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REVIEW

Safety, Efficacy, and Patient Acceptability of the Copper T-380A Intrauterine Contraceptive Device

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Abstract: The ParaGard Copper T 380A intrauterine device (CuT380A) provides reversible contraception that is as effective as sterilization for up to 20 years. The CuT380A is a mainstream, first-line contraceptive option for most healthy women, including nulligravid women, as well as many women who have serious medical problems. Because it is the most cost-effective method of birth control, the CuT380A is the preferred IUD, except for women who desire lighter or no menstrual blood loss. Surveys reveal that 95% of US CuT380A users are "very" or "somewhat" satisfied with their method. This article describes current candidates for IUD use, discusses the mechanisms of action of the CuT380A, provides guidance to reduce barriers to IUD access, suggests counseling points for patients, and outlines techniques to reduce the risks and side effects that can be associated with use of the CuT380A.

Keywords: copper intrauterine device, CuT380A IUD, ParaGard, patient satisfaction, efficacy, side effects

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Introduction

Worldwide, intrauterine devices are the most commonly used form of reversible contraception with 160 million women currently relying on this method.[1] Highest rates of utilization are found in China, Southeast Asia and the Middle East, but as many as 24% of women in select European countries use IUDs.[2] The impact that provider enthusiasm for IUDs has on their utilization can be seen in isolated reports of unusually high acceptance rates. Only about 1.5% of Brazilian contracepting women use any IUDs but in one Sao Paulo clinic, about 40% of women use the CuT380A.[3]

Copper IUDs are the most commonly used type of IUD; over 106 million women worldwide use them.[4] The CuT380A (ParaGard® Copper T380A IUD, Teva Women's Health Inc., Pomona, NY) has been found to be the most effective copper IUD[5,6] and is the only nonhormonal IUD currently available in the United States. The CuT380A is a T-shaped device, which measures 32 mm vertically and 36 mm horizontally. Its plastic frame is composed of polyethylene with barium sulfate to enhance its radiographic visibility. A thin copper wire with 200 mm^2 surface area is wrapped around the stem and a sleeve of solid copper is located on each of the two arms, which raises the total surface area of copper to 380 ± 23 mm^2. At the base of the vertical stem is a 3 mm bulb through which are threaded the monofilament polyethylene tailstrings that can enable the patient to monitor for the ongoing presence of the device and facilitate later removal of the IUD. This IUD is sold in a sterilized package that also includes the introducing tube and the stabilizing rod needed for placement.

The introduction of the CuT380A was delayed for 3 years after its FDA approval in 1985, until 1988 because of the extremely unfavorable medicolegal environment for IUDs at the time.[7] When it was ultimately introduced, product labeling was very stringent, reflecting liability concerns from both manufacturer's and providers' perspectives. In addition to extensive contraindications, which were largely based on theoretical concerns, a new type of filter was applied to reduce potential users—a "recommended patient profile" requiring parity, stable mutually monogamous relationship, and no history of PID or ectopic pregnancy.

As experience with the CuT380A has grown in the US and scientific evidence has been more frequently used as a basis for product labeling,[8] dramatic changes have been made in the circumstances in which this IUD is offered. The CuT380A has become a mainstream, first line contraceptive option for women seeking top tier, intermediate to long term contraception. It is an excellent choice for women desiring to delay pregnancy and also is an important alternative to irreversible sterilization. When fewer than 30% of women fill their prescriptions for hormonal contraception on time for 12 months[9] and 1 million pill users become pregnant each year, there is a clear need for an effective contraceptive that requires virtually no effort to make it work. As a result of its high efficacy and its long duration of action, the CuT380A is the most cost-effective method of birth control.[10–12] As more insurance companies cover this method, the total cost of reproductive health care will be reduced. For uninsured women, self-pay programs and patient assistance programs have considerably extended potential accessibility.

Despite these attractive features, it is estimated that only 5.5% of contracepting women in the United States use any type of IUD,[13] and only a minority of those women utilizes the copper IUD. In part, this may reflect lack of professional enthusiasm for the method. A recent survey of clinicians reported that 40% did not offer IUDs to *any* patient seeking contraception.[14] A curious pattern of inherent bias appeared in another study of physician responses to standardized patient videos, in which it was found that physicians tended to offer IUDs only to low SES women of color and high SES white women.[15]

It is clear that if CuT380A were used more often, unintended pregnancy rates would be lower, as would reduce repeat pregnancy among adolescent mothers and repeat abortions among women seeking pregnancy termination.[16–19] For all these reasons, expanding use to younger women has been declared to be a national priority.[20] In order to better appreciate the potential that this method offers women, this article will provide a comprehensive review of the literature about mechanisms of action, product safety and efficacy, patient satisfaction and approaches to reduce the risks and side effects that can be associated with the use of CuT380A.

Mechanisms of Action

There has been significant confusion about the mechanisms of action of the Copper IUD, but all the classic scientific evidence demonstrates that the IUD is a contraceptive, which acts a functional spermicide, to prevent the sperm from reaching the fallopian tube to fertilize the ovum.[21–24] The copper ions stimulate an intrauterine inflammatory reaction that is cytotoxic to the sperm and phagocytizes them; no viable spermatozoa remain in the endometrial cavity 18 hours after natural insemination.[25] Copper has a direct adverse effect on sperm motility and on sperm ability to penetrate through the cervical mucus.[21,26–28] The copper ions also incite inflammatory changes around the oocyte at the time of ovulation, a situation that is similar to that seen in women with endometriosis.

There is no evidence that the IUD works after implantation. Women using IUDs, who were followed with serial measurements of serum β-human chorionic gonadotropin, demonstrated no pattern suggestive of abortion (initial increase with subsequent disappearance of that hormone).[29–31] The evidence that IUDs do not work after fertilization by blocking implantation comes from several different experimental designs. When laparoscopic tubal flushings were studied, no sperm were found.[25,32] By studying ova retrieved during sterilization procedures from women who had mid cycle coitus, it was seen that none of the specimens from women using IUDs displayed normal cellular division indicating successful fertilization. However, 50% of the ova from the women who used no method showed such division.[33] Similarly, no eggs were recovered from the uterine cavities of 56 IUD users within 132 hours after the LH peak compared to 4 eggs found in the 115 control women.[33] In addition, the fact that CuT380A dramatically decreases ectopic pregnancy risks supports the fact that the site of action is before the fallopian tube—that fertilization is blocked. Recent studies have revealed that the copper IUD decreases endometrial HOXA10 expression, which is essential for endometrial receptivity, but the clinical significance of those changes is not known.[34]

When the CuT380A is placed postcoitally, it functions very successfully as an interceptive, but it may be that the placement procedure itself (with its substantial intrauterine manipulation) is responsible for that protection. The inflammatory changes seen in the endometrium, which are responsible for its excellent contraceptive efficacy, take time (at least days) to become established and cannot completely explain the ability of the CuT380A to provide immediate emergency contraception (see below).

Efficacy as Ongoing Contraceptive Method

IUDs are among the most effective and safest methods of contraception. A 2008 Cochrane Systemic Review concluded that the first year failure rate of the CuT-380A ranged from 0% to 1.0%; the cumulative pregnancy rate by 10 years was 2.1% in non-Chinese study centers, but 4% in Chinese centers, which tended to have less loss-to-follow-up.[5] Similar estimates were obtained by a later review in which the CuT380A was found to have a 5 year failure rate of 0.3%–0.5%.[35] These rates compare very favorably to the pregnancy rates seen with tubal ligation.[36]

Longer follow-up studies have demonstrated that the CuT-380A provides highly effective contraception beyond 10 years. Excellent protection was reported in one study for up to 15 years.[37] Bahamondes et al reported that 228 women age 35 and older who had used their CuT380A for 10 years and were followed for another 366 woman-years had no pregnancies.[38] More recently, Sivin has shown that excellent pregnancy protection extends to 20 years; no pregnancies were reported in that study after the seventh year of use.[39]

Success of the CuT380A is independent of the user's behavior, or put another way, there is virtually nothing that the woman has to do to maintain its efficacy, and there is nothing she can do (short of removing her IUD herself) that will compromise its efficacy. The efficacy of the CuT380A is not adversely affected by any drug-drug interactions, including concomitant use of anti-inflammatory drugs.[40] This conclusion is important, not only because an early case-control study had suggested that NSAIDs, especially aspirin, might have been responsible for IUD failures[41] but also because NSAIDs are extensively relied upon to treat the bleeding and cramping that can be associated with IUD use.

Copper IUDs increase serum copper levels, but that has not been shown to have any adverse clinical effects[42] except among the rare woman with copper

allergies.[43] IUDs containing smaller amounts of copper have measurably higher failure rates than the CuT380A.[26] For example, the Nova T with only 200 mm^2 of copper has a first year failure rate of 1.42%.[5] Some investigators have suggested that the intrauterine concentrations of copper ions, especially the early burst effect, might induce cytoxic and genotoxic effects on endometrial cells.[44] Higher concentrations be responsible for early spotting and bleeding, but have no long term carcinogenic impacts on the endometrium.[44]

Copper IUDs for Emergency Contraception

In a review of 8400 postcoital copper IUD placements, Trussell and Ellerson reported that pregnancy rates ranged between 0.1% and 0.7%.[45] A 2-year study compared 98 women who had IUDs placed postcoitally for both emergency and future contraception with a control group of women who had routine IUD placement for pregnancy protection only; it found no difference in rates of pregnancy, expulsion or removal for medical reasons between the 2 groups.[46]

In the first prospective study of the effectiveness of the CuT380A as an emergency contraceptive, none of 1963 women who had that IUD placed within 120 hours of unprotected intercourse experienced pregnancy in the first year. The 12 month continuation rate among the 1493 women who remained in the study was 94.3% for multiparous women and 88.2% for nulliparous ones.[47] In another multicenter study involving 1933 Chinese women who had the CuT380A placed within 120 hours of unprotected intercourse, the observed first year pregnancy rate was 0.13%.[48] Confirming these high levels of efficacy is a trial of another IUD with slightly less copper (375 mm^2) as an emergency contraceptive, in which the pregnancy rate was 0.2 per 100 women-years.[49] These rates compare very favorably to the single episode failure rate (2.0%) of the levonorgestrel emergency contraceptive pill. As seen, women often utilize the CuT380A for ongoing contraception. In a prospective comparative trial of women choosing CuT380A vs. oral levonorgestrel tablets for emergency contraception, it was found that at 6 months, 61% of women continued to use their IUDs and another 8% had switched to another effective method whereas only 52% of the oral EC users was using an effective method.[50]

Other Health Benefits Provided by CuT380A

Because the CuT380A provides such effective protection against pregnancy, it also significantly reduces a woman's risk of developing an ectopic pregnancy. Women who use no method of contraception are 2–10 times more likely to experience an ectopic pregnancy than are CuT380A users.[51,52] If a woman does become pregnant while using the CuT380A, her risk of having an extrauterine implantation (8%) is lower than women who get pregnant while using the LNG-IUS or following tubal sterilization.[53] The CuT380A has also been associated with a 50% to 60% reduction in the risk of endometrial adenocarcinoma, although the mechanism of action for this protection is not clear.[54–58]

Patient Satisfaction

The success of the CuT380A can be measured not only in terms of efficacy, but also in terms of acceptance and continuation rates. Worldwide the popularity of the copper IUDs reflects high acceptance where the devices are available.[59] In the United States, a tremendous potential for IUD utilization has been demonstrated by studies in which long acting methods are provided for free.[60]

Patient satisfaction with the IUD is generally among the highest of all methods.[61] Continuation rates with the CuT380A reflect that satisfaction; first year continuation rates are relatively high, 85%–90%,[39] compared to continuation rates with other reversible methods. A WHO study found that 44% of women continued to use their CuT380A for at least 7 years.[62] Not only do women use IUDs for longer than they use other methods, they use them more effectively. There is no intermittent or inconsistent use of the CuT380A, as is routinely seen with other methods.[63,64]

One of the most common reasons for early IUD removal is a desire for pregnancy; on average women use the copper IUD 4 years before requesting removal for this reason.[65] Cost effectiveness is established in less than 2 years.[12] A removal request provides an opportunity for preconception care, which is not routinely available with most other methods. Women who

experience side effects tend to request slightly earlier removal, which might be affected by the patients' concerns about the impact of the side effects.[66]

Candidates for IUD Use

The United States Medical Eligibility Criteria published by the CDC in May 2010 lists only a limited number of medical conditions as Category 4 (contraindications) for use of the CuT380A.[67] These conditions can be grouped into 4 major categories—1) uterine issues (unexplained uterine bleeding; 2) endometrial cavities that are distorted or too small (<6 cm) or too large (>9 cm)), known or suspected carcinoma of the uterus (endometrial, cervical); 3) recent uterine infection (cervicitis, endometritis, pelvic inflammatory disease); 4) behavioral conditions (those which place the women at high risk for PID). Other than those considerations, the CuT380A is a viable option to provide top tier contraception to women with serious medical problems[68] including hypertension, diabetes,[69] ovarian carcinoma,[70] thyroid dysfunction, organ transplant,[71] obesity, breast cancer, history of stroke or myocardial infarction. Some of these conditions are discussed in more detail below. It is interesting to observe that even after a simplified checklist reflecting WHO MEC for IUD use was provided, clinicians continued to rely on their prior "knowledge" of IUD eligibility and denied the IUD to 30% of MEC-eligible women.[72] Perhaps, this may explain why, women are so ill-informed about the IUD.[73]

Nulliparous women

Nulliparity has never been a contraindication to the use of any IUD. However, in the wake of the Dalkon Shield lawsuits (which linked IUD use and PID-related infertility),[74,75] parity was a requirement in the recommended patient profile for each of the US IUDs. This ignored the rich history in the US of IUD use by young, nulliparous women. In fact, in the 1970s, the Copper-7® IUD (Ortho-McNeil, Raritan NJ) was developed specifically for and used successfully by nulliparous women.

In 2005, the FDA removed the recommended patient profile in its entirety from the product labeling for the CuT380A. The data that persuaded the FDA to make this substantial change came from studies that demonstrated 3 important conclusions: 1) that prior IUD use was not a risk factor for infertility, 2) that the presence of an IUD did not increase a user's risk of having a cervical infection ascend into the upper genital tract, and 3) that discontinuation rates among nulliparous women were acceptable.

Hubacher et al provided the greatest reassurance that prior IUD use was not associated with infertility. In a case-control study of 1895 nulliparous woman with primary infertility, no increase in the prior use of IUDs was found in 358 women in the tubal occlusion group when they were compared either to the 958 infertile controls or to 584 pregnant controls. Tubal infection was not related to the duration of IUD use but was associated with the presence of chlamydia antibodies.[76] Doll et al found that delivery rates for the former IUD users were very comparable to delivery rates seen in women who stopped oral contraceptive use.[77] It is not clear if longer duration of IUD use is associated with lower fertility rates.[77,78] Hov et al found no difference in overall return to fertility between women who had their IUDs removed in order to conceive and those who had their IUDs removed because of an IUD complication.[79] Not only is future fertility not effected by IUD use, but return to fertility is very rapid after IUD removal.[79,80]

The concern for an increased risk of PID among nulliparous women was one of the reasons the IUD was lost from the US market in the mid-1980s,[74,75] but conditions have radically changed since then. The possibility that an IUD might permit the ascent of the pathogens from the vagina through the cervical mucus into the upper genital track was credible with the multifilament tailstrings of the Dalkon Shield.[74,81] However, the monofilament tailstrings used with modern IUDs do not pose that risk. When adjusted for relationship stability, modern IUD users have been found to have no increased risk of PID over the general population.[74,82] The only time women are vulnerable to any IUD-related increase in upper tract infection is within the first 20 days following IUD placement.[83,84] Another convincing answer to the concern that IUD use might impact upper tract infection comes from the fact that the treatment of PID in IUD users is the same as it is for other women; the CDC STD Treatment Guidelines no longer call for routine IUD removal as part of the initial treatment of PID in IUD users.[85]

The final concern—that there would be higher rates of side effects and discontinuation by nulliparous women—was addressed in another series of studies. The expulsion rate among nulliparous IUD users was found to be only slightly higher than parous IUD users.[86,87] Veldhuis et al reported that nulliparous women using "copper IUDs" did not show higher rates for complications than parous users did: PID rates were 3.5 per 1000 women-years; ectopic pregnancy rates were 0.6% to 1.1% per year; and rates of expulsion were 0.0% to 1.2% per year. There was also no excessive removal of IUDs among nulliparous women compared to parous ones.[88]

Even though ACOG recommends that IUDs and implants be first-line choices for both nulliparous and parous adolescents,[89] teens are rarely even told about IUDs. Recent studies have shown that only half of the pregnant women aged 14–25 had ever heard about an IUD and only slightly more than one half knew of its efficacy.[90,91] Although physicians recommend IUDs to only 42%–86% of women of all ages,[15] young women comprise the age group to whom practitioners are least likely to offer IUDs.[14] In a survey of California women age 14–27 (85% nulliparous), only 45% had heard of the IUD and not one woman had used one. Very interestingly, after reading a brief description of the IUD, only 11% said they might be interested in using one.[92] However, another study showed that a brief (3 minute) educational intervention significantly impacted on the attitudes that young women had towards IUDs. At baseline, only 14.7% of women aged 14–24 expressed a positive attitude toward the IUD, but, after the educational intervention, 53.8% held a positive attitude.[93]

Breastfeeding women

Breastfeeding women are excellent candidates for the CuT380A once uterine involution is achieved. While lactational amenorrhea is a very effective method for the first 6 months following delivery, many women discontinue breastfeeding early and without consulting their providers.[94] Having the IUD in place provides protection during those gaps and simplifies the woman's life at a time when extensive demands are being placed on her time.

Breastfeeding women are more likely than non-breastfeeding women to have a smooth, pain-free IUD placement and less post-placement bleeding and problems.[95] A prospective study of breastfeeding women using CuT380A IUD compared to those using a progesterone-releasing vaginal ring demonstrated the safety of IUD use in this population. Among the 97 women using the IUD, there were no insertion failures, no perforations, no pelvic infections, and no accidental pregnancies during the 12-month follow-up period. The total discontinuation rate over that year for the IUD was 2.3%, which compared very favorably to the 65.4% discontinuation rate seen with the progestin-only vaginal ring in the same time period.[96]

In another prospective randomized trial of IUD use by breastfeeding women, it was shown that mean infant weights were at or above the 50 percentile. No negative influence on infant development was observed among IUD users. By 12 months, 90.9% of women were still using the copper IUD.[97]

Women with uterine leiomyoma

Leiomyoma pose several potential problems for successful IUD use. Fibroids that distort the endometrial cavity can block entry into the endometrial cavity, preventing correct placement of the IUD at the fundus or they can prevent the IUD arms from extending completely. Another concern is that by eroding against the leiomyoma, the IUD could cause unscheduled bleeding or heavy and prolonged menses. The depth of the cavity and the location of the fibroids can be evaluated ultrasonographically prior to attempting IUD placement. Saline infusion sonography can separate the endometrial walls and better identify any submucosal fibroids. If imaging studies are not available, the endometrial cavity can be adequately assessed using the uterine sound at the time of attempted IUD placement. If the sound can be advanced easily to the fundus, the uterine depth can be confirmed and obstructing fibroids can be ruled out. Lateral (side to side) movement of the sound at the fundus confirms that there is adequate space for the IUD arms to open completely. Women who have small leiomyoma and heavy menstrual bleeding are often better served by the LNG IUS[98] or other hormonal methods but, in the absence of excessive menstrual bleeding and cramping, women with small fibroids may still reasonable candidates for the CuT380A.

Women with HIV

Women with HIV infection may also use IUDs. In a prospective 2-year trial of HIV-infected women

randomized post partum to receive a CuT380A or hormonal contraceptive (either DMPA or oral contraceptives), the safety and efficacy of IUD use this population was established.[99] Pregnancy rates were lower in the women randomized to CuT380A compared to those assigned to hormonal contraception (2.0/100 women-years vs. 4.6/1000 women-years). There was one case of PID in the 296 women randomized to the CuT380A. Finally, the CuT380A users had a lower progression of their disease as measured by death or by a CD4+ lymphocyte count below 200. Other investigations have verified that HIV-infected IUD users have no higher levels of complications than HIV-negative IUD users.[100,101]

Risks of IUD Placement

Uterine perforation

Rare complications can occur with IUD placement. Perforation occurs in about 1 in 1000 cases (0.21/1000 to 3.6/1000 placements).[62,102–104] All perforation starts at the time of IUD placement, but the diagnosis of IUD perforation is often delayed.[105,106] There is no evidence that the IUD can migrate completely through the myometria of non-pregnant women, although the IUD is known to wander within the endometrial cavity.[107] However, if a portion of the IUD is pressed into the myometrium during initial placement, the IUD may work its way through the remainder of the wall to be later expelled into the peritoneal cavity. Rates of perforation are higher when the uterus is markedly verted or fixed. Operator experience also plays an important role. For all postpartum women, it is recommended that IUD placement be done either immediately after delivery of the placenta (see below) or after uterine involution is complete. For many women, involution may be sufficiently complete by 4–6 weeks, but other women may need 8 weeks to normalize their uteri following delivery. Prior C-section does not seem to increase the risk of perforation.

Close adherence to all steps of the placement is important to minimize the risk of perforation. This includes placement of the tenaculum to stabilize the uterus and to straighten its axis. Sounding of the uterus prior to placement will reveal the uterine angle as well as size of the cavity to verify that the depth of the uterus (external os to fundus) is within labeling recommendations (6–9 cm). Additional recommendations to limit the risk of perforation are discussed below in Table 1.

Uterine perforation is suggested when the tailstrings of the IUD shorten or disappear from the vagina entirely. Probe the endocervical canal for the

Table 1. Management of IUD complications.

Challenges	Suggestions
Obesity making bimanual exam inconclusive	Rectal exam can provide assessment of uterine size, mobility, position, etc.
Stenotic cervical os	Progressively dilate cervix with cervical os finder. If unable to dilate cervix, consider misoprostol.[163]
Vasovagal reaction anticipated	Provide a paracervical block—wait at least 3 to 5 minutes. Always be prepared with smelling salts, oxygen, etc. If patient experiences a strong vasovagal reaction, remove cause (IUD, tenaculum, etc.).
Perforation risk	Place tenaculum on cervical lip that is more difficult to reach to more completely straighten the axis of uterus.
Pain with tenaculum placement	Use of slender tipped tenaculum (Goldstein Grippers) decreases pain and results in less bleeding after removal. Do ***not*** have the patient cough with tenaculum placement but having her valsava prior to and throughout may help distract her and stabilize her cervix for tenaculum placement.
Perforation potential with uterine sound	Gently bend (metal) tenaculum to match uterine flexion. Hold tenaculum as if it were a pencil. Stabilize your hand against patient's thigh. Advance though os using only force of fingers. Advance into cavity in direction of uterus determined during pelvic exam.
Loading of IUD into tubing	Tuck IUD arms into tubing through packaging. No sterile gloves needed.
Prevent future tailstring complaints	Cut tail strings long enough to tuck around cervix (eg, behind cervix of anteverted uterus or anterior to cervix of posterior uterus).
Pain immediately following procedure	Prophylactic NSAIDs do not reduce pain scores[166] but administration with onset of symptoms may be helpful.

IUD or twist a cytobrush in the canal to determine if the tail strings are present there and can be snagged and brought back into the vagina. If the IUD is not found in the cervix, its localization is usually made ultrasonographically. If ultrasonography is not available, the CuT380A can clearly be seen on X-ray studies. However, X-rays will not be able to ascertain the location of the device within the pelvis. Markers, such as a uterine sound, help define the endometrial cavity on cross table and lateral X-ray films. If X-ray studies are not available, the CuT380A can often be located within the endometrial cavity and removed with alligator forceps, RetrieveHC® or the Emmett Thread Retriever®.[108] IUD hooks, which were helpful in removal of S-shaped Lippes Loop IUDs, should **not** be used to remove T-shaped devices because they are associated with an increased risk of uterine perforation.

If the CuT380A is extrauterine, it should be surgically removed, especially if the patient is symptomatic. This is because the copper may establish a sterile abscess in the peritoneal cavity, which can lead to adhesion formation. These adhesions may cause chronic pelvic pain and infertility. IUDs have also been found to cause bowel perforation.[109] There are case reports of delayed abdominal abscesses, up to 35 years after placement.[110] Laparoscopic removal is generally successful.[111] However, with unusual placement (such as within the bladder,[112] rectum, or broad ligament), other surgical approaches may be required. If the patient is asymptomatic and is a poor surgical risk, it has been suggested that she may be intermittently monitored radiographically and symptomatically.[113]

Expulsion

Symptoms of expulsion include vaginal discharge, cramping or pelvic pain, unscheduled spotting or bleeding, dyspareunia (patient or partner), lengthening tail strings, or an IUD palpated in the vagina.[114] A Cochrane systematic review reported that first year expulsion rates ranged from 2.4%–5.2% for the CuT380A.[5] A multinational trial with 7 years of follow-up found that the cumulative discontinuation rate due to expulsion was 1.8 per 100 women-years of use.[115] Expulsion rates are affected by the experience of the clinician, the parity of the patient, severe dysmenorrhea, and the cycle day of placement.[116,117] Nulliparous women have a statistically (but not clinically) significantly higher rates of expulsion compared to multiparous women.[86] Expulsion rates are highest when IUDs are placed when women are on menses; delaying IUD placement until cycle day 6 can reduce expulsions in the first 3 months by 30%–50%.[118] Breastfeeding women who experience more uterine contractions were found to have no higher expulsion rates than women who menstruated.[96] A woman who has experienced one prior expulsion has a 30% chance of expelling a subsequent copper IUD.[119]

In a large multicenter clinical trial, Walsh et al observed that early (during the first 8 weeks) expulsions were obvious to the patient. However, between 8 to 12 weeks, asymptomatic partial expulsions tended to replace those overt, complete expulsions. This observation has provided the impetus for the new recommendations which change the timing of the first follow-up visit to 10–12 weeks following placement.

Infection

As noted above, the risk of pelvic inflammatory disease (endometritis/salpingitis) is elevated among IUD-users only for the first 20 days following IUD placement.[83,84] After that time, the risk for acquiring PID mirrors the rate found in the general population. These observations confirm the concept that early PID results from endometrial contamination at the time of placement and that subsequent infections (with the exception of actinomycotic infection) are due to the same risk factors that non-IUD users have for PID, eg, multiple sex partners combined with lack of condom use.

The absolute rate of PID with early IUD use varies with the prevalence of cervical infections in the population. In studies from the US and Norway, the incidence early infection was approximately 1:1000.[120,121] In a systematic review, Mohllajee et al reported that the absolute risks of PID were 0.27% for women without STDs at the time of IUD placement and 0.5% among women with chlamydia or gonorrhea.[122] These were confirmed by Faundes et al.[123] These observations underscore the need to screen women carefully for risk factors which might place them at risk for having current cervicitis. They also highlight the need for fastidious attention to correct techniques with IUD placement to minimize endometrial contamination.

However, routine antibiotic prophylaxis at the time of IUD placement is not warranted.[8,120] Cervical infections and upper genital tract infections acquired during IUD use can generally be treated with the IUD in place according to CDC STD Treatment Guidelines,[85] unless the patient fails to respond to antibiotic therapy or actinomycotic PID is suspected.[83,124]

Pelvic actinomyces is an extremely rare disease that can occur in women who use IUD for a long duration. Because it is so rare and because it is not a reportable disease, there are no secure estimates of its incidence. *Actinomyces* are obligate anaerobic Gram-positive bacilli that are commensal organisms found in the mouth and gastrointestinal tract. They are fastidious and slow growing, which makes testing for them challenging. They tend to form granulomatous abscesses with tissue fibrosis and sinus formation. The original abscess may be unilateral, but the colonies spread aggressively, often into the bowel. Unless a patient presents with a surgical emergency (obstruction, etc.), long term (at least 30 days) antibiotic therapy with penicillin, clindamycin, erythromycin or tetracyclines can be quite effective.[125] In contrast to PID caused by STDs, it may be prudent to remove the IUD after initiating antibiotics in women with suspected actinomycotic infection.[126,127]

Unfortunately, there are no screening tests to identify at-risk women and few tests to confirm the diagnosis of actinomycotic infection. Vaginal culture is not helpful.[128] Pap smears are very insensitive and nonspecific for detecting the presence of *Actinomyces*; only about 50% of women with *Actinomyces* abscesses have pap smears reporting the characteristic "sulfur granules". The test also results in frequent false positive results, because many other organisms (*Candida, Aspergillus, Nocardia, Leptothrix*, botryomycosis, coccobacilli and even synthetic fibers) can cause similar appearing "sulfur granules" on pap smears.[129] The prevalence of *Actinomyces*-positive smears in studies of IUD users were found to vary from 0% to 31%, with an average of 7%.[130,131] Given its prevalence, an incidental finding of actinomyces-like organisms in a pap smear obtained from an asymptomatic woman requires no treatment.[129]

IUDs are not generally recognized as a risk factor for vaginal infection but, there are some isolated reports of an increase in the incidence of bacterial vaginosis in IUD users.[132] In addition, Chassot et al have reported the IUD might serve as a reservoir for Candida albicans.[133]

Side Effects

On average, menstrual blood loss may increase by 35%–80% with use of the CuT380, but this rarely leads to anemia.[134] In the first year of use, heavy menses and dysmenorrhea are the most common reasons for CuT380A removal;[135] up to 15% of users discontinue use due to those side effects.[5] Many more women complain of these problems but tolerate them. A long-term study of copper IUD users found that mean hemoglobin levels were not changed from baseline but women over age 30 were less likely to complain of heavy bleeding.[39] Nonsteroidal anti-inflammatory agents (NSAIDs) are frequently recommended to treat each of those side effects. In a systematic review of 15 randomized, controlled studies involving more than 2700 women, Allen et al found that all types of NSAIDs (including alclofenac, diclofenac, flufenamic acid, ibuprofen, indomethacin, mefenamic acid, naproxen and suprofen) reduced bleeding. However, prophylactic use of NSAIDs to *prevent* development of those side effects is not supported by evidence.[136] If NSAIDs are not successful as first line therapy for heavy or prolonged bleeding, then tranexamic acid may be helpful. For women who have a CuT380A placed at the time of abortion, the number of days of bleeding and spotting rapidly stabilizes at about 8 days per month.[137]

The prevalence of bleeding and painful side effects over time was studied in a 52 week clinical trial of 1947 copper IUD users, in which only 15 subjects were lost to follow-up. In the first 9 week period, 35% of participants reported more menstrual pain with the IUD.[138] Over the remainder of the 1 year period, about one third of women reported more menstrual pain with the IUD, but about a quarter reported less menstrual pain. Bleeding was found to decrease over time, but intermittent spotting and bleeding complaints remained unchanged with longer term use.

One recent report suggests that in women who complained of excessive bleeding or cramping, a three-dimensional (3D) pelvic ultrasound study, can be helpful in identifying malpositioned IUDs (that may be causing those problems).[139] Doppler studies have searched for underlying vascular changes, which could account for these complaints but no consistent

findings have emerged. Jimenez et al demonstrated that women, who have severe dysmenorrhea and/or bleeding with the CuT380A, have increased subendothelial blood flow, but no increase in pulsatility index or in resistance index in the midluteal phase 3 months after placement.[140] The increased blood flow persisted even after corrections were made for age, IUD type and parity. Yigit et al studied IUD users in the early phase of the menstrual cycle and found that women with increased bleeding scores had significantly lower uterine artery pulsatility indices compared to IUD users without bleeding problems.[141]

Because changes in bleeding patterns are among the most common reasons for IUD discontinuation, Stanback and Grimes sought to determine if such removals could be predicted at a one-month follow-up visit. They found that women who complained at their first visit of intermenstrual bleeding were 2.9 times more likely to request early removal and those with excessive menstrual flow were 3.5 times more likely to discontinue use. These authors suggested that these women would benefit from more intensive counselling and treatment with non-steroidal anti-inflammatory drugs to reduce the risk of early discontinuation.[142]

Placement Techniques

The procedure to place the CuT380A is very straightforward. Failures occur in 1 in 300 attempts.[5] The manufacturer's instructions are clearly described in the package labeling[143] and didactic aids are available from various organizations, including the Association of Reproductive Health Professionals.[144]

Timing

The CuT380A IUD can be placed at any time in a woman's cycle when she is not pregnant. It is preferable to avoid IUD placement during menstruation, especially during heavy flow days to reduce the risk of expulsion during the first 3 months.[118] Since the Copper IUD is an excellent post coital contraceptive (see above), recent unprotected intercourse is not a contraindication to IUD placement. The ACOG Committee on Gynecologic Practice urged clinicians adopt Same Day IUD placement protocols.[145]

Post abortal placement

The safety and efficacy of IUD placement immediately following first or second trimester abortions, is well established.[146,147] Placement at this time has many attractive features. The patient's motivation is generally quite high, especially following an elective pregnancy termination. From the patient's perspective, the convenience of having an IUD placed immediately can be important. The cervix is open, making the procedure less uncomfortable and the bleeding related to IUD placement may be masked by postabortal bleeding. The alternative—delayed placement—may not be feasible because studies have shown that up to two-thirds of women, who asked for an IUD at the time of the abortion but were told to return at a later date, never got an IUD placed.[148,149] Not unexpectedly, IUD use was higher overall among those given the IUD immediately after the procedure.[150]

The disadvantages of IUD placement immediately following an abortion have also been chronicled. The greatest theoretical risks are for perforation, expulsion and infection. Studies, which have compared immediate to delayed placement of the CuT380A, have reported that continuation rates by 6 months were equivalent. By 12 months, expulsion rates were higher in the postabortal arm but ranged from 1%–15%.[150] Expulsion rates are generally higher following placement done after 2nd trimester abortions than after 1st trimester procedures.[150,151]

Postpartum placement of IUDs

Immediate postpartum placement of IUDs is a common practice in Mexico, China, and Egypt. The convenience to the woman of having an IUD placed immediately (within 10 minutes) after delivery of the placenta is obvious; however the potential for significantly higher risk of expulsion may offset that convenience. Early followup may be appropriate.[152] In an early retrospective study, which followed 235 women in whom the CuT380A IUD was placed immediately following removal of the placenta, the unplanned pregnancy rate was 0.7% and continuation rates at 6 and 12 months were 87.6% and 76.3%.[153] In another study, which compared immediate postpartum IUD placement to delayed postpartum placement, one year pregnancy rates were higher in the early placement group—4.7% vs. 2.4%.[154] In a trial comparing 910 women given immediate postpartum placement either digitally or with instruments, 6 month followup revealed no pregnancies, no infections, no perforations, and expulsion rates of 13.3% vs. 12.7%.[155]

Adding appendages to the IUD has been found not to be helpful.[152]

Post cesarean-section placement

Case series of IUD placement at the time of cesarean section have demonstrated high levels of device retention[156–159] and low levels of complications.[155,158,160] Many of the early reports were with tailless IUDs. A recent pilot study of women undergoing elective C-sections had TCu380As placed through the uterine incisions and the elongated tailstrings were threaded within the placement tubing through the cervix and into the vagina; all IUDs stayed in a fundal position throughout uterine involution and tailstrings were always available in the vagina to facilitate easy IUD removal should complications develop.[161]

Preparing for placement

Once a history has been obtained to determine if the patient has any contraindications to use of the CuT380A, a pelvic exam should be done to assess uterine size, position and mobility. No specific laboratory tests are needed; in particular, routine screening for STDs is not needed. Similarly, routine pretreatment with antibiotic prophylaxis or with[162] or with misoprostol is not recommended.[163] Suggestions to increase successful IUD placement are outlined on Table 1.

Infection issues with IUD placement

Known acute cervicitis is an absolute contraindication to IUD placement until the infection has been cleared. However, routine screening for STDs or cervical cytology is not required.[140] If testing is done, it may be obtained on the day of the procedure. One study of 975 IUD placements found that none of the women, who were diagnosed with chlamydia immediately following placement, developed PID when all the infected women were treated within 7 days of IUD placement.[121] The risk of developing clinical PID attributable to an IUD has been estimated to be 0.15% when the prevalence of gonorrhea and chlamydia in the population was 1% and there was screening for STDs.[164]

There is also no longer any concern about CuT380A placement in the face of vaginal infections, such as bacterial vaginosis or candidal infection. Women who have trichomoniasis should be re-evaluated as candidates since they have demonstrated their vulnerability to STDs in a sexual relationship. If a woman has bacterial vaginosis, IUD placement should not be delayed, but she should be given oral antibiotic therapy, not vaginal treatments, for her condition.

Managing discomfort during IUD placement

Every effort should be made to reduce discomfort and the fear of discomfort with IUD placement. There are several potential steps in the procedure which might cause pain or discomfort. Most women rate their discomfort as mild to moderate. Occasionally, the pain is more severe and may be accompanied by nausea, dizziness and vasovagal reactions. Cramping and pain may last for a few days. Risk factors for pain include nulligravidity, age over 30 and more time since menses. Expectations also affect the perception of pain.[66] Early studies of pain with placement of the Dalkon shield found that pain scores were unaffected by pretreatment with NSAIDs.[165] Other trials with NSAIDs of different doses and different formulations have also failed to find a benefit. In one study, median pain scores on a scale of 1 to 10 were 1.8 in the ibuprofen group and 2.0 in placebo users.[166] Misoprostol given sublingually with diclofenac does not reduce pain and may increase side effects.[167] Double-blind, randomized, placebo controlled studies of the effect of misoprostol failed to show any positive impact on pain scores or the ease of placement of the IUDs.[163,168] However, in a small pilot project, use of misoprostol 400 mcg given vaginally 1 day prior to IUD placement enabled women, who had previously failed placement due to cervical stenosis, to receive an IUD.[169]

Management of pregnancy with IUD use

Once pregnancy has been diagnosed, it is important to localize both the IUD and the pregnancy. If the copper IUD fails, the chance that the pregnancy is extra-uterine rises to about 5%–8%,[170] which is far less than is seen with either tubal ligation or the progestin-releasing IUDS. On the other hand, of the most frequent reason for pregnancy in an IUD user is that the IUD has been lost or dislocated.[171] If the pregnancy is intrauterine and diagnosed in the first trimester, the CuT380A should be removed if removal

can be accomplished without an invasive procedure.[172] Early removal reduces the risk of spontaneous abortion, septic abortion, and pre-term delivery.[21] Women with no available tailstrings should be counselled about the signs and symptoms of preterm labor, but advised that they face no increased risk of fetal anomalies due to the presence of the CuT380A within the endometrial cavity.

Other Issues

Women who require biopsies of endocervical area and endometrium can generally have them done without disruption of the IUD. LEEP procedures can be done either by lifting the tailstrings away from the area, tucking them temporarily inside the cervix or protecting them within a plastic tubing.[173]

Women who need imaging can safely undergo magnetic resonance imaging without concerns for heating the CuT380A or rotational forces being applied to the unit.[174]

Counterfeit IUDs are now available on line and have tempted providers who wish to make the devices available to their patients. Unfortunately, these devices are not allowed by the FDA and use of them has been found to constitute insurance fraud. The manufacturer has programs in place (patient payment plans and patient assistance programs) to reduce the initial upfront cost so that women can enjoy the long term cost effectiveness, and other benefits of the CuT380A.

Looking into the Future

The benefits of the CuT380A are well documented. (See Table 2), and should become better recognized with time. Utilization of IUDs in the US will continue to grow, especially as smaller devices are introduced for use in nulliparous women, as more women learn of the convenience and efficacy of IUDs and as more clinicians have success placing them. The CuT380A, in particular, may well gain more favor when cost effectiveness becomes a more important focus for the health care system. It is not clear if the more innovative applications (including immediate postabortal or postpartum placements and use of the copper IUD as an effective emergency contraceptive) will be more generally adopted, since each of them would require changes in the way payments are made. In particular, if global fees continue to be provided for obstetrical care, it is unlikely that immediate postpartum placements will increase. Copper IUDs that are coated with NSAIDs or related compounds may reduce early spotting and unscheduled bleeding. Versions of the copper IUD that rest in the cervix rather than within the endometrial cavity could greatly increase the number of clinicians capable of offering this device.

Table 2. Key points: CuT380A in 2011.

- The Copper T380A is the most cost effective method of birth control available in the United States.
- The efficacy of the CuT380A in typical use matches that of sterilization and places it in the top tier of methods. Therefore, the CuT380A is a mainstream, first choice method for all women, except those who do not want monthly bleeding.
- Off label, the CuT380A may be used for up to 20 years.
- Return to fertility is rapid following removal of the CuT380A.
- Patient satisfaction is among the highest and continuation rates are generally higher than seen with other reversible methods.
- The CuT380A is a good choice for nulliparous women and for many women with serious medical problems needing effective contraception .
- Same day placement is preferred. Immediate placement following abortion, C-section and vaginal deliveries have acceptable expulsion rates and give great convenience.
- The risks of IUD placement (infection, uterine perforation) are low, each about 1:1000.
- The most common side effects are increased bleeding and cramping; NSAIDs can provide effective treatment of these problems in most cases.
- The CuT380A is the most effective method of post coital contraception.
- The safety record with the CuT380A is impressive.
- The CuT380A offers convenient, private contraception, which reduces the risk of ectopic pregnancy and endometrial cancer.

Disclosure

This manuscript has been read and approved by the author. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The author serves on the TEVA Advisory Board for hormonal contraception, has received honoraria from them for promotional talks, and her clinic is receiving grant funding for contraceptive research. The peer reviewers of this paper report no conflicts of interest. The author confirms that they she has permission to reproduce any copyrighted material.

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