

Management of the Pregnant Oral and Maxillofacial Surgery Patient

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Pregnancy causes many changes in the physiology of the female patient, providing the oral and maxillofacial surgeon with many challenges. These alterations are sometimes subtle but can lead to disastrous complications if proper precautions are not taken. There are many myths regarding the gravid patient—some of them are true, and many of them not. In this article, these myths are either dispelled or clarified. Physiologically, changes occur in the cardiovascular, hematologic, respiratory, gastrointestinal, and genitourinary systems (Table 1). These changes are reviewed.

Cardiovascular System

There are several changes that occur in the hemodynamic/cardiovascular systems of the gravid patient. Cardiac output increases 30% to 50% during pregnancy, secondary to a 20% to 30% increase in heart rate as well as a 20% to 50% increase in stroke volume.^{1,2} Increased stroke volume is predominantly responsible for the early increase in cardiac output, possibly due to increased left ventricular mass and blood volume.¹ It has also been shown in multiple studies that peripheral vascular resistance decreases early in pregnancy, but the mechanism of the decrease is poorly understood.^{3,4} The most likely explanation is that there is a peripheral vasodilatation from circulating progesterone, prostaglandin, prostacycline, and nitric oxide.⁵ The exact timing of all of these cardiovascular changes has not been described adequately, but it is clear clinically that cardiac output increases in the first trimester, plateaus in the second

trimester, and has a minimal increase in the third trimester.⁶ Pressures in the right ventricle, pulmonary artery, and pulmonary capillaries remain at normal, nonpregnant levels throughout the gestation; this is due to the low-pressure/high-capacitance characteristics of the pulmonary vasculature.⁷

During the second and third trimesters, a decrease in blood pressure and cardiac output can occur while the patient is in a supine position. This has been attributed to the decreased venous return to the heart from the compression of the inferior vena cava by the gravid uterus, which can result in a 14% reduction in cardiac output.^{3,8} Compression of the descending aorta can also occur, which leads to decreased blood flow to the common iliac arteries.⁹ Hypotension, bradycardia, and syncope characterize supine hypotension syndrome.¹⁰ Not all patients become symptomatic in the supine position, but in the ones that do, an increase in heart rate and blood pressure may initially occur and then they decrease.¹¹ It must be noted that while the supine pregnant patient may be asymptotic, a substantial decrease in uteroplacental perfusion can still occur. Placing the patient in a 5% to 15% tilt on her left side can relieve supine hypotension. If hypotension is still not relieved, a full left lateral position may be needed.¹¹

Hematologic System

Maternal plasma volume and red blood cell changes account for a substantial increase in overall blood volume. Maternal blood volume increases about 25% to 52% and red blood cell mass increases 20% over nongravid values by late pregnancy.^{12,13} This disproportionate rise accounts for the "hemodilution" or physiologic anemia of pregnancy that is maximal by approximately 30 to 32 weeks' gestation.³ Blood volume changes have at least 2 clinically significant purposes. The first is to protect the mother from volume depletion due to excessive peripartum hemorrhage. The second is to lessen the chance of thrombotic event occurrence. Some investigators have determined that the optimal maternal hematocrit is approximately 30% to 38% and that patients above this range have an increased incidence of maternal and

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Table 1. SUMMARY OF PHYSIOLOGIC CHANGES DURING PREGNANCY

Cardiovascular	Uterine compression of the inferior vena cava, leading to venous stasis and deep venous thrombosis Decreased oncotic pressure leading to lower extremity edema Increased red blood cell volume, heart rate Flattened T waves on electrocardiogram Extra heart sounds (S3, systolic murmur) Increased cardiac output, increased plasma volume
Respiratory	Increased airway mucosa fragility leading to an increased risk of edema Decreased Pao ₂ in supine position Increased risk of epistaxis with placement of nasal airway, nasogastric tube Progesterone-induced hyperventilation Decreased functional residual capacity
Hematologic	Increased risk of thromboembolic disease (hypercoagulable state) Leukocytosis
Gastrointestinal	Increased plasma volume creates a physiologic anemia Decreased lower esophageal sphincter tone leading to and increased incidence of gastroesophageal reflux disease Decreased gastric motility Increased intragastric pressure
Renal	Increased glomerular filtration rate Increased urinary stasis leading to urinary tract infections Progesterone-induced dilation of renal tree
Immune	Suppression of the maternal immune system, secondary to decreased neutrophil chemotaxis, cell-mediated immunity, and natural killer cell activity

intrauterine thrombotic events.¹⁴ Pregnancy stimulates an elevation in the leukocyte count, leading to a physiologic leukocytosis of pregnancy. Increased circulation of catecholamines and cortisol lead to a demargination of mature leukocytes from the endothelial lining of the vascular system, producing an increase by 5,000 to 10,000 cells.¹²

Pregnancy increases the chance of thromboembolism 5-fold compared with the nonpregnant patient.¹⁵ During pregnancy, all coagulation factors are increased, except factors XI and XIII, which are decreased.¹⁶ Thrombin-mediated fibrin generation increases throughout pregnancy, which, combined with the increased amount of clotting factors and increased hematocrit, leads to the hypercoagulable state of pregnancy. Compression of the inferior vena cava and iliac vein by the gravid uterus causes a venous obstruction, leading to stasis. Venous stasis in turn creates endothelial cell wall damage, which leads to thrombus formation. During pregnancy, an overall incidence of 0.09% has been reported.¹⁷ Pulmonary embolism (PE) has been reported in 15% to 25% of patients with untreated deep venous thrombosis (DVT), resulting in a 12% to 15% mortality rate.¹⁸

Anticoagulation is recommended for the treatment of established DVT and PE, and for prophylaxis against venous thromboembolism in women with a previous history of thromboembolic disease. Heparin is the anticoagulant of choice during pregnancy; it is a very large molecule that does not cross the placenta, unlike coumadin, which does cross the barrier and

poses a significant fetal risk. Its anticoagulant effect is due to its high affinity binding sequence to antithrombin III, which undergoes a conformational change that accelerates its ability to inactivate the coagulation factors Ia, Xa, and IXa. A retrospective study of 100 consecutive pregnancies in which heparin was used reported that the rate of adverse fetal and neonatal outcomes was comparable to that in normal pregnancies.¹⁹ There are 2 major considerations when using heparin on the pregnant patient. The first is heparin-induced thrombocytopenia (HIT). HIT is secondary to heparin-dependent IgG antiplatelet antibodies, which result in a serotonin-induced platelet aggregation and thus pose a substantial risk of a thromboembolic event. HIT usually occurs between 5 and 15 days after the start of therapy, but it has been reported within hours in patients who have previously been exposed to heparin.²⁰ Patients on heparin should therefore receive frequent platelet counts 5 to 15 days after therapy. Heparin-induced osteoporosis is also a concern during pregnancy. Fractures during pregnancy have been reported to be rare, occurring mainly in the pelvic region with no reported maxillofacial fractures.

Low-molecular-weight heparin (LMWH) was recently introduced in the United States; it has been used extensively in Europe. There are several advantages to using LMWH over unfractionated heparin. Because the half-life of LMWH is longer and there is less protein binding, the dose response is much more predictable, allowing for unmonitored administration.

More important, it has been shown to be more effective than unfractionated heparin in preventing the recurrence of clot, as well as less likely to cause major bleeding because of minimal effects on platelets and vascular permeability.²¹

Acute thromboembolism during pregnancy requires intravenous anticoagulation for 5 to 10 days, followed every 8 to 12 hours by subcutaneous injections to prolong the partial thromboplastin time at least to 1.5 times control throughout the dosing interval. The weight-based protocol for nonpregnant patients is 80 U/kg bolus followed by an 18 U/kg/hr infusion. The current regimen for a gravid woman at risk for DVT includes 5,000 U heparin twice a day in the first trimester, 7,500 U twice a day in the second trimester, and 10,000 U twice a day in the third trimester. In patients with a previous thromboembolic event, the American College of Chest Physicians recommend heparin 5,000 U every 12 hours or heparin adjusted to level of 0.1 to 0.2 IU/mL or clinical surveillance with periodic surveillance ultrasonography or, finally, coumadin prophylaxis postpartum for 4 to 6 weeks.²¹ The use of sequential pneumatic compression devices can also be used concurrently.²²

Respiratory System

During pregnancy, roughly 30% of all gravid patients experience severe symptoms of rhinitis. These changes have been attributed to the direct effects of estrogen and the indirect effects of increased blood volumes, but scientific proof is still lacking. Rhinitis of pregnancy begins at the beginning of the second trimester and increases in severity until delivery, when it often resolves within 48 hours. Alterations in the upper respiratory tract during pregnancy are not limited to the nasal mucosa. Mucosa in the upper airways also may become generally more edematous and friable.²³

Pulmonary changes also occur in the gravid patient. Hyperventilation begins in the first trimester and may increase up to 42% in late pregnancy.²⁴ The mechanism is associated in part with a resting arterial carbon dioxide tension below 30 mm Hg that is accompanied by increased renal bicarbonate excretion.²⁴ There also is a postural effect that must be considered, as well as the respiratory stimulant effects of progesterone.²⁵ Moderate hypoxemia was observed in 25% of supine gravid women.²⁶ The supine position was also associated with an abnormal alveolar-arterial oxygen tension gradient that significantly improved when women shifted back to the sitting position.²⁶ Therefore, the gravid patient can be expected to have a mild respiratory alkalosis (pH 7.40 to 7.46) and blood gas parameters (serum bicarbonate between 18 and 22 mEq/L) that are affected by maternal position.²⁷

Thus the use of nonpregnant ventilatory patterns may result in respiratory acidosis in the fetus and in the mother.⁷

Approximately 50% of pregnant women complained of dyspnea by gestation week 19, which increased to 75% by 31 weeks.²⁸ The dyspnea cannot be correlated with any single parameter of respiratory function; therefore women who complain of dyspnea may only be more aware of the increased ventilation of pregnancy.

Anatomically, the diaphragm is displaced upward approximately 4 cm, which is compensated for by an increase in the transverse diameter of the thorax and the chest circumference, resulting in a 40% increase in the vital capacity.²⁹ The diaphragmatic displacement leads to a 15% to 20% reduction in functional residual capacity.³⁰ There also is a baseline 15% increase in oxygen consumption by the gravid uterus. These 2 facts result in a significant depletion in the oxygen reserve of the gravid patient.³ The lowered oxygen reserve increases the hypoxia during periods of hypoventilation, so inspired oxygen concentrations should be obtained before periods of apnea.⁷

Gastrointestinal System

The gastrointestinal disorders in pregnancy are mostly due to significant displacement of the stomach by the enlarging uterus onto the spleen and liver. This displacement causes a high intragastric pressure. Concurrently, a decrease in the lower esophageal sphincter tone occurs due to inhibition of the production of the peptide hormone motilin by the increased amounts of progesterone.³¹ Motilin normally has a stimulatory effect on the smooth muscle of the gastrointestinal tract. These 2 disorders result in pyrosis (heartburn) in approximately 70% of all pregnant women,³² as well as increased gastric emptying time that is almost double compared with that of nonpregnant women.³³

The lowered esophageal sphincter tone, the elevated gastric pressure, and the slowing of gastric emptying set the stage for increased episodes of gastric reflux and regurgitation. Prevention of gastric content aspiration during surgery remains a major concern when performing surgery on the gravid patient. Maternal death after aspiration has been estimated to occur in 10% to 25% of reported cases, with the additional fact that the more acidic the aspirate, the greater is the chance of maternal death.³⁴

Antacid therapy was first proposed by Mendelson in 1946 to reduce the morbidity of gastric aspiration. Particulate antacids (magnesium and aluminum hydroxide) were used until about 1979, when it was shown that these types of antacids did not prevent pulmonary edema and impaired oxygenation after as-

piration.³⁵ Further studies have shown that sodium citrate (30 mL) and Bicitra (30 mL; Baker Norton Pharmaceutical, Miami, FL) are effective in buffering gastric contents to a pH greater than 2.5 in 88% of obstetric patients.^{36,37} Simultaneous to the research on antacids, H2 antagonist cimetidine and ranitidine have also been able to decrease the pH of gastric secretions.^{38,39} Unfortunately, there are no published studies that show with hard evidence, that antacids or histamine antagonist use decreases maternal mortality from pulmonary aspiration.

Genitourinary System

Genitourinary changes also occur during pregnancy. Urethral length increases as pregnancy progresses owing to passive elongation as the uterus enlarges. Urethral length increases by 4 to 7 mm.⁴⁰ The bladder is drawn passively upward and anterior as the uterus enlarges, becoming more an abdominal organ rather than a pelvic organ. The detrusor muscle hypertrophies due to increased estrogen levels, whereas the bladder becomes hypotonic secondary to increased progesterone. These 2 factors combine to create an increase in bladder capacity. This is limited in the third trimester by fetal engagement, which causes a reduction in bladder capacity.⁴¹ The most significant physiologic urinary tract change is ureteral dilation. Hydroureter is found in almost 90% of pregnancies by the third trimester.⁴² This is caused primarily by mechanical compression by the enlarging uterus, although there is some muscle hypotonia caused by progesterone. The relative urinary stasis may account for the higher incidences of pyelonephritis during pregnancy.

Asymptomatic bacteruria in pregnancy can adversely affect pregnancy outcome. The prevalence of asymptomatic bacteriuria in pregnancy is 2% to 8%.⁴³ The incidence of asymptomatic bacteriuria in pregnancy increases with age parity, sexual activity, presence of sickle cell trait, and lower socioeconomic status.⁴³ Asymptomatic bacteruria may progress to lower and upper urinary tract infection, and 33% of cases will advance to pyelonephritis if not treated.⁴⁴ Theoretically, if pregnant patients have an increased susceptibility to urinary tract infections, then catheter placement should probably be avoided to prevent bacterial seeding. The increase in urinary tract infection due to catheterization has not been studied. Normal pregnancy is characterized by increases in renal plasma flow (RPF) and glomerular filtration rate. RPF increases to a peak 60% to 80% above nonpregnant levels during the second trimester and then decreases to 50% to 60% above normal in the third trimester. Glomerular filtration rate increases to 30% to 50% in the first trimester, but unlike the RPF, the levels are

sustained to term.⁴⁵ This results in increased creatinine, uric acid, and urea clearance levels, with resultant decreases in serum creatinine, blood urea nitrogen, and uric acid levels.⁴⁶ When drugs with renal clearance are used in pregnancy, their doses may need to be increased to account for their more rapid clearance.

Fluid volume levels are also altered during pregnancy. Approximately 6 to 8 L of body water is accumulated during pregnancy, with most of the fluid stored in the extracellular compartment. About 1,200 mL is distributed into the plasma volume. The remainder resides in the interstitial space. Concurrently, serum osmolality drops from 280 to 270 mOsm/kg. This decrease appears to be secondary to a resetting of the osmostat, which causes a release of antidiuretic hormone.⁴⁷

Sodium levels are maintained by an altered homeostasis. Excretion is promoted by the increases in the filtered load of sodium, serum progesterone, and prostaglandin. Increased levels of aldosterone, deoxycorticosterone, and estrogen promote reabsorption. The net result is the retention of approximately 950 mg of sodium during pregnancy.⁴⁸

Anesthetic and Pharmacologic Considerations

While medications are commonly used in oral and maxillofacial surgery practice during pregnancy, careful attention must be given to their effect on maternal and fetal health (Table 2).

LOCAL ANESTHETICS

Pregnancy may affect nerve sensitivity to local anesthetics. The time required for 50% depression of the action potential of A, B, and C vagal fibers from pregnant and nonpregnant animal models was determined after the application of bupivacaine. Onset time for conduction blockade in each type of nerve fiber was faster in fibers from pregnant as opposed to nonpregnant animals and the differences were shown to be highly significant.⁴⁹ Preliminary findings suggest a slowing of nerve conduction velocity in humans with the progression of pregnancy.⁵⁰

Local anesthetics freely cross the placental barrier, so the issue of fetal toxicity must be considered. The majority of amide type agents are bound to α_1 -acid glycoprotein. Pregnancy reduces α_1 -acid glycoprotein levels, resulting in increases of free local anesthetic plasma concentration and thus the potential for toxic reactions, especially in bupivacaine.⁵¹ In general, the direct effects of local anesthesia on the neonate seem to be minimal, even at higher doses. There are few statistically significant effects, and these are transient and so small that they probably

Table 2. SUMMARY OF COMMONLY USED MEDICATIONS IN THE ORAL AND MAXILLOFACIAL SURGERY PRACTICE AND THEIR USE IN PREGNANCY

Drug	FDA Category	Use During Pregnancy	During Breastfeeding
Local anesthetics			
Lidocaine	B	Yes	Yes
Mepivacaine	C	Yes	Yes
Prilocaine	B	Yes	Yes
Bupivacaine	C	No, may cause hypotension	Yes
Analgesia			
Aspirin	C/D	No, associated with IUGR	No
Acetaminophen	B	Yes	Yes
Ibuprofen	B/C	Avoid in third trimester; may close the PDA	Yes
COX-2 inhibitor	C	Avoid in third trimester; may close the PDA	Yes
Codeine	C	Associated with first trimester Malformations; can use in second or third trimester	Yes
Oxycodone	B/C	Yes	Yes
Morphine	B	Yes	Yes
Fentanyl	B	Yes	Yes
Antibiotics			
Penicillins	B	Yes	Yes
Erythromycin	B	Yes	Yes
Clindamycin	B	Yes	Yes
Cephalosporins	B	Yes	Yes
Tetracycline	D	No	No
Sedatives			
Hypnotics			
Benzodiazepines	D	No, risk for fetal craniofacial anomalies	No
Barbituates	D	No, risk for fetal craniofacial anomalies	No
Nitrous oxide	Not assigned	Controversial	Controversial

lack clinical significance.⁵² The Collaborative Perinatal Project showed that the administration of benzocaine, procaine, tetracaine, and lidocaine during pregnancy did not result in an increased rate of fetal malformations.⁵³

When local anesthesia is administered in oral and maxillofacial surgery, it is commonly dispensed in a 1:100,000 epinephrine concentration, or 10 μg mL. There has been a hesitancy to use epinephrine with local anesthesia in the gravid patient. The concern is that the accidental intravascular injection of 15 μg of epinephrine will cause uterine artery vasoconstriction and decreased uterine blood flow. In animal models, the decrease in the uterine blood flow occurs transiently, but the magnitude and duration of this decrease are equal to the decrease in uterine blood flow caused by a single uterine contraction.⁵⁴ However, clinically significant doses of α -adrenergic agents must be avoided to preserve placental perfusion and fetal viability.

GENERAL ANESTHETICS

The use of general anesthesia in the pregnant patient, regardless of the agent used, presents with 3 main considerations in relation to the fetus. The first is maintenance of fetal oxygenation, the second is avoidance of teratogenic agents, and the third is the

prevention of premature labor. Fetal oxygenation is obtained by maintenance of normal maternal Paco_2 and Pao_2 , uterine vascular resistance, and maternal blood pressure.⁵⁵ Hypoxemia can occur with rapid onset during general anesthesia administration in the gravid patient. Short-term administration of high levels of oxygen present no risk to the fetus; even with a maternal Pao_2 of 600 mm Hg, the fetal Pao_2 does not rise above 50 to 60 mm Hg. Thus there is no risk of retroplacental fibroplasia or premature closure of the ductus arteriosus in utero secondary to increased maternal oxygen content.⁵⁵

The normal state of uterine vasculature is wide dilation, but under certain conditions, a severe constriction can occur. Maternal alkalosis, which can commonly be caused by hyperventilation, will cause direct vasoconstriction that will reduce intervillous blood flow. Another common intraoperative cause of uterine vasoconstriction is α -adrenergic vasopressor administration.

Maternal hypotension is probably of the greatest concern intraoperatively. Deep levels of inhalation agents will cause rapid maternal hypotension, which can result in fetal hypoxia. Therefore lighter levels of general anesthesia agents should be used to attenuate surgical stress but not sufficient to decrease maternal blood pressure.⁵⁵ If maternal hypotension does occur,

treatment should be administered immediately. Treatment consists of intravenous fluid administration, repositioning patient to a lateral position, decreasing the anesthetic concentration, and use of an indirect acting vasoconstrictor. Direct acting α -adrenergic vasoconstrictors such as phenylephrine will cause uterine vasoconstriction and must be avoided. Indirect agents like ephedrine are the agents of choice during maternal hypotension.

Of the general anesthetic inhalation agents in use today in oral and maxillofacial surgery, the most common, and potentially the most teratogenic, is nitrous oxide. The potential teratogenic effects of N_2O are related to its ability to inactivate methionine synthetase. Methionine synthetase is responsible for the conversion of homocystiene and methyltetrahydrofolate to methionine and tetrahydrofolate. Methionine is an essential amino acid and tetrahydrofolate is needed for the synthesis of DNA.⁵⁶ The effect has not proved to be clinically significant in humans, but it has been suggested that all patients undergoing anesthesia with N_2O receive prophylactic doses of folic acid, methionine, and vitamin B_{12} . Two studies, following chronic nitrous oxide gas exposure, were reviewed. The first study followed Swedish midwives who were exposed to nitrous oxide. It concluded that night work and high workload increase the risk of spontaneous abortion, not nitrous oxide.⁵⁷ The second study followed female dental assistants. An elevation in risk of spontaneous abortion was seen among women who worked with nonscavenged nitrous oxide for 3 or more hours per week.⁵⁸

Other general anesthetic inhalation agents have been studied for their affects. In animal models, a high incidence of both intrauterine death and congenital anomalies has been reported, but the experimental methods in these investigations allowed for extended exposure to high concentrations of the agents at levels much higher than commonly given doses.⁷ Some studies showed no conclusive teratogenicity has been proved.^{59,60} Exposure to volatile gas agents in the first trimester of pregnancy is estimated to carry a relative risk of 0.5% in humans.⁶¹

Although general anesthetics have minimal risk of teratogenicity, there is a tendency for increased risk of premature delivery. One study showed an approximate premature delivery of 9% with a 7.5% perinatal mortality. The norm for premature delivery in this study was 2.2%.⁶⁰ The difficulty in evaluating this and other studies that compare general anesthetics and premature delivery is that the affect of the agent and the affect of the surgical stress on the patient cannot be differentiated. It is possible that the surgical stress is causing the premature delivery, not the agent.

ANTIBIOTICS

Blood volume and creatinine clearance increase in the pregnant patient. This can lead to a lower serum concentration of antibiotics in the pregnant patient versus the nonpregnant patient.

Most antibiotics do cross the placenta and thus have the potential to affect the fetus. Penicillin, a β -lactam structured cell wall inhibitor, has been used in clinical practice since the 1940s. Of more than 3,500 fetuses included in the Collaborative Perinatal Project, there was no increase in congenital anomalies or other adverse effects after exposure to penicillin in the first trimester.⁶² Penicillin remains the antibiotic of choice in treating the gravid patient with an oral infection.

Cephalosporins are the most commonly prescribed antibiotic in general use today. Although there have been no large studies of the safety of cephalosporin use in pregnancy, there have been no teratogenic effects reported. All cephalosporins, regardless of their generation, have a Food and Drug Administration (FDA) classification B, which is presumed safe based on animal models.

The macrolide family of antibiotics is composed of erythromycin, clindamycin, azithromycin, and clarithromycin. Unlike most other antibiotics, the macrolides cross the placenta only minimally. Erythromycin and clindamycin are used extensively for oral infections in patients with allergies to penicillin or with resistant bacteria. All the macrolides, except clarithromycin are FDA class B. Clarithromycin are class C, which implies uncertain safety.

Aminoglycosides include streptomycin, gentamicin, tobramycin, kanamycin, amikacin, and netilmicin. Gentamicin is the most widely used aminoglycoside during pregnancy. It has an FDA category ranking of C. Gentamicin rapidly crosses the placenta, with peak cord serum levels of approximately 40% of maternal levels in 1 to 2 hours.⁶³ There have been no reported congenital anomalies resulting from gentamicin and no reports of neonatal ototoxicity or nephrotoxicity after in utero exposure.

The use of metronidazole in pregnancy is controversial. The reduced form of the drug is teratogenic, but humans are not capable of reducing metronidazole and so should not be at risk.⁶⁴ It has not been reported as teratogenic in animal models. Although it has not been associated with adverse fetal effects, it is currently recommended for use in the second and third trimesters only, with an FDA classification of B.⁶⁴

Vancomycin is a drug of choice in *C difficile*-induced pseudomembranous colitis, for which vancomycin is administered by mouth. It is also used intravenously for the treatment of methicillin-resistant

Staphylococcus aureus (MRSA). There has been controversy regarding the potential for fetal ototoxicity and nephrotoxicity. It appears that standard doses of vancomycin pose no threat to the fetus; it is listed as FDA category C.⁶⁵

Fluoroquinolones include norfloxacin, ciprofloxacin, ofloxacin, and enoxacin. There are no large epidemiologic studies of the use of fluoroquinolones in pregnancy, but these agents have been reported to cause irreversible arthropathy in immature animals. Their safety during pregnancy is not established.

Sulfonamides are the oldest class of antibiotics, introduced in the 1930s. They are bacteriostatic and interfere with bacterial synthesis of folate. Sulfonamides cross the placenta and reach 75% to 90% of maternal levels within hours. If given before shortly before delivery, they can bind to albumin and displace bilirubin, which can cause hyperbilirubinemia with kernicterus.⁶⁶ However, in one study in which 94 infants were exposed to sulfadiazine in utero, no increased risk of hyperbilirubinemia or kernicterus was found.⁶⁷

Tetracyclines are bacteriostatic antibiotics that reversibly bind the 30S ribosome and inhibit bacterial protein synthesis. They have a very broad spectrum of coverage. Tetracyclines cross the placenta and deposit in fetal decidua teeth, causing yellow-brown discoloration if given after 5 months' gestation.⁶⁸ Despite earlier reports, tetracycline does not cause enamel hypoplasia, and they do not inhibit fibula growth in the preterm infant.⁶⁹ Tetracycline has an FDA classification of D and should be avoided in pregnant patients.

ANALGESICS

Codeine, a common postsurgical analgesia, has been associated with fetal toxicity beneath the maternal toxic doses in mice and hamster models, resulting in decreased fetal body weight. It should be noted that codeine did not induce any increase in structural malformations in mice.⁷⁰ Meperidine and morphine both appear to be safe when administered for anesthesia and analgesia for short periods of time, although chronic use has been shown to cause fetal growth retardation and neonatal withdrawal.⁷

Nonsteroidal anti-inflammatory drugs (NSAIDs) gained popularity in the late 1970s. Inhibition of prostaglandin synthesis by NSAIDs raised concerns about premature fetal ductus arteriosus constriction, which will induce primary pulmonary hypertension and closure, as well as fetal bleeding tendencies.

Obstetricians have discouraged pregnant women from taking analgesic doses of aspirin, mainly because of the wide spread availability of acetaminophen, which causes less gastric irritation, but also because of the concerns listed earlier. These fears were largely

derived from studies on patients taking large doses of aspirin and extrapolations from other NSAIDs.⁷¹ Bleeding tendencies, specifically intracranial hemorrhage, were found only in infants whose mothers had ingested 5 to 10 g of aspirin 5 days before delivery. No bleeding tendencies occurred if the aspirin was taken at least 6 days before delivery.⁷² Most cases reported of premature ductus arteriosus closure occurred secondary to indomethacin administration for tocolysis. Ibuprofen, the most widely used NSAID, had no published reports linking its use with congenital defects.⁷¹ A new class of anti-inflammatory analgesics, cyclooxygenase (COX)-2 inhibitors (celecoxib and rofecoxib) is classified as category C medication based on animal studies. Like other NSAIDs, COX-2 inhibitors should be avoided in late pregnancy because they may cause premature closure of the ductus arteriosus; they are also classified as category C medications.

HYPNOTICS

The use of benzodiazepines has shown increased incidences of cleft palate, central nervous system dysfunction, and dysmorphism after in utero exposure.⁷³ Neurotransmitters regulate palate shelf reorientation. Gamma-aminobutyric acid (GABA) inhibits reorientation. The theory is that benzodiazepines, diazepam specifically, may mimic GABA, thus causing incomplete palatal closure.⁷⁴ Unfortunately, the data for these studies are not reliable, due to a secondary drug exposure variable in the patient pool. Barbiturates have been found to cause congenital anomalies in animals, but teratogenic human affects have not been reported.⁷⁵

Management Modifications for the Gravid Oral and Maxillofacial Surgical Patient

Based on the earlier review of gravid and fetal physiology, the adjustments documented here in the treatment of the pregnant patient should be implemented by the oral and maxillofacial surgeon. Initial assessment includes a comprehensive review of the patient's medical and surgical history. If there is a question of pregnancy, treatment, unless emergent, should be deferred until a definitive documentation of gravid status is obtained, usually by the patient's primary care physician. All elective procedures, such as orthognathic and cosmetic, should be postponed until postpartum. Minor/outpatient oral and maxillofacial surgical procedures should follow some basic guidelines. The supine position should be avoided for a variety of reasons: to avoid the development of the "supine hypotensive syndrome" in which a spine position causes a decrease in cardiac output, resulting in hypotension, syncope, and decreased uteroplacental

perfusion. In addition, the supine position may cause a decrease in arterial oxygen tension (P_{aO_2}) and increase the incidence of dyspepsia from gastroesophageal reflux secondary to an incompetent lower esophageal sphincter. Finally, the supine position poses an increased risk of developing DVT, by compression of the inferior vena cava, leading to venous stasis and clot formation. The ideal position of the gravid patient in the dental chair is the left lateral decubitus position with the right buttock and hip elevated 15°.

Dental radiographs should also be kept to a minimum with appropriate patient shielding and collimation; however, animal and human studies have shown that greater than 10 cGy total exposure to radiation, or more than 5 cGy during the first trimester, is associated with intrauterine growth retardation and congenital fetal abnormalities. A full mouth radiographic examination exposes 0.0001 cGy, and an orthopantomogram delivers 0.008 cGy; thus a minimal use of dental radiographs is acceptable for the gravid patient. A computed tomography scan of the head and neck produces 0.01 cGy. The only radiographs that truly pose a risk to the fetus are pelvic and abdominal films. Head and neck films using a lead shield pose minimal risk to mother or child.

The use of local anesthetics in the gravid patient, as noted earlier, is acceptable, with the standard maximum utilization to avoid toxicity. However, controversy does arise with the use of vasoconstrictors; some practitioners avoid its use, as the vasoconstrictor (usually epinephrine) if injected intravascularly, may result in uteroplacental vasoconstriction with subsequent fetal hypoxia. Ultimately, its use is acceptable as long as care is taken to ensure that no intravascular injection occurs. The use of nitrous oxide is also controversial. It has been found that high doses of nitrous will inhibit the enzyme methionine synthetase, required for production of the essential amino acid methionine. It is therefore thought that the use of nitrous oxide in the gravid patient is acceptable as long as it is less than 50% of the inhalant, with the other part being oxygen. In addition, the patient should be given supplemental vitamins, specifically to replace methionine, as a precaution.

The pregnant trauma patient has some unique considerations: the basic of advanced trauma life support should be followed, keeping in mind that the gravid patient has an increased plasma volume; therefore increased fluid resuscitation is required. Maternal shock decreases uteroplacental blood flow, causing fetal hypoxia—the primary cause of fetal death after maternal trauma. Unless a spinal cord injury is suspected, the gravid trauma patient should be kept in the left lateral decubitus position to avoid the supine hypotensive syndrome. Direct acting vasopressors should also be avoided because they may vasocon-

strict the uteroplacental blood flow. As part of the primary survey, an obstetric consultation and examination are paramount. The maternal genitourinary organs (uterus, bladder, and kidneys) are at increased risk of blunt injury due to their larger, more prone position and as such should be evaluated quickly. Also, evaluation of uterine rupture (abdominal pain, guarding, rigidity, palpation of fetal parts, or inability to palpate the uterine fundus) should be assessed. Fetal heart tones should be assessed as well. As part of the secondary survey, if a diagnostic peritoneal lavage is indicated, it should be performed superior to the umbilicus to avoid penetration of the gravid uterus. Vaginal bleeding coupled with uterine contractions may indicate placental abruption (tearing of the placenta from the uterine wall), which in turn leads to maternal hemorrhage and disseminated intravascular coagulation. Definitive diagnosis is made via ultrasonography, and treatment is removal of the placenta and fetus via cesarean section. Other elements of the gynecologic examination include checking for cervical effacement and assessing the amniotic fluid pH (if 7 to 7.5, may indicate rupture of membranes and impending premature labor). Finally, there may be mixing of the maternal and fetal blood. If the mother is Rh negative and the fetus is Rh positive, maternal antibodies to the Rh factor may develop, causing congenital damage and/or death of the fetus in a subsequent pregnancy. Therefore the gravid patient should be administered RhoGam (Rh immunoglobulin) to minimize the risk of Rh antibody formation.

If maxillofacial trauma occurs in the gravid patient, head and neck computed tomography scans or plain films are acceptable given the minimal radiation exposure (with a lead shield) to rule out facial fractures. If possible, maxillomandibular fixation should be avoided, and maxillofacial fractures treated with rigid fixation. This allows the quick restoration of adequate nutrition. If maxillomandibular fixation is necessary, parenteral nutrition supplementation is recommended. The mucosa of the oropharynx is also friable and easily susceptible to edema; therefore, the airway must be closely monitored for obstruction and subsequent intubation. If endotracheal intubation is not feasible, tracheostomy may be considered. Fetal monitoring should also be followed thorough to ensure uteroplacental perfusion and fetal well-being.

Maxillofacial infections in the pregnant patient should be addressed immediately. The gravid patient is more susceptible to infection for a variety of reasons. Hormonal changes make the mucous more friable, with subsequent chronic gingivitis. In addition, as noted earlier, there is a mild immunosuppression caused by the gravid state. Management of mild infections should be managed via incision/drainage under local anesthetic with subsequent antibiotic coverage.

It is essential to aggressively treat the gravid patient to minimize the risk of infection spreading to the fascial spaces. Fascial space infection should be handled in a standard fashion: airway assessment (if any doubt, intubate), imaging (computed tomography scan), and to the operating room for adequate incision and drainage. Postoperatively, if the patient is unable to maintain oral intake, parenteral nutritional support must be instituted. Until the results of the culture/sensitivity are returned, empirical penicillin therapy is appropriate. More severe infections should be managed in the operating room under general anesthesia with intravenous antibiotics and incision and drainage. Other issues with the gravid patient who is hospitalized for an extended period of time include avoiding bladder catheterization to minimize the risk of urinary tract infections and the use of subcutaneous heparin.

Summary

It is important to remember that treatment is being rendered to 2 patients: mother and fetus. All treatment should be done only after consultation with the patient's gynecologic specialist. If there is an uncertainty about the diagnosis of pregnancy, all treatment (unless emergent) should be postponed unless a definitive determination of pregnancy can be obtained. Patients may be unsure of their pregnancy status. In a study of 12- to 21-year-old females in a day surgery visit, 1 in 200 tested pregnant after universal screening.⁷⁶ With these findings, it is best to avoid drugs and therapy that would put a fetus at risk in all women of child-bearing age for whom a negative pregnancy test has not been ensured.

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