



# Intrauterin Devices: What Has Changed?

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## ABSTRACT

Intra-uterine devices (IUDs) are one of the most common, long acting, reversibly-used methods of contraception in the world. IUDs are safe and effective T shaped designed plastic framed devices including copper or levonorgestrel. The purpose of this review was to outline the types, mechanisms, benefits, and adverse effects of IUDs and to help for selection of candidates and devices. The most important role in the mechanism of action is to cause sterile inflammation in the uterine cavity. Hormonal IUDs have also non-contraceptive benefits like reduction in heavy menstrual bleeding, dysmenorrhea, pelvic pain, endometrial hyperplasia and anemia. Pelvic inflammatory disease (PID), ectopic pregnancy, anemia and progestin related complaints including acne, weight change, headache, mood changes, hirsutism and nausea are some undesirable effects of IUDs. IUDs are highly preferred in the world and will not be abandoned in the future. They are easily accessible, cheap and cost-effective for contraception.

**Keywords:** Intrauterine devices, levonorgestrel, patient selection, types of IUDs, contraception

## ÖZ

### Rahim İçi Araçlar: Neler Değişti?

Rahim içi cihazlar (RIA), dünya çapında en yaygın, uzun etkili, geri dönüşümlü olarak kullanılan doğum kontrol yöntemlerinden biridir. RIA'lar, bakır veya levonorgestrel içeren güvenli ve etkili T şeklinde tasarlanmış plastik çerçeveli cihazlardır. Bu derlemenin amacı, RIA'ların türlerini, mekanizmalarını, yararlarını, yan etkilerini ana hatlarıyla belirtmek ve hastaya uygun araç seçimine yardımcı olmaktır. Etki mekanizmasındaki en önemli rolü rahim içinde steril enflamasyona neden olmaktır. Hormonal RIA'ların ayrıca yoğun adet kanaması, dismenore, pelvik ağrı, endometrijal hiperplazi ve anemi tedavisi gibi kontraseptif olmayan faydaları vardır. Pelvik enflamatuvar hastalık (PID), ektopik gebelik, anemi, progestin içeren RIA'lar için akne, kilo değişikliği, baş ağrısı, duygudurum değişiklikleri, kılınma ve mide bulantısı gibi bazı istenmeyen etkiler görülebilir. RIA'lar dünya çapında oldukça fazla tercih edilmektedir ve gelecekte de terk edilmeyecektir. Doğum kontrolü için kolay erişilebilir, ucuz ve uygun maliyetlidirler.

**Anahtar Kelimeler:** Rahim içi araçlar, levonorgestrel, hasta seçimi, RIA çeşitleri, doğum kontrolü

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## INTRODUCTION

Family planning is basically determined as allowing people to have as many children as they want and whenever they want. Although there are many methods of contraception, IUDs are the most known (1). They are one of the most common, long acting, reversibly-used methods of contraception in the world (1,2). The average usage of IUDs is between 2 to 40 percent depending on the countries, for instance, it is 40 percent in China and approximately 50 percent in Korea (2,3). IUDs are T shaped designed plastic framed devices including copper or levonorgestrel (1). Intra-uterine devices has the lowest discontinuation rate of contraception (4,5). This method, which had started by placing stones in the uterus of camels in ancient times, was developed

into tools placed in the uterus over time (1,6). In the 1970s, the hormone releasing part was added to the IUDs, which started from the silk ring in the 1920s and evolved over time to the T-shaped copper-containing format in the 1960s. (7). The purpose of this review was to outline the types, mechanisms, benefits, and adverse effects of IUDs and to help for selection of candidates and devices.

### Types of IUDs

- 1. Inert IUDs (No Additives-No Drugs):** They are made of stainless steel or plastic and their most important advantage is effectiveness for many years without needing replacement. It is widely used in China but due to the high failure rates (1 to 4.8 per 100 women years), copper or hormonal IUDs are now recommended especially for women younger than 40 years of age (8).
- 2. Copper IUDs:** These are some with added barium sulfate, consisting of a body of polyethylene structure and containing copper (some of which also contains silver to extend its lifespan) notched or flat T shaped IUDs. The number in their name as mm<sup>2</sup> specifies the area of its copper surface. TCu 380A (contains 380 mm<sup>2</sup> copper) is the most common used type and approved by U.S. Food and Drug Administration (FDA) for ten years of use (9,10).
- 3. Hormonal IUDs (Levonorgestrel IUDs):** This type is determined as T shaped devices mainly releasing progesterone. The first levonorgestrel (LNG, a type of progesterone) releasing IUD was Mirena (released 20 µg levonorgestrel per day and can be used for five years) (11). There are four types of hormonal IUDs approved by the FDA according to the amount of LNG they contain and daily LNG releasing amounts. These are 52 mg LNG (Mirena, Liletta), 19.5 mg LNG (Kyleena), and 13.5 mg LNG (Skyla). The difference between Mirena and Liletta is the diameter of insertion tube ranging from 4.4 to 4.8. Among them, Mirena is the longest acting hormonal IUD, effective up to seven years, Liletta has a similar effect but is not most affordable. Kyleena is effective up to five years but releases less LNG than Mirena. Skyla is the smallest type, least hormone-releasing one and effective up to three years (12-15).
- 4. Frameless IUDs:** They first appeared in the 1980s and contain either copper (Gynefix) or LNG (Fibroplant). Since all uterine cavities are not the same size or shape, frameless IUDs are discovered. They contain beads attached to a non-resorbable filament and have an anchoring system to retain in the uterine cavity (16,17).

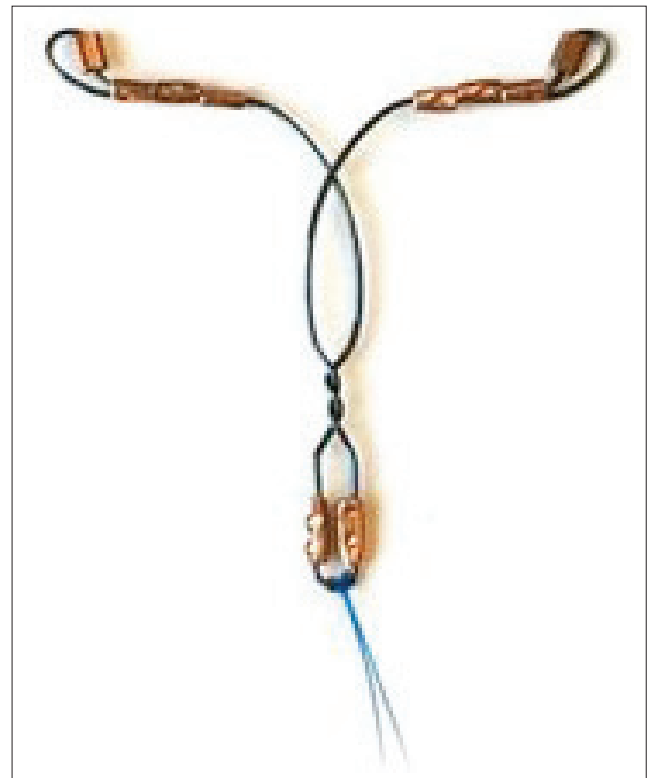
### 5. Types of IUDs Still in Development

**Veracept:** A novel, flexible, low-dose copper IUD which has nitinol frame with copper beads all including 175 square-mm<sup>2</sup> of copper surface area (18). Different than traditional IUDs with plastic frames, nitinol has flexibility and memory that allows the arms to compress inward with pressure from the uterine walls (Figure 1).

**Levocept:** Similar to Veracept but includes levonorgestrel instead of copper and its phase 2 clinical trial in the United States is a work in progress.

**Copper Indomethacin Intrauterine Device:** This type of IUD, which is only available in China, contains indomethacin in addition to copper. The copper and indomethacin do not interfere with each other. The aim of this IUD is to release menstrual pain or other complaints related to copper (19). Different shapes of this type of IUD can be found in China (20,21).

It is best known that the only way of contraception without side effects is avoiding intercourse. Clinicians and researchers are trying to produce new IUDs with the least side effects and more protection.



**Figure 1.** VeraCept, low-dose copper IUD.

Image source: Sebela Pharmaceuticals.

### Mechanisms of Action for IUDs

The most important role in the mechanism of action of IUDs is to cause sterile inflammation in the uterine cavity. The effects can be divided as before and after fertilization. Mechanisms of action before fertilization are the inhibition of sperm motility and viability at the level of the cervix and endometrium; acceleration or deceleration of ovum transport in the tubes and fragmentation of ovum during pre-fertilization (22). After fertilization, IUDs prevent the implantation of the embryo before it reaches the uterus. They affect the transport rate of the embryo in the tubes (rapidly or slowly) and cause fragmentation of the embryo (22). All IUDs cause impaired fertilization.

Moreover, hormonal IUDs thicken the cervical mucus and cause to block sperm transport from the cervix (23). The copper inhibits the motility of the sperm. All IUDs make changes in the endometrium (atrophy, anti-implantation and spermicidal effect) and cause some changes in endometrial gene expression (24).

### Benefits of IUDs (25)

IUDs have a high contraceptive effect. (Pregnancy prevention >99 percent, are used for emergency contraception even five days after intercourse).

- Systemic metabolic side effects are not observed.
- They provide long-term protection.
- Suitable for lactating women.
- There is no delay in returning to fertility after removal.
- Their effects are independent of sexual intercourse.
- They are useful, safe, cost-effective and rapidly reversible.
- They reduce risk of cervical, endometrial and ovarian cancers (26,27).

Hormonal IUDs have also non-contraceptive benefits like reduction in heavy menstrual bleeding, dysmenorrhea, pelvic pain, endometrial hyperplasia, anemia and pelvic inflammatory disease (28-31).

### Negative Aspects of IUDs

- Application and removal require trained personnel.
- Does not protect from sexually transmitted disease (STDs).
- There is a risk of uterine perforation if the appropriate technique is not used.
- The application can be a little painful.

- There could be lower abdominal pain in the form of cramps and intermenstrual spotting in the first three months after application.

- It can slide from the uterus to the cervix and be thrown into the vagina (expulsion).

- The patient could not stop contraception by herself.

### Adverse Effects of IUDs

There are some adverse effects and complications associated with intrauterine devices, and for this reason, IUD use has lost its popularity in some countries. Pelvic inflammatory disease (PID), menstrual blood loss, infertility, ectopic pregnancy and anemia are some undesirable effects after its application.

### Failure, Expulsion and Perforation

Young age under 25 years is mostly related to failure and expulsion (32). The reason of failure is explained due to increased fertility in this group of patients. IUD expulsion rates ranges from 2% to 10% among all IUD users, and it is up to 14% in adolescent patients (31,32). There is no consensus on a clear relationship between increased expulsion rates and the adolescent age group.

The risk of expulsion is increased during delayed postpartum or postabortion period especially after second trimester abortions (33,34). Regardless of IUD type (copper or hormonal), uterine perforation risk has been found higher in patients undergoing IUD application during breast feeding (35). Other risks such as expulsion or pelvic pain are similar to non-breast-feeding patients (34,35). The overall uterine perforation risk is 1 percent approximately, and the risk gets six-fold in breastfeeding patients (36).

Contrary to popular belief, the retrovert uterine position was not associated with high failure or expulsion rates compared to antevert uterine position. Similarly, length of uterine cavity does not constitute a risk factor for IUD failure or expulsion (37). Moreover, nulliparity does not affect the failure rate of IUD insertion (38).

Distorted uterine cavities due to anomalies or leiomyomas are related to increased risk for IUD expulsion. IUDs are not recommended for patients with uterine anomalies (39-41).

Intra-uterine devices preferences vary according to uterine cavity size. When we talk about special uterine cavity size, the ones that come to mind are those smaller than 6 cm and larger than 9 cm. Hormonal IUDs are recommended in cavity sizes over 9 cm because of decreased effectiveness in copper IUDs. In cavities <6 cm, smaller framed IUDs like LNG 19.5 or 13.5 could be recommended to avoid migration or expulsion (42).

In a recent study, the authors have explored whether sonographic measurements of the uterus and IUD positioning at insertion are associated with displacement (43). Uterine and cervical sizes, endometrium and the distance between the tip of the IUD and the fundus have been all measured in 384 patients who had TCU380A devices inserted at a tertiary hospital. All measurements have been performed at insertion, at one month, three months, and six months after insertion. The authors have revealed that women with 7.5 mm distances between IUD and endometrium and uterus width less than 41.5 mm has a higher risk for displacement (43).

Perforation or expulsion risk will decrease with the use of uterine size measurement, along with the use of ultrasound. Moreover, new shaped IUDs will be developed.

Perforation management depends on the stability of the patient. Type of surgery either with laparoscopy or laparotomy should be planned (44). Expectant management of displaced IUDs in asymptomatic patients is not recommended due to risks of bowel or bladder perforation, intestinal obstruction and chronic pelvic pain as well as complicated pelvic abscesses (46). Initial evaluation including kidneys, ureter, bladder and intestines should be performed. Vaginal delivery is not a contraindication after IUD perforation (44).

**String Problems:** Patients are no longer recommended for routinely check of IUD strings by themselves (45,46). If the IUD strings are not visible during speculum examination, an ultrasound check should be performed. After confirming the IUD in the correct uterine location, a cytobrush can be gently placed and rubbed to pull the strings down or out of the cervical os. If this method fails, no further intervention is necessary. Patients should be counselled that during the time of removing, special forceps should be used under ultrasound guidance.

**Ectopic Pregnancy:** Intra-uterine devices do not increase the risk of ectopic pregnancy (47). The possibility of ectopic pregnancy in IUD users is 50% lower than those who do not use any contraceptive method. It is thought that risk of ectopic pregnancy is higher in IUD users. The reason for this false belief is that risk assessment is done incorrectly. It is well known if a woman using an IUD becomes pregnant, the probability of ectopic pregnancy is 3-4%, which is higher than the ectopic pregnancy rate of the general population (0.8-1.5%). The risk of being ectopic is higher with copper IUDs because failure rate is higher than hormonal IUDs (47).

**Pelvic Inflammatory Disease (PID):** Pelvic inflammatory disease and pelvic abscess are rarely seen in long-term IUD

users (48). Rates of IUD removal due to PID within five years was 0.8% and 2.2 % in hormonal IUD copper IUD users, respectively (49). Increased PID risk with IUD use has only been connected to the insertion period and STDs status during insertion (50).

It has been shown that there is no evidence for intrauterine contraception (Cu-IUD or LNG-IUS) altering the vaginal microbiota composition. Therefore, the use of intrauterine contraception is unlikely to alter susceptibility to infection (51).

**Bleeding Disorders:** Copper IUDs can cause excessive and prolonged menstrual bleeding, increase in dysmenorrhea and intermenstrual spotting and cramping in the first few cycles after administration (52). Decreased hemoglobin concentration by 0.36 to 0.94 g/dL in one year period has been found in copper IUD users (53) Non-steroidal anti-inflammatory drugs (NSAIDs) are recommended to alleviate menstrual blood and cramping pain. Hormonal IUDs reduce menstrual bleeding day and menstrual blood loss with LNG which suppresses endometrium that is sensitive to enlargement by ovarian estrogen (54,55).

**Hormonal Side Effects:** These related side effects are related to LNG. Although systemic release is known to be limited, progestin related complaints have been reported such as acne, weight change, headache, mood changes, hirsutism and nausea (54,56). There is a conflicting interest about hormonal IUDs regarding quality of life and sexual functioning. In a recent review, the authors have revealed that hormonal IUD has no effects on mental health and sexual functioning. Future larger studies are needed for women vulnerable to adverse effects of hormonal IUDs (57).

#### **Device Selection: Copper or LNG?**

The pros and cons of IUDs are shown in Table 1 (54,56).

#### **Candidates for IUDs**

- Those who do not want to get pregnant for a long time, but want to get pregnant for later in any age or parity,
- Those who no longer consider pregnancy but do not accept sterilization,
- Women unwilling to be reminded of a contraception method every day or before every sexual intercourse,
- Those who breastfeed,
- Those who cannot use pills because of the estrogen they contain,
- Those who have low risk of genital tract infections or STD.

**Table 1.** Comparison of the advantages and disadvantages of copper and hormonal IUDs

	Copper IUD	Hormonal IUD (LNG)
Advantages	<p>Longer contraception time.</p> <p>Cheap and safe.</p> <p>Low device discontinuation rates.</p> <p>Higher patient satisfaction due to regular menses.</p>	<p>Lower risks for menstrual blood loss.</p> <p>Therapeutic effects on dysmenorrhea and pelvic pain.</p> <p>Noncontraceptive benefits (endometrial, ovarian cancer).</p> <p>Lower risks for ectopic pregnancy.</p> <p>Lower risks for PID.</p>
Disadvantages	<p>More cramping and heavy bleeding.</p> <p>No non-contraceptional therapeutic effects.</p> <p>Higher ectopic pregnancy risk.</p> <p>Higher contraception failure.</p>	<p>Insertion difficulties.</p> <p>Higher incidence of oligo-amenorrhea and/or amenorrhea.</p> <p>Unscheduled bleeding.</p> <p>Higher removal rate for hormone-related side effects.</p> <p>Higher risks for functional ovarian cysts.</p>

## CONCLUSION

In this review, the basic features of IUDs in general are presented and summarized for easy use in clinical information. Although there is no major change compared to previous literature, there have been new developments in IUD types. Hormonal IUDs are more preferred in terms of comfortable gynecological use. The only hormonal IUD in the literature includes LNG, and possibly in the future, novel research would be designed releasing different progesterone types such as dienogest. Or patients may have IUDs sized according to personal predisposition, demographic characteristics or uterine type. IUDs are highly preferred in the world and will not be abandoned in the future because they are easily accessible, cheap and cost-effective form of contraception.

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