

Antibiotic use in endodontic treatment during pregnancy: A narrative review

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Abstract

More than half of pregnant women are usually affected by odontogenic pain affects. Pain often accompanies periapical or pulp infections and increases the risks to pregnant patients and their fetuses. The American Dental Association, in partnership with the American College of Obstetricians and Gynecologists, has offered a strong declaration reaffirming the significance of suitable and timely oral health care as an indispensable constituent of a healthy pregnancy. However, there is lack of knowledge about the use of antibiotics in endodontic treatment. Therefore, the present study would review the researches done in this area and tries to provide comprehensive and complete information about the use of antibiotics in endodontic treatment during pregnancy. Based on the results, it can be said that using antibiotics during pregnancy are allowed, and they can be used normally and safely by pregnant women.

Key Words:Antibiotics; endodontic therapy; pregnancy.

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Oral disease in pregnant women is a major public health issue worldwide.¹ Pregnancy does come with inherent risks and the idea that dental treatment should not be implemented due to pregnancy is not debatable. Special concerns are necessary as a pregnant woman seeks dental care;^{2,3} hence, the treatment related to these patients may need more attention to reduce treatment time and make changes in the type of dental treatment and prescribed drugs.⁴ Appropriate risk assessment for the mother and fetus should be performed.³ According to results of a novel study about pregnant women, it was recognized that more than 43% of them have oral health problems, containing odontogenic infections and pain.⁵ It is normal that most of odontogenic infections develop quickly to deep-seated infections that ultimately endanger the airway of oropharyngeal.² Moreover, dental infections usually present with symptoms of pain and swelling in the mouth.⁶ Misuse of drugs instead of receiving proper dental treatment may consequently lead to damaging effects on the pregnant patient and fetus; so, during pregnancy, it is necessary to notice that odontogenic infections must be treated quickly at any time. One of the suggested treatments is endodontic treatment, which includes cleaning and removing the pulp of a patient's teeth. Root Canal Therapy (RCT) may include radiography, local anesthesia, root

cleaning, and intracanal drugs such as analgesics and antibiotics.² During endodontic treatment, radiography is essential, and to have appropriate diagnosis, proper obstruction, length of work, and assessment after treatment, radiographs are needed. As X-rays during intraoral radiography are directed to the mouth and not the abdomen, it is considered safe for pregnant women. In addition, when performing radiography, a protective method like collimation, high-speed film, lead apron, and filtration is also applied.⁷ It is recommended that concerned pregnant patients be reassured that the as Low as Reasonably Achievable (ALARA) standard will be used in all circumstances requiring radiographs and that only the necessary radiographs for both treat and diagnosis will be obtained.⁸ During pregnancy, local anesthesia is considered rather safe if it is managed properly and in the exact amount.⁹ The overall idea is that sometimes there is a need to administer an increased quantity of anesthesia and that the effects of stress are more dangerous than those of the increased quantity of local anesthesia. Most anesthesia contain vasoconstrictor epinephrine. A maximum dose of 0.1 mg has been added to local anesthesia. No side impacts or abnormalities have been reported, even after the implementation of epidural anesthesia during childbirth.¹⁰ Local anesthesia with epinephrine, used as an intravascular injection, has been reported to at least

cause a decrease in placental uterine blood flow.⁹ It has been reported that for healthy pregnant women, a concentration of 1: 100,000 epinephrine applied in dentistry is considered safe accompanied with an appropriate aspiration procedure and limited to the minimum necessary dose.^{11,12} During pregnancy, RCT is applied to achieve the goals such as preserving a healthy oral environment, controlling the illness, and avoiding possible problems that may happen during the post-childbirth time or in late pregnancy.¹² None of the detergents, hypochlorites and root canal fillers used in endodontic are claimed to be harmful to the fetus.² In addition, some antibiotics and analgesics can be safely prescribed by your dentist as an adjunct to endodontic treatment.¹³

Management of emergencies and acute disease

In situations such as mild cellulite, drugs like cephalexin, penicillin and amoxicillin, as first-line antibiotics would probably be selected. Also, in the case of allergy to penicillin, Erythromycin or clindamycin (Cleocin) may be applied. The pregnant patient with severe cellulite should be treated at a hospital with an intravenous infusion of clindamycin or cephalosporin. To relieve toothache, Acetaminophen can be prescribed. Besides, controlled use of oxycodone and Ibuprofen are proper.¹⁴

Some common kinds of dental techniques that can be implemented in each trimester

First trimester: The most vital period for fetal growth. Emergency treatment should be implemented whether or not organogenesis is complete, there are precautions to be made and the patient's obstetrician should be consulted if organogenesis is incomplete, but emergency treatment is vital. If a pregnant patient experienced a toothache, the dentist can make an emergency opening, eliminate the inflamed pulp (or) drain the pus, and release the pain. Intracanal drugs such as chlorhexidine/metronidazole and calcium hydroxide can be used. In addition, programs containing Plaque diet control for pregnant patient can be initiated.¹⁵

Second trimester: During the second trimester of pregnancy, it is the safest phase for treating patients. So, elective and emergency dental treatment can be administered in the second trimester. Also, other treatments can be done like periodontal surgery, tooth extraction, and root canal treatment.¹⁶

Third trimester: If the patient has a toothache, emergency treatment can be administered and if possible, transfer definitive treatment to the post-childbirth time.¹⁷

In 2012, the American Dental Association issued a statement reaffirmed in 2019. It underlines the significance of oral health for pregnant patients at the correct time and in the suitable place. Treatment, the inhibition and control of odontogenic infections as an appropriate treatment is necessary to a healthy pregnancy,¹⁸ yet, it has been reported that oral

treatments during pregnancy are avoided by numerous dental treatment providers.^{19,20} Evidence for the use of antibiotics as complementary medicine in endodontic treatment is given below. According to the obtained results of some studies in Canada and Netherlands, about 25% to 50% of pregnant women have received antibiotics.^{21,22} However, it is necessary to prescribe antibiotics to pregnant women after evaluating their disadvantages and advantages.²³ It should also be noted that infections can be dangerous for both mother and fetus. For example, one of the risks of spreading infection from the mandibular second molars is the possibility of Ludwig's angina.^{24,25}

Indications for antibiotics in dentistry

According to studies, the use of antibiotics in some cases such as surgery to remove benign tumors, surgery for extraction of impacted teeth, surgery for an implant, bone grafting, and periapical surgery, is prescribed for patients. In treatment of acute infections like invasive localized periodontitis, ulcerative gingivitis, acute apical abscess, periodontal abscess, peri-implantitis, cellulite and pericoronitis, the antibiotics are also suggested.^{6,26-29}

Transport across the placenta

Antibiotics have high fat solubility and low molecular weight. This maintains a high concentration of antibiotics in the blood and facilitates their transfer through the placental barrier. In addition, oral antibiotics are safer than Systemic antibiotics because of their lower absorption.^{30,31}

Classification of antibiotics

The FDA has divided antibiotics into five categories based on their side effects during pregnancy:

Category A: This category includes antibiotics that have been adequately controlled in studies and have not reported any specific side effects during pregnancy.

Category B: Antibiotics have not been observed any specific complications in humans during pregnancy, but side effects have been observed in animals.

Category C: Antibiotics do not have sufficient information about their side effects in pregnant women or animals.

Category D: Antibiotics that have side effects, but they have been proven in pregnancy, but when necessary, their benefits are more than their disadvantages.

Category X: Antibiotics whose side effects have been proven in humans and animals and their disadvantages are more than their advantages.³²

The next part is a list of the most common antibiotics applied in dentistry during pregnancy.

Penicillin

To treat odontogenic infections, Penicillins are suggested as beta-lactam antibiotics. Amoxicillin, ampicillin (category B), and penicillin VK are suggested as common dental antibiotics. According to the statement of the FDA, no relation has yet been reported

linking the implementation of amoxicillin during pregnancy to the miscarriage, the main birth defects, or fetal and maternal side effects. The same results were reported by the Teratogen System Information (TERIS) by examination of 25,000 implementation of penicillin in pregnancy and the increased danger of pregnancy outcomes.¹⁸ Nevertheless, there are some evidences that confirm the congenital defects of the oral-maxillofacial complex like cleft lip and palate and hypomineralization in tooth enamel as results of the use of amoxicillin during pregnancy.³³⁻³⁵

As a beta-lactamase inhibitor antibiotic, the combination of amoxicillin and clavulanic acid (co-amoxiclav) is very effective in treating sever odontogenic infections. No evidences have been reported of the relationship between increased dangers of fetal or congenital defects by exposure to therapeutic doses of this combination drug during pregnancy (18). It is worthy to point that the danger of a severe disease called necrotizing enterocolitis in the newborn is increased by use of this drug in the third trimester.³⁶ While the complete danger of infection is not high, this combination drug should be eluded in the third trimester of pregnancy.¹⁸

Cephalosporin

They are considered a kind of beta-lactam antibiotics with a broad range. There is no evidence approving an increased danger of spontaneous abortion or miscarriage in pregnant patients used cephalosporins.³⁰ The reports about the relationship between congenital defects in infants and prenatal implementation of cephalosporins are conflicting. Based on results of an examination working on the impacts of cephalosporins in initial use, no adverse effects were reported. It is worthy to mention that some studies approved the relationship between implementation of cephalosporin, anorectal atresia, and atrial septal deficiency in infants.³⁷⁻³⁹ Yet, the danger of developing abnormalities is not high.

Clindamycin

This drug is frequently applied for patients with a previous hypersensitivity to beta-lactam. There is not enough clinical information on the safety of this

category (B). While clindamycin is not associated with outcomes of pregnancy and abortion on the fetus, its use has been associated with congenital cardiovascular and musculoskeletal abnormalities.^{30,31}

Metronidazole

Metronidazole is a very effective category B drug derived from nitroimidazole. The antibiotic metronidazole is prescribed against anaerobic bacteria, usually in combination with penicillin, to treat odontogenic infections. Concerns about the mutagenicity and carcinogenicity of metronidazole have been reported in animal studies; while in human studies the absence of these cases has been confirmed.^{40,41}

There are not same obtained results regarding prenatal metronidazole use and a developed danger of miscarriage.³¹ No meaningful relationships have been reported between prenatal metronidazole use and fetal deficiencies or adverse pregnancy.^{26,32,42-50}

Tetracycline

Tetracyclines are the same as tetracycline, oxytetracycline, minocycline, and doxycycline. They are all broad-spectrum antibiotics classified in category D.^{51,52} A study has reported a statistically significant relationship between the use of tetracycline antibiotics and spontaneous abortion of the fetus.³¹ In addition, the use of tetracyclines has been shown to stain permanent teeth and discolor them.^{22,53} Therefore, it is recommended that tetracycline be avoided during pregnancy except there is a convincing cause.

Macrolide

Macrolides are similar in antibacterial range to penicillin and usually used for patients with allergy to penicillin. In dentistry, the most frequently used of this group are azithromycin (category B), erythromycin (category B), and clarithromycin (category C)..

Based on the new findings, macrolide use has not been related to cardiovascular defects in newborns and the previous beliefs were rejected.⁵⁴⁻⁵⁶ According to gained results of a novel meta-analysis, an increased danger of cerebral palsy-epilepsy, miscarriage, and gastrointestinal abnormalities were reported as the results of macrolide use during pregnancy.⁵⁷ Based on

Table 1. Management of antibiotics for pregnant patients in dentistry.

	Acceptable drugs during pregnancy	Food and Drug Administration Category	Unacceptable drugs during pregnancy	Food and Drug Administration Category
Antibiotics	Penicillin	B	Tetracyclines	D
	Amoxicillin	B	Erythromycin	D
	Cephalosporins	B	(estolate form)	
	Clindamycin	B	Quinolones	C
	Erythromycin (except for estolate form)	B	Clarithromycin	C

another finding, acetate macrolides are not relatively safer than basic form of erythromycin.⁵⁸

Fluoroquinolones

They are broad-range category C antibiotics with restricted usage. For odontogenic infections, they are just applied for patients with allergy to penicillins or treatment of bacteria unaffected by other antibiotics. Meanwhile, their implementation for odontogenic infections in endodontics is restricted. Meta-analysis findings have not been able to reveal the use of fluoroquinolones, especially ciprofloxacin, that upsurge the danger of preterm delivery, miscarriage, and fetal abnormalities.^{59,60}

Table 1. shows management of antibiotics for pregnant patients in dentistry.

Benefits and harms of antibiotics

Most pregnant women are prescribed to use a variety of medicines. The drugs may have teratogenic influences on the fetus during pregnancy. In addition, drugs used during breastfeeding can have severe effects on the health of the baby. During pregnancy and lactation, one of the most used drugs is antibiotics frequently prescribed by doctors.⁴²

Infections and Preterm labor

According to the definition of The World Health Organization, preterm labor is labor that happens at more than 20 weeks and less than 37 weeks gestation.⁴³ The frequency of preterm labor in developed countries differs between 7 and 11%.^{44,45} In the last 40 years, in spite of all progresses in midwifery care, the danger of prematurity has not reduced.⁴⁶ In developed countries, prematurity is recognized as one of the main reasons of mortality and neonatal morbidity and it is the cause of 60% to 80% of neonatal mortality deprived of congenital abnormalities. Despite the low percentage of births less than 32 weeks' gestation (only 1% to 2% of all births), they are reason for 50% of long-term neurological problems as well as 60% of prenatal deaths.^{43,47} Pointing to the financial issues, preterm labor is remarkably significant as one-tenth of the cost of general child care and one-third of the cost of caring for infants is related to preterm labor.^{48,61} During the two past decades, many kinds of investigations have underlined the reasons of preterm labor and consequently various correlated risk elements have been recognized.⁶² Most common reported ones are congenital causes of infectious origin.⁶³⁻⁶⁵ The possible associations between preterm labor and infection can be explained by models that claim that preterm labor is initiated by an inflammatory reaction to pro-inflammatory cytokines such as IL-6, IL-8, interleukin (IL) -1 beta, and TNF-alpha.⁶⁶ Based on the evidences from clinical and laboratory examinations, there is a relationship between labor and systemic infections and spontaneous preterm labor.^{63,67} As a result, it is widely an accepted logical assumption that antibiotics play an

effective role in the handling of preterm labor.^{68,69} Although the relationship between inflammation and infection with the increased danger of preterm labor is crucial, yet it is not identified whether antibiotic handling can inhibit it. Moreover, it is believed that antibiotic treatment to inhibit preterm labor can be dangerous.^{67,70-71}

Side effects of misuse of antibiotics

Antibiotic resistance is a natural phenomenon, but it can be caused by the misuse of antibiotics.⁷² The plans to inhibit his misuse of antibiotics can have consequent worldwide results for inhibiting the expansion of antibiotic-resistant bacterial strains.²⁶ There is some data that antibiotic implementation can lead to severe side effects such as gastrointestinal abnormalities, allergic reactions, and cardiac arrhythmias, and death⁷³ The expansion of resistant bacteria is recognized as a main problematic issue linked to the overuse of antibiotics.^{74,75} It is claimed that the use of antibiotics during fetal-neonatal life has an opposing and long-term influence on the maternal intestinal microbiota and the maternal vaginal microbiota. Furthermore, it can lead to the expansion of allergic illnesses. Antibiotics may also inhibit and delay with the beginning colonization of the baby's gut microbiota.⁷⁶ This inhibition may restrict the development and growth of the baby's immune system, causing diseases and allergies.^{77,78} Overuse of antibiotics for pregnant women is linked to the presence of many antibiotic-resistant organisms, as the rate of erythromycin-resistant Streptococcus (Group B) -one of the selective antibiotics after premature rupture of membranes (PROM) prescribed in most British hospitals- and reaches 35%.⁷⁹⁻⁸¹

In conclusion, according to the results of researches, aspecifically evidences published by the American Dental Association with American Obstetricians, the use of some antibiotics during pregnancy are allowed and can be used normally and safely by pregnant women.

List of acronyms

ALARA - as Low as Reasonably Achievable
FDA – U.S. Food and drugs administration
IL - interleukin
PROM - premature rupture of membranes
RCT - Root Canal Therapy
TERIS - Teratogen System Information

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