World Journal of Gastroenterology

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DOI: 10.3748/wjg.v20.i41.15241

World J Gastroenterol 2014 November 7; 20(41): 15241-15252
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

REVIEW

Gastrointestinal endoscopy in pregnancy

Nurten Savas

Nurten Savas, Department of Gastroenterology, Baskent Universitesi Hastanesi, 06990 Istanbul, Turkey
Author contributions: Savas N designed and performed the study, and wrote the paper.
Correspondence to: Dr. Nurten Savas, Department of Gastroenterology, Baskent Universitesi Hastanesi, Oymacı Sokak No. 7, Altunizade, 06990 Istanbul, Turkey. nakyurek2000@yahoo.com
Telephone: +90-216-5541500 Fax: +90-216-4749596
Received: January 10, 2014 Revised: May 25, 2014
Accepted: July 29, 2014
Published online: November 7, 2014

Abstract

Gastrointestinal endoscopy has a major diagnostic and therapeutic role in most gastrointestinal disorders; however, limited information is available about clinical efficacy and safety in pregnant patients. The major risks of endoscopy during pregnancy include potential harm to the fetus because of hypoxia, premature labor, trauma and teratogenesis. In some cases, endoscopic procedures may be postponed until after delivery. When emergency or urgent indications are present, endoscopic procedures may be considered with some precautions. United States Food and Drug Administration category B drugs may be used in low doses. Endoscopic procedures during pregnancy may include upper gastrointestinal endoscopy, percutaneous endoscopic gastrostomy, sigmoidoscopy, colonoscopy, enteroscopy of the small bowel or video capsule endoscopy, endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography. All gastrointestinal endoscopic procedures in pregnant patients should be performed in hospitals by expert endoscopists and an obstetrician should be informed about all endoscopic procedures. The endoscopy and flexible sigmoidoscopy may be safe for the fetus and pregnant patient, and may be performed during pregnancy when strong indications are present. Colonoscopy for pregnant patients may be considered for strong indications during the second trimester. Although therapeutic endoscopic retrograde cholangiopancreatography may be considered during pregnancy, this procedure should be performed only for strong indications and attempts should be made to minimize radiation exposure.

Key words: Pregnancy; Endoscopy; Colonoscopy; Endoscopic retrograde cholangiopancreatography; Safety

Core tip: Gastrointestinal endoscopy has a major diagnostic and therapeutic role in most gastrointestinal disorders; however, limited information is available about clinical efficacy and safety in pregnant patients. Endoscopic procedures during pregnancy may include upper gastrointestinal endoscopy, percutaneous endoscopic gastrostomy, sigmoidoscopy, colonoscopy, enteroscopy of the small bowel or video capsule endoscopy, endoscopic retrograde cholangiopancreatography and endoscopic ultrasonography. All gastrointestinal endoscopic procedures in pregnant patients should be performed in hospitals by expert endoscopists and an obstetrician should be informed about all endoscopic procedures.

Savas N. Gastrointestinal endoscopy in pregnancy. *World J Gastroenterol* 2014; 20(41): 15241-15252 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i41/15241.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i41.15241

INTRODUCTION

Although gastrointestinal (GI) endoscopy is usually safe, the safety of this procedure during pregnancy must be evaluated. The best option may be to postpone the procedure until the third trimester or postpartum. When therapeutic intervention is necessary in specific clinical situations, GI endoscopy may be a safe alternative to radiography or surgical intervention.

However, many potential risks are associated with endoscopy during pregnancy[1]. Over sedation may cause maternal hypotension, maternal hypoxia and potentially,

Table 1 General principles for endoscopy in pregnant women[1]

1	Always have a strong indication, particularly in high-risk pregnancies
2	Endoscopy should be postponed to second trimester whenever possible
3	Lowest effective dose of sedative medications should be used
4	Especially category A or B drugs should be used
5	Procedure time should be very short
6	To avoid vena caval or aortic compression, pregnant women should be positioned in the left pelvic tilt or left lateral position
7	Fetal heartbeat should be detected before sedation and also after the endoscopic procedure
8	Obstetric support should be available whenever pregnancy-related complications occur
9	Placental abruption, imminent delivery, ruptured membranes, or eclampsia are defined as obstetric complications of endoscopy

[1]Based on Qureshi *et al*[2] (2005).

fetal hypoxia. The fetus may be exposed to potentially teratogenic drugs, radiation and premature birth risk[1-6]. In addition, the pregnant woman's uterus may apply pressure to the inferior vena cava, causing decreased uterine blood flow and fetal hypoxia. Therefore, the American Society for Gastrointestinal Endoscopy has issued guidelines for endoscopy in pregnant women (Table 1)[2].

The purpose of this article was to review GI endoscopy in pregnancy including indications and treatment options.

FETAL SAFETY OF DRUGS USED IN ENDOSCOPIC PROCEDURES

To prevent hypoxia and hypotension during GI endoscopy, pregnant patients may be positioned in the left lateral position and given prompt intravenous hydration with normal saline or other high osmolar solutions. The use of analgesics and sedatives should be minimized and the endoscopic procedure may be terminated prematurely when necessary[5-6]. A major challenge for anesthesiologists is sedation in pregnant women. Inhalational or local anesthetic drugs have no proven teratogenic effects in humans; however benzodiazepines are associated with congenital anomalies. Any drugs that are given during pregnancy must be used with caution. Antidepressant drugs may affect the fetus because they could cross the placental barrier[5-7].

Endoscopic procedures are associated with teratogenic risk in the first trimester and premature labor in the third trimester. Therefore, endoscopic procedures should be considered with caution in pregnant patients with anesthesiology assistance. The United States Food and Drug Administration (FDA) have defined five categories of drugs in terms of safety to pregnant women (Table 2)[8]. Category A drugs are considered safe during pregnancy and category B drugs also may be used during pregnancy (Table 2). Category C drugs may be used when required during pregnancy, but there may be risks to the fetus. Category D drugs usually are contraindicated during pregnancy and are used only with extreme caution. Category X drugs are absolutely contraindicated during pregnancy (Table 2)[8].

There are no category A drugs that are used for endoscopy. During endoscopic procedures, category B and when necessary, category C drugs may be recommended (Table 3). Category D drugs may be used when the benefits outweigh the risks. These categories are of limited use in determining the safety of one-time use; therefore, consultation with an obstetrician about drugs should be considered. For most procedures, anxiolytic drugs or moderate sedation may be adequate. Heavy sedation, when necessary, should be administered by an anesthesiologist[2].

The opiate analgesic meperidine was commonly used for GI endoscopy for the general population; however, it has been replaced by short-acting analgesics because of adverse events (respiratory depression and seizures) (Table 3). After intravenous administration, meperidine is transferred rapidly across the human placenta and is metabolized to normeperidine, which has a longer half-life than meperidine. Repeated administration of meperidine at high doses may cause progressive accumulation of normeperidine, maternal respiratory depression and maternal seizures. Meperidine is a drug in category B for regular use, but is category D for prolonged use at high doses. Meperidine use should be limited to 50-75 mg for endoscopic procedures in pregnant women[4,5,9]. Fentanyl (category C) is a potent narcotic that has a rapid onset of action and a shorter recovery time than meperidine; fentanyl is usually safe in low doses (< 125 mg) during pregnancy (Table 3)[2-5].

Benzodiazepines (diazepam and midazolam) are commonly used before GI endoscopy to reduce anxiety, induce brief amnesia and produce muscle relaxation. Prolonged use of diazepam during early pregnancy may be associated with cleft palate malformations; however, this association is unproven[10-13]. The use of diazepam in the first trimester of pregnancy, however, is not safe because of a strong relation between diazepam use and mental retardation or neurological defects, cardiac defects and Mobius syndrome (a neurological disorder with normal intelligence but sixth and seventh nerve palsies)[11,14,15]. There are limited data about the use of midazolam, but there is no known association of midazolam with oral cleft palate. However, midazolam may be associated with transient depression of neonatal neurobehavioral responsiveness during labor[16,17]. When meperidine cannot be used, the preferred benzodiazepine is midazolam (category D) because associated fetal abnormalities have not been reported.

Propofol (category B) is commonly used for anesthesia during endoscopy. It is a short-acting anesthetic agent with a short recovery period. It is usually administered by anesthesiologists because of its narrow therapeutic index and potential for respiratory depression. Endoscopy societies have recommended the use of propofol for patients who are difficult to sedate or have complicated clinical situations. Propofol is considered safe during pregnancy, but there are insufficient data available about the use of

Table 2 United States food and drug administration categorization of drug safety during pregnancy[1]

Category	Risk	Description
A	No risk has been shown in controlled studies	Sufficient, well-controlled studies have not demonstrated a risk to the fetus in any trimester of pregnancy
B	No risk in humans	Sufficient, well-controlled studies have not demonstrated an increased risk of fetal abnormalities despite adverse findings in animals or, in the absence of adequate human studies, animal studies show no fetal risk. The chance of fetal harm is very low but still is a possibility
C	Risk cannot be ruled out	Sufficient, no well-controlled human studies, where animal studies have shown a risk to the fetus. There is a chance of fetal harm if the drug is administered during pregnancy, but the potential benefits should be considered and may outweigh the potential risk
D	Positive evidence of risk	Studies in humans, or investigational or postmarketing data, have demonstrated fetal risk. Nevertheless, potential benefits from the use of the drug may outweigh the potential risk. For example, the drug may be acceptable if needed in a life-threatening situation or for serious disease for which safer drugs cannot be used or are ineffective
X	Contraindicated in pregnancy	Studies in animals or humans (investigational or postmarketing reports) have demonstrated positive evidence of fetal abnormalities or risk that clearly outweighs any possible benefit to the patient

[1]Adapted from Food and Drug Administration (1980)[8].

Table 3 Safety of anesthetics commonly used in gastrointestinal endoscopy

Drug	FDA category in pregnancy	Key points about drug safety
Narcotics		
Meperidine	B, but D at term	Repeated use of high dose and prolonged administration can cause respiratory depression and seizures
Fentanyl	C	It is safe in low doses
Propofol	B	Generally suggested for use in patients who are sedated with difficulty and in complicated clinical situations
General anesthetics		
Ketamine	B	Data are limited with humans; animal data suggest prolonged use is not safe
Sedatives		
Diazepam	D	Some congenital malformations and mental retardation may be associated with diazepam, the use of diazepam during pregnancy is restricted
Midazolam	D	As a benzodiazepine member, its use is restricted during pregnancy, especially in the first trimester
Reversing agents		
Naloxone	B	It probably is safe but should be used only in respiratory depression, systemic hypotension, or unresponsiveness in a closely monitored pregnant woman after endoscopy
Flumazenil	C	Fetal risks are unknown, but it should be given carefully in small doses

FDA: United States Food and Drug Administration.

propofol in the first trimester[4,5,18].

Ketamine (category B) can be used for endoscopy when there is insufficient sedation with propofol. Ketamine has a rapid onset of action and a short duration of effect, but data are limited about use of ketamine during the first trimester of pregnancy, prolonged use or overdose[19].

Naloxone (category B) is a fast-acting narcotic antagonist that may be administrated to reverse narcotic overdose during endoscopy. Naloxone crosses the placenta within 2 min[2,20]. It is used to treat respiratory depression, systemic hypotension or unresponsiveness in closely monitored settings during or after endoscopy. Naloxone is given in small, graded doses and titrated to the required effect during pregnancy, because there has been one neonatal fatality that was attributed to naloxone use[21]. Naloxone is contraindicated in narcotic-dependent pregnant patients because of the risk of opiate withdrawal syndrome[22]. Flumazenil (category C) is a benzodiazepine antagonist that is used to reverse over sedation from benzodiazepines that are administered during endoscopy. Its fetal risks during pregnancy are unknown and is used only to reverse benzodiazepine overdose. Flumazenil overdose may cause maternal seizures, especially when given to patients who are chronically habituated to benzodiazepines. The risk of benzodiazepine overdose may be minimized by careful and slow titration of minimal doses of benzodiazepines required for endoscopy[19-23].

UPPER GASTROINTESTINAL ENDOSCOPY

It would be ideal to postpone endoscopic procedures until after delivery; however, pregnant patients may develop conditions that require urgent upper endoscopy. The most common indications for esophagogastroduodenoscopy (EGD) in pregnant patients include major or continued GI hemorrhage, dysphagia, and refractory nausea and vomiting (Table 4). The EGD procedure is reasonably safe for the fetus and may be performed when strongly indicated during pregnancy.

In a multicenter retrospective study of 83 pregnant women concerning the safety and clinical efficacy of EGD in pregnant patients, indications for endoscopy in-

Table 4 Indications for endoscopy in pregnancy

No.	Indication
1	Major or continued bleeding
2	Severe or refractory nausea and vomiting or abdominal pain
3	Dysphagia or odynophagia
4	High suspicion of colonic mass
5	Severe diarrhea with negative evaluation
6	Biliary pancreatitis, CBD stones, or cholangitis
7	Biliary or pancreatic ductal injury

Based on American Society for Gastrointestinal Endoscopy.

cluded GI bleeding, abdominal pain and vomiting[24]. The most common causes of the GI bleeding were Mallory-Weiss tear and peptic ulcer, which were significantly lower than the reported frequencies in non-pregnant patients The diagnostic yield for upper GI bleeding was 95% and there were no patients who had premature labor or congenital fetal malformation.

During pregnancy, increased progesterone and estrogen levels mediate lower esophageal sphincter relaxation, with 50% decreased lower esophageal sphincter pressure during, compared with before, pregnancy and decreased gastric emptying that may cause symptoms of gastroesophageal reflux disease (GERD). As pregnancy progresses, the frequency and intensity of GERD symptoms may increase because of changes in GI motility during pregnancy and the physical effects of the gravid uterus[25,26]. The EGD procedure is rarely helpful or indicated for nausea or vomiting during pregnancy or hyperemesis gravidarum. In patients who have major upper GI bleeding, severe nausea and vomiting accompanied by abdominal pain that is refractory to medical treatment or signs of gastroduodenal obstruction, EGD may be appropriate for diagnosis of major peptic ulcers, diagnosis of gastric outlet obstruction or treatment of a bleeding site. Debby *et al*[27] reported a study of patients who had EGD in the first trimester of pregnancy, in that study, 49 patients had intractable nausea with or without epigastric pain and 11 patients had nausea and upper GI bleeding; the diagnostic yield of EGD was similar for patients who had GI bleeding or intractable vomiting. The endoscopic findings changed the treatment of patients who had nausea and vomiting minimally, and they concluded that EGD may be useful for treatment of upper GI bleeding, but not nausea, vomiting or hyperemesis gravidarum[27].

Acute nonvariceal upper GI bleeding (NVUGB) is a common clinical emergency that causes 50-160 hospitalizations per 100000 adults annually. Mortality may be decreasing but remains at 10%-14%[28]. Endoscopy for NVUGB may provide an assessment of the risk of rebleeding and enable therapeutic hemostasis that could reduce bleeding, frequency of surgery and risk of death. In a population-based study of NVUGB, there were 1210 pregnant women and 6050 nonpregnant women who had NVUGB. The most common causes of NVUGB were Mallory-Weiss tear in pregnant women and peptic ulcer disease and gastritis in nonpregnant women[29]. Pregnant women had lower frequencies of blood transfusion, hypovolemic shock or EGD than nonpregnant women. The proportion of EGD procedures that led to therapeutic intervention was similar for pregnant (8.9%) and nonpregnant women (7.2%). The frequency of maternal mortality and fetal loss were < 1% and it was concluded that it was appropriate to defer endoscopy in most patients who were hemodynamically stable and who had self-limited NVUGB[29].

Patients who have cirrhosis are not likely to become pregnant because they may have hypothalamic-pituitary dysfunction and associated disturbance of estrogen and endocrine metabolism. The exact incidence of pregnancy in cirrhosis is not known, but only 45 cases of cirrhosis occur in every 100000 women of reproductive age. On the other hand, women with noncirrhotic portal hypertension have normal frequency of fertility and these patients may have 45% incidence of variceal bleeding during pregnancy and 18%-50% associated mortality. The variceal bleeding typically occurs during the second or third trimester. The high severity of variceal bleeding in pregnancy may be attributed to increased fluid retention and cardiac output in pregnancy. Women who have esophageal varices or severe liver disease should be advised about the high risk of variceal bleeding and hepatic decompensation during pregnancy. Nonselective β-blockers may be given to patients who have esophageal varices or severe liver disease, but the safety of β-blockers is controversial because of reports of premature labor, fetal growth restriction, neonatal apnea, bradycardia and hypoglycemia. Furthermore, myometrial relaxation of the gravid uterus is a β_2-receptor-mediated process and nonselective β-blockers, such as propranolol, may counteract the effect of β_2-receptor stimulation. The pregnant patient should be informed about the possible benefits and adverse effects of β-blockers during pregnancy.

THERAPEUTIC ENDOSCOPY

Endoscopic hemostatic techniques for nonvariceal bleeding include injection therapy (epinephrine, sclerosing agents, thrombin or cyanoacrylate), ablative therapy (electrocoagulation, thermocoagulation, photocoagulation or argon plasma coagulation), and compression (hemoclips, detachable snares, graspers or sutures)[30]. Although there are numerous techniques, there are few case reports about the fetal safety of endoscopic hemostasis for NVUGB, including epinephrine injection, thermocoagulation or electrocoagulation. In the available reports, hemostatic techniques were successful in all patients except for one patient who required surgery. The fetal outcomes were all healthy infants without any fetal malformations[24,27,30,31].

Epinephrine (category C) may cause a decrease in uterine blood flow. Although there are limited data from case reports, no adverse events from epinephrine injection have been reported and the benefits (cessation of hemorrhage and prevention of rebleeding) may outweigh the risks[1,2,26,32]. Electrocautery is safe when used for hemostasis, but amniotic fluid may conduct electrical cur-

rent to the fetus; therefore, during electrocoagulation, a grounding pad should be placed such that the uterus is not between the electrical cord and the grounding pad, and bipolar electrocautery should be used to minimize the risk of stray current going through the fetus.

There are limited data about hemostasis for nonvariceal bleeding in pregnant patients, and the therapeutic technique is chosen from expert opinion that is based on results of clinical studies in nonpregnant patients. Prophylactic or urgent endoscopic injection sclerotherapy (EIS) and endoscopic band ligation (EBL) are safe procedures during pregnancy. When bleeding is not stopped endoscopically in cirrhotic patients, an emergency transjugular intrahepatic portosystemic shunt (TIPSS) is indicated, but data about pregnant cirrhotic women are limited[33-39]. There are only a few case reports about the treatment options for esophageal varices, and further studies are needed about the treatment of hemorrhage during pregnancy. In the early 1980s, EIS was a first-line treatment procedure for bleeding esophageal varices. However, only a few cases of EIS with sclerosing agents (polidocanol, absolute alcohol or sodium tetradecyl sulfate) have been reported during pregnancy[36-39]. There are no studies available about the effects of these sclerosing agents on the fetus; however, the procedure is considered safe and effective in controlling active variceal bleeding. Vasoactive drugs that are used to achieve hemostasis are contraindicated during pregnancy because these drugs (vasopressin and terlipressin) may induce labor or fetal malformations.

EBL may be an effective treatment option for active variceal hemorrhage and prophylaxis for this severe complication during pregnancy. There are several case reports that describe successful hemostasis without fetal complications[40-41]. When EBL is used, there is no risk of migration of a toxic substance to the placenta. Studies of EBL *vs* EIS in nonpregnant patients have shown improved reduction in rebleeding and mortality with EBL[40,42]. However, there are no studies that directly compare EBL to EIS in pregnant patients.

In a previous study, 17 patients had acute variceal bleeding during pregnancy because of noncirrhotic portal hypertension that was caused by extrahepatic portal vein obstruction or portal fibrosis. These patients underwent EIS with either absolute alcohol or sodium tetradecyl sulfate[43]. There were two patients who required EBL after failure of EIS to obliterate esophageal varices[43]. In an another report, 10 patients underwent EIS with absolute alcohol for treatment of active variceal bleeding (five patients) or prophylaxis against variceal bleeding (five patients). Hemostasis was achieved in the five patients who had active variceal bleeding and all 10 patients delivered healthy infants[44]. In pregnant patients, EBL may be a reasonable option for the treatment of acute variceal bleeding and prophylaxis against variceal bleeding. EIS may be a secondary choice for acute variceal bleeding because of probable detrimental effects on fetal safety.

When endoscopic and pharmacologic therapy fail, TIPSS may be a salvage procedure for pregnant women who have variceal bleeding that is recurrent, difficult to treat or unresponsive to endoscopic or pharmacologic treatment. However, adequate controlled trials are lacking, and this procedure should be limited to a selected group of patients. TIPSS placement is associated with radiation exposure to the patient and fetus because the procedure usually requires prolonged fluoroscopy. There are several reported cases of TIPSS placement in pregnancy in which the fetal dose of radiation was 5.2 mSv to 2.1 mGy[35,45,46].

The average person in the United States receives 0.0036 Sv (0.36 rem) ionizing radiation annually, including 0.0006 Sv (0.06 rem) from manmade sources, such as diagnostic radiography. Fetal radiation exposure may cause developmental abnormalities, especially when the exposure occurs during the first trimester. Fetal radiation exposure should not exceed 0.001 Sv (0.1 rem) during the first trimester and later exposures > 0.001 Sv (0.1 rem) during neuron development and migration may be associated with microcephaly, seizures, decline in mental ability and childhood cancer. The maximum permitted dose of ionizing radiation to the fetus during the entire pregnancy is 0.005 Sv (0.5 rem)[47-49]. Therefore, in patients who have upper GI bleeding all therapeutic procedures that are used in nonpregnant patients can also be used in pregnant patients. In cirrhotic patients, pregnancy is not an absolute contraindication for TIPSS placement for the treatment of relapsing bleeding varices, but minimizing the duration of radiation exposure is important to prevent toxic radiation exposure to the fetus.

PERCUTANEOUS ENDOSCOPIC GASTROSTOMY

During pregnancy, optimal nutrition is important to minimize maternal and neonatal morbidity[50,51]. Nausea and vomiting are observed in 80% pregnancies but are usually mild and self-limited. Patients who have severe hyperemesis gravidarum with dehydration and ketonuria should be hospitalized and treated with intravenous hydration and antiemetic drugs. When the hospitalization is prolonged and there is no oral intake, supportive nutrition with enteral feeding or total parenteral nutrition may be considered. Long-term nasogastric feeding is limited by patient intolerance and nasal septal necrosis. Adverse events may limit the use of long-term total parental nutrition during pregnancy[52].

Percutaneous endoscopic gastrostomy (PEG) is an important option for long-term enteral feeding. Placement of PEG tubes in pregnant women may be limited because of risks of uterine damage, fetal injury, premature labor and infection, but there were no major complications associated with PEG tube placement in several reported cases[53-60]. In previous studies, PEG enteral nutritional support was provided for an average 14 wk. During pregnancy, PEG tube placement is feasible for optimal enteral nutrition in the critical care setting and in the third trimester of pregnancy. A major risk of PEG

during pregnancy is puncture of the uterus or fetus during transabdominal needle insertion, but this risk may be minimized by demarcating the upper border of the uterus before PEG and inserting the PEG needle ⩾ 5 cm cephalad.

Placement of a PEG tube is reserved for severe refractory cases of impaired nutrition of the mother and fetus. The pregnant woman should be informed about the risks of the procedure and potential placental injury. If possible, less invasive alternative techniques, such as a nasoenteric feeding tube or peripherally inserted catheter for parenteral nutrition, should be considered, and PEG tube placement may be offered when other methods are unsuccessful or declined by the patient. When refractory nausea and vomiting persist despite PEG tube placement, and the risk of aspiration pneumonia is increased, the PEG may be converted to a percutaneous endoscopic gastrojejunostomy[50,61].

SIGMOIDOSCOPY

Most pregnant patients are young, healthy women and the gestational period is 40 wk. Therefore, most patients do not need to have flexible sigmoidoscopy or colonoscopy during pregnancy. Lower GI endoscopy is avoided for weak indications during pregnancy and deferred until after the first trimester or postpartum[62]. However, sigmoidoscopy or colonoscopy is indicated for the evaluation of major lower GI bleeding, suspicion of colonic mass or severe diarrhea.

Sigmoidoscopy is usually safe during pregnancy and indications include rectal bleeding, chronic diarrhea, abdominal pain and rectal pain. Guidelines for colonoscopy during pregnancy are limited because of insufficient data, but colonoscopy is typically safe and effective when obstetrical consultation and close monitoring are performed[63,64].

The safety and efficacy of flexible sigmoidoscopy during pregnancy was studied in a case controlled study of 45 patients undergoing sigmoidoscopy[65]. In that study, the most common clinical indication was hematochezia in 29 patients, diarrhea in 10 patients and abdominal pain in 4 patients. The most common sigmoidoscopic diagnoses were reactivated or newly diagnosed inflammatory bowel disease, bleeding internal hemorrhoids and other types of colitis. In 29 patients who had hematochezia, 8 patients had *de novo* or recurrent episodes of ulcerative colitis, 7 patients had *de novo* or recurrent episodes of Crohns disease, 3 patients had proctosigmoiditis, 2 patients had bleeding internal hemorrhoids, 1 patient had pseudomembraneous colitis and 1 patient had a sigmoid colon adenoma. Hematochezia gave the highest diagnostic yield compared with other clinical indications. Therapeutic changes because of the sigmoidoscopic findings occurred in 24 patients, including changing or starting drugs for inflammatory bowel disease in 15 patients, steroid enemas for nonspecific proctitis in 2 patients, avoiding surgery in 2 patients and treatment of hemorrhoids in 2 patients.

Other studies of sigmoidoscopy performed during pregnancy have included case reports and a mailed survey[26,66-70]. Multiple case reports describing flexible sigmoidoscopy in pregnant patients have confirmed the safety of this procedure. These studies suggested that sigmoidoscopy during pregnancy may not induce labor or cause congenital malformations. Thus, sigmoidoscopy is not contraindicated and may be considered in medically stable patients who have important indications. Sigmoidoscopy should be performed with maternal monitoring (electrocardiography and pulse oximetry) after obstetric consultation and after medical stabilization. Medical stabilization may include blood transfusion and supplemental oxygen[62,64]. For evaluation of a change in bowel habits, abdominal pain, family history of colon cancer or routine screening or surveillance, sigmoidoscopy is not recommended during pregnancy but is deferred until > 6 wk postpartum[63,64].

COLONOSCOPY

There are insufficient data about the safety of performing a colonoscopy during pregnancy. The largest case control study about colonoscopy in pregnancy included 20 patients who were evaluated for symptoms including hematochezia, diarrhea, bloody diarrhea and abdominal pain[71]. In that study, colonoscopy was performed in 16 patients in the second trimester and in 4 patients in the first or third trimester; colonoscopic diagnoses included ulcerative colitis, Crohn disease, ischemic colitis and lymphocytic colitis. Colonoscopy resulted in a change in therapy in seven (35%) patients. Most patients had favorable fetal outcomes (18 healthy infants) and there was one involuntary abortion and one infant who was born with a cardiac defect (septum secundum)[71].

In another study of eight pregnant women who had colonoscopy (10 different medical centers) there were 6 healthy infants born, 1 elective abortion and one fetal death that was unrelated to colonoscopy[65]. Outcomes were independent of the trimester during which colonoscopy was performed. In addition, several case reports about colonoscopy during pregnancy have shown 8 healthy births, 2 stillbirths unrelated to colonoscopy and 1 unknown fetal outcome[72-80].

With limited data about safety and adverse events, colonoscopy should be limited to patients who have strong indications or life-threatening emergencies during the second trimester. However, colonoscopy may be considered in lieu of surgery during the first and third trimester for evaluation of suspected colon cancer, colonic mass, uncontrolled severe colonic hemorrhage, colonic stricture of unknown cause or colonic pseudo-obstruction. When required before urgent colonic surgery, colonoscopy should be considered, even in the first and third trimester. Otherwise, colonoscopy for elective indications, such as surveillance for prior history of colon cancer or colonic polyps usually is deferred in any trimes-

ter until after delivery.

When colonoscopy is performed, especially in late pregnancy, patients should not be placed in the decubitus or prone position. External abdominal pressure should be avoided and when required, applied pressure should be minimal and directed away from the uterus. Limited information is available about the safety of bowel cleansing agents during pregnancy. The systemic absorption of polyethylene glycol is minimal and abdominal bloating and gas symptoms are less common with polyethylene glycol than with other laxatives[81]. However, polyethylene glycol solutions (category C) have not been studied during pregnancy. Sodium phosphate solutions (category C) may cause fluid and electrolyte disturbance, and should be avoided during pregnancy. In addition, newborns may have bone demineralization and bone growth failure because of maternal phosphate overload[82], but one-time use in pregnancy may not be detrimental. Furthermore, sodium phosphate preparations may be associated with the risk of phosphate nephropathy[83]. Bowel preparation with phosphate enemas before flexible sigmoidoscopy may be safe, but has not been studied in pregnancy. Underprepared sigmoidoscopy is generally not recommended because of the risk of overlooking lesions; instead, sigmoidoscopy with tap water enemas may be sufficient.

Therefore, flexible sigmoidoscopy with tap water enemas is preferred instead of colonoscopy. However, in patients who have strong indications or life-threatening emergencies or when the alternative treatment is surgical decompression, colonoscopy may be considered, even during the first and third trimesters.

THERAPEUTIC COLONOSCOPY

Therapeutic colonoscopy is applied for the management of lower GI bleeding, colonoscopic polypectomy and colonic stenting. All the hemostatic techniques that are mentioned above for upper GI bleeding can be applied during lower GI bleeding. These are mainly injection therapies, ablative therapies, hemoclips, detachable snares, graspers, or sutures[30]. Epinephrine is commonly used to treat GI bleeding and may cause hemostasis by vasoconstriction. Numerous studies have confirmed the fetal safety of epinephrine administration during labor, and epinephrine is commonly added to spinal epidural anesthesia. A previous study showed no congenital defect in 35 infants who had first trimester in utero exposure to epinephrine[10]. However, the dosage of epinephrine (category C) during pregnancy is kept low because of α-adrenergic effects and decreased uterine blood flow.

Electrocautery may provide hemostasis during lower GI bleeding and is used during polypectomy or biopsy. Electrocautery of lesions may be required, in which case bipolar electrocautery should be used. Removal of nonbleeding polyps may be postponed until after delivery[4,5,62].

Colonic tattooing is performed with India ink or methylene blue in nonpregnant patients, and India ink may persist for the entire life of the patient. A literature search showed no reports of long-term complications of India ink tattooing. Although methylene blue tattooing during pregnancy has not been studied, there are reports of methylene blue examination during amniocentesis and in the detection of ruptured membranes. In these reports, fetal death and jejunal atresia were reported and methylene blue has been labeled as teratogenic. Although the safety of colonic injection with methylene blue has not been studied, its use should be avoided during pregnancy[62,84,85].

ENTEROSCOPY AND VIDEO CAPSULE ENDOSCOPY

Enteroscopy of the small bowel is a procedure with long duration and anesthesia time. There are no case reports of enteroscopy during pregnancy and the safety of enteroscopy to the fetus is unknown.

Video capsule endoscopy (VCE) is a major advance in the investigation of small bowel diseases. The main indications include obscure GI hemorrhage, Crohn's disease, celiac disease, small bowel tumors and polyposis syndromes. The main contraindications include known or suspected GI obstruction, strictures, fistulas, cardiac pacemakers and swallowing disorders[86]. During pregnancy, the growing gravid uterus pushes and compresses the GI tract, and GI motility decreases because of inhibition of the intestinal smooth muscle by gestational progestin. These effects raise concerns about capsule impaction during VCE in pregnant women[87]. According to the United States FDA, pregnancy is a relative contraindication for VCE.

There is a report of VCE use in a young, acutely bleeding pregnant patient in whom endoscopy and colonoscopy showed no lesion except fresh blood exiting the terminal ileum. On VCE, an actively bleeding jejunal lesion was shown and pathological examination showed that this lesion was a jejunal carcinoid tumor. After the procedure the pregnant patient and fetus did well[88]. Therefore, VCE may be considered during pregnancy for strong indications, and it is not absolutely contraindicated during pregnancy.

ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

Pregnancy is associated with an increased risk of gallstone formation. Complications of cholelithiasis, such as cholecystitis, common bile duct (CBD) stones and pancreatitis are uncommon, and are frequently treated nonoperatively. However, patients may develop complications of gallstones that require intervention during pregnancy, and these complications are among the most frequent indications for nonobstetric surgery during pregnancy[89-93].

There is controversy about the safety of endoscopic retrograde cholangiopancreatography (ERCP) during pregnancy, and data are limited. Major concerns are asso-

ciated with radiation exposure to the fetus and the risk of the procedure on the outcome of pregnancy. In women who have an acute biliary tract disorder during pregnancy, it is advisable to provide nonoperative treatment whenever possible and delay surgery until after pregnancy or the second trimester, when the surgical risks of pregnancy are lowest. There are numerous reports about ERCP during pregnancy, especially during the past 10 years. The largest series included 65 pregnant patients, and the most common indications for ERCP during pregnancy were recurrent biliary colic, abnormal liver function tests and a dilated bile duct on ultrasonography[94]. There were 68 ERCP procedures performed in 65 pregnant patients (trimester: first, 17 patients; second, 20 patients; third, 31 patients). The median fluoroscopy time was 1.45 min and most patients had a therapeutic procedure. Pancreatitis after ERCP developed in 11 patients (16%), but no patient had a severe course. Most patients achieved term pregnancy (89%); only 5 babies (8%) were born prematurely or with low birth weight, and there were no congenital malformations[94].

In another series of 23 patients who had ERCP (therapeutic, 20 patients; diagnostic, 3 patients), complications included pancreatitis after ERCP (1 patient), spontaneous abortion (1 patient) and neonatal death at 26 h after delivery (1 patient)[95]. The neonatal death and post-ERCP pancreatitis occurred in the same patient who had three ERCP procedures (2 during the first trimester; 1 during the third trimester) with pancreatic duct stenting for treatment of pancreatic orifice stenosis after a previous surgical sphincteroplasty.

In a study of 18 pregnant women who had biliary sphincterotomy for CBD stones during pregnancy (trimester: first, 4 patients; second, 6 patients; third, 8 patients), short-term complications occurred in 2 patients (postsphincterotomy bleeding, 1 patient; mild post-ERCP pancreatitis and preterm labor, 1 patient); however, no long-term maternal complications were observed after a median of 6 years (range, 1-11 year)[96]. In 11 families that were contacted retrospectively, all 11 children were healthy at a mean of 6 years postpartum[96].

In a prospective study of therapeutic ERCP during pregnancy, a single 10-French stent was placed without sphincterotomy and all patients had uncomplicated pregnancy and delivery of healthy infants[97]. All women had ERCP with sphincterotomy and stent extraction postpartum: eight patients had stones extracted. In two patients, the 10-French stent remained in place for 7 to 8 mo and no patient developed cholangitis[97].

During ERCP, radiation exposure to the fetus may increase the risk of intrauterine fetal death, malformations, disturbance of growth and development, mutations and cancer. Therefore, these risks should be discussed with the pregnant patient and her family before ERCP. Lead shielding should be used to minimize radiation exposure to the uterus. When the radiation source is underneath the patient, the lead apron shield must be placed underneath the patient and not draped over the abdomen. External shielding may not completely eliminate fetal exposure because of internally scattered radiation, and efforts should be made to avoid performing ERCP during the first trimester. Although the harmful effects of radiation exposure are unlikely to develop below a threshold radiation dose, the threshold associated with the risk of childhood cancers, such as leukemia, is unknown and no long-term studies (10-20 years after exposure during pregnancy) are available.

The use of ERCP without fluoroscopy has been reported, including a 2-step procedure with (1) biliary sphincterotomy and stenting without fluoroscopy and (2) definitive ERCP with stone extraction after delivery[98,99]. In this study, initial CBD cannulation was performed with a double lumen sphincterotome; deep cannulation was achieved and bile was aspirated to confirm CBD position[98]. After deep CBD cannulation, the guide wire was passed and complete biliary sphincterotomy was performed over the guide wire. When deep CBD cannulation was not possible, the sphincterotome was removed and needle knife sphincterotome was used. After the biliary orifice was identified, a complete biliary sphincterotomy was performed using a double lumen sphincterotome. A 7-French double pigtail stent was placed in the CBD. After delivery the stent was removed and definitive ERCP was performed[98].

In another study of ERCP without fluoroscopy, the procedure included cannulation of the bile duct and sphincterotomy[99]. The endoscopist controlled the wire-guided cannulation, and the cannula was not advanced into the duct unless the endoscopist was confident that the CBD had been cannulated (as assessed by the presence of bile flowing around the wire from the papillary orifice). After biliary cannulation was confirmed, a wire-guided biliary sphincterotomy was performed using a papillotome. When bile was not observed flowing around the guide wire, the catheter was not advanced to aspirate fluid, but a 5-French stent was inserted over the wire and drainage from the stent was observed. The color of the draining fluid was used to assess whether the stent was in the bile or pancreatic duct. When the stent showed bile flow, a stent-guided biliary sphincterotomy using a needle knife was performed. The stent was removed after biliary sphincterotomy[99].

Although these techniques may be less risky for the pregnant woman and fetus, ERCP should be avoided for weak indications, such as preoperative cholangiography in patients who have low probability of having CBD stones. All women of childbearing age should be asked about the possibility of pregnancy and a pregnancy test should be ordered based on clinical history. Other methods of diagnosis without radiation exposure should be considered. Magnetic resonance cholangiopancreatography may provide diagnostic information for various hepatobiliary conditions, and endoscopic ultrasonography is highly sensitive and specific for CBD stones. However, ERCP with or without fluoroscopy is indicated in patients who have CBD stones, biliary pancreatitis, cholangitis and bile

duct dilation on abdominal ultrasonography with known gallstones and abnormal liver function tests.

ENDOSCOPIC ULTRASONOGRAPHY

Endoscopic ultrasonography is commonly performed for the diagnosis of GI and pancreatobiliary diseases. Endoscopic ultrasonography may reduce unnecessary interventions in patients who have a low or moderate probability of developing CBD stones and it is a safe alternative to fluoroscopy for the evaluation of biliary disorders during pregnancy. Case reports about the use of endoscopic ultrasonography for pregnant patients are available. The largest study included endoscopic ultrasonography performed in six pregnant patients for suspected CBD stones[99] Endoscopic ultrasonography findings in this study included CBD stones (two patients), biliary sludge (two patients) and nonspecific findings (two patients). All six patients had ERCP after endoscopic ultrasonography and there were no maternal complications; fetal outcome was favorable for five infants and unknown for one infant[99].

In another report, endoscopic ultrasonography was performed for acute pancreatitis of unknown cause in three pregnant patients. Biliary pancreatitis without CBD stones was observed in two patients and pancreatitis caused by an unspecified pancreatic anomaly was observed in one pregnant patient. There were no reported maternal complications and two healthy infants were delivered; however, there was one fetal death because of recurrent cholangitis at 10 wk after endoscopic ultrasonography[100].

Endoscopic ultrasonography may prolong the evaluation. However, when endoscopic ultrasonography is normal, ERCP intervention may be avoided. In addition, endoscopic ultrasonography may provide other useful information, and the added time for endoscopic ultrasonography may be only several minutes. Further studies are required to evaluate the potential benefits of endoscopic ultrasonography in the treatment of pregnant patients. It may be acceptable to perform endoscopic ultrasonography when CBD stones are suspected, the diagnosis is unproven and magnetic resonance cholangiopancreatography is an undesirable alternative.

CONCLUSION

All GI endoscopic procedures in pregnant patients should be performed in hospitals by expert endoscopists, and an obstetrician should be informed about all endoscopic procedures. GI endoscopy may be performed safely in pregnant patients when there are strong indications. To minimize fetal risks from drugs during endoscopy, category D drugs should be avoided, drug use should be minimized and an anesthesiologist should attend at endoscopy. The EGD and flexible sigmoidoscopy may be safe for the fetus and pregnant patient and may be performed during pregnancy when strong indications are present. Colonoscopy for pregnant patients may be considered for strong indications during the second trimester. Although therapeutic ERCP may be considered during pregnancy, this procedure should be performed only for strong indications and attempts should be made to minimize radiation exposure.

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P- Reviewer: Akyuz U, Farmer AD, Tang D **S- Editor**: Qi Y
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ISSN 1007-9327