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A REVIEW ON INTRAUTERINE DRUG DELIVERY SYSTEM

Harendra Prasad*[1], Ram Chandra Bharati[2], Navneet Kumar Verma[3] and Shekhar Singh[3]

[1]Associate Professor, Rajeev Gandhi College of Pharmacy, Nautanwa, Maharajganj, UP, India- 173164.
[2]Assistant Professor, Rajeev Gandhi College of Pharmacy, Nautanwa, Maharajganj, UP, India- 173164.
[3]Associate Professor, Suyash Institute of Pharmacy, Hakkabad, Gorakhpur, UP, India-273016.

***Corresponding Author: Harendra Prasad**
Associate Professor, Rajeev Gandhi College of Pharmacy, Nautanwa, Maharajganj, UP, India- 173164.

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ABSTRACT
An intrauterine contraceptive device, or IUD, is inserted into the uterus. It is a tiny copper or plastic device. There are numerous sorts, and depending on the type, they can endure three to ten years. A long-acting, reversible method of birth control is the IUD. The delicate, slender T-shaped IUD is secured with a nylon string. This device is inserted into the uterus by a licensed physician or other healthcare provider. The IUD has a 98% success rate in stopping pregnancies. Because getting an IUD implanted might be uncomfortable, you might want to take an analgesic before having one put in. They hinder fertilization by obstructing the passage of sperm and eggs. They also alter the uterine lining and interfere with implantation. Intrauterine system for levonorgestrel (LNG- IUS), it can be used to treat endometriosis or as an alternative to hysterectomy in situations of menorrhagia. It is more successful than copper IUDs at lowering bleeding and dysmenorrhea. The review covered the importance of intrauterine drug delivery systems, their advantages and disadvantages, and the development and application of intrauterine devices (IUDs).

KEYWORDS: Intrauterine Drug Delivery System, Intrauterine Contraceptive Device, or IUD.

INTRODUCTION

In order to postpone pregnancy, contraceptives are devices or processes that either delay the implantation of the fertilized egg or stop the male sperm from fertilizing the female egg. Unintended pregnancy is expensive for both women and society in terms of medical costs, the cost of caring for extra children, and the cost of pursuing personal and professional aspirations.[1] Various contraceptive methods have been developed, including intrauterine devices (IUDs), intrauterine systems (IUS), hormonal contraceptives (oral contraceptives, implants, injections, contraceptive patch, and vaginal rings), barrier devices with or without spermicides (male condom, diaphragm, cervical cap, female condom), natural family planning methods, male sterilization (vasectomy), and female sterilization (tubal ligation).[2,3] One of the most efficient, secure, and cost-effective forms of contraception available today is the intrauterine device (IUD). More women than any other reversible method of birth control use it globally. The two IUD types now in use in the United States—the copper- and levonorgestrel-containing IUDs—have comparable success rates in preventing pregnancy, with failure rates of 0.08% and 0.02%, respectively. This raises their ability to prevent pregnancies to almost 99%.[5] The use of long-acting reversible contraception (LARC) has increased in the United States since 1995. This use has been increasing year over year, with 14% of women who use contraception opting to use a specific type of LARC.[4] The frequency of unwanted pregnancies has decreased along with the increased use of LARC.[5] IUDs provide a lot of additional benefits, such as effectiveness, usability, reversibility, and patient satisfaction, particularly when you take into account the time commitment needed for long-term use and the expense.[6] A small, typically T-shaped birth control device called an intrauterine device, sometimes known as an intrauterine coil, is placed inside the uterus to prevent conception. It is within the category of long-acting reversible contraception.[7] The intrauterine device (IUD) is one of the available contraceptive treatments that is both effective and feasible nowadays.[8] Fig. 1 shows several IUD shapes and sizes. About 100 million women globally, especially in underdeveloped countries, utilize IUDs.[9-10] Between 1982 and 2002, the estimated percentage of women who utilized an IUD dropped from 8% to 2%.[11] 2% is the cumulative global pregnancy rate after five years, regardless of the technique used.[12] Owing to the advantages of IUDs—safety, low side effects, high rate of continuation, and use regardless of

age or parity.[13] They ought to be regarded as one type of first-line contraceptive option for any woman without a medical reason not to use them to avoid an unintended pregnancy.[13]

Fig. 1: Various current and historical intrauterine devices.

Historical background

In 1909, Richard Richter in Germany[14] used a silkworm gut-made ring as an intrauterine device for the first time, ushering in the modern era of the IUD. This device was the original IUD. Sadly, no clinical data were ever released because Dr. Richter's discovery at the time was of no medical significance and had no bearing on the usage of birth control. Ernst Gräfenberg claimed that a contraption with a silkworm stomach core encased in a copper, nickel, and zinc alloy was highly effective at preventing pregnancy in 1929.[15] His study's conclusions triggered a contentious discussion on PID (pelvic inflammatory disease) induction, and the theory was rejected by European medical experts. The results of Tenrey Ota's investigation of the use of elastic metallic rings as IUDs in Japan in 1934 were fortunately presented. As soon as the proposal was authorized, IUD use started. Ishihama's findings in Japan and Oppenheimer's findings in Israel caused a change in IUD views in Europe around 1950. These tests and investigations led to the 1960s seeing the introduction of the first IUDs.

Development of IUDs

An analysis from 2008 found that IUDs are one of the most effective contraceptive methods, with an efficacy rate comparable to female sterilisation.[11] The most effective IUD types seem to be levonorgestrel-releasing intrauterine devices (LNG-IUD) and, to a lesser extent, TCu380A devices, with cumulative 5-year pregnancy rates for LNG-IUD of 0.5% and between 0.3% and 0.6% for TCu380A devices at five years.

1. InertplasticIUDs

The Lippes Loop (1961), Margoulis coil (1961), Dalk Shield (1971–1974), and other first inert plastic IUDs were introduced to the market at the start of the 1960s. Some inactive devices may be left in place after menopause.[19] In the 1960s and 1990s, it was determined that The Dalkon Shield caused severe harm to a disproportionately high percentage of women (for instance, sepsis), which led to numerous lawsuits and its removal from the U.S. market in 1975. Since then, devices made of copper wire (Cu-IUDs) have increasingly replaced all previous inert devices as a result of a widespread phobia of illumination.

2. Cu-IUDs

Some of the Cu-IUDs are Flexi Gard, NOVA-T 380 IUD, Multi Load-Cu 375, and T Cu 380A (Para Gard). The Cu T 380A IUD is the only long-acting, reversible, non-hormonal form of contraception currently approved by the U.S. Food and Drug Administration (FDA).[20] The frequent process of intrauterine copper corrosion, which predominantly affects the IUD's cervical region and has the potential to completely remove the metal, is common. Its beginning and growth are quite variable from person to person. The inclusion of copper to inert polyethylene devices has reduced but not completely eliminated the fundamental drawback of these devices, bleeding problems. A high rate of Cu-IUD dissolution may increase the amount of copper ions in endometrial tissue and may trigger the endometrium's release of vascular endothelial growth factor, which could ultimately result in abnormal uterine bleeding.[21]

3. Long-acting reversible levonorgestrel-releasing intra-uterine deliverysystem(LNG-IUS)

Every day, LNG-IUS releases levonorgestrel into the body to inhibit implantation.[22] The Mirena, Jaydess, Liletta, Levosert, and Avibella are just a few examples of the several ING-IUSs that are being offered.[23] A total of 0.2/100 women-years of them became pregnant.[24] Following device implantation, they are only permitted to be used for a maximum of five years, even though accumulating scientific evidence indicates that they may be useful for up to seven years.[25] Lidocaine therapy before to insertion appears like a good option for nulliparous women to lessen pain and increase usage.[26] For Mirena, levonorgestrel is first released into the uterus at a rate of approximately 20 g/d; for Jaydess, the rate is approximately 12 g/d. It gradually decreases to 1012 g/d after five years[27] and stays there. In the first two to three months following the placement of this device, intermenstrual spotting was frequently experienced. After that, bleeding issues are rare and far less common than those seen with Cu-IUDs.[28] In a randomised comparative examination of TCu380A and 52 mg LNG-IUS involving 3 755 women, amenorrhea and decreased bleeding were the primary reasons for removing the LNG-IUS, whereas increased bleeding was the primary reason for removing TCu380A.[29] The surface epithelium erodes much less than inert plastic or Cu-IUDs.[30] Additionally, compared to women who utilize inert and copper-IUDs, endometrial regression under these conditions has produced much less endometrial tissue.[31]

Mechanism of Action

There is still much to learn about how the IUD works to give contraception. IUDs, especially copper-based ones, trigger a potent local inflammatory response that, in turn, activates lysosomes and results in additional inflammatory changes that are spermicidal. Following fertilization, the developing embryo experiences the same inflammatory responses every time. The efficiency of inert devices like the Lippesloop is increased with increased size and depth of contact with the endometrium. Several metals, especially copper, considerably increase the contraceptive impact of inert devices. This is most likely because copper causes a higher local intrauterine inflammatory response. The progesterone carrying devices lead to atrophic endometrial changes that make the endometrium an unfavorable site for implantation if fertilization and efficient tubal transport have occurred. There are numerous mechanisms of action for the levonorgestrel-releasing IUS, none of which can be distinctly distinguished. The contraceptive efficacy of the device is primarily caused by insufficient cervical mucus and severe endometrial suppression. Due to the local effects of progesterone, the cervical mucus thickens. The chronically elevated circulating levels of levonorgestrel cause the cervical mucus to remain thick and sparse, unlike in women with levonorgestrel-releasing implants, where it generally diminishes around mid-cycle. Data on the effects of the levonorgestrel-releasing IUS on cervical mucus changes, which have a substantial impact on the efficacy of contraceptives, are insufficient. Another strategy for preventing conception involves limiting sperm activity and movement inside the uterus and fallopian tubes, which limits fertilization and endometrial expansion. Early studies on the progestogen 2 mg/day device imply that the contraceptive effect occurs before fertilization because beta human chorionic gonadotropin (bHCG) levels have not been demonstrated to rise and fertilized eggs from the reproductive tract have not been discovered.[32] Despite the fact that ovulation is inhibited in some women, it is not thought to have a significant impact on the effectiveness of contraception. There is also a foreign body effect, comparable to that of other intrauterine contraceptive methods.

Advantages

One of the most widely used contraceptive methods is the IUD because it is simple to insert and remove, especially for long-term reversible contraception.

Its advantages include

- It can be used by practically any woman, including nulliparous women, and has a success rate of 98–99 percent over five years of IUD use. Its action lasts for ten years if it is not removed in that time.
- The action starts right away.
- It does not require sexual activity.
- It doesn't hinder sexual activity
- It is safe for nursing mothers.
- Fertility quickly returns after stopping.
- Contrary to hormonal contraception, it is safe for use by women taking any kind of medicine. It is not related with cancer of any organ. It does not result in weight gain. It typically has no impact on mood or sex drive.

It is also appropriate for females who are unable to utilise estrogen-containing birth control, such as those having a history of venous thromboembolism, stroke, myocardial infarction, or other types of vascular illness, long-term diabetes, migraine susceptibility, and heavy smokers over 35 years of age.

Disadvantages

An IUD has both minor and significant downsides despite its evident advantages, such as

- Menorrhagia, dysmenorrhea, and polymenorrhea are common complaints. These are also the main causes of IUD discontinuation.
- It provides no defence against STIs (sexually transmitted illnesses).
- A uterine infection during IUD placement has a 1% chance of occurring within 20 days of the procedure. If the woman is predisposed to STIs, this is enhanced. Before insertion, women should be tested for gonorrhoea, chlamydia, and any other organisms upon request. Fortunately, pelvic infections with an IUD in pregnancy can be effectively treated without taking the device out of the body.
- Without proper treatment, pelvic inflammatory disease may develop in a woman who has a STI and an IUD in place.
- The IUD may expel itself, particularly after or during the first three months' worth of periods. This is more frequently the case in nulliparous women, or in those who had it put in right after giving birth or having an abortion. There is a 5% chance of it happening. Backup contraception should be used right away if the device is expelled and the loss is discovered a few days later.
- 0.1% of women may get uterine perforation during implantation. Lower abdomen ache could be one symptom of this. Surgery will be required to remove the perforation.
- Pregnancies with an IUD in situ are relatively uncommon, but there is an increased risk of an ectopic pregnancy if conception happens.

Contraindications

The use of the IUD is contraindicated in women who have

- Present-day or recent history of pelvic infection;
- Current dysmenorrhea or menorrhagia that could be made worse by the IUD;
- Undiagnosed irregular vaginal bleeding that could be caused by cancer of the female reproductive organs

Malignant trophoblastic illness, ovarian, cervical, or endometrial cancer, structural heart disease with a

history of bacterial endocarditis.Small or irregularly formed uteri.[33,34,35]

CONCLUSION

Intrauterine contraceptive devices (IUDs) have been widely used to reduce female fertility because they are inexpensive, dependable, efficient, and reversible. The IUD still maintains a reasonable level of acceptability for family planning, although in recent years, that acceptability has drastically declined. One of the key reasons for this decrease is the bleeding episodes linked to its use. Due to the IUD's widespread use, numerous investigations on its mechanism of action have been carried out. But it's still unknown exactly how the IUD works. New IUDs are being designed with changes to increase patient and physician acceptance. The modifications are designed to lessen removals brought on by discomfort and bleeding, make insertion and removal easier, and lessen the risk of expulsion. Intrauterine contraceptive devices (IUDs) have been widely used to reduce female fertility because they are inexpensive, dependable, efficient, and reversible. The IUD still maintains a reasonable level of acceptability for family planning, although in recent years, that acceptability has drastically declined. One of the key reasons for this decrease is the bleeding episodes linked to its use. Due to the IUD's widespread use, numerous investigations on its mechanism of action have been carried out. But it's still unknown exactly how the IUD works. To improve patient and physician acceptance, adjustments are being made to the design of new IUDs. The changes are intended to reduce removals due to pain and bleeding, facilitate insertion and removal, and reduce the danger of expulsion.

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