Contraception

Contraception 95 (2017) 529–537

Clinical Guidelines

Use of intrauterine devices in nulliparous women

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Received 18 August 2017; accepted 23 August 2017

Abstract

Five intrauterine devices (IUDs) are available in the United States: four levonorgestrel-releasing intrauterine systems (two containing 52 mg, one containing 19.5 mg and one containing 13.5 mg) and one copper-bearing device (Copper T 380A). All IUDs have very low typical-use failure rates and high acceptability ratings, yet they are used by a minority of women, with nulliparous women less likely to do so than parous women. The objective of this clinical review is to give evidence-based recommendations for the use of IUDs in nulliparous women. Intrauterine devices are safe and effective for the majority of women including those who are nulliparous, and should be routinely included in the contraception options offered to them.

Keywords: Intrauterine device; Intrauterine contraception; Intrauterine system; IUD; IUS; Nulliparous

This guideline revises and replaces the first version published in 2009. During the past 7 years, there have been significant contributions to the literature on the use of intrauterine devices (IUDs) in nulliparous women. These data have enabled us to make more confident statements about the effectiveness, acceptability and low complication rate of IUD use in this group. They have also provided concrete information on the role of preinsertion agents, which do not appear to provide any benefit. In addition, although some studies have shown that nulliparous women may be more likely to experience difficult or painful insertions, the vast majority of women, regardless of parity, experience successful and well-tolerated insertions. Recent research, like earlier studies, shows that both providers and women frequently have an inadequate understanding of IUDs. This lack of knowledge is a major barrier to wider use.

This guideline is not itself a systematic review of the literature, although we include the results of systematic reviews where available. Some of the questions addressed in this guideline are not amenable to systematic reviews because of the limitations of the information available on the IUDs currently being marketed. Rather, this document provides guidance for clinical practice based on a synthesis of expert opinion and available evidence.

In summary, data published since 2009 have confirmed that IUDs are an excellent contraceptive option for nulliparous women. However, the health care community and the public need to be educated about their safety, effectiveness and acceptability in this group to improve access and an informed choice of contraceptive method.

1. Background

IUDs are highly effective, safe and well-tolerated contraceptives with typical-use failure rates similar to that of surgical sterilization [1]. These characteristics make the IUD an excellent contraceptive for the majority of women, including those who are nulliparous.

The overall use of IUDs has increased in recent years. In 2002, 2% of currently contracepting women reported use of an IUD [2]. This proportion rose to 10.3% by the period 2011–2013. Use of IUDs has also grown among nulliparous women, although to a lesser extent. In 2002, only 0.5% of women currently using contraception who had never had a birth were using an IUD. This grew to 4.8% in 2011–2013.

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http://dx.doi.org/10.1016/j.contraception.2016.08.011
0010-7824/

The belief that women must have had at least one vaginal delivery to be eligible for an IUD remains a barrier to provision to women who are nulliparous. A survey obstetrician-gynecologists in the United States found that only two thirds considered nulliparous women appropriate candidates for IUDs [3]. Another study based on a questionnaire completed by clinicians, including physicians, physician assistants, certified nurse midwives, nurse practitioners and nurses, found that 30% of respondents had misconceptions about the safety of IUD use in nulliparous women [4]. Particular concerns cited are the risk of pelvic inflammatory disease (PID) and infertility, and the safety and difficulty of insertion [5–7].

Outdated and some current prescribing information may also contribute to misperceptions about the relationship between parity and eligibility for an IUD. For example, when the Copper T 380A was first marketed in the United States, it included a history of childbirth as part of a recommended patient profile. Although the label was changed in 2005 to remove this recommendation, many current providers may not be aware of the change [8]. The prescribing information for one of the 52-mg levonorgestrel intrauterine systems (brand name Mirena) currently recommends the device for women who have had one child [9]. Neither the label for the more recently marketed 52-mg system (brand name Liletta) [10] nor that of the devices designed for smaller uteri, the 19.5-mg levonorgestrel-releasing intrauterine system (LNG-IUS; brand name Kyleena) [11] or the 13.5-mg LNG-IUS (brand name Skyla) [12], mentions parity with regard to eligibility. While not explicitly addressed, the prescribing information of these products includes data on their use in parous and nulliparous participants, suggesting no limit based on a history of previous birth.

In its Medical Eligibility Criteria for Contraceptive Use (U.S.-MEC), the Centers for Disease Control designate intrauterine contraception for nulliparous women as Category 2 (advantages generally outweigh risks), while for parous women, it is Category 1 (no restriction) [13]. The U.S.-MEC states: "The data conflict about whether IUD use is associated with infertility among nulliparous women, although well-conducted studies suggest no increased risk." Although the Selected Practice Recommendations [14] make clear that parity need not influence eligibility for an IUD, such statements may discourage use of IUDs in nulliparous women.

Many young women appear to have limited or no awareness of IUDs [15–19]. However, nulliparous women who do use IUDs have a generally positive view of them [20].

This guideline reviews the evidence on IUD use in nulliparous women. While other devices are available worldwide and will be discussed briefly, this review focuses on the five available in the United States:

- The Copper T 380A, a copper-bearing T-shaped IUD measuring 36 mm by 32 mm with an approved duration of use of 10 years (Paragard)
- Four T-shaped LNG-IUSs:
  - o Two LNG-IUSs that contain 52 mg of levonorgestrel and measure 32 mm by 32 mm. One (Mirena) is approved for 5 years of use, while the other (Liletta) is currently approved for 3 years. With continued follow-up of women in the Phase III trials, the duration of use of Liletta will likely be extended to 7 years.
  - o A smaller LNG-IUS containing 19.5 mg of levonorgestrel, which measures 30 mm by 28 mm and is approved for 5 years of use (Kyleena). Like the device itself, the diameter of the insertion tube is smaller than those of other IUDs.
  - o A smaller LNG-IUS containing 13.5 mg of levonorgestrel, which measures 30 mm by 28 mm and is approved for 3 years of use (Skyla). Like the device itself, the diameter of the insertion tube is smaller than those of other IUDs.

2. Clinical questions

2.1. What is the failure rate of IUDs in nulliparous women?

Intrauterine contraception has a low failure rate in both multiparous and nulliparous women. In the first year, the failure rate during typical use is 0.2% for the 52-mg LNG-IUS and 0.8% for the Copper T 380A [1]. Perfect-use failure rates are 0.2% and 0.6%, respectively. Although typical-use failure rates for the 13.5-mg LNG-IUS or the 19.5-mg LNG-IUS are not yet available, a Phase III randomized trial of 1432 women (including 556 nulliparous women) who used the smaller devices for up to 3 years found cumulative failure rates of 0.9% and 1%, respectively. Seven hundred and seven women randomized to the 19.5-mg system elected to enter into a two-year extension study [22], enabling a 5-year cumulative failure rate to be calculated which was 1.5% [22].

Comparisons of IUD failure rates by parity confirm a low rate in nulliparous women. Sivin and Stern reported on 11 trials of the Copper T380A performed by the Population Council in the early 1970s in which 64% of participants were nulliparous, and found no marked difference by parity [23]. A more recent multicenter retrospective chart review of 2138 women aged 13–35 who used either the 52-mg LNG-IUS or the Copper T 380A also found no significant differences in rates of pregnancy between women of differing parity [24]. Life-table analysis of 1600 16–35-year-old women (including 989 nulliparous women) in a Phase III study of the newer 52-mg LNG-IUS (Liletta) yielded a pregnancy rate of 0.14 [95% confidence interval (CI) 0.04–0.57] through 1 year and 0.55 (95% CI 0.24–1.23) through 3 years [25]. Two pregnancies were reported in 989 nulliparous women and 4 of 611 parous women, suggesting no difference. A subanalysis of the Phase III trial of the 13.5-mg and 19.5-mg LNG systems and the extension study of the 19.5-mg LNG-IUS also demonstrated no difference in efficacy by parity [22,26].

A number of smaller studies of IUD use in nulliparous women demonstrate their high, expected effectiveness in this group. In a randomized trial by Suhonen et al., comparing the 52-mg LNG-IUS with oral contraceptives (OCs) [27], no

pregnancies occurred in 94 nulliparous women assigned to the LNG-IUS during 1 year of use. In another prospective pilot study [28], there were no pregnancies among a cohort of nulliparous women using either the 52-mg LNG-IUS (n=9) or copper-bearing devices (n=104) at 1 year. Lastly, a study from Belgium of a T-shaped levonorgestrel-releasing device similar to a 52-mg LNG-IUS included 112 nulliparous women and reported no pregnancies over the 5-year study period [29].

2.2. Is intrauterine contraception acceptable to nulliparous women?

High satisfaction and continuation rates are reported in studies of both the Copper T380A and LNG-IUS. Among women enrolled in the Contraceptive CHOICE project, 85% of LNG-IUS users (n=1551) and 80% of Copper T380A users (n=385) were very or somewhat satisfied at 12 months, rates that the authors reported were unaffected by parity [30]. Continuation rates, also unaffected by parity, were 88% and 84%, respectively. A small prospective study of 109 nulliparous students at a university health clinic found that 83% of users were "happy" or "very happy" with the IUD, and 87% reported that they were "likely" or "very likely" to recommend it to a friend [31]. There were no statistically significant differences in satisfaction between users of the LNG-IUS and those of the Copper T 380A in that study.

In Europe and the Near East, a survey of 8680 users of the LNG-IUS (8% of whom were nulliparous) found that 93% of nulliparous women reported satisfaction with device (62% very satisfied and 31% rather satisfied) compared with 95% of women with children (66% very satisfied and 29% rather satisfied) [32]. Overall, 86% and 91% of nulliparous women and women with children, respectively, would recommend the LNG-IUS to a friend, while 87% and 91% stated their intention to have LNG-IUS fitted again. The randomized trial by Suhonen et al. found that 90% of women in the LNG-IUS group and 88% in the OC group assessed their methods as being moderately to very good (p=.36) [25]. However, 86% of LNG-IUS users who completed the 1-year study were willing to continue with the same method compared to only 68% of OC users (p=.003).

In the subanalysis of the Phase III trial of the smaller 13.5-mg LNG-IUS and a 19.5-mg LNG-IUS, 2116 of 2884 women in the full analysis set completed a user satisfaction questionnaire either at the end of 3 years (those who completed the study) or at their last study visit (those who discontinued prematurely): 802 and 1314 were nulliparous and parous, respectively [26]. Across all parity subgroups, >90% of women were either "very satisfied" or "somewhat satisfied" with these devices.

2.3. Is the rate of IUD expulsion higher among nulliparous women than among parous women?

In 2007, Hubacher published a systematic review comparing the performance of a range of copper IUDs in nulliparous and parous women [33]. Expulsions were rated as higher for nulliparous women in 13 of 20 studies examined; however, for the Copper T380A, performance differed only slightly between nulliparous and parous women [23].

More recent studies have reported equivalent or lower rates of expulsion in nulliparous compared to multiparous women. In the multicenter retrospective study by Aoun et al., of 2138 IUD users aged 13–35 years, the overall rate of IUD expulsion was 6%, which did not significantly differ by parity (p=.79) [24]. The Contraceptive CHOICE project, which included 4219 women choosing the LNG-IUS and 1184 choosing the Copper T 380A, found a cumulative expulsion rate of 10.2 per 100 IUD users over a 36-month study period, with no differences by IUD type [34]. The cumulative rate of expulsion was lower in nulliparous women compared with parous women (8.4 vs. 11.4; p<.001). After adjusting for confounders and stratifying by IUD type, expulsion was lower for nulliparous LNG-IUS users (adjusted hazard ratio 0.59, 95% CI 0.44–0.78) and was higher for copper IUD users, but this did not reach statistical significance, (14.3 compared with 8.2, p=.10). Similarly, in the 3-year efficacy trial of the newer 52-mg LNG-IUS (Liletta), expulsion occurred less frequently in nulliparous women than parous women (2% vs. 5.6%, p<.0001) [25]. Lower rates of expulsions among nulliparous women were also reported in subanalysis of the Phase III trial of the smaller 13.5-mg and 19.5-mg LNG systems [26].

2.4. Are side effects higher in nulliparous women than in parous women?

Expected side effects of the LNG-IUS devices are lighter menstrual bleeding and a tendency toward amenorrhea. In the first 3 months, there may be irregular bleeding. Common side effects reported for the Copper T 380A are increased menstrual bleeding and pain.

Hubacher reported that removals of copper-bearing IUDs for pain and bleeding were higher in nulliparous than in parous women and that IUD size and shape play a role in performance [33]. The one study included in this analysis that investigated the Copper T 380A found a removal rate attributed to bleeding and pain at 2 years of use to be significantly higher for the Copper T 380A than the Copper T 200 in the double-blind studies (23.7 vs. 18.9 per 100, p<.01) [21]. The differential was strongly marked in the nulliparous acceptors at 2 years (24.6 vs. 17.6, p<.01).

Aoun's multisite retrospective study of the copper IUD and LNG-IUS [24] also found that nulliparous women were more likely to report pain with IUD use than were parous women (p=.02), although the incidence of discontinuation was not greater in the nulliparous group (p=.13). Comparison between the two devices was not made, however. Suhonen documented that, among nulliparous women randomized to the LNG-IUS, pain was the most common reason for IUS discontinuation at 12 months, reported in 6 of 94 women [27]. Most of the discontinuations for pain (4 out of 6) occurred during the first 3 months after insertion. A

change in menstrual bleeding pattern (including amenorrhea) was the indication for discontinuation of both the 13.5-mg and 19.5-mg LNG-IUS in approximately 5% of women in the Phase III efficacy trial but did not differ by parity [26].

While pain and problematic bleeding appear to be more common in nulliparous users of copper-bearing devices and short-term changes in menstrual pattern occur with the LNG-IUS regardless of parity, in most cases, they are not sufficiently problematic to result in device removal.

Symptomatic ovarian cysts are a known adverse event associated with LNG-IUS use. Eisenberg et al. reported on cyst formation in parous and nulliparous women in the Phase III trial of the 52-mg LNG-IUS (Liletta) [25]. Fifty-nine (3.4%) women had a symptomatic ovarian cyst, including 3.2% of nulliparous women and 3.7% of parous women (p=.15).

2.5. Is the risk of perforation at IUD insertion higher in nulliparous women than in parous women?

The overall risk of uterine perforation with IUD insertion is low. In a European multinational, prospective, noninterventional cohort study, the rate reported with the LNG-IUS was 1.4 per 1000 insertions (95% CI 1.1–1.8) and 1.1 per 1000 insertions (95% CI 0.7–1.7) for copper IUDs [35]. This risk could theoretically be higher in nulliparous women because of their smaller uterine cavity and greater cervical resistance to dilation, but evidence for a difference is limited.

One prospective follow-up study reported that increasing parity reduced the risk of perforation with insertion of the Copper T 380A, but included only two nulliparous women in a total of 8343 women [36]. Neither Suhonen et al. nor Brockmeyer et al. reported perforations during their studies of IUDs in nulliparous women [27,28]. Veldhuis et al. reported no perforations among 461 women (129 nulliparous and 332 parous) who had one or more Copper IUD or LNG-IUS insertions between 1981 and 2000 in general practice in the Netherlands [37].

2.6. Is the risk of PID higher in nulliparous than in parous users of intrauterine contraception?

An older epidemiologic study [38] found small transitory increase in the incidence of pelvic infection in the first 20 days after IUD insertion, thought to be related to either cervical infection at the time of insertion or transmission of vaginal bacteria into the uterus. However, a systematic review of more recent direct and indirect evidence found that IUD placement in women with asymptomatic gonorrhea or *Chlamydia* infection or at high risk of sexually transmitted infections did not have an increase in the risk of PID compared to initiating other contraceptive methods [39]. Prospective observational data from the Phase III trial of the 52-mg LNG-IUS (Liletta) provide further evidence that there is no increased risk of PID in the weeks following insertion among a low-risk population [40]. It is important to note that even in the presence of risk factors and undiagnosed infection, the absolute risk of PID is low. Screening for cervical infection can be performed at the time of insertion, followed by treatment as indicated.

Although studies reporting comparisons are few, parity does not seem to affect the risk of PID after IUD insertion. Veldhuis et al. reported no difference in the rate of PID among nulliparous and parous women who had either a copper IUD or LNG-IUS placed [37]. Over up to 3 years of the 13.5-mg LNG-IUS or 19.5-mg LNG-IUS use, nulliparous women were at no higher risk PID than parous women (crude PID incidence: 0.1% vs. 0.6%, respectively) [26]. In Suhonen's randomized controlled trial of 193 nulliparous women aged 18–25 years randomized to LNG-IUS or OCs, no PID cases were reported among the total study population over 12 months [27].

2.7. Are nulliparous users of IUDs at higher risk of infertility than parous users?

Intrauterine devices have long been believed to cause PID and subsequent tubal infertility. However, in a landmark case–control study, Hubacher et al. demonstrated that infection with *Chlamydia trachomatis*, not previous use of a copper IUD, is associated with an increased risk of tubal occlusion among nulligravid women [41].

One older study of return to fertility among nulliparous women discontinuing OCs, the copper IUD or a barrier method found the return of fertility to be slowest in the first 12 months among OC users, the fastest in those discontinuing barrier methods with those discontinuing copper IUDs midway between [42]. By 18 months, the differences had disappeared. More recent data regarding the LNG-IUS and a copper-based IUD still widely used in Europe found no delay in return of fertility after discontinuation [43]. The only study directly comparing the return to fertility in nulliparous and parous users after cessation of use of the GyneFix device (a frameless copper-based IUD not available in the United States) found no difference between the two groups [44].

2.8. Is IUD insertion more painful or difficult in nulliparous women?

Most IUD insertions in nulliparous women occur without complication [45] but may be more painful, more difficult and less likely to be successful compared to IUD insertion in parous women.

2.8.1. Pain

Several studies have found that women with a prior vaginal delivery report less pain at IUD insertion than women with no prior vaginal delivery. The magnitude of the recorded difference in pain varies across studies. One study found the mean pain score on a 0–100-mm visual analog scale (VAS) to be 51.2 (SD 29.2) for nulliparous women and 34.7 (SD 31.6) for parous women (p=.009) [46]. In a retrospective review, a small but statistically significant increase in insertion discomfort was found for nulliparous

women, but the authors doubted the clinical importance of the finding [47].

In a study showing no benefit of preinsertion ibuprofen, Hubacher [48] found a low but statistically significant difference between pain ratings in nulliparous and multiparous women (2.7 and 1.9 on a 10-cm VAS, respectively). Another study showing no benefit of ibuprofen prior to IUD insertion found higher pain scores overall than those reported by Hubacher's group and also reported a significant difference between nulliparous and parous women (54.6 and 35.0 on a 100-mm VAS, respectively) [49]. Other studies have found similarly high VAS scores, between 5 and 6, for nulliparous women undergoing IUD insertion, although these studies do not include parous women for comparison, limiting the potential to draw a definitive conclusion from these data [50,51].

In an effort to reduce discomfort, some clinicians routinely provide an oral nonsteroidal anti-inflammatory drug prior to insertion. While these medications have a low cost and a low incidence of side effects, a Cochrane review of the available evidence found that they are not effective at reducing pain during or after insertion [52]. Ketorolac given 30 min prior to IUD insertion was studied and found to decrease pain with uterine sounding (8.4 cm vs. 6.0 cm on a 10-cm VAS, p=.04), at IUD placement (8.1 cm vs. 5.4 cm, p=.02) and at 15 min postprocedure (4.8 cm vs. 1.8 cm, p=.02) [53]. Unfortunately, at 15 min postinsertion, 20% of the subjects also rated the pain of injection as equivalent to the pain of IUD insertion. Other measures that have been studied and are not effective are 1% or 2% lidocaine gel via the cervical [54] and vaginal [55] routes, and nitroglycerin gel via the cervical [56] and vaginal [57] routes. One randomized controlled trial of 218 nulliparous women receiving administration 4% viscous lidocaine delivered to the portio, cervix and uterus did find significantly lower pain scores within 10 min of insertion (28.3 mm vs. 44.2 mm on a 100-mm VAS, p<.0001) [58]. This study did not adequately measure the pain of study drug application. Misoprostol, a prostaglandin analogue administered for cervical priming before a range of gynecological procedures, is used by many clinicians before IUD insertion in nulliparous women [59]. However studies have consistently shown that misoprostol is not effective at reducing pain or difficulty of insertion [50,51], and in two studies, it increased discomfort [60,61].

2.8.2. Difficult and unsuccessful insertion

In a prospective observational trial of women undergoing copper IUD insertion for emergency contraception, 27 of 138 (19.6%) IUD insertions in nulliparous women were unsuccessful compared with 8 of 59 (13.6%) in parous women, although the study was not large enough for the results to be statistically significant [adjusted odds ratio (AOR) for unsuccessful insertion=2.31, 95% CI 0.90–6.52, p=.09] [62]. Notably, the rates of unsuccessful insertions in both groups were significantly higher than those reported in other studies.

In a prospective study of 996 insertions in New Zealand, factors associated with an abandoned insertion included nulliparity (AOR=5.19, 95% CI 2.49–10.82). Practitioner-reported difficulty with insertion was also associated with nulliparity (1.98; 95% CI 1.11–3.54); however, 80% of insertions in nulliparous women were rated as "easy" by the inserting doctor. The rate of unsuccessful insertion was 2.3% in women with prior vaginal delivery and 11.2% in nulliparous women (p<.001) [45].

2.8.3. Differences by device

Diameter of the insertion tube and size of the inserted product could theoretically be associated with level of pain or with ease of insertion in a nulliparous population. In a study comparing the 13.5-mg LNG-IUS, 19.5-mg LNG-IUS (both with smaller insertion tube and smaller product) and the 52-mg LNG-IUS in nulliparous and parous women, no difference was found in ease of insertion or severe patient-reported pain [63]. An analysis of the nulliparous women showed 0.8% severe pain with insertion of the smaller devices and 1.6% severe pain with the 52 mg LNG-IUS, not a significant difference [64]. In a mixed cohort of 2884 women, of whom 39% were nulliparous, placement of a smaller framed (30 mm × 28 mm) LNG-IUS device containing either 13.5 mg or 19.5 mg LNG was successful in 95.5% of cases on first attempt and in 99.7% after two attempts. Investigators rated placement of these smaller systems as "easy" in 84% of women, and 42% of women reported their pain as either "none" or "mild" [21]. In another study evaluating the ease of placement of the 52-mg LNG-IUS in 509 women (99.8% of whom were parous), 95.9% were inserted at the first attempt and 92% of investigators rated the procedure as "easy." Most (68.2%) subjects felt either mild pain or no pain during the insertion procedure [65].

In conclusion, nulliparity appears to be associated with increased pain at IUD insertion and increased risk of difficult and unsuccessful insertion. However, most IUD insertions in nulliparous women — as in all women — are well tolerated and successful. Use of ketorolac or 4% viscous lidocaine appears to decrease pain for nulliparous women having IUD insertions, although not without pain from drug administration. Providers should bear in mind that use of non-evidence-based preprocedure agents may impose additional barriers on women wishing to use an IUD but provide no benefit.

2.9. Are adolescents appropriate candidates for intrauterine contraception?

Adolescent women in the United States are of particular relevance to this guideline because the vast majority (approximately 89%) are nulliparous [66]. According to the American Academy of Pediatrics [67] and American Congress of Obstetricians and Gynecologists [68], IUDs should be considered a first-line contraceptive option for adolescent women. Seventy-five percent of pregnancies among U.S. teenagers are unplanned, representing 15 % of

all unintended pregnancies annually [69]. As a group at high risk for unintended pregnancy and given the few contraindications to use, adolescents desiring effective contraception should not be discouraged from considering IUDs. An analysis of data from the National Survey of Family Growth found that from 2008 to 2013, long-acting reversible contraception (LARC) use rates in teens aged 15–19 years old increased from 2.1% to 5.9% (p<.001), and 72% of LARC devices were IUDs [70]. Young nulliparous women were significantly less likely than their parous counterparts to have used an IUD (AOR for parous adolescents=11.43, 95% CI 3.61–36.16) [71].

A retrospective review of 233 IUD insertions in women younger than 21 showed 5-year continuation rates of 50% in those younger than 18 years and 71.5% in those aged 18–21 (p<.001) [72]. Teenagers younger than 18 were at greater risk of discontinuation due to either removal or expulsion [hazard ratio (HR)=2.85]. Another retrospective cohort study of 307 adolescents, 77% of whom were nulliparous, found that while the discontinuation rate was higher than those reported in studies of adults, it was lower than rates reported among adolescents using other forms of contraception, and the overall continuation rate at 6 months was 83.3% [73]. A cohort study of 179 adolescents in New Zealand, 73% of whom were nulliparous, using the 52-mg LNG-IUS for a variety of indications including contraception found a similarly high 1-year continuation rate of 85%. The expulsion rate was 8% [74].

More recent data from the CHOICE study, which included 529 women aged 14–19 years, showed a relatively high rate of expulsion of approximately 18% in this group. Compared with older women, adolescent women were significantly more likely to experience an expulsion over a mean follow-up time of 22 months (52-mg LNG-IUS: HR for expulsion 2.26, 95% CI 1.68–3.06; copper device: HR 3.06, 95% CI 1.75–5.33), but there were no differences by parity among adolescents (18.7 per 100 in nulliparous adolescents vs. 18.9 in parous adolescents, p=.47). Continuation rates were otherwise similar in adolescent and older women [34].

The literature clearly demonstrates that more education of health care providers is needed to ensure that they have adequate knowledge about the use of IUDs in adolescent women. In a survey of adolescent health care workers, only 77% of respondents said they believed that IUDs are safe for adolescents, and 18% of those respondents stated that they would be unlikely to recommend an IUD to a woman younger than 20 [75]. Other articles have highlighted the challenge of educating providers about the use of IUDs in nulliparous women and adolescents in particular [4,6,7].

In conclusion, although expulsion appears to be more common in adolescents than in older women, the rate of expulsion remains low, and IUD use is safe and effective in this group. The majority of adolescents are excellent candidates for IUDs, given the excellent efficacy and high rate of continuation of the devices.

2.10. Are IUDs designed specifically for nulliparous women superior to standard devices?

Smaller and "frameless" (lacking the horizontal arms) IUDs have been developed specifically to fit more easily inside the smaller uterine cavity of nulliparous women. A large prospective trial of 1170 women in Mexico showed a dramatic difference between the performance of the Copper T 380A and that of two copper-based devices designed specifically for nulliparous women [76]. The continuation rate at 1 year was 29.5% for the Copper T 380A compared with approximately 85% for the two smaller devices. These studies, however, suffered from methodological flaws: the study investigators were not blinded to the method, and complication and removal rates of the Copper T 380A were markedly higher than rates in other published research [77].

To date, there is no reliable evidence that other devices, including the 13.5-mg LNG-IUS now available in the United States, confer greater benefits than the 52-mg LNG-IUS and the Copper T 380A in nulliparous women [24,63,78].

3. Conclusion and recommendations for IUD use in nulliparous women

The following recommendations are based on good and consistent scientific evidence (Level A):

- The 52-mg, 19.5-mg and 13.5-mg LNG-IUSs and the Copper T 380A IUDs are effective and safe for nulliparous women and should be offered routinely to women of all parities seeking contraception.
- Nulliparous women seeking highly effective reversible contraception should be advised of the high satisfaction and continuation rates with IUDs.
- Providers and women can be reassured that nulliparous women who use the IUD do not appear to have higher risks of pelvic infection than parous users and that following IUD removal, fertility is not impaired.
- Providers and women can be reassured that IUD expulsion rates are not higher among nulliparous women compared to parous women.
- Use of cervical or vaginal nitroglycerine gel is not recommended to reduce pain during IUD insertion because neither is effective for this indication.
- Use of 4% viscous lidocaine gel may be beneficial in reducing pain during IUD insertion, although further study is needed to assess pain of gel administration.
- Use of intramuscular ketorolac may reduce pain during IUD insertion if administered 30 min before the procedure. One fifth of patients felt that the pain of the injection equaled the pain of the IUD insertion.
- Use of preprocedure misoprostol is not recommended as a method of making IUD insertion easier or less painful.

The following recommendations are based on limited or inconsistent scientific evidence (Level B):

- Both nulliparous and parous adolescent women should be considered candidates for IUDs.
- Provideres and women can be reassured that although nulliparity appears to be associated with increased pain at IUD insertion and increased risk of difficult and unsuccessful insertion, most IUD insertions in nulliparous women are well tolerated and successful.

The following recommendations are based primarily on consensus or expert opinion (Level C):

- Providers should advise women that pain and bleeding with copper IUDs may be greater in nulliparous women than in parous women.
- Women and providers may be reassured that the risk of perforation at IUD insertion is not higher among nulliparous women than among parous women.

4. Important questions to be answered

Further research is needed to define the risks and benefits of different IUDs in nulliparous women. Research into methods to reduce discomfort or make insertion technically easier may be of particular benefit to nulliparous women.

Sources

PUBMED, MEDLINE and the Cochrane Database were searched for articles related to the use of IUDs in nulliparous and adolescent women published during the period 1980–2016. In addition, the references of publications found through these databases were reviewed to capture any additional articles that may have been missed.

Authorship

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Conflict of interest statement

None of the authors report any significant relationships with industries relative to these guidelines. The Society of Family Planning receives no direct support from pharmaceutical companies or other industries.

Intended audience

This guideline is for Society of Family Planning fellows and any other health care professionals involved in the provision of contraception services. It may also be of interest to those involved in sexual and reproductive health education. This evidence-based review should help guide clinicians providing this care, but it is not intended to dictate clinical care.

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