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ORIGINAL ARTICLE

Endodontic Consideration for the Usage of Drugs in Pregnant and Lactating Mothers

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ABSTRACT

The pregnant or lactating patient presents with a number of unique management problems for oral health care providers. Practitioners with minimal training in gestational medicine may be hesitant to treat their pregnant patients. Because of a fear of injuring either the mother or unborn child, some practitioners may withhold care or medications from their patients, inadvertently causing harm. An understanding of the patient's physiological changes, the effects of chronic infection or illicit drugs and the risks or benefits of medications are necessary to adequately advise a patient on her options regarding medical/dental care.

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Introduction

Many dental professionals may be apprehensive about providing dental care to their gestational patients due to fears of inadvertently harming the foetus. The need to minimize systemic infection and the disease is of utmost importance during this period [1],[6] and so, all dental procedures are not contraindicated during pregnancy. They should be performed with added precautions and drug modifications. With respect to the field of endodontics, if dental caries is a source of pain or acute infection in an otherwise healthy gestational woman, a dentist should provide invasive care, no matter what the patient's phase of pregnancy is [1],[13]. Dental decay also presents an additional source of bacterial load on the patients. The endodontic treatments performed to alleviate the pain and infection, along with proper drug selection to reduce the side effects of drugs on pregnant females and their unborn foetuses.

Additionally, there is no contraindication in using radiographs during diagnostic procedures which are deemed necessary, such as radiographs with normal safety precautions. These precautions include beam collimation, high speed films, limited exposure and lead apron for the patients [6]. It is estimated that an average full mouth dental film series may expose the foetus to $1x10^{-5}$ rads of radiation, far below the teratogenic risk to an unborn child [11],[14],[16].

Drugs And Pregnancy

Medications may be either a boon or liability during a woman's pregnancy. This determination can only be made if the weight of her medical/dental condition, the foetus's risk of exposure and the need for dental treatment are evaluated and balanced [3]. Physicians, dental professionals, or patients may have an irrational belief that all medications may be harmful to the unborn child. However, some medical or dental conditions, if left untreated, may be more detrimental to the foetus. This may lead to progressive maternal disease status, teratogenesis, impaired foetal growth or development, premature birth, spontaneous miscarriage, or abortion [9]. While some medications may be harmful to a foetus, safe alternatives are often available to treat many of these dental conditions. Both the patients and the dentalprofessionals need to make an informed choice in this matter.

In the United States, the FDA has developed a five-category system to determine foetal risks of medications [12]. The categories range from A, the

safest listing, to the final category, X, which is completely contraindicated during pregnancy [18] [Table/Fig 1] .

(Table/Fig 1) FDA Drug Categories during Pregnancy: Level and outcome of testing required to determine a pregnancy risk factory category.

Category	US Food and Drug Administration risk stratification of drugs
A	Controlled studies in humans have failed to demonstrate a risk to the fetus, and the possibility of fetal harm appears remote.
B	Animal studies have not indicated fetal risk, and human studies have not been conducted; or animal studies have shown a risk, but controlled human studies have not.
C	Animal studies have shown a risk, but controlled human studies have not been conducted; or studies are not available in humans or animals.
D	Positive evidence of human fetal risk exists, but in certain situations the drug may be used despite its risk.
X	Evidence of fetal abnormalities and fetal risk exists based on human experience, and the risk outweighs any possible benefit of use during pregnancy.

Data from Refs. [3,5,18].

The dental professionals must use scientific literature and study reviews; confer with the patient's obstetrician, physicians, or pharmacists who are familiar with pregnancy interactions; or make use of reliable published reference sources.

Many factors play roles in determining the foetal risk of medications. First, it should be determined if a drug is tetragenic in nature. Most foetal organogenesis occurs during the first trimester, which is the period of most concern for many medication effects on the foetus. The next matter of concern would be the degree of foetal exposure to a medication. Not all drugs readily pass through the placental barrier. For example, drugs with little or no foetal contact are those that bind to proteins or that which are made up of large molecules that cannot transfer through the barrier [9].

The drugs that would readily go across the placental barrier include lipid-binding drugs, acidic medications, or those that depend on renal clearance [17]. Though tetracycline and minocycline are both effective antibiotics, both known to be associated with abnormalities in both bone and dentaldevelopment. These drugs are thus not advised for pregnant patients [18]. Alcohol is also contraindicated during gestation, as it has been proven to cause neurodevelopmental defects after repeated or high-dose exposure [2].

The pharmacokinetics of a drug may be altered by pregnancy. For example, vasodilation leads to increased hepatic metabolisms and renal clearance rates. The increase in blood volume causes a larger volume of distribution of a given medication [14]. Pregnancy is also associated with slower peristalsis and gastric emptying, as well as increased cardiac output, blood volume, body fat, and glomerular filtration [9],[10]. Thus, unbound free drugs may be transferred across the placenta and drugs that are usually cleared by the kidney do so at a faster rate. This leads to lower serum drug concentrations and thus lower effectiveness, unless the dosage is adjusted [9].

Drugs Used In Endodontics

Fortunately, many drugs in a dental office's armamentarium are considered to be generally safe for both pregnant patients and their unborn children. Most dental professionals should have access to a medication reference if questions arise regarding a proposed drug's efficacy or safety. However, if a dental professional has any doubts about either dental medication choices or the risk factors for pregnant patients, he or she should refer to the patient's obstetrician.

1. Local Anaesthesia

Local anaesthetics are among the most commonly used medications by dentists. Lidocaine and prilocaine have been given an FDA category B rating when given in a therapeutic range and should be the first-line choices for local anaesthesia for pregnant women who do not have any contraindications, such as allergy [4],[18]. Bupivicaine, mepivicaine, and articaine have each been given FDA category C ratings. Bupivicaine's rating stems from animal studies demonstrating embryo death with higher-than-therapeutic dosages.

Mepivicaine and articaine have been rated as category C drugs because of insufficient animal studies [5]. None of the above listed local anaesthetic agents have been associated with poor foetal outcomes when given in dental therapeutic dose ranges [4,5]. Additionally, the use of vasoconstrictors such as epinephrine or levonorderfrin, is not contraindicated when they are a part of the commercially available local anaesthetics. Though

given a C rating, these vasoconstrictors, when used in low concentrations in pre-packaged local anaesthetic cartridges, cause no foetal harm as long as normal precautions are taken. These precautions include avoiding injection within the blood vessels and maintaining total dosages at or below therapeutic ranges such as 0.04 mg for epinephrine and 0.2 mg for levonorderfrin [4],[5].

2. Antibiotics

Frequently, the best treatment option for a patient is to immediately address pain or infections at the source [1],[5],[11]. However, there are occasions when infections cannot be treated immediately with invasive dental care and antibiotics may be a necessary course of action. Many of a dentist's first line antibiotics are rated by the FDA as category B for pregnancy risk. These include the penicillin family, the erythromycins (except for the estolate form), azithromycin, clindamycin, metronidazole, and the cephalosporins [18]. However, tetracycline, minocycline, and doxycycline are given D ratings due to their likelihood of chelating in bones and teeth. Thus, tetracycline, minocycline, and doxycycline should be normally avoided [18].

3. Analgesics

When discussing pain, the dental professional should be aware of many potential pitfalls. Not all nonsteroidal anti-inflammatory drugs are safe for the foetus. Neither aspirin nor diflusinal are recommended for a pregnant woman. Aspirin and diflusinal have both been associated with prolonged gestation and labour, anaemia, increased bleeding potential and premature closure of the ductus arteriosus of the heart [5]. Even ibuprofen, ketoprofen, and naproxen are contraindicated in the third trimester of pregnancy, where they are considered as FDA category D choices, due to their risks of prolonged labour, haemorrhage risk during delivery and premature closure of the ductus arteriosus. However, these three analgesics are given a category B rating for the first two trimesters of pregnancy [5]. The first-line nonsteroidal anti-inflammatory drug of choice should be acetaminophen. Acetaminophen has earned an FDA B rating for all three trimesters of pregnancy [18]. If stronger pain medication is necessary, most narcotic combinations are relatively safe for short durations, despite their risks for foetal growth retardation or foetal dependency if prescribed for long periods. Oxycodone has received a B rating for short-term usage, while meperidine, hydrocodone, propoxyphene and codeine are FDA category C narcotic medications, though they are still considered to be reasonably safe for short-duration pain control [18]. However, long-term narcotic usage is ill-advised, as the foetus may develop either neonatal depression or withdrawal symptoms [12].

4. Anxiolytics

When treating anxiety in the dental setting, nonpharmaceutical methods are preferred because they reduce the foetus's exposure to medication. Most benzodiazepines for anxiolytic relief must be administered with extreme caution and consultations with the patient's physician because most drugs in this class are classified in categories C or D for pregnancy risk [1,5]. Triazolam which is listed by the FDA in category X is absolutely contraindicated in gestational patients [5]. Intranasal nitrous oxide use is very controversial because there is risk of reduced uterine blood flow or tetratogenic effects when it is used in high concentrations [1]. Short-term (ie, %30 minutes) use of nitrous oxide, when used in combination with 50% oxygen for nonelective dental procedures, may be warranted if patient management is not possible without anxiolytic management. However, anecdotal reports have indicated risks of cleft palate development which are associated with the short-tern use of nitrous oxide in combination with oxygen [1],[13].

Herbal Medication

Herbal medications have been used throughout human history and are once again gaining popularity in Western cultures. While physicians commonly prescribe vitamin supplements for their pregnant patients, they may be unaware or may be uncomfortable in discussing other natural products with patients. Americans are more frequently adding dietary supplements to their daily routine and may be using these agents during their pregnancies. Because herbs are considered to be natural products, patients may not perceive them as risky [9]. The FDA, in conjunction with the Dietary Supplement Health and Education Act of 1994, has recently begun reviewing the efficacy and safety of herbs. Controlled scientific studies which are related to herbs are needed. The effects and risks associated with most natural substances are dose related. For example, garlic and ginger have been used as spices for generations without any reported effects on pregnancy. Yet, high doses of garlic may increase the risk of heavy

bleeding by its antiplatelet aggregation properties [3]. Other herbs such as blue cohosh and passionflower may alter uterine contraction patterns, which may then affect labour [3].

Drugs And Lactation

With the increasing recognition of the benefits of breast-feeding, clinicians must often weigh the benefits versus risks of drug therapy in lactating women. Mechanisms of the excretion of drugs in breast milk include both passive diffusion and carrier-mediated transport. The amount of a drug excreted in breast milk depends on the characteristics of the drug, such as the drug's molecular weight, lipid solubility, pK_a, and plasma protein bonding [7],[8]. Small, water-soluble non-electrolytes pass into milk by simple diffusion through aqueous channels in the mammary epithelial membrane that separates plasma from milk. With larger molecules, only the lipid soluble, non-ionized form passes through the membrane. The pH of milk is generally lower (more acidic) than that of plasma and milk can act as an "ion trap" for weak bases. At equilibrium, basic drugs may be more in concentration in milk as compared to plasma. Conversely, acidic drugs are limited in their ability to enter milk, because the concentration of the nonionized free form in the milk is higher than that in plasma and a net transfer of the drug from milk to plasma occurs.

The factors that determine the advisability of using a particular drug in a nursing mother includes the potential for acute or long-term, dose-related and non-dose-related toxicity; dosage and duration of therapy; age of the infant; quantity of milk consumed by the infant ; and the drug's effect on lactation. To minimize the infant's exposure to medication in milk, clinicians should consider the following strategies: withhold drug therapy, delay drug therapy temporarily, advise the mother to avoid nursing at peak plasma concentrations of the drug, administer the drug to the mother before the infant's longest sleep period and/or withhold breast-feeding temporarily. Drugs that are prescribed for women who are lactating are listed in [Table/Fig 2].

(Table/Fig 2) Drugs of choice for dental care during pregnancy and lactation

Therapeutic agents	FDA pregnancy category	During lactation
Anxiolytic agents		
Diphenhydramine	C	Use with caution
Benzodiazepines	D	Avoid
Barbiturates	D	Avoid
Nitrous oxide	Avoid	Safe
Local anesthetic agents		
Lidocaine	B	Safe
Mepivacaine	C	Safe
Benzocaine	C	Safe
Analgesics		
Acetominophen	B	Safe
Ibuprofen	B (D, in third trimester)	Safe
Oxycodone	B	Avoid
ASA	C (D, in third trimester)	Avoid
Codeine	C (D, in third trimester)	Use with caution
Tramadol	C	Use with caution
Antibacterial agents		
Penicillins	B	Safe
Cephalosporins	B	Safe
Clindamycin	B	Safe
Metronidazole	B	Safe

Conclusion

Every gestational woman should be encouraged to seek medical and dental care during her pregnancy, as failure to treat developmental problems affects the health of both the mother and the unborn child. Dental care professionals should educate themselves by gaining a basic understanding of the underlying physiological changes of pregnancy, the influences related to the use of medications or illicit drugs or substances during gestation and how these may interact with the delivery of dental care. This understanding aids the development of a treatment plan and the delivery of the necessary medical, nutritional and dental care, as well as it prepares the professionals for counseling their pregnant patients on relevant issues such as nutritional supplement usage or the need to avoid chemicals or substances that may be harmful to either the mother or the child.

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