

Hysteroscopic sterilization using a micro-insert device: results of a multicentre Phase II study*

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BACKGROUND: Unlike laparoscopic surgery for interval tubal sterilization, a hysteroscopic approach obviates surgical incision and requires only local anaesthesia or intravenous sedation. The safety, tolerability and efficacy of an hysteroscopically placed micro-insert device was evaluated. **METHODS:** A cohort of 227 previously fertile women participated in this prospective international multicentre trial. Micro-inserts were placed bilaterally into the proximal Fallopian tube lumens under hysteroscopic visualization in outpatient procedures. **RESULTS:** Successful bilateral micro-insert placement was achieved in 88% of women. The majority of women reported that intraprocedural pain was less than or equal to that expected, and 90% rated tolerance of the device placement procedure as good to excellent. Most women could be discharged in an ambulatory state within 1–2 h. Adverse events occurred in 7% of the women, but none was serious. Correct device placement was confirmed in 97% of cases at 3 months. Over 24 months follow-up, 98% of study participants rated their tolerance of the micro-insert as very good to excellent. After 6015 woman-months of exposure to intercourse, no pregnancies have been recorded. **CONCLUSIONS:** Hysteroscopic sterilization resulted in rapid patient recovery without unacceptable post-procedure pain, as well as high long-term patient tolerability, satisfaction and effective permanent contraception.

Key words: contraceptive devices/hysteroscopic sterilization/transcervical sterilization/tubal occlusion

Introduction

In the USA and other developed countries, most interval sterilization procedures are laparoscopic procedures performed under general anaesthesia in a day surgery setting (MacKay *et al.*, 2001). While generally safe and effective, laparoscopic surgery does entail risks of operative complications. Moreover, laparoscopic occlusion techniques such as clips and rings, which have become increasingly popular because of a reduced risk of bowel injury and potential of reversibility, are usually associated with significant post-operative pain that can result in nausea, vomiting and even unanticipated hospital admissions (Davis and Millar, 1988; Benhamou *et al.*, 1994; Tool *et al.*, 1997).

A safe, simple and highly effective alternative to incisional procedures for interval tubal sterilization such as transcervical sterilization has long been sought. Despite numerous past approaches and attempts—primarily during the 1970s and 1980s—an acceptable transcervical method of sterilization has still not been developed. Previous attempts using various hysteroscopic sterilization methods have resulted in unacceptable rates of ectopic or intra-uterine pregnancy, expulsion of devices, infection, perforation or damage to surrounding organs. The less controllable destructive techniques involving the intra-uterine or intratubal injection of sclerosing agents, tissue adhesives, electrocoagulation or cryosurgery were associated with side effects related to tissue destruction such as abnormal uterine bleeding, discharge, infection and pelvic pain. The various mechanical tubal occlusive devices failed to gain acceptance because of their tendency towards expulsion and an associated unacceptable pregnancy rate (Cooper, 1992; Kerin, 1995). During the past 10 years, miniaturization of endoscopes, improved light transmission and optical resolution, continuous flow technology and the development of

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Table I. Patient selection criteria

Selection criteria	Details
Inclusion criteria	Age 23–45 years Regular menses Demonstrated prior fertility (\geq one live birth) Able and willing to use alternative contraceptive method (barrier or oral) for first 3 months following device placement Willing to keep coital and menstrual log for 6 months following device placement Available for all study follow-up visits Comprehension of study participation risks and benefits
Exclusion criteria	Uncertainty as to desire for permanent birth control Known anatomic abnormalities possibly preventing tubal cannulation Cervical or uterine neoplasia or its precursors Untreated acute cervicitis or history of acute pelvic inflammatory disease Unexplained abnormal uterine bleeding History of chronic pelvic pain, severe dysmenorrhoea or severe dyspareunia Prior Fallopian tube surgery Any unresolved tubal, ovarian or endometrial pathology Allergy to contrast media Inability to comply with protocol requirements

over-the-wire variable softness catheters with a hydrophilic coating have improved the navigation and tracking properties of delivery systems into the Fallopian tube (Kerin *et al.*, 1992). In addition, there has been a trend to use less invasive technology for surgery in general, and this provided encouragement to reinvestigate the challenge of hysteroscopic sterilization.

In this report of a Phase II study, the experience is described with a new, irreversible transcervical method to occlude the Fallopian tubes. The Essure™ permanent birth control device (Conceptus, Inc., San Carlos, CA, USA) is a dynamically expanding micro-insert which is placed in the proximal section of the Fallopian tube using a hysteroscopic approach for cannulating the Fallopian tube (Kerin *et al.*, 1992). The micro-insert achieves tubal sterilization through mechanical occlusion of the Fallopian tube by inducing a local fibrous tissue in-growth from the surrounding tubal walls. Over a 3-month period the tissue in-growth completely occludes the tubal lumen (Valle *et al.*, 2001). In a recent report of experience at a single centre, the procedure was found to be safe and encouragingly acceptable to women (Kerin *et al.*, 2001). Herein, the findings are reported of a multicentre study evaluating the success of device placement, safety and patient acceptability of the procedure, and the experience of women up to 3 years after placement. The design, quality control and monitoring of the five investigational sites was carried out in accordance with the Food and Drug Administration (FDA) requirements in order to comply with the conditions set down for premarket approval (PMA). The data from this Phase II study which commenced in 1998 followed by a Pivotal Multicentre Study that started in 2000 were assessed by the Obstetrics and Gynecological Devices Advisory Committee of the United States FDA and approval granted on November 5, 2002. It is believed that the Essure micro-insert is the first medical device to gain FDA approval for hysteroscopic sterilization in a clinical setting.

Materials and methods

Study design

This Phase II study was an international, multicentre, single-arm clinical trial among women of childbearing age seeking permanent birth control. The study results detailed in this article evaluated: (i) the safety of the micro-insert placement; (ii) tolerance of and recovery from the placement procedure; (iii) patient experience during the 3 years after placement; (iv) evaluation of tubal occlusion; and (v) effectiveness at preventing pregnancy. Women who met the patient selection criteria (Table I) gave their written informed consent in the knowledge that this sterilization procedure was both investigational and irreversible, prior to undergoing pelvic examinations and screening for *Neisseria gonorrhoea* and *Chlamydia trachomatis* infection. All five investigational sites, located in the USA, Europe and Australia, conducted the study according to the same protocol, and each obtained approval from their respective Institutional Review Board or Ethics Committee before study commencement.

Procedural techniques

The micro-insert, previously known as STOP (Selective Tubal Occlusion Procedure), consists of a flexible stainless steel inner coil, a dynamic outer coil made of nickel titanium alloy (commonly known by the tradename Nitinol™), and a layer of polyethylene terephthalate (PET) fibres running along and through the inner coil. Over a 3-month period, the PET fibres elicit a benign localized tissue in-growth from the surrounding tubal wall into and around the device to completely occlude the tubal lumen (Valle *et al.*, 2001). The micro-insert is designed to be placed transcervically, and can be delivered through a 5 Fr (1.7 mm internal diameter) operative channel of a 5 mm outer diameter hysteroscope of varying manufacture. The entire system is attached to a handle for one-handed release of the micro-insert. During insertion, the micro-insert is maintained in a wound-down configuration through the use of a release catheter that is sheathed in a hydrophilic delivery catheter to improve tracking along the Fallopian tube. Optimal positioning of the insert occurs when 3–8 mm of the proximal end of the micro-insert is visible at the ostium. The guidewire attached to the device's inner coil aids placement. When released from the delivery catheter, the outer coil of the micro-insert

Table II. Category and primary reason for failure of bilateral device placement in 27 women

Category	Reason for failure	n (%)
Anatomic	Stenosis, occlusion, spasm or extremely lateral/tortuous tubes	13 (48)
Procedural	Inability to cannulate or advance the catheter for unknown reasons	6 (22)
	Micro-insert perforation adjacent to the true ostium	1 (4)
Device-related	Deficient catheter performance	5 (19)
Unspecified	–	2 (7)
Total		27 (100)

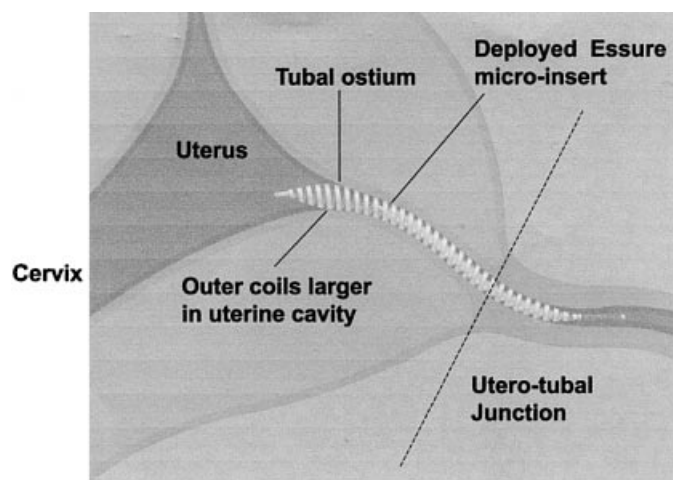


Figure 1. Illustration depicting the Essure™ micro-insert *in situ*. This cross-sectional view of the uterus and Fallopian tube shows the device placed across the uterotubal junction (external).

expands to span the intramural and proximal isthmic portions of the Fallopian tube. This expansion serves to anchor the micro-insert in the tubal lumen (Figure 1). Permanent placement of the micro-insert is achieved upon subsequent fibrous tissue in-growth.

Procedure management

The hysteroscopic sterilization procedure was performed in both the follicular and luteal phase of the menstrual cycle. Women using barrier methods of contraception were advised to abstain from intercourse during the procedure-related menstrual cycle, whereas those women using hormonal contraception were not advised to abstain from intercourse. A urine pregnancy test was performed within 24 h of the procedure. Pre-operative analgesia, if given, consisted of a non-steroidal anti-inflammatory drug given 30–60 min prior to the procedure.

Women received a paracervical block only, or in some cases, with intravenous sedation. General anaesthesia was rarely used. For paracervical block (recommended to all clinical investigators), 10 ml of 1% lignocaine was drawn into a 10 ml syringe to which a long 22 gauge spinal needle was attached. The needle was inserted into the paracervical tissue at the cervicovaginal reflection to a depth of 1–1.5 cm at the 12, 3 and 9 o'clock positions. Aspiration at each point was performed to ensure that the needle tip was not in the rich paracervical blood supply. An aliquot of 1% lignocaine (3 ml) was inserted at each point and an interval of 5 min allowed to elapse prior to hysteroscope insertion. Physiological saline irrigation was used gently to dilate the cervix and distend the endometrial cavity, as well as simultaneously provide forward vision for safe introduction of the hysteroscope. Mechanical dilatation of the cervix was rarely required. The endoscopic image of the uterine cavity allowed the women to

Table III. Predominant anaesthesia^a

Anaesthesia	n (%)
Intravenous sedation	112 (49)
Local anaesthesia	94 (41)
General anaesthesia	10 (4.4)
Analgesia	7 (3.1)
None	5 (2.2)
Regional	1 (0.4)
Total	227 (100)

^aMethod of anaesthesia primarily responsible for pain relief during device placement.

visualize their Fallopian tube openings and the entire procedure. Devices were placed bilaterally.

Follow-up

Each woman completed a questionnaire one week after device placement, recording the occurrence of any bleeding, discomfort or other symptoms experienced following the procedure, as well as their perceptions of the placement procedure. Women kept daily diaries for 6 months and recorded menstrual bleeding, sexual intercourse events, any untoward symptoms experienced and medications taken. Women were then followed up at 3, 6, 12, 18, 24 and 36 months. During the first 3 months of wearing the device, women used an alternative form of contraception (either barrier methods or oral contraceptives) to allow adequate time for a localized tissue in-growth into the micro-insert to occur. At 3 months after micro-insert placement, these women underwent a hysterosalpingogram (HSG) in order to evaluate device location and Fallopian tube occlusion. Given satisfactory device location and tubal occlusion, the women were advised that they could rely on the micro-inserts for permanent birth control and were instructed to cease alternative contraception.

Statistical analysis

Tests of differences in proportions were calculated using the χ^2 statistic. Differences in means were evaluated using *t*-tests.

Results

Demographics

Of the 269 women who were enrolled into the study, device placement was attempted in 227. The other 42 either voluntarily withdrew or failed screening assessments. Of these 227 women, 130 were from Australia, 44 from the USA and 53 from Europe. Their average age was 35 years (range 23–45); among subjects, 16 women (7%) were aged <28 years, 53 (23%) were aged between 28 and 33 years, and 158 (70%) between 34 and 45 years. The average (\pm SD) height of

Table IV. Incidence of side effects following hysteroscopic procedures

Type	Management	n	%
Pain during procedure	Intravenous sedation 49%; paracervical block 41%	153/227	67
Pain post procedure	–	156/206	76
No analgesia required	–	52/156	33
Analgesia required	48% given ibuprofen; 50% given codeine-containing medication	104/156	67
Bleeding post procedure	Resolved within 1 day in 27% of cases; 3 days in 64%; 7 days in 96%; and 15 days in 100%	171/206	83
Dyspareunia (first 3 months based on diaries)	Resolved in all cases	18/206	9
Pain during menses (first 3 months based on diaries)	–	27/206	13

subjects was 163 ± 12 cm, average body weight was 70 ± 16 kg, average gravidity 2.6 ± 1.3 and average parity 2.2 ± 0.9 .

Device placement

Among the 227 women in whom the procedure was attempted, bilateral device placement was successful in 200 cases (88%; CI 83–92%). The average time for device placement recorded from the start of hysteroscopic insertion to its removal from the uterine cavity was 18 min, and there was no significant difference in the procedure time between the five clinical investigators. In four of the women, a second procedure by the same investigator was required in order to accomplish bilateral placement. This left a total of six women with a unilateral placement. Causes of failure of bilateral device placement among the 27 women are summarized in Table II. Included in this group were two women who had bilateral placement failure after two attempts. Each failure was classified as anatomic, procedural, device-related or unspecified. In all, 13 women (48% of all placement failures) had anatomic reasons for device placement failure; these could be due to normal variants of tubal anatomy, spasm, stenosis or occlusion. It was not possible to differentiate between these anatomic factors during the procedure. Procedure-related failures occurred on the day of the device placement in seven women (22% of all placement failures), while device failure occurred in five women (19%). The day of the menstrual cycle did not appear to affect bilateral placement rates (Fisher's exact test, $P = 0.9$). The bilateral placement rate was 87% (97/111) for women between days 1 and 14, 89% (95/107) between days 15 and 35, and 100% (4/4) among women from day 35 or greater after menstrual day 1. Data were not available from five women.

Anaesthesia

Non-steroidal anti-inflammatory medications were taken prior to the procedure in 70% of the hysteroscopic placement attempts. The predominant anaesthesia regimens used among the 227 women are listed in Table III. Intravenous sedation (including when accompanied by paracervical block) or paracervical block only were the predominant choices. Only 10 women (4%) received a general anaesthetic as the primary method of pain relief.

Post-procedure pain

Among the 206 women who had either a bilateral or unilateral device placement, 156 (76%) reported pain following the procedure (Table IV). Post-operative pain was evaluated independently of investigator involvement on the day of the procedure by asking the women to complete an analogue pain scoring system ranging from very severe, severe, moderate, mild or no pain, where the reference point, moderate, was equivalent to their usual degree of menstrual cycle discomfort. Post-procedure pain was resolved within 1 day in 59% of these women, within 3 days in 88%, and within 1 week in 99% of all women reporting pain. Pain was resolved within 2 weeks for the remaining two women (1%). The pain was most commonly described as being similar to menstrual cramps.

Post-procedure bleeding

Post-procedure bleeding was reported by 171 of the 206 respondents (83%) who had a device placed (Table IV). Compared with normal menses, post-procedure bleeding was reported as the same or less in 89% of 171 women, a little more by 8%, and a lot more by 3%. Post-procedure bleeding was resolved within 1 day in 27% of cases, within 3 days in 64% of cases, and within 1 week in 96% of cases. In the remaining 4% of cases, bleeding was resolved within 15 days. Due to variations in menstrual period timing compared with device placement date, some women may have experienced their normal menses within a week after device placement. Therefore, it is presumed that these women captured bleeding associated with both device placement and normal menses in some cases.

Adverse events

Details of adverse events related to micro-insert placement and reported by 15 of the 227 women (7%) are shown in Table V. These adverse events did not result in serious side effects in any of the women. Six perforations of the uterine wall or tubal lumen were reported; in four of these cases the perforation was thought to be due to the use of a support catheter which was subsequently discontinued. Four of the women elected to undergo a laparoscopic sterilization procedure, three by use of the Filshie clip technique and one by tubal electrocautery. No

Table V. Incidence of adverse events following 227 hysteroscopic procedures

Type	Management/outcome	n (%)
Vaso-vagal response	Atropine	2 (1)
Device proximal band detachment ^a	No clinical sequelae	3 (1)
Unsatisfactory device location	One expulsion, six perforations; two unsatisfactorily placed devices; no serious side effects reported in any of these women	9 (4)
Broken device tip ^a	Breakage occurring during intraprocedural hysteroscopic device removal: no clinical sequelae	1 (<1)
Total		15/227 (7)

^aProblems addressed by subsequent design/manufacturing improvements

damage to the uterus or tubes could be visualized. In two cases the perforated micro-insert was located on the parietal peritoneum, either just below the ovary or Fallopian tube. Each device was superficially adherent to the peritoneum, without any surrounding inflammation or adhesion formation, and was gently dissected free and removed. The contralateral devices could be seen extending from the uterotubal junction to occupy the proximal sections of the isthmic tube. The overlying coverings of the tube and peritoneum appeared healthy and normal, and these devices were left *in situ*. In the third woman the device could not be located, but was suspected to be lying between loops of small bowel, as judged by its midline position above the sacral promontory on the HSG films. The fourth woman had a partial perforation that did not extend completely through the myometrium, which was asymptomatic and therefore left *in situ*. One case of perforation was diagnosed after 2 years of micro-insert placement. This woman requested that her micro-inserts be removed following a 6-month history of pain. The pain was described as a scratchy irritating pain in the pelvic region on the right side, which was not associated with any systemic upset or change in blood picture normality. The surgeon involved performed a small transverse suprapubic laparotomy incision and confirmed a partial perforation where one-third of the micro-insert was coiled under the peritoneum just below the right uterotubal junction. There was no evidence of inflammation or adhesion formation. A bilateral cornual resection containing each micro-insert was performed. The pain settled post-operatively and the woman has remained pain-free following 18 months of follow-up. Histological evaluation revealed that the device had perforated the tube half way along its intramural segment and continued parallel to the underside of the peritoneum adjacent to the uterotubal junction. There was no evidence of any infection present.

Device location and tubal occlusion

An HSG was performed at the 3-month follow-up visit to assess device location and tubal occlusion in the 200 women who had successful bilateral placement. Correct device location was confirmed in 191 cases (96%), and unsatisfactory device location in six cases (3%). Bilateral occlusion was reported in 191 women (96%), unilateral occlusion was demonstrated in six women (3%), and three women (1.5%) had an equivocal HSG. In consultation with radiologists, a

protocol was produced to standardize the technique of hysterosalpingography in order to maximize the accuracy of micro-insert position and assessment of tubal occlusion.

Nine of the 200 women were found to have some evidence of dye passage (patency) past the micro-insert into the distal tubal lumen or peritoneal cavity at an HSG carried out 3 months after device placement. One of these women had unilateral patency due to an expelled device, and the other due to inadvertent device placement into the myometrium adjacent to the tubal ostium. The remaining seven women with some evidence of tubal patency underwent a repeat HSG 3 months later (6 months post-placement), and all had achieved bilateral tubal occlusion at this time. Thus, of the 200 women with initial bilateral placements, 198 (99%) had developed bilateral occlusion and were subsequently able to rely on the micro-insert for contraception. Four of the 198 women with demonstrated bilateral occlusion on HSG were found to have an unsatisfactory device placement according to the study criteria, where a device was located either too far or not far enough into the tube. This unsatisfactory placement was defined when the proximal segment of the device was >2 cm away from the opacified uterine cavity, or when >50% of the device length was present in the opacified uterine cavity. However, provided that bilateral occlusion was demonstrated, these women could rely on these devices for contraception.

Device-wearing tolerance

During the post-procedure follow up, satisfaction with wearing the micro-insert was rated as very good to excellent by 96% of the women at the 3, 6, 12, 18 and 24 month evaluation points. Only 4% rated their tolerance to wearing the device at any time point as good to fair, and none rated their tolerance to the device as poor.

Pregnancy prevention

The micro-insert effectiveness was measured, beginning 3 months post-placement, after the HSG had demonstrated bilateral tubal occlusion and the woman ceased alternative contraception. As of November 2002, 6015 woman-months of effectiveness data have been accumulated. The length of time during which women have been relying on the micro-insert ranges from 21 to 45 months. In total, 198 women have relied on the micro-insert for at least 12 months, 181 women have

relied on it for at least 2 years, and 34 women for >3 years. To date, there have been no reports of pregnancies following micro-insert placement. One woman with a previously discontinued version of the device in an earlier trial became pregnant; this prototype device did not contain the dynamic outer coil that now provides superior post-placement stability within the tubal lumen. Therefore, the 1-year effectiveness rate is 100% (95% CI 98.47–100%) using the Essure™ micro-insert, and the 2-year rate is 100% (95% CI 98.45–100%). There is also one woman with a unilateral Essure™ micro-insert and confirmed contralateral proximal tubal occlusion who has been relying on the micro-insert for 40 months.

Discussion

Hysteroscopic interval tubal sterilization using the Essure™ micro-insert appears to offer an attractive alternative to standard laparoscopic approaches. In the present study, this non-incisional method was associated with rapid recovery, high patient satisfaction and effective permanent contraception after 6015 women-months of follow-up. Following placement, there have been no serious side effects, nor any need for hospitalization. Tubal occlusion using a laparoscopic approach is generally regarded as highly effective in preventing pregnancy (Ryder and Vaughan, 1999), and any alternative approach must achieve comparable success rates. After 6015 woman-months of reliance, no pregnancies have occurred in those women in the study who have been relying on this micro-insert device. Thus the 1-year effectiveness rate was 100% (95% CI 98.47–100%), which is equal to the high success rates reported for various laparoscopic approaches after a comparable follow-up period (Ryder and Vaughan, 1999). Starting 3 months after the micro-insert placements, 191/200 (96%) of the women with successful bilateral placement had developed tubal occlusion and were able to discontinue other forms of contraception. Among the remaining nine women, seven had achieved occlusion at 6 months (total 198/200; 99%); of the remaining two women, one suffered a device expulsion and one had a device placed into the myometrium adjacent to the tubal ostium. In clinical practice, the need to perform a routine HSG at 3 months after insertion should not be necessary, provided that the placement position falls within the recommended guidelines where three to eight coils remain visible proximal to the tubal ostium following deployment. Where the physician feels unhappy about device placement, or the placement falls outside the recommended guidelines, an HSG should be performed at 3 months. Unfortunately, reinvestigation by HSG where confirmation of correct micro-insert placement and tubal occlusion is considered necessary may limit the suitability of this procedure in communities where such resources are either limited or unavailable. Although the success of bilateral placement of the micro-insert was not influenced by timing within the menstrual cycle, it was considered easier to see the tubal opening during the second half of the follicular phase when the endometrial lining was thinner and less prone to congestion. In clinical practice, it would be preferable to perform this procedure prior to ovulation in order to minimize the risk of pregnancy occurring

following ovulation. It is acknowledged that a urinary or blood pregnancy test would not exclude an early conception when the procedure was performed in the luteal phase. All the women in the study were using contraception in order to minimize this risk.

An advantage of this hysteroscopic approach for permanent contraception is that it offers a less invasive and taxing procedure that might broaden the appeal of interval tubal sterilization. The great majority of women (96%) tolerated this procedure with either sedation only or no sedation at all. In the small minority (4%) who required a general anaesthetic, this was either by request or it was considered necessary when difficult cervical dilatation was required due to pre-existing cervical stenosis, secondary to cone biopsy. Following the procedure, most of the women were able to walk from the procedure room to a recovery room, and could be discharged home 1–2 h later. In contrast, the time to discharge following laparoscopic tubal sterilization has been reported to average 4–5 h (Bordahl *et al.*, 1993).

Laparoscopic tubal sterilization procedures can result in significant postoperative pain, which can prevent women from resuming regular activities (Fraser *et al.*, 1989). In one study, 85% of the women reported that pain and/or fatigue slowed their recovery, with an average delay in return to normal activity level of 4.4 days, not including the day of surgery (Fraser *et al.*, 1989). The most powerful predictor of return to normal activity was the total amount of pain experienced. In contrast, in the present study, post-procedure pain was most commonly described as similar to menstrual cramps and resolved within one day in the majority of women. Overall, when interviewed during the 24-month follow-up period, 96% of women rated their tolerance to wearing the device as good to excellent, and a high level of satisfaction with the wearing comfort of the device continued for up to 36 months of follow-up.

In the present study, successful bilateral micro-insert placement was achieved in 88% of the women, and the most common reasons for failure to achieve satisfactory placement were tubal obstruction, stenosis, spasm, tortuosity or difficult access to the proximal tubal lumen, accounting for almost half of failures. Some undetectable anatomical barriers, possibly resulting from subclinical inflammatory or infective conditions, pose an unavoidable hurdle to this transcervical approach. Procedure- or device-related difficulties (potential avoidable factors) were primarily responsible for the other instances of unsatisfactory placement. It is believed that both of these latter causes can be improved upon or eliminated, so that successful bilateral micro-insert placement rates can be expected to improve further in future study populations.

Over the course of the present study, a number of adjustments—such as discontinuing the use of a support catheter and adding a black bump on the delivery catheter to signal optimal micro-insert positioning—were made that addressed many of the early device-related complications. In the early part of the study, this support catheter was used to increase column strength of the delivery catheter and provide more forward progression. However, it was soon realized that when the device encountered increased resistance in the tubal lumen, this

extra force predisposed to perforation through the tubal wall and into the surrounding myometrium of the intramural tube or more distally into the peritoneal cavity. Following removal of the support catheter, there were only a further two perforations in the larger portion of procedures performed. Over the course of the first five Essure sterilization procedures, all five physicians became more confident and time-efficient in gently introducing the hysteroscope along the endocervical canal, identifying and obtaining co-axial alignment of the scope to the tubal lumen, cannulating the tube and deploying the device. This acquisition of procedural skills was associated with a shortened procedure time that in turn resulted in less uterine distension, reduced leakage through a slowly dilating cervix, reduced endometrial oedema (J.F.Kerin, unpublished data) and enhanced patient tolerance to the procedure.

Even with the learning curve that is typically associated with a new procedure and device, the adverse events did not result in any serious clinical complications. Though perforations with the device did occur, only one woman developed symptoms of pelvic pain which required surgical removal of the micro-insert. In this case the micro-insert had undergone a partial perforation where one end remained fixed in the smooth muscle of the uterus and the other end was free to irritate the adjacent peritoneum, omentum or other surrounding structures. It is possible that symptoms of pain may be generated under these circumstances. In contrast, a complete perforation does not appear to cause pain, as the micro-insert lies freely until it attaches to the underlying peritoneum. The woman with the micro-insert remaining in her peritoneal cavity has remained asymptomatic after 3 years of follow-up. No uterine perforations associated with the hysteroscopic part of the procedure has occurred.

There was no clinical evidence of infection in relation to the micro-insert sterilization procedure at the 1-week follow-up review or clinical assessments at 3 months following placement. Prophylactic antibiotics were infrequently administered prior to or during the hysteroscopic sterilization procedure, and the evidence suggests that this procedure does not appear to carry a risk of intra-operative or post-operative infection. None of these women required hospitalization for any procedure-related reason. In contrast to the unacceptable rates of expulsion reported for past hysteroscopic sterilization approaches (Sciarrà and Keith, 1995; Ligot-Veneman *et al.*, 1999), only one expulsion was observed in the present study, and this resulted from the incorrect placement of the micro-insert. Accurate micro-insert placement across the narrowest diameter of the tubal lumen (Kerin *et al.*, 1992), where the intramural segment meets the isthmic segment at the uterotubal junction, and subsequent fibrous tissue ingrowth combines these primary and secondary factors to firmly anchor the micro-insert. Although the external junction of the tube to the uterus is described as the uterotubal junction (Lindblom and Norstrom, 1986), its endothelium contained in the smooth muscle envelope continues as the intramural tube to terminate at the ostium.

Before women consent to this hysteroscopic sterilization procedure, it is considered most important that they understand this to be an irreversible method of permanent contraception,

which cannot be surgically reversed. Despite careful pre-procedure counselling about the surgical irreversibility of the micro-insert sterilization procedure, some women will eventually regret this decision and wish to become pregnant. The only potential solution would be IVF, followed by embryo transfer into the uterine cavity. To date, seven women have undergone hysteroscopic procedures between 4 and 43 months following device placement for unrelated gynaecological conditions. A progressive tissue encapsulation of the device has been observed over time. The average post-placement uterine cavity micro-insert length of 6 mm had decreased to 1.3 mm over the 4- to 43-month period. In addition, the micro-insert is composed of inert biocompatible materials, which do not break down. These observations lend support to the hypothesis that the presence of the Essure micro-insert is unlikely to interfere with implantation following embryo transfer, but until embryo transfer and implantation rates are analysed in women carrying these micro-inserts this question will remain unanswered.

The other important factor to consider during the pre-procedure counselling involves the observation that up to 12% of women will not achieve bilateral micro-insert placement. The present authors' experience has been that most women will accept this potential failure rate of device placement because the alternative of laparoscopic surgery under general anaesthesia is less attractive to them. Those women with failed micro-insert placement can still pursue the option of laparoscopic sterilization or remain on their current contraception; alternatively, their partner might consider a vasectomy. With the hysteroscopic approach used to place the micro-insert, most women remain sufficiently alert to view the procedure on a video screen. It was noted consistently that those women who were awake and observed the procedure from the video screen commented that the experience gave them a sense of control and understanding of what was happening. The clinician could describe the appearance of the tubal opening and the placement of the micro-insert. The women could lateralize some discomfort to the appropriate tube and, most importantly, the clinician could demonstrate the inability of the device to advance when tubal resistance was encountered. The combination of pre-procedure counselling about the risk of failed placement and a visual validation of failed advancement of the device appeared to assist the woman in coping with this disappointment.

The age range considered in the present study was planned in an attempt to match the age range of the U.S. Collaborative Review of Sterilisation, where the median age of the 10 685 women at the time of sterilization was 30 years (Peterson *et al.*, 1996). This study revealed that the cumulative 10 year failure rate of various forms of sterilization was higher than previously realized, especially for women aged <28 years. It was also considered important to have a representative group of women aged <28 years whose natural fecundity would also test the efficiency of the micro-insert over time. Particular care was taken to counsel the younger cohort of women about the irreversibility of the procedure.

The present findings from this Phase II trial indicate that a hysteroscopic sterilization procedure using a dynamically

expanding micro-insert can achieve permanent contraception, with high patient acceptance and tolerability, and minimal morbidity. The 1-year effectiveness estimate equals that of conventional transabdominal sterilization approaches. One of the most important lessons learned was the need to improve the bilateral placement rate, and this is already being addressed by procedure- and device-related changes. The micro-insert hysteroscopic tubal sterilization procedure also has the potential to be cost-effective as it does not require the use of an operating room, general anaesthetic and the staff support required for a laparoscopic procedure. In addition, the recovery, turn-around time, earlier return to normal activity (J.F.Kerin, unpublished data) and the potential reduction in the rare but serious complications related to general anaesthesia and laparoscopic surgery may be realized. For these reasons, Essure™ hysteroscopic sterilization is likely to provide women with a reliable choice and a welcome alternative for permanent contraception.

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