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Hysteroscopic Sterilization: 10-Year Retrospective Analysis of Worldwide Pregnancy Reports

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ABSTRACT

Study Objective: To identify factors that might contribute to pregnancies reported after hysteroscopic sterilization worldwide.

Design: Retrospective review of commercial data compiled from the MAUDE database, medical literature, and manufacturer reports received during commercial distribution of hysteroscopic sterilization micro-inserts from 2001 through 2010 (Canadian Taskforce classification III descriptive study).

Measurements and Main Results: From 2001 through 2010, 497,305 hysteroscopic sterilization kits were distributed worldwide, and 748 pregnancies were reported, i.e., 0.15% of the estimated user population based on the number of distributed kits. The data were sufficient to enable analysis of 508 pregnancies for potential contributing factors and showed most to be associated with patient or physician noncompliance (n = 264) or misinterpreted confirmation tests (n = 212). Conceptions deemed to have occurred within 2 weeks of the procedure and therefore too early for detection were identified in 32 cases.

Conclusion: Although there are limitations to the dataset and the study design is retrospective, it represents the largest body of cumulative hysteroscopic sterilization data available to date. Of the 748 pregnancies reported, it is apparent that some might have been prevented with greater patient and clinician attention to interim contraceptive use and counseling and with more rigorous evaluation and informed interpretation of the procedure confirmation tests. Although the estimated pregnancy rate based on such a dataset is likely an underestimation, it does suggest that the evaluable field performance of hysteroscopic sterilization micro-inserts is consistent with the labeled age-adjusted effectiveness of 99.74% at 5 years. Journal of Minimally Invasive Gynecology (2014) 21, 245–251 © 2014 AAGL. All rights reserved.

Keywords: Contraception; Essure; Female sterilization; Hysteroscopic sterilization; Permanent birth control

Background and Rationale

Essure (Conceptus, Inc., San Carlo, CA), the first hysteroscopic sterilization method approved for use, has been distributed worldwide for >10 years and has been supported as an effective permanent minimally invasive female sterilization technique by the American College of Obstetricians and Gynecologists [1]. The system is composed of 2 micro-inserts, one for each oviduct, for intraluminal occlusion that are positioned using a disposable delivery system. Each micro-insert consists of a stainless steel inner coil, a nickel–titanium (nitinol) expanding outer coil, and polyethylene terephthalate fibers wound in and around the inner coil. When released from the delivery system, the outer coil expands to a diameter of 1.5 to 2.0 mm to anchor the micro-insert in the varied diameters and shapes of the proximal fallopian tube. The currently-available insert (ESS305) was modified slightly so that the proximal portion of the...
outer coil was reduced to a half band from the full band found in the earlier model (ESS205) (Fig. 1). Each model has some unique design features that result in a slight difference in appearance on radiographs or hysterosalpingograms (HSGs) (Fig. 1).

Using hysteroscopic guidance, the micro-inserts are placed across the uterotubal junction to occupy the proximal portion of the fallopian tube. The polyethylene terephthalate fibers elicit a local fibrotic tissue response designed to result in luminal occlusion, which typically is complete within 3 months. As a result, patients must use an alternative form of contraception until a confirmation test is performed at 3 months after the procedure. The confirmation test is designed to evaluate micro-insert location and, in either selected instances (outside of the United States) or in all instances (within the United States), to demonstrate proximal tubal occlusion. The types of imaging vary with the region and regulatory environment in which hysteroscopic sterilization is approved for use. In the United States, the approved hysteroscopic sterilization confirmation test is the modified HSG, which enables confirmation of satisfactory location of both radiopaque micro-inserts and bilateral tubal occlusion (Fig. 2). Flat-plate radiography was the standard first-line confirmation test in Europe; however, transvaginal ultrasound has recently been approved as an alternate confirmation method in Europe, Canada, South Africa, and Australia and is used primarily to identify satisfactory location of the micro-inserts. If there is reason to suspect unsatisfactory location on transvaginal ultrasound or flat-plane radiography, the patient is referred for HSG. From independent studies in the literature, the requirement for HSG for further confirmation occurs in approximately 15% of cases [2–7].

Evidence demonstrates that the hysteroscopic sterilization approach is highly effective when used either as an in-office procedure or in the outpatient operating room [8–12]. Effectiveness in the commercial setting was previously evaluated in the 2007 summary of 64 reported pregnancies in an estimated 50,000 Essure hysteroscopic sterilization procedures [13]. That analysis also revealed that most pregnancies were the result of noncompliance and misread confirmation tests and thus were preventable. The present analysis was designed to similarly evaluate all available data from the reported post-Essure pregnancies that have been received from initial release through December 2010. The primary goal was to identify factors that might have affected the effectiveness of the procedure in this population. A secondary goal of this assessment of the 10-year commercial experience was to estimate the pregnancies reported during 10 years of worldwide hysteroscopic sterilization as a percentage of distributed kits.

Methods

Design

This was a retrospective identification and review of pregnancies that occurred after use of the Essure system and was designed to identify potential factors that contributed to the pregnancies. In addition, confirmation test image review was performed by an expert panel and compared with the written report provided by the local radiologist. The number of pregnancies identified was compared with the number of Essure kits distributed worldwide during the study period.

Subject Identification

Pregnancy data were gathered via retrospective review of commercial pregnancies compiled from the medical literature, the US Food and Drug Administration (FDA) Manufacturer and User Facility Device Experience (MAUDE) database, and voluntary reports directly received by the manufacturer from 2001 through 2010. The MAUDE data comprises voluntary reports from manufacturers and users including clinicians and hospitals or other facilities. The nature of such data dictates that it not be used either to evaluate the rates of adverse events (AEs) or to compare AE occurrence rates across devices. Additional voluntary reports received by the manufacturer were from a number of sources.
including patients, providers, company representatives, and institutions and were processed within FDA AE reporting requirements. No patient names or identification parameters are included in the MAUDE database or the FDA AE reporting documents; cases are identified only by AR number and reported as such to the FDA.

The MAUDE database was searched from January 2001 to December 2010 to identify all records containing the brand name Essure and/or the manufacturer name Conceptus, Inc. A MEDLINE search through December 31, 2010, was conducted using the PubMed search engine for articles using the keywords “Essure” and/or “hysteroscopic sterilization.”

When the Product Surveillance Team at Conceptus received a pregnancy report, regardless of the source, a case was created. When the complaint source was indirect (e.g., via MAUDE database or a literature search), the Product Surveillance Database was searched to determine whether the case had been previously reported (i.e., an Original Report). If a previous report (a match) was not identified, a new case was created. When assessing each pregnancy report, the evaluation team at Conceptus collected all of the available clinical information to determine the most likely cause of failure. The team attempted to i) estimate the date of conception related to placement date of hysteroscopic sterilization micro-inserts; ii) determine compliance with the use of interim contraception before an appropriate confirmation test; and iii) facilitate a thorough review of the Essure Confirmation Test, if made available to the review panel, including both radiologic images and the radiology report describing the findings. Fields for follow-up and additional comments were also included.

Because the data included in this retrospective review were deidentified, no institutional review board approval was required.

**Confirmation Test Review**

When confirmation test images were obtained from providers, they were reviewed by a team of professionals with extensive training and experience in interpreting confirmation test images. The review panel included advanced practice nurses employed by Conceptus and external physician consultants, who together evaluated each case with respect to image quality (interpretability), presence (number of micro-inserts), lie (how the micro-insert was positioned on the scout film), orientation, symmetry, location of the micro-insert in relation to the filled uterine cornua, and presence or absence of bilateral tubal occlusion. After panel review, the physician consultant provided interpretation of the images and the probable cause of pregnancy.

**Timing of Pregnancy and Use of Interim Contraception**

Each pregnancy report was assessed to determine the likely timing of conception with respect to placement of the Essure micro-inserts. When possible, using a combination of last menstrual period, the dates and results of a pregnancy test, including those performed on the day of the procedure, and other relevant evidence, the conception date was estimated and compared with the procedure date. If the baseline pregnancy test results were negative and the estimated date of conception was determined to be <2 weeks before the
hysteroscopic sterilization procedure, the early pregnancy was classified as occurring during the luteal phase at the time of micro-insert placement. If the pregnancy was deemed to have occurred after micro-insert placement, the records were examined for both physician instructions and patient compliance with use of interim contraception. If conception was perceived to have occurred after micro-insert placement but before a satisfactory confirmation test, the pregnancy was deemed to be secondary to either interim contraception noncompliance or failure of the interim contraception method selected. Pregnancies that occurred after a satisfactory confirmation test were potential methodologic failures, but were subject to evaluation for other factors that could have contributed to the conception including appropriate confirmation test interpretation and noncompliance on the part of the physician who performed the procedure.

Estimation of Number of Procedures Performed

The number of procedures performed worldwide was estimated using the number of Essure hysteroscopic sterilization kits sold from 2001 through 2010. Although the precise number of placement procedures performed is not known, the quantity of product distributed was considered the only available surrogate because, according to Conceptus, product orders have been consistently small and frequent, which suggests rapid use and low inventory levels.

All data were compiled on an Excel spreadsheet (Microsoft Corp., Redmond, WA).

Results

Worldwide Commercial Pregnancy Reports

Total Pregnancies

From 2001 through 2010, 497,305 kits were distributed worldwide, including 133,000 of the original model ESS205 (no longer available) and 365,000 of the currently available model ESS305. As of December 31, 2010, 748 pregnancies had been identified (Fig. 3). Data collection did not capture model numbers in all cases; thus an analysis according to model could not be performed. Of the 748 pregnancies, 602 reports originated from physicians, 68 from patients, 65 from the medical literature, and 13 from the MAUDE database.

The 748 reported pregnancies represent 0.15% of the Essure kits distributed during the 10 years. Of these, 660 (88%) were reported in the United States, and 88 (12%) outside the United States, where the confirmation test is flat-plate radiography or transvaginal ultrasound. For those reports for which confirmation tests were available, evaluations were performed. Despite repeated follow-up attempts, insufficient data were available to enable detailed analysis of 240 reports, which were therefore deemed unevaluable. For the purposes of this analysis, the 508 evaluable pregnancy reports were reviewed.

Pregnancy Timing

Of the 508 evaluable pregnancies, detail regarding conception timing was available in only 403 but none were determined to have occurred ≥2 weeks before micro-insert placement.

Fig. 3

Distribution of the 508 evaluable pregnancies occurring after placement of Essure micro-inserts through December 2010, and potential causative factors.
However, there seem to have been 32 instances (6.3%) in which gestations existed that were &lt;2 weeks after conception at the time of Essure placement and were therefore categorized as luteal phase pregnancies. A total of 16 pregnancies (3.1%) were deemed to have occurred following placement and &lt;3 months after hysteroscopic sterilization, 194 (38.1%) at 3 to 11 months after placement, 154 (30.3%) at 12 to 36 months after placement, and 7 (1.3%) at &gt;36 months after placement; for 105 reports (20.7%) further detail regarding the timing of conception was unknown (Fig. 4).

Ectopic Pregnancy

A likely diagnosis of ectopic pregnancy was found in 30 cases, a rate of 0.006%, using as the denominator the number of kits distributed. Of these 30 cases, 1 was reported as a luteal phase pregnancy, 5 occurred after the procedure but before the confirmation test, and the remaining 24 occurred after the confirmation test. Eleven of the 30 cases were successfully treated surgically; 8 were treated with methotrexate; and despite follow-up attempts, the outcomes and treatments remain unknown for the remaining 11 cases.

Factors That Contributed to Pregnancy

Misinterpreted HSGs

In total, in 212 of 508 pregnancies (41.7%) HSGs were determined to have been misinterpreted, including 24 (4.7%) missed micro-insert expulsions and 95 (18.7%) perforations in which at least 1 micro-insert penetrated the fallopian tube, cornua, or uterine corpus (Fig. 5). Unreported patency of one or both tubes was found in 20 patients (3.9%), as determined by visualization of contrast medium flowing beyond the distal end of the micro-insert (Fig. 5). The review panel identified unsatisfactory micro-insert location not described in the report in 45 (8.9%) of the evaluable cases (Fig. 5). This occurred when micro-inserts were located within the fallopian tube but positioned either too distally, defined by the proximal mark of the inner coil located &gt;30 mm from the cornua, or too proximally, defined as &gt;50% of the inner coil in the endometrial cavity. The review panel categorized 28 of the confirmation tests as “inadequate,” including HSGs that failed to demonstrate adequate fill or distension of the endometrial cavity and cornual regions or inadequate views or image resolution rendering determination of satisfactory micro-insert location and bilateral tubal occlusion impossible or equivocal (Fig. 6).

Patient Noncompliance and Interim Contraception Failure

Patient noncompliance included failure either to use contraception after micro-insert placement or to return for the confirmation test. These combined categories of patient noncompliance were found to be factors in 45% of the evaluable post-hysteroscopic sterilization pregnancies. The study records contained no documentation of a confirmation test in 178 pregnancies (35.0%).

Contraception Noncompliance or Contraception Failure

Of 51 patients who did not comply with the use of post-Essure placement contraception, 16 pregnancies were determined to have occurred before the 3-month confirmation test. Thirteen of these patients did not comply with post-placement contraception, and 3 seem to have experienced contraceptive method failure.

Conception After the 3-Month Confirmation Test

Twenty of 51 pregnancies attributed to lack of contraceptive compliance were determined to have occurred after the 3-month confirmation test. In each of these cases, patients were counseled to continue alternative contraception after an unsatisfactory 3-month HSG, but failed to do so. For the remaining 15, we were unable to determine, with adequate precision, the time of conception.

Physician Noncompliance

The placement of a single micro-insert was identified in 35 of 508 reports (6.9%). These procedures were generally performed in women thought to have had a previous salpingectomy or a contralateral tube thought to be previously occluded. However, this category also included cases in which only a single micro-insert could be placed. In some instances, tubal occlusion was demonstrated at HSG but, absent a micro-insert, could possibly represent artifactual cornual occlusion secondary to tubal spasm. As a result, such cases were categorized as examples of physician noncompliance.
Discussion

Although the present review is limited by the both the nature of the data sources and the retrospective design, it represents the largest body of cumulative Essure hysteroscopic sterilization data available to date. Our findings are consistent with previously published data that indicate that most unintended pregnancies occur in association with evidence of noncompliance and/or documented misinterpretation of the confirmation test, usually HSG [13–17]. Consequently, it is likely that the already low pregnancy rates associated with the use of Essure can be further reduced with improved patient and surgeon compliance and, notably, with consistent and accurate evaluation of the post-procedure confirmation test.

Of particular importance for the gynecologist is counseling about appropriate use of an effective interim contraceptive system until both tubal occlusion and satisfactory location of the inserts have been documented or, outside of the United States, implied, on the basis of imaging that documents presence and suggests appropriate location of the inserts. The frequent low compliance with either interim contraception requirements or post-procedure HSG confirmation has prompted some physicians to institute changes in their clinical practice, integrating reminder systems to help patients comply with the post-insertion protocols [9,14].

Misinterpretation of satisfactory micro-insert location was the leading factor in pregnancies due to misread and misinterpreted category. Essure confirmation test interpretation sometimes seemed to be incorrectly focused only on documenting tubal occlusion because location was often not described in the radiology report. These observations suggest that there is need for better education about the reporting requirements of the Essure confirmation test for both radiologists and other clinicians involved with the use of the Essure hysteroscopic sterilization system.

For the radiologist or other clinician interpreting the confirmation test, it is important to understand that the purpose of the post-hysteroscopic sterilization HSG is different from that performed for infertility and that modifications in technique are necessary. This understanding can be facilitated by knowledge of the Essure mechanism of action and that proximal tubal spasm can exist even in the presence of tubal patency. Consequently, the presence, location, and configuration of the micro-inserts, in addition to evaluation for tubal patency, must be consistently included in the

![Fig. 5](image_url)

(A) Expulsion. Right Essure micro-insert (arrowhead) is located in the endometrial cavity. Left micro-insert is in proper place, with occlusion. (B) Perforation. Note proximal marker of left micro-insert and position of inner coil. Asymmetry with abnormal lie suggests perforation of left Essure micro-insert without evidence of tubal patency. Right micro-insert is in proper position, with occlusion. (C) Patency observed beyond the distal end of the left micro-insert positioned properly in the tube. (D) Unsatisfactory placement. Proximal location of the right Essure micro-insert (>50% of inner coil in endometrial cavity), without evidence of patency.

![Fig. 6](image_url)

Example of an inadequate confirmation test. Note a large filling defect in the left cornual region. Consequently, location and occlusion of the left micro-insert are indeterminate.
evaluation and subsequent report. Without confirmation of satisfactory micro-insert location, patients should not be counseled to rely on Essure despite occlusion.

Outside of the United States, hysteroscopic sterilization confirmation testing follows an algorithm that starts with simple radiography or transvaginal ultrasound evaluation as primary techniques, leveraging data showing almost certain tubal occlusion at 3 months if the micro-inserts are maintained in appropriate position in the tubes [15–17]. If the first-line confirmation test is inadequate or inconclusive, HSG is performed for confirmation of location and occlusion. The ability to visualize the micro-inserts as they span the uterotubal junction has been well-demonstrated [7,15,16].

Important limitations of the present study must be acknowledged, and largely reflect issues related to the retrospective design. It is almost certain that a number of pregnancies that occurred after placement of the hysteroscopic sterilization micro-inserts were not captured. In contrast, because the method did not totally preclude any one pregnancy from being reported from a number of potential avenues, there was potential for overreporting. However, given our method, it is unlikely that this deficiency in the database affects the actual number of pregnancies reported. Consequently, we must assume that the method results in underestimation of the actual pregnancy rate. Nevertheless, the 0.15% rate of pregnancy based on kits distributed still suggests a high level of effectiveness and is similar to that reported in the pivotal clinical trials and other well-designed post-marketing studies [14–17].

Conceptus confirms that it has reported all known pregnancies to the FDA regardless of the potential causative factor, and these data have been included in the most current revision of the Essure Instructions for Use. Most pregnancies were associated with noncompliance or misinterpreted confirmation tests. These data suggest that future pregnancies can be reduced because proper adherence to compliance and confirmation test requirements are variables that can be improved.

Acknowledgments

Drs. Munro, Nichols, Levy, Vleugels, and Veersema are consultants for Conceptus, Inc.

References