> Usually, the dentist is not sure about the specific microorganism responsible for certain infection, considering that cultures of pus & exudate

are not regularly made therefore antibiotic prescription is empirical. According to epidemiological data, dentists should suspect the germs that could be involved in the infectious process and decided treatment on suggested reasons.<sup>29</sup> For that reason, broad spectrum antibiotic is largely prescribed. The sensitivity of the bacteria to

many antibiotic decreased & types resistant strains increase in a significant manner.<sup>30</sup>

The antibiotic prescription could have interactions with the prescription of non-steroidal anti-inflammatory drugs. The non-steroidal anti-inflammatory drugs cause reduction of antibiotic bioavailability and thus reduce its effect<sup>31,31</sup>, for example some drug combinations like cephalosporin and profen, or tetracycline with naproxen or diclofenac have been shown to increase in the bioavailability of the antibiotics.<sup>1</sup>

Since the major etiological factor of gingivitis & periodontitis are poly-microbial type of infection, systemic & topical antibiotics in addition to mechanical removal of microbial biofilms is indicated. The acquired resistance of dental bacteria to antibiotics prompted the extensive approaches to find alternative remedies, such as toothpaste, mouth rinses, & gingival gels, to prevent and decrease local bacterial overload.<sup>33</sup>

Non-clinical factors also affecting the choice of antibiotics like patient preference, availability in the pharmacy, cost of antibiotic. Therefore, nonclinical alternative factors that might increase understanding of variation in antibiotic prescribing should be considered. It was found that antibiotic prescribing is affected by the doctor/patient relationships, patient expectation, doctors' characteristics, patients' social background and circumstances, a sense of social responsibility and, a balancing act between what is 'clinically best' against perceived patient expectations.<sup>17</sup>

#### **Precautions with antibiotic use**

#### **Pregnancy:**

The limitations of human clinical trials to estimate the safety of antibiotic in pregnant women lead to doubts about their use for such patients. Food and Drug Administration "FDA" set up 4 drug risk levels during pregnancy: (A) no risks; (B) no effects in the animal; (C) no studies conduction in both animals and humans, or teratogenic effects recorded in animals without evaluation in humans; and (D) teratogenic effects. No antibiotics for groups (A), group (B) contains the followings: "azithromycin, cephalosporins, erythromycin, metronidazole and penicillins with or without beta-lactamase inhibitors", group (C) includes "clarithromycin, the fluorquinolones and the sulfa drugs (including dapsone)", lastly, group (D) contains "the aminoglycosides and tetracyclines".<sup>28,34</sup>

#### **Kidney & Liver failures:**

Antibiotics are excreted by kidneys. Therefore problems in renal function need dose adjustment "by reducing the amount administered in each dose or by increasing the interval between doses" to stay away from greatly elevated plasma drug levels that could result in toxic effects.

In liver failure patients, the use of antibiotics that are metabolized and /or eliminated in the liver should be limited in order to prevent overdose toxicity. Antibiotics like erythromycin, clindamycin and metronidazole have need of dose adjustments when given to patients with such failure.<sup>28,35,36</sup>

### **Diabetes & hypertension:**

The rates of the whole antibiotic prescriptions in a medically compromised patient with various systemic diseases were less than in normal healthy individuals. Thus, diabetes & hypertension are not critical factors that affect the rate of antibiotic prescriptions.<sup>37</sup>

### **Age of patient & Genetic factors**

Age may affect the pharmacokinetics of many drugs. Chloramphenicol conjugation & excretion is inefficient in new-born, thus larger doses produce grey baby syndrome. Also Sulphonamides can cause kernicterus by displacement of bilirubin from protein binding sites in the neonate. On another example, the  $t_{1/2}$  of aminoglycosides is prolonged in the elderly and they are more prone to develop nerve toxicity. It is well known that tetracyclines accumulate in the developing teeth & bone causing discolouration and weakness of which makes them contraindicated below the age of 6 years. Some drugs like sulphonamides & chloramphenicol cause haemolysis in G-6pd deficient patient.<sup>(38)</sup>

### **CONCLUSIONS**

To summarise, the definitive indications for antibiotics in dentistry are limited & specific (see Table 1 & 2). In dentistry, most cases of infection can be treated by the elimination of their focus & they respond in good manner to the special antibiotic. Rational prescription of antibiotics by dental practitioner is necessary in the scope of the global issue of antimicrobial resistance. Education is

mandatory during the training as well as in programs of continuous dental education.

The practice of antibiotic prescription by dental specialists is still poorly understood. It is an art & science. There are many variables, such as specific pathogens, the virulence of the infection, pharmacokinetic of the drug, mechanism of action of the antibiotic, the health status of the patients, and their defense mechanisms, that control & regulate antibiotics prescription. This review highlights some points about this subject. Future studies are necessary to evaluate this practice including antibiotic prescribing patterns and its role in the development of resistance to antibiotics.

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