New Sterilization Device Nears Market

BY PATRICE WENDLING
Chicago Bureau

The Adiana transcervical sterilization system appears to be easy to use, safe, and effective, according to phase III data, Dr. Alan Johns reported at the annual meeting of the AAGL (formerly the American Association of Gynecologic Laparoscopists).

The Adiana Complete system is available only for experimental use, but U.S. Food and Drug Administration submission is anticipated in mid-2006, said Dr. Johns, one of the clinical investigators in the trial.

The FDA approved Essure, currently the only nonincisional approach to female sterilization, in November 2002.

The Adiana system "is the next step in the evolution of hysteroscopic devices," Dr. Johns said in an interview. It may be better than Essure simply because it doesn't require as much manipulation and the whole device is altogether shorter and easier to put in and cannulate, he said.

"More importantly, in contrast to the Essure system, after the Adiana matrix has been deployed, nothing remains in the endometrial cavity."

This may be important in women who subsequently choose to undergo in vitro fertilization or endometrial ablation, because these options can be limited by the presence of a portion of a device in the endometrial cavity, he said.

The Adiana system also differs from Essure in that it uses radio frequency energy before the placement of the polymer matrix in the fallopian tubes. This process is designed to stimulate vascularized tissue ingrowth into the matrix material, said Dr. Johns, who practices in Fort Worth, Tex. He accepted payment to enroll and treat patients in the trial but said he has no financial interest in Adiana Inc.

As of September 30, 2005, the Evaluation of the Adiana System for Transcervical Sterilization Using Electrothermal Energy in Women study (EASE) had enrolled 770 women at 16 sites. Almost half (47%) were aged 28-33 years.

A total of 655 patients were taken for hysteroscopy, and 10 were excluded for hysteroscopic findings. The remaining 115 patients either withdrew from the study or were excluded from the study protocol.

Treatment was attempted in 645 patients and bilateral placement was achieved in 614 (95%).

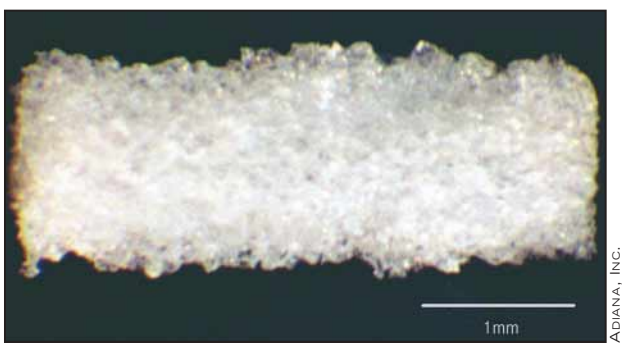
This placement rate is comparable with that attained by Essure in its clinical trials, he said. Lateral location of the ostia is the most common reason for failure of placement of hysteroscopic sterilization devices.

The average procedure time from insertion to removal of the hysteroscope was 12 minutes. Local and oral anesthesia was used in 35% of patients, local anesthesia plus intravenous sedation in 48% and local plus intravenous analgesia in 17%.

Nine patients were lost to follow-up or are awaiting 3-month hysterosalpingogram (HSG).

Failure of tubal occlusion occurred in 26 (4.29%) of women, and there were 2 pregnancies. One pregnancy occurred after proper placement of the device and HSG confirmation of occlusion. The second occurred when a physician misinterpreted the HSG and retreated the patient but placed the device in the occluded tube instead of the patent tube.

There were no device-related significant adverse events. One procedure-related incident of hyponatremia was reported. All other events were minor and included spotting, cramping, and headache. ■



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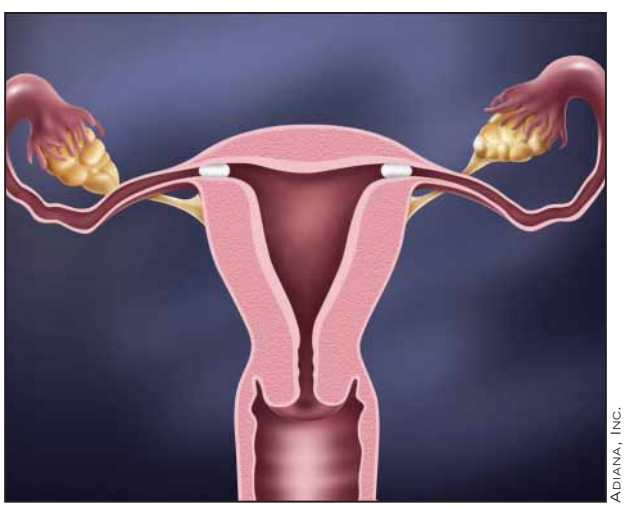
The matrix is porous and bioengineered to provide a scaffold for tissue in-growth and tube closure.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Adiana implants are inserted into the intramural portion of the fallopian tube.

DRUGS, PREGNANCY, AND LACTATION

GI Agents: Part II

BY GERALD G. BRIGGS, B.PHARM.

The second part of this three-part series examines the safety of drugs used to treat several gastrointestinal diseases that cause significant morbidity in pregnant women.

▶ ***Helicobacter pylori* infection:** The bacteria *H. pylori* are associated with chronic active antral gastritis, duodenal ulcer, and gastric ulcer. Although controversial, several studies have associated this infection with severe nausea/vomiting of pregnancy, including hyperemesis gravidarum. Eradication regimens involve dual, triple, or quadruple therapy, typically given for 2 weeks, combining one or two anti-infectives and an antisecretory agent. Bismuth and ranitidine bismuth citrate are sometimes added to the regimen. If clinically acceptable, the wisest course is to delay therapy until after the first trimester. Of the four anti-infectives used in these regimens (amoxicillin, clarithromycin, metronidazole, and tetracycline), only tetracycline clearly causes developmental toxicity, but the carcinogenic potential of metronidazole has not been adequately assessed.

Two proton pump inhibitors, lansoprazole (Prevacid) and omeprazole (Prilosec, Zegerid), are the antisecretory agents of choice in *H. pylori* eradication regimens because neither appears to represent a significant risk in pregnancy. Although ranitidine (Zantac) is compatible with pregnancy, both the salt form ranitidine bismuth citrate (Tritec) and bismuth alone are best avoided because the limited human data prevents an accurate assessment of bismuth's risk to the embryo or fetus.

Amoxicillin, clarithromycin, and tetracycline are compatible with breast-feeding. All of the other agents used for *H. pylori* infection are best avoided in lactation because of potential toxicity in the nursing infant.

▶ **Cholelithiasis:** Only one gallstone-solubilizing agent, ursodiol (Actigall, Urso), is available in the United States. Reports of exposure to this agent early in pregnancy are limited, but there are more data in the second half of pregnancy, which indicates that the drug does not appear to represent a risk in pregnancy or lactation.

▶ **Digestive enzymes:** Two digestive pancreatic enzymes—pancreatin and pancrelipase—are used for various conditions that result in deficient pancreatic secretions, such as cystic fibrosis and chronic pancreatitis. These enzymes metabolize fats, proteins, and starches in the duodenum and upper jejunum. Only fragments of pancreatin and pancrelipase are absorbed systematically. Although human data are limited, animal data suggest these enzymes are low risk in pregnancy and lactation. Of note, the enteric coating on many of these products is diethyl phthalate, and high doses of some phthalates may cause developmental toxicity. However, the very small quantities that the embryo or fetus may be exposed to from the enteric coating suggest that the risk of reproductive and developmental toxicity is probably minimal to negligible.

▶ **Ulcer prophylaxis:** Sucralfate (Carafate) inhibits pepsin activity and protects against ulceration. Only very small amounts of the drug are absorbed systemically, and it is compatible in both pregnancy and lactation. The prostaglandin misoprostol (Cytotec) is also indicated for ulcer prophylaxis, but this use is contraindicated in pregnancy (see GI Agents: Part I, FAMILY PRACTICE NEWS, Dec. 1, 2005, page 47).

▶ **Flatulence:** Two antiflatulents available over the counter are the silicone product simethicone (multiple trade names) and activated charcoal. They also are combined in a single product (Flatulex). Because neither agent is absorbable, they present no risk to the embryo, fetus, or nursing infant.

▶ **Obesity:** There is no human pregnancy experience with the lipase inhibitor, orlistat (Xenical). The drug inhibits the absorption of dietary fats. The animal reproduction data and minimal systemic bioavailability suggest that the drug represents a low risk in pregnancy and lactation.

▶ **Inflammatory bowel disease (IBD):** Mesalamine (5-aminosalicylic acid, 5-ASA) (Asacol, Canasa, Pentasa, Rowasa) is compatible with pregnancy. Reports have described several hundred pregnant women who had received the drug without apparent harm to embryo or fetus. Two other agents in this class, balsalazide (Colazal) and olsalazine (Dipentum), are broken down in the colon to 5-ASA. Both of these agents appear to be compatible with pregnancy.

A third agent, sulfasalazine (Azulfidine), is metabolized to 5-ASA plus sulfapyridine. Sulfapyridine readily crosses the placenta to the fetus. When sulfapyridine is used close to delivery, neonatal jaundice and/or kernicterus secondary to displacement of bilirubin from albumin is a theoretical concern but has not been reported. Although the human experience is limited, sulfasalazine appears to be compatible with pregnancy.

However, all of the IBD agents should be used cautiously during lactation. Multiple episodes of diarrhea were reported in one nursing infant that appeared to be related to the mesalamine rectal suppositories used by the mother. In another case, persistent bloody diarrhea was attributed to the mother's use of sulfasalazine. Because of these cases, close observation of the nursing infant is required if the mother is taking any of these agents.

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