

Original Article

Analysis of Adverse Events With Essure Hysteroscopic Sterilization Reported to the Manufacturer and User Facility Device Experience Database

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ABSTRACT **Study Objective:** The Manufacturer and User Facility Device Experience database may be useful for clinicians using a Food and Drug Administration–approved medical device to identify the occurrence of adverse events and complications. We sought to analyze and investigate reports associated with the Essure hysteroscopic sterilization system (Conceptus Inc., Mountain View, CA) using this database.

Design: Retrospective review of the Manufacturer and User Facility Device Experience database for events related to Essure hysteroscopic sterilization from November 2002 to February 2012 (Canadian Task Force Classification III).

Setting: Online retrospective review.

Patients: Online reports of patients who underwent Essure tubal sterilization.

Intervention: Essure tubal sterilization.

Measurements and Main Results: Four hundred fifty-seven adverse events were reported in the study period. Pain was the most frequently reported event (217 events [47.5%]) followed by delivery catheter malfunction (121 events [26.4%]). Post-sterilization pregnancy was reported in 61 events (13.3%), of which 29 were ectopic pregnancies. Other reported events included perforation (90 events [19.7%]), abnormal bleeding (44 events [9.6%]), and microinsert malposition (33 events [7.2%]). The evaluation and management of these events resulted in an additional surgical procedure in 270 cases (59.1%), of which 44 were hysterectomies.

Conclusion: Sixty-one unintended poststerilization pregnancies were reported in the study period, of which 29 (47.5%) were ectopic gestations. Thus, ectopic pregnancy must be considered if a woman becomes pregnant after Essure hysteroscopic sterilization. Additionally, 44 women underwent hysterectomy after an adverse event reported to be associated with the use of the device. *Journal of Minimally Invasive Gynecology* (2013) 20, 825–829 © 2013 AAGL. All rights reserved.

Keywords: Essure; Manufacturer and User Facility Device Experience; Microinsert; Sterilization

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Permanent female sterilization remains the most common method of contraception in the United States [1]. Essure per-

manent birth control (Conceptus Inc., Mountain View, CA) was the first hysteroscopic sterilization technique to be

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approved by the US Food and Drug Administration (FDA) in 2002. Essure microinserts are inserted hysteroscopically through a delivery catheter and anchor in the proximal fallopian tube. They have an inner stainless steel coil and an expanding outer coil of nitinol. The inner coil houses the polyethylene terephthalate fibers, which induce benign, localized tissue ingrowth, resulting in occlusion of the tubal lumen [2].

Since its clinical use in 2002, Essure hysteroscopic sterilization has been proven to be a safe and effective method of sterilization that is feasible in the ambulatory setting. Essure sterilization has shown good overall patient satisfaction and cost-effectiveness when compared with laparoscopic sterilization [3–5]. Consequent to the increase in Essure use, data became available in the literature describing complications and adverse events associated with the procedure. These data can be used to reduce complications and improve patient outcomes.

The Manufacturer and User Facility Device Experience (MAUDE) database is a reporting system mandated by the FDA for postmarket surveillance. MAUDE data represent reports of adverse events involving medical devices. The data consist of user facility reports since 1991, distributor reports since 1993, voluntary reports since June 1993, and manufacturer reports since August 1996 [6]. Our objective was to explore and evaluate adverse events and complications related to Essure hysteroscopic sterilization that were reported to the MAUDE database.

Materials and Methods

The MAUDE database was accessed through the FDA Web site [6], and an online search was performed. The following search terms were used: “Essure,” “Conceptus,” “sterilization,” and “micro-inserts.” We analyzed the reports of Essure adverse events in the MAUDE database from the time of its approval in the United States in 2002 through February 2012.

The following data were collected from each case: event number, event date, report date, type of complication, brief description of the event, report source, who reported the event, and device catalog number. Some duplicate reports were identified and removed after comparing the event number, date, and description. For several reports, no report date was specified; in these cases, the date the report was received by the FDA was used for the purpose of this study.

The reports included events that occurred and were identified during the procedure (e.g., delivery catheter malfunction), symptoms the patient experienced afterward (e.g., pain), and findings diagnosed after the procedure (e.g., malposition or pregnancy). Some reports had more than 1 complication, so the total number of complications is greater than the total number of reports. In analyzing these reports, we further categorized the events into those requiring imaging (other than the required poststerilization hysterosalpingogram), surgical intervention, or hospital admission. Results

were collected and tabulated. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS version 19 for Mac; SPSS Inc., Chicago, IL).

Results

The MAUDE database was searched using the previously described search terms for the period of November 2002 to February 2012. Five hundred twelve events were reported during this period or an average of 51.2 reports per year; 55 of these were found to be duplicate or not relevant. This brought the total number of reported events to 457. The first 5 reported events were in 2004, and the number of reported events increased in subsequent years to 114 reported events in 2011 (Fig. 1). At the time this search was performed, there were no reports in the database for 2012. Events were not mutually exclusive and were categorized as pain (217 events [47.5%]), delivery catheter malfunction (primarily failure to deploy or microinsert detachment) (121 [26.4%]), perforation (90 [19.7%]), pregnancy (61 [13.3%]), abnormal bleeding (44 [9.6%]), microinsert malposition (33 [7.2%]), allergic reaction (20 [4.4%]), and other (24 [5.3%]).

Pain was the most frequently reported event in 217 cases (47.5%). The timing of pain ranged from pain experienced during the procedure when performed in the office setting to pain experienced by the patient immediately after or weeks to years after the procedure. In 54 of these cases (24.9%), perforation was discovered during subsequent imaging or surgery.

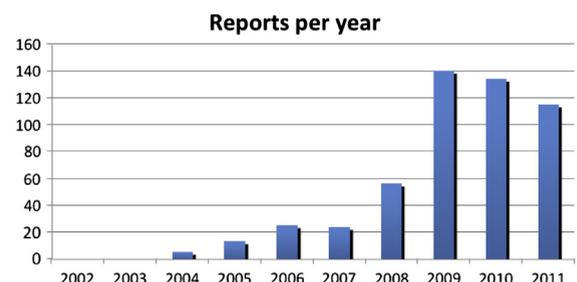
Sixty-one events were associated with pregnancy, of which 29 (47.5%) were ectopic pregnancies. In 23 of the reported pregnancies (37.7%), hysterosalpingography (HSG) completed after the procedure documented tubal occlusion. Four reports mentioned that pregnancy occurred within the first 3 months after sterilization.

For the reports related to allergic reactions, including possible hypersensitivity to nickel, symptoms ranged from itching and nausea to abdominal pain. Allergy testing was mentioned and was positive in 4 of these reports. The microinserts were surgically removed in 11 cases.

Further imaging studies were described in 140 reports (30.6%); ultrasound was mentioned in 45 event reports (9.8%), computed tomography scan in 22 (4.8%), x-ray in

Fig. 1

The number of events per year as reported in the MAUDE database.



22 (4.8%), and magnetic resonance imaging in 3 (0.7%). The evaluation and management of these events resulted in an additional surgical procedure in 270 cases (59.1%), which included laparoscopy in 131 (28.6%) events, hysteroscopy in 47 (10.3%), hysterectomy in 44 (9.6%), laparotomy in 9 (2.0%), and dilatation and curettage in 5 (1.1%); the procedure was not specified in 34 (7.4%) cases.

Sources of the event reports included the manufacturer in 237 (51.9%) cases, the facility where the event took place in 141 (30.8%), and the patient in 79 (17.2%). These reports described the occupation of the reporter as being a physician in 221 cases, a patient in 77, a risk manager in 46, a nurse in 26, and other in 87 event reports.

Discussion

Essure permanent birth control is a medical device that is regulated by the FDA and is subject to premarketing and postmarketing surveillance and regulatory controls. Post-market surveillance is designed to better identify uncommon but potentially serious adverse events related to the use of the device in the general public [7].

The MAUDE database is a searchable online database that is updated quarterly. Searching the MAUDE database is useful for clinicians using a specific medical device. The MAUDE database is particularly useful because most clinical trials are performed by experts and conform to rigorously defined protocols that might not translate into what can be expected in general use. Second, not all physicians are willing to publish their own complications. Third, infrequent complications might only occur after large numbers of procedures have been performed. Finally, there is often a significant time lag in event occurrence and subsequent peer review publication [8].

Events related to the Essure device have been reported to the MAUDE database since 2004, and more reports have been submitted each year since, possibly related to the cumulative increase in device use. The slight decrease in reported events after 2009 may be the result of simple variation in reporting or it may be because of increased familiarity with the device resulting in fewer adverse events. However, it is important to note that the MAUDE database data are not intended to be used to evaluate rates of adverse events or to compare adverse event occurrence rates across devices [6]. Limitations of the MAUDE database in general include underreporting of events, insufficient or inadequate information, inability to establish causality, and inability to establish rates of adverse events because there would not be an accurate denominator or a known exact number of procedures performed. The numbers and percentages of events described in this report are only in reference to the total number of adverse events reported to the MAUDE database regarding this device. Additionally, voluntary reporters may use layman terminology, which may not be specific. Similar articles have appeared in the medical literature attempting to summarize adverse events in

the MAUDE database for various medical devices. The advantage of using these reviews instead of independently searching the database is the avoidance of extraneous information [8].

For the Essure device, pain was the most frequently reported event. In general, when compared with laparoscopic methods of sterilization, Essure has been associated with decreased immediate postoperative pain, improved patient tolerance, and reduced hospital time [9]. However, there are rare reports of persistent pelvic pain that resolved after the removal of the device [10]. Pain after tubal ligation has been described before along with other symptoms collectively referred to as “posttubal sterilization syndrome.” This syndrome is believed to be a misnomer because the pain experienced may be the result of an increase in menstrual flow and dysmenorrhea in women who were previously on oral contraceptives [11]. Although pain has been described even with proper microinsert placement [10,12], pain that persists after the procedure should alert the physician to the possibility of complications such as improper placement or perforation [13].

During early studies for Essure sterilization, correct device location was reported in 96% of cases; device location was unsatisfactory in 4%, whereas 1.7% were unsatisfactory because of perforation [14,15]. Expulsion of a microinsert from the fallopian tube was reported to occur in 1.3% to 3.6% of cases and was typically caused by incorrect insertion of the microinsert, mostly concerning placement too proximal in the tube [4,13].

Malposition was reported in 25 events (7.0%) in the MAUDE database. These were not believed to be perforations because they were noted to be in a wrong position in the tube or embedded in the endometrium. Malformation and abnormalities of the uterine cavity or fallopian tubes are associated with placement failure, and tubal spasm is also suspected to have a negative influence on proper microinsert placement [16,17]. It is also thought that fluid collection under the endometrium could complicate the correct placement of a microinsert because the insert may be placed under a layer of endometrium instead of in the tubal ostium [15]. Even in the hands of experienced surgeons, misplacement, perforation, and expulsion of Essure microinserts can occur [15]; therefore, it has been advised that patients with difficult placement or suboptimal conditions during the procedure be screened earlier than 3 months after the initial placement to determine if the position of the microinserts is appropriate [14]. A transvaginal ultrasound or pelvic x-ray after the patient’s first period or withdrawal bleed could be used for this assessment [15].

Pregnancies after Essure sterilization have been reported in the literature in a few reports from the United States and worldwide [18,19]. The overall effectiveness of Essure has been stated as 99.83% based on closely monitored clinical trials [20]. In the MAUDE database, 61 events were associated with pregnancy. Approximately one third of these cases mentioned that there was documented bilateral tubal

occlusion by HSG after Essure placement. The goal of the post-Essure HSG is to evaluate tubal occlusion and proper device placement. In pregnancies that have occurred subsequent to Essure sterilization, misinterpretation of the HSG has been described in which the abnormal location of a microinsert was not recognized [19]. This occurrence highlights the importance of interpretation of the HSG by an experienced physician who is familiar with the Essure procedure to ensure proper device location and tubal obstruction at the cornua [18]. In addition, HSG has been reported by 1 group to have moderate sensitivity to detect tubal patency [21] because of the high occurrence of tubal spasm. Of the total number of reported pregnancies, 29 (47.5%) were ectopic pregnancies. Ectopic pregnancy has also been reported to have a higher incidence (25%–50%) among women who conceived after other forms of tubal sterilization failed [22,23]. Because of the high percentage of women who developed ectopic pregnancies among women who conceived after Essure sterilization, ectopic pregnancy needs to be considered in a patient who is confirmed to be pregnant after undergoing Essure sterilization.

Hypersensitivity reaction to nickel after Essure microinsert placement is a rare occurrence [24]. Although there were 20 cases related to allergic reactions after Essure placement reported to the MAUDE database, only 4 reports mentioned confirmatory allergy testing. In a recent study, adverse events suspected to be related to nickel hypersensitivity were estimated to occur in approximately 0.01% of cases, questioning whether nickel reactions are clinically relevant in the use of nitinol containing Essure microinserts [25]. In 2011, the FDA approved the removal of the nickel hypersensitivity contraindication from the Essure instructions for use.

Sixteen reports mentioned the concomitant use of Essure with endometrial ablation techniques. Pain was the most frequently reported symptom in those cases. Two of the cases reported the need for hysterectomy because of persistent pain. In 1 of the patients who underwent hysterectomy, the resultant pathology was described as endometritis and salpingitis. Additionally, 1 event described a bowel injury occurring after concomitant Her Option cryoablation (CooperSurgical, Inc., Trumbull, CT) and another bowel injury after concomitant NovaSure bipolar radiofrequency ablation (Hologic Inc., Newark, DE) with the subsequent need for surgical intervention. Endometrial ablation is a fairly common procedure that is performed as a substitute to hysterectomy in the treatment of abnormal uterine bleeding. Endometrial ablation performed simultaneously with Essure microinsert placement has been investigated. The Thermachoice Uterine Balloon Therapy System (Ethicon Inc., Cornelia, GA) was shown to be safe without damaging the Essure microinserts or increasing the temperature in the microinserts that could result in tissue damage [26]. In contrast, it was found that performing NovaSure ablation in patients who may have an undiagnosed perforation, such as those with difficult or atypical procedures, poses the risk of thermal injury to the bowel or

bladder [27]. However, other studies that assessed the concomitant use of these endometrial ablation devices have suggested feasibility and apparent safety [28]. As stated in the instructions for use, the Essure procedure should not be performed concomitantly with any endometrial ablation technique because intrauterine synechiae that result from ablation can compromise the interpretation of the HSG confirmation test for tubal occlusion [27]. Therefore, endometrial ablation procedures should only be performed after HSG is completed.

To summarize, we encourage physicians to review the MAUDE database when using medical devices because it is an excellent tool to assess uncommon but major problems that could be associated with a medical device. Knowledge of such events will assist health care providers in counseling patients before performing a procedure with a specific medical device. Furthermore, we strongly encourage facilities and physicians to report adverse events associated with medical devices to the MAUDE adverse event reporting program.

References

1. Chapman L, Magos A. Currently available devices for female sterilization. *Expert Rev Med Devices*. 2005;2:623–634.
2. Connor VF. Essure: a review six years later. *J Minim Invasive Gynecol*. 2009;16:282–290.
3. Andersson S, Eriksson S, Mints M. Hysteroscopic female sterilization with Essure in an outpatient setting. *Acta Obstet Gynecol Scand*. 2009;88:743–746.
4. Kerin JF, Cooper JM, Price T, et al. Hysteroscopic sterilization using a micro-insert device: results of a multicentre phase II study. *Hum Reprod*. 2003;18:1223–1230.
5. Thiel JA, Carson GD. Cost-effectiveness analysis comparing the essure tubal sterilization procedure and laparoscopic tubal sterilization. *J Obstet Gynaecol Can*. 2008;30:581–585.
6. Available at: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/Search.cfm>. Accessed February 10, 2012.
7. Department of Health and Human Services. Postmarket surveillance. Final rule. *Federal Register*. 2002;67:38878–38892.
8. Gurtcheff SE. Introduction to the MAUDE database. *Clin Obstet Gynecol*. 2008;51:120–123.
9. Duffy S, Marsh F, Rogerson L, et al. Female sterilisation: a cohort controlled comparative study of ESSURE versus laparoscopic sterilisation. *BJOG*. 2005;112:1522–1528.
10. Lannon BM, Lee SY. Techniques for removal of the Essure hysteroscopic tubal occlusion device. *Fertil Steril*. 2007;88:497e13–497e14.
11. Rulin MC, Turner JH, Dunworth R, Thompson DS. Post-tubal sterilization syndrome—a misnomer. *Am J Obstet Gynecol*. 1985;151:13–19.
12. Beckwith AW. Persistent pain after hysteroscopic sterilization with microinserts. *Obstet Gynecol*. 2008;111:511–512.
13. Mahmoud MS, Fridman D, Merhi ZO. Subserosal misplacement of Essure device manifested by late-onset acute pelvic pain. *Fertil Steril*. 2009;92:2038e1–2038e3.
14. Kerin JF, Carignan CS, Cher D. The safety and effectiveness of a new hysteroscopic method for permanent birth control: results of the first Essure pbc clinical study. *Aust N Z J Obstet Gynaecol*. 2001;41:364–370.
15. Gerritse MB, Veersema S, Timmermans A, Brolmann HA. Incorrect position of Essure microinserts 3 months after successful bilateral placement. *Fertil Steril*. 2009;91:930e1–930e5.

16. Cooper JM, Carignan CS, Cher D, Kerin JF. Microinsert nonincisional hysteroscopic sterilization. *Obstet Gynecol.* 2003;102:59–67.
17. Ubeda A, Labastida R, Dexeus S. Essure: a new device for hysteroscopic tubal sterilization in an outpatient setting. *Fertil Steril.* 2004; 82:196–199.
18. Levy B, Levie MD, Childers ME. A summary of reported pregnancies after hysteroscopic sterilization. *J Minim Invasive Gynecol.* 2007;14: 271–274.
19. Veersema S, Vleugels MP, Moolenaar LM, et al. Unintended pregnancies after Essure sterilization in the Netherlands. *Fertil Steril.* 2010;93: 35–38.
20. Conceptus Inc. *Conceptus(R) Reports Second Quarter Financial Results.* Mountain View, CA: Conceptus Inc.; 2012.
21. Swart P, Mol BW, van der Veen F, van Beurden M, Redekop WK, Bossuyt PM. The accuracy of hysterosalpingography in the diagnosis of tubal pathology: a meta-analysis. *Fertil Steril.* 1995;64:486–491.
22. Peterson HB, Xia Z, Hughes JM, Wilcox LS, Tylor LR, Trussell J. The risk of ectopic pregnancy after tubal sterilization. U.S. Collaborative Review of Sterilization Working Group. *N Engl J Med.* 1997;336: 762–767.
23. Barnhart KT. Clinical practice. Ectopic pregnancy. *N Engl J Med.* 2009; 361:379–387.
24. Al-Safi Z, Shavell VI, Katz LE, Berman JM. Nickel hypersensitivity associated with an intratubal microinsert system. *Obstet Gynecol.* 2011; 117:461–462.
25. Zurawin RK, Zurawin JL. Adverse events due to suspected nickel hypersensitivity in patients with Essure micro-inserts. *J Minim Invasive Gynecol.* 2011;18:475–482.
26. Valle RF, Valdez J, Wright TC, Kenney M. Concomitant Essure tubal sterilization and Thermachoice endometrial ablation: feasibility and safety. *Fertil Steril.* 2006;86:152–158.
27. Conceptus Inc. Essure Instructions For Use, 2012. Available at: essuremd.com. Accessed November 3, 2012.
28. Donnadieu AC, Defieux X, Gervaise A, Faivre E, Frydman R, Fernandez H. Essure sterilization associated with endometrial ablation. *Int J Gynaecol Obstet.* 2007;97:139–142.