July 2016 - Vol. 28 - N.3 - Monograph - ISSN 2385 - 0868

Italian Journal of Gynæcology & Obstetrics

The Official Journal of the Società Italiana di Ginecologia e Ostetricia (SIGO)

Monograph

From recommendation to action.
Expert consensus statements on:
1. Drivers and barriers to the proper use of intrauterine systems.
2. Detailed intrauterine system counselling for women.
3. Practical aspects related to the insertion of intrauterine systems.

Partner-Graf


SOCIETA ITALIANA DI OSTETRICIA E GINECOLOGIA
MDCCCXCII

Italian Journal
of

Gynæcology & Obstetrics

The Official Journal of the
Società Italiana di Ginecologia e Ostetricia
(SIGO)

Monograph

Partner-Graf

Management, Administrative office

Partner-Graf Srl - Via F. Ferrucci, 73 - 59100 Prato
Tel 0574 527949 - Fax 0574 636250
E-mail: info@partnergraf.it

The Italian Journal of Gynaecology & Obstetrics is a digital magazine.
You can download it freely from
www.italianjournalofgynaecologyandobstetrics.com or
www.italianjog.com

Table of contents


SOCIETA ITALIANA DI OSTETRICIA E GINECOLOGIA
MDCCCXCII

Italian Journal of
Gynæcology & Obstetrics
July 2016 - Vol. 28 - N. 3 - Monograph - ISSN 2385 - 0868

From recommendation to action. Expert consensus statements on: 1. Drivers and barriers to the proper use of intrauterine systems. 2. Detailed intrauterine system counselling for women. 3. Practical aspects related to the insertion of intrauterine systems.

The TRAIN group:
Drivers and barriers to the proper use of intrauterine systems

Vincenzina Bruni[1] (coordinator)

Carlo Bastianelli[2], Stefano Bianchi[3], Giampiero Capobianco[4], Ettore Cicinelli[5], Manuela Farris[2], Novella Russo[6]

[1] Ginecologia e Ostetricia, Firenze
[2] Sapienza Università di Roma
[3] Ospedale San Giuseppe, Università di Milano
[4] Ginecologia e Ostetricia, Università degli Studi di Sassari
[5] Università degli Studi "A. Moro", Bari; Azienda Ospedaliero Universitaria Policlinico Consorziale, Bari
[6] Centro Medico Demetra Grottaferrata, Roma

Detailed intrauterine system counselling for women

Attilio Di Spiezio Sardo[7](coordinator)

Tommaso Bignardi[8], Agostino Menditto[9], Cinzia Polo[10], Massimo Stomati[11], Silvia Von Wunster[12]

[7] Università degli Studi di Napoli "Federico II"
[8] U.O. Ginecologia e Ostetricia, ASST Grande Ospedale Metropolitano Niguarda, Milano
[9] Unità Operativa Ginecologia e Ostetricia Clinica Mediterranea, Napoli
[10] Casa di Cura Città di Rovigo
[11] U.O. Ostetricia e Ginecologia - P.O. "D. Camberlingo" Francavilla Fontana, ASL Brindisi
[12] Ospedale di Alzano Lombardo, ASST Bergamo Est

Practical aspects related to the insertion of intrauterine systems

Emilio Arisi[13] (coordinator)

Siri Braekhus[14], Valeria Dubini[15], Alessandro Gambera[16], Giampietro Gubbini[17], Maria Cristina Meriggiola[18]

[13] Società Medica Italiana per la Contraccezione
[14] Ginecologia e Ostetricia, Borgoricco, Padova
[15] Struttura Complessa, Ginecologia Territoriale USL Centro Firenze
[16] Ginecologia Endocrinologica, Spedali Civili di Brescia/Università di Brescia
[17] Endoscopia Ginecologica, Casa di Cura Villa Laura, Bologna
[18] U.O. Ginecologia e Fisiopatologia della Riproduzione, Università di Bologna, Azienda Ospedaliero - Universitaria S. Orsola - Malpighi

ABSTRACT

Intrauterine contraceptive methods are the most effective in their typical use and the most popular reversible contraception methods. In Italy their popularity is growing, but the use of such systems is still hampered by some "common beliefs", counselling challenges and problems encountered by some gynaecologists when inserting intrauterine devices. These are the reasons why a group of experts was invited to discuss this topic and provide clinical practice recommendations. This document is the result of this process and offers three separate sections addressing the following subjects: "Drivers and barriers to the proper use of intrauterine systems", "Detailed intrauterine system counselling for women" and "Practical aspects related to the insertion of intrauterine systems".

Keywords: Intrauterine contraception, intrauterine systems, barriers, placement, insertion, counselling

SOMMARIO

Gli anticoncezionali intrauterini sono i metodi contraccettivi reversibili più efficaci nel loro uso "tipico" e più usati al mondo. In Italia la loro diffusione seppur in aumento è limitata. Alcuni "falsi miti", la difficoltà nel counselling e la scarsa pratica nell'inserimento da parte di alcuni ginecologi sono elementi che potrebbero frenare la diffusione di questi metodi contraccettivi. Un gruppo di esperti si è riunito, utilizzando una metodologia tipica delle conferenze di consenso, per discutere tali tematiche e produrre raccomandazioni per la pratica clinica. Il presente documento è il risultato di questo processo e propone tre sezioni separate che affrontano le tematiche: "I *driver* e le barriere per un corretto uso dei sistemi intrauterini", "Il corretto counselling alle donne relativamente all'uso dei sistemi intrauterini" e gli "Aspetti pratici nell'inserimento del sistema intrauterino".

INTRODUCTION

"Long acting" contraceptive methods, and in particular intrauterine systems, are the most effective in their typical use and the most popular reversible contraceptive method. Use rates of IUS (hormone-releasing intrauterine devices)/IUD (copper intrauterine devices), among fertile women with a stable relationship, reach values of about 40% in some Asian countries and are growing in Italy, with a use rate (among women using hormonal methods or IUDs) of 12% in 2015, which means 110,000 women approximately[1,2]. Moreover, the latest data show that in Italy the average age of women who use new intrauterine systems is lower and lower, with more than two-thirds of patients under 40 years of age and a quarter of patients under 30 years of age, whereas in the past these systems were used by an older population.

However, in our country, the use of such systems is still hampered by some "common beliefs", counselling challenges and problems encountered by some gynecologists when inserting intrauterine devices. This consideration led Bayer to invite some gynecologists to participate in the drafting of some consensus statements on decision drivers and barriers to the use of IUS, detailed counselling for women and practical aspects related to the insertion of these devices.

METHODS

To do that, the consensus conference method was chosen, providing a list of recommendations by a jury at the end of a presentation, and expert consultations summarizing scientific knowledge on a given subject. The critical analysis of the literature allows the jury to compare the available evidences and opinions and expert reports.

This method involves:

-definition of the questions;
-identification of the relevant literature;
-preparation of a first consensus statement draft by a group of participants
-discussion by a panel of experts and preparation of the final document.

The experts called to participate in the drafting of such consensus statements attended a first workshop on November 26, 2015. During this workshop, the participants, divided into three working groups, defined the working methodology and the assessment tools to ensure equity and consistency between the different opinions expressed and also identified the questions to be addressed in the consensus document.

During the following three months, under the guidance of a coordinator, the three working groups discussed and critically assessed all relevant documents on statement issues identified through a PubMed research carried out by using the following keywords: "intrauterine device/insertion/counselling/barrier" to draft a first version of the Consensus Documents.

During a second workshop held on 26 February 2016, the three documents were presented by the coordinator of the group to all the experts in plenary session to be discussed and approved.

This document is the result of this process and has

Correspondence to: emilio.arisi@gmail.com

DOI: 10.14660/2385-0868-46

been approved and issued by all experts.

For the purposes of this document, unless otherwise specified, IUC means all intrauterine contraceptive methods, IUD means non-medicated intrauterine devices and IUS means medicated intrauterine systems containing 13.5 mg or 52 mg of levonorgestrel (LNG).

1. Drivers and barriers to the proper use of intrauterine systems

While drawing up the document, the working group used, as a basis for discussion, the results of a recent survey which aimed at identifying and assessing drivers and barriers to the use of intrauterine systems.

The research was conducted in October 2013-December 2014 through an online survey submitted to doctors (gynecologists for Italy) which administer intrauterine contraceptive (IUDs, that is copper intrauterine devices or IUS, that is levonorgestrel-releasing intrauterine devices such as LNG-IUS 13.5 mg, Jaydess® and LNG-IUS 52 mg such as Mirena®) and to women.

The study involved 670 health workers from 11 countries and 1,356 women from 13 countries.

In Italy 100 gynecologists aged between 25 and 65 years were selected with the following characteristics: working at clinics for at least 70% of their time; with at least 3 years of work experience; personally prescribing contraceptive methods to their patients; visiting at least 20 patients per month in order to prescribe contraceptive methods and knowing at least one intrauterine system (IUS/IUDs). 110 women aged between 18 and 45 years were also selected; they were interested in contraception and they had not undergone hysterectomy or sterilization surgeries.

The data collected showed that women had a good knowledge of the main contraceptive methods. 25% of them where on the pill, 31% used condoms, despite the fact that these are not the best birth control method, and 9% of them were using intrauterine methods.

Gynecologists were reported as the primary source of information (48%), followed by groups of girlfriends (37%), friends (28%) and the Internet (27%). As for the last source of information, women used mainly search engines, contraception websites and forums.

Specifically, the women interviewed revealed not to have a thorough knowledge of intrauterine systems: 58% of them, indeed, claimed to know them superficially, while only one woman out of four had a good knowledge of these systems.

Despite the lack of a thorough knowledge of the method, about half of the women interviewed stated they were interested in intrauterine systems. The main reasons for this choice are the high contraceptive efficacy and the long duration of action. Furthermore, many have pointed out the advantage of using a low amount of hormones (13.5 mg for LNG-IUS) and the absence of oestrogen. Ease of use and local action would also push women to choose an intrauterine contraceptive (**Table 1**).

Table 1.
Drivers and barriers to the use of IUS: women and gynaecologists (excluding some aspect relating to welfare for gynaecologists and costs for women) identify very similar drivers and barriers to the use of IUS.

FROM WOMEN'S POINT OF VIEW	FROM GYNECOLOGIST'S POINT OF VIEW
DRIVERS • Ease of use • Long-acting methods • Contraceptive effectiveness • Absence of oestrogen • Local action and minimal side effects • Small size (for LNG-IUS 13.5 mg)	DRIVERS • Easy placement procedure thanks to the small size of the system LNG-IUS 13.5 mg • Long-acting methods • Contraceptive effectiveness • Absence of oestrogen • And local action • Possible benefits not concerning contraception (for LNG-IUS) • Maximum adherence
BARRIERS • Concern for possible complications • Costs • Concern for the procedure/pain • Menstrual irregularities • Foreign body sensation	BARRIERS • Concern for the risk of PID/ infertility/ectopic pregnancy, especially in nulliparous women • Fear of causing pain during the procedure and making mistakes • The risk of irregular bleeding that requires continuous contact with the patient • The time required for counselling

However, there are some downsides that would prevent women from choosing an intrauterine system, such as the fear of foreign body sensation, the fear of experiencing pain during the placement procedure and possible complications that might arise from it. In addition, many women mistakenly think that these methods may affect their menstrual cycle.

Pros and cons of intrauterine contraception for women are very similar to those reported by gynaecologists who may recommend or not this method. If, on the one hand, contraceptive effectiveness, long duration of action, low amount of hormones, local action, absence of oestrogen and ease of insertion, in the case of LNG-IUS 13.5 mg, given its small size (**Table 1**) are undoubtedly some of the advantages of this method, on the other, the placement procedure is still a barrier, especially for nulliparous women, not just because physicians are afraid to cause pain to the patient but also for the risks of PID, ectopic pregnancies and infertility. These barriers are just common myth-conceptions, due to complications arising from the use of old copper spirals, which will be discussed later. Compared to copper spirals, some gynaecologists see an advantage in the bleeding profile of IUS compared to IUDs, while others think they are the same thing. Although some tend to confuse the two methods, gynaecologists say they are much more likely to recommend the use of IUS than IUD, although some claim that the IUD placement procedure is easier than the IUS placement procedure.

This survey was considered as an important source of information, also in consideration of the consistency of the results with other studies. For example, in a study conducted in Europe and Canada which assessed barriers and myths influencing the use of IUC in nulliparous and involved 1,103 physicians, the main barriers reported were: nulliparity, the risk of PID, difficulty/pain during the placement procedure and the risk of infertility, especially for nulliparous women[3].

1.1. In the light of the information that emerged from the survey, what are the good points to be proposed/actions to be implemented to support the use of IUS/IUD?

1.1.1. Long duration of action/contraceptive effectiveness

For women

For women, benefits include the contraceptive duration of IUS equal to 3/5 years.

In other words, this means not having to use a daily/weekly or monthly contraception method. Moreover, these methods are safer than combined hormonal contraceptives (COC).

For gynaecologists

Gynaecologists should be aware of the fact that LNG-IUS are among the modern reversible contraceptive methods with the best efficacy, in particular due to the combination of efficacy and "perfect" and "typical" use[4]. The increased efficacy of long-acting methods is due to the peculiarities of their route of administration and to the reduced role of medication adherence. Moreover, IUS/IUDs do not interfere with other medications and their effectiveness is not reduced due to malabsorption problems (**Table 2**).

Table 2

Contraceptive efficacy of different methods according to perfect use and typical use. Source: [4]modified.

**used in clinical practice*
***off label use in Italy*

Method	*% of unintended pregnancy within the first year of use*	
	*Typical use**	*Perfect use*
Combined contraceptives or mini pill (progesterone)	9	0.3
Contraceptive patch	9	0.3
Contraceptive ring	9	0.3
DMPA injection**	6	0.2
IUC		
IUD-Cu	0.8	0.6
IUS-LNG	0.2	0.2
Subcutaneous implantation	0.05	0.05

1.1.2. Absence of oestrogen exposure, local action, and reduced side effects

For women

Many women are not taking oral contraceptives due to the presence of oestrogen, both because they are concerned about hormones and because of their possible side effects.

LNG-IUS is just a hormonal progestin method acting locally, therefore side effects are reduced.

The most common side effects are headache, abdominal pain, changes in menstrual flow. These effects, however, tend to diminish over time.

For gynaecologists

The absence of oestrogen and the local action of IUS are important safety aspects which make this method suitable not just for women who are looking for a long-term, very effective, well tolerated and safe contraception method, but also for those women for whom the use of oestrogen is not recommended, for example women at increased risk of thromboembolism.

1.1.3. Ease of use and maximum adherence

For women

When using an IUS, patients can forget daily administration typical of pills. An IUS is a "fit and forget" method, because, once the device has been placed by a gynaecologist, women can forget about it and the only thing they have to do is schedule a medical examination after placement and an annual medical examination, which, however, is required for all women.

For gynaecologists

Using an IUS requires minimum compliance; moreover, its safety and maximum adherence to the treatment guarantee high continuity of use.

To simplify counselling, a timetable for medical examinations to be scheduled after placing an IUS can be delivered to women and discussed with them (**Table 3**).

Table 3
Example of timetable for periodic medical examinations

After placing an IUS:

- Schedule a follow-up visit after the first menstrual cycle (after 4-6 weeks) following placement.
- Schedule an annual gynaecological examination, as usual.
- No additional checks are required, except in the presence of symptoms that require medical supervision.

1.2. In the light of the barriers pointed out by the survey, what are the good points to be proposed/actions to be implemented to overcome these barriers?

1.2.1. Concern for the risk of PID/infertility/ectopic pregnancy

For women

Women should be informed of the possible rare adverse events that might occur after placing an IUS and, as for all contraceptive methods, of the risks/benefits associated with it.

For gynaecologists

As for IUS devices, no increased risk of PID was reported, if not in the first 20 days after placement, affecting future infertility.

During each counselling session, gynaecologists should emphasize that IUS are not characterised by the same risk profile of copper intrauterine devices used in the 70s. Such devices are certainly associated with an increased risk of PID causing infertility and ectopic pregnancy.

The high contraceptive efficacy of IUS results in a lower absolute risk of ectopic pregnancy if compared to sexually active population that does not use any form of contraception(5,6).

(See also paragraph 2 of the document "Detailed intrauterine system counselling for women").

Fertility is immediately restored after removing the IUS.

Comments

A study on 57,728 insertions reported a PID rate of 0.54% in the first 90 days after placement, confirming that an increased risk is associated exclusively with the insertion procedure[7].

A systematic review that included all contraceptive methods reported that the PID rates were similar with the use of Depo-Provera® shots, Mirena® systems and COC[8].

A Cochrane review of 2010 showed that the risk of PID after the IUC insertion is low, and that the administration of 500 mg of azithromycin or 200 mg of doxycycline does not reduce the risk[9]. ACOG does not recommend routine antibiotic prophylaxis, but an infectious disease evaluation for women at high risk of STDs at the time of insertion and to treat as soon as possible only women with positive results[10]. Even the RCOG does not recommend routine antibiotic prophylaxis, but suggests to consider antibiotic prophylaxis for women at high risk of infectious diseases in whom the results of infectious diseases screening are not available at the time of insertion of the IUC[11].

Finally, a recent review of the literature has documented that, after a year of discontinuation of hormonal contraceptives or intrauterine devices, fertility is immediately restored[12].

1.2.2. Cost or cost-effectiveness for women

For both women and gynaecologists

It is important to inform women of the cost of IUS compared to other methods, emphasizing the fact that these are long-term methods (see paragraph 2 of the document "Detailed intrauterine system counselling for women").

Women, in fact, might refuse such methods due to a higher initial investment, but should be advised that, being these methods used for a three-year period, the same amount would cover the use of COC for just one year.

Moreover, when planning outpatient activities gynaecologists should be aware that, from the point of view of public health, the use of intrauterine systems involves significant savings compared to other contraceptive methods, particularly because LARC present greater efficacy in reducing the risk of abortion.

Comments

In Italy, the phenomenon of repeat abortions is relevant. The 2012 ISTAT data show that the percentage of women who undergo repeated abortion procedures is 26.6%. This results in a high cost for public expenditure, given that the total cost of repeat abortions is about 30 million euros per year.

The Committee on Gynaecologic Practice Long-Acting Reversible Contraception Working Group of ACOG has identified cost as a barrier to the use of IUS emphasizing, however, that "the implant and the IUDs are highly cost-effective, even with relatively short-term (12–24 months) use"[13].

In 1999, the British government introduced a health policy known as Teenager Pregnancy Strategy aimed at reducing the number of unintended pregnancies and, consequently, the number of voluntary abortions, through the use of LARC methods[14]. The goal was to reduce unintended pregnancies by 50% in girls younger than 18 years by 2010, by investing 26.8 million pounds in contraception. The obtained reduction was not 50%, as planned, but 34%. It was calculated that the use of LARC (especially implants) allowed to save 17,300 pounds for each avoided pregnancy. Only in 2009, 53 million pounds were spent for unintended pregnancy interruption procedures for girls younger than 20 years.

1.2.3. Concern for the insertion procedure

For women

Information is the main tool to overcome this barrier. The use of drawings or models may help women to understand the insertion technique.

For gynaecologists

The lack of a training for the insertion of IUS is not a limitation but it could be a barrier to the use of these devices for gynaecologists.

According to scientific literature, insertion difficulties are not greater for nulliparous women (see paragraph 3.4. of the document).

1.2.4. Menstrual irregularities

For women

Some women who use IUC may experience some menstrual irregularities, which have little clinical relevance.

Women should be informed about the differences between IUDs and IUS and the absence of oestrogen that characterises both systems, but should also know that the two systems have a different influence on the menstrual pattern. In particular, as for IUS, after the first few months of use , women can experience reduced menstrual flow or periods of amenorrhea.

For gynaecologists

Correct information prevents the request for information to the gynaecologist and a discontinuation of use[15].

Table 4 shows the main differences between IUDs and IUS in relation to the menstrual cycle.

Table 4
Influence of IUDs and IUS on the menstrual pattern

IUD	IUS
• Intermenstrual spotting or long and heavy bleeding are quite common[16].	• Abnormal bleeding occurs in a small percentage of cases.
• Menstrual flow increased by 20-50% compared to the menstrual flow prior to insertion[17].	• The frequency of abnormal bleeding varies depending on the levels of progestin released[18].
	• Reduced menstrual flow and, in some cases, within one year after the system placement, women can experience temporary amenorrhea[19].

1.2.5. Time required for IUS insertion procedure counselling

For gynaecologists

Contraceptive counselling best practices should include an exhaustive presentation of all the most effective contraceptive methods.

Consequently, the time required for counselling on IUD/IUS or other methods is substantially similar.

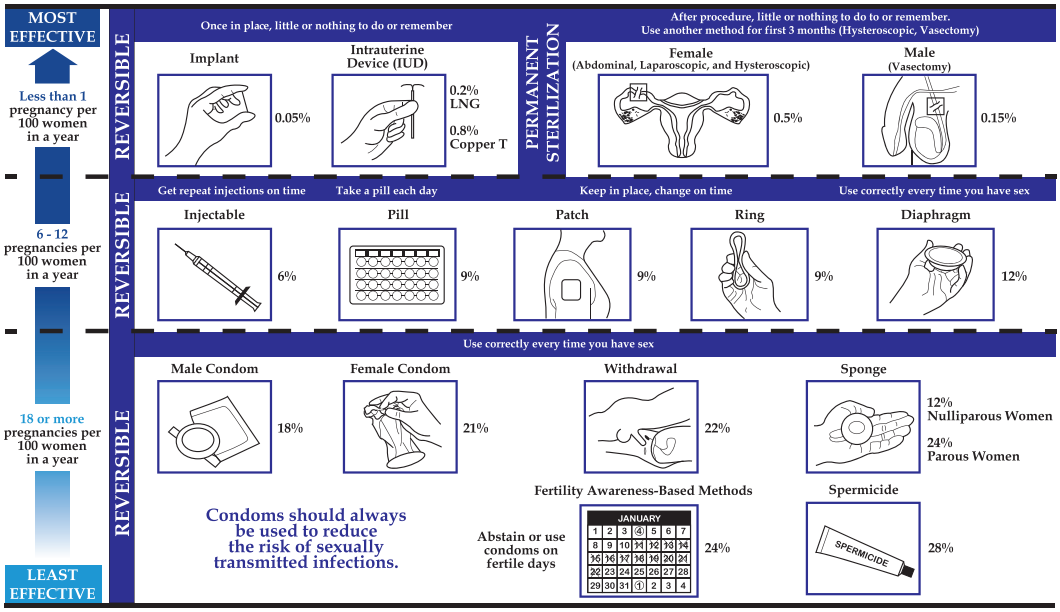
This barrier can be overcome through the availability of information materials specifically prepared for both patients and doctors.

According to the contraceptive method chosen, different aspects have to be investigated, but the time required is the same.

Figure 1

Effectiveness of family planning methods.

The percentages indicate the number out of every 100 women who experienced an unintended pregnancy within the first year of typical use of each contraceptive method.



Adapted from World Health Organization (WHO) Department of Reproductive Health and Research, Johns Hopkins Bloomberg School of Public Health/Center for Communication Programs (CCP). Knowledge for health project. Family planning: a global handbook for providers (2011 update). Baltimore, MD; Geneva, Switzerland: CCP and WHO; 2011; and Trussell J. Contracpetive failure in the United States. Contraception 2011; 83:397-404

2. Proper counselling supporting the choice of the right intrauterine system

2.1. What are the preliminary questions to be asked during contraception counselling?

When developing appropriate strategies to facilitate decision making and adherence to contraception, gynaecologists must take into account the fact that the choices made must necessarily be in harmony with the ideal of femininity and must meet the needs of each single woman.

It is crucial to understand what are the needs of each single woman by asking some preliminary questions that are general but also crucial to advise patients, such as:

-Are you looking for a reliable method of birth control?
-Is there a baby in your near future?
-Are you already using a contraceptive method, if so which one?
-What do you think about it?
-Have you used a hormonal contraceptive or another method of contraception in the past?
-Did you stop contraception in the past? If so, why?
-Are there any medical conditions precluding the use of certain methods of contraception (e.g., family history of deep vein thrombosis)?

Comments

Today, women want to choose a method that suits their lifestyle and, at the same time, that is in harmony with their body. A method that does not interfere with the biological mechanisms of sexuality, enhancing awareness of sexuality. Loss of libido, as well as changes in mood and a reduced menstrual flow, are among the most important causes of discontinuation of oral contraception use. Indeed, side effects seem to justify a rate of oral contraception discontinuation of 30% for "new users" and 15% for women who had already experienced at least one other type of hormonal contraception. The fact that oral contraception is a user-dependent method and that women who miss a pill may experience intermenstrual bleeding which impairs contraception reliability, are both examples of low compliance[20].

According to scientific literature, women and gynaecologists agree in saying that there is room for improvement in adherence to contraceptive methods and counselling plays an important role[21].

In addition, most women, if properly informed, prefer a long-acting method[22].

2.2. How to explain the difference between SARC (short-acting reversible contraception) and LARC (long-acting reversible contraception) methods in terms of duration and methods of use, advantages and disadvantages?

When explaining the differences between SARC and LARC methods, some basic information must be provided (see also the **Table 5** for a better presentation of the differences between the two methods):

-SARC includes short-acting contraceptive methods requiring daily, weekly or monthly administration, such as combined pills, patches and vaginal rings;
-LARC includes long-acting contraceptive methods administered by a gynaecologist, such as intrauterine contraceptive devices (IUS and IUDs), injectable and implantable contraceptives. These are administered every three months (injectable contraceptives) or every 3-5 years.
-LARC methods do not depend on user compliance;
-among all SARC and LARC methods, only IUS/IUDs act locally and not systematically;
-IUC and implantable systems are the LARC methods currently available in Italy, while injections are not recommended for contraception;
-there are two types of intrauterine contraceptive devices available today: levonorgestrel-releasing devices (LNG-IUS 52 mg, Mirena® and LNG-IUS 13.5 mg, Jaydess®) and non-hormonal copper devices (IUD). IUS can be effective for up to 3-5 years, while some copper IUDs can be effective for 10 years;
-since they do not contain oestrogen, LARC methods can be considered a viable alternative for those patients for whom combined hormonal contraceptives are not recommended. Long-acting reversible contraception, indeed, is contraindicated only in rare cases;
-LARC methods are extremely safe, with an efficacy greater than 99%;
-the contraceptive effectiveness of SARC methods depends on a 'typical' use, while the effectiveness of LARC does not depend on compliance or proper use of contraception;
-continued use rates of LARC methods are higher than those reported for oral contraceptives;
-the efficacy and tolerability profile of LARC methods is better than that of short-acting contraceptives;
-the effectiveness of LARC is not reduced by problems of malabsorption;
-IUS/IUDs do not interfere with other medications.

Table 5
Main differences between LARC and SARC methods.

	Long-acting reversible contraeception (LARC)			Short-acting reversible contraeception (SARC)
	Copper IUD	LNG - IUS	Subcutaneous implant	Combined pill, patch, ring
Mechanism of action	Non-hormonal, local	Hormonal, local	Hormonal, systemic	Hormonal, systemic
Presence oestrogen	No	No	No	Yes
Failure rate after one year of use	0.8%	0.2%	0.05%	9%
Administration frequency	5-10 years	3-5 years	3 years	Daily, weekly or monthly
Community of use after one year	83%	88%	83%	49-55%
Return to fertility following discontinuation	No delay	No delay	No delay	No delay
Menstrual pattern	Heavier and longer menstrual bleeding for 20-50% of women	Reduced and shorter menstrual bleeding	Decreased blood loss but and longer menstrual bleeding	Reduced and shorter menstrual bleeding

Comments:

According to clinical studies, LARC methods are 20 times more effective at preventing unintended pregnancies than pills, patches or rings[23]. Studies involving different populations have shown a significant association between the use of LARC and a decrease in unintended pregnancies in adolescents[24]. Patients younger than 21 years, whose compliance to medication is typically low, are a group of women at high risk of unintended pregnancies (almost twice as much than older women)[25]. LARC methods do not require any user-dependent treatment adherence after their placement, therefore LARC failure rates for an 'ideal' use are equivalent to failure rates related to a 'typical' use. LARC failure rates are close to those of tubal sterilization, but LARC methods are reversible. SARC methods, on

the other hand, require daily, weekly or monthly treatment adherence among users. Consequently, while SARC failure rates for an 'ideal' use can be compared to those of LARC methods, failure rates for a 'typical' use are significantly higher[26].

If we consider patients who decide to stop taking the pill, only one third of them decides to stop contraception due to side effects (spotting, nausea, breast tenderness). In fact, among the most frequent causes of discontinuation of birth control pill, patches and rings we find difficulties related to treatment adherence[20]. Due to these difficulties in adherence to contraception, in 2012, ACOG recommended to promote the use of LARC methods, especially among teenagers[27].

Knowing the mechanism of action of IUC systems is very important, since we are talking about a local action, which is quiet different from other contraception systems: copper IUDs induce a marked foreign body reaction associated with a cytotoxic effect of copper ions on sperm in the cervical mucus, the tubal and uterine fluid[28,29]. The mechanism of action of levonorgestrel-releasing devices, on the other hand, is more complex and multifactorial compared to that of copper IUDs.

Some studies showed how 20 µg/day levonorgestrel-releasing devices modify the cervical mucus, thus resulting in a negative ferning test with consequent impedance of sperm penetration[30,31]. Downregulation of estrogen and progesterone receptors has a clear anti-proliferative effect causing insensitivity to circulating levels of estradiol. As a result, the endometrial thickness is uniformly reduced (atrophy-wasting) with a reduction in number and size of the endometrial glands, decidualized stromal cells, and increased apoptosis[32]. Another response of the endometrium is a foreign body reaction with modifications of cytokines and integrins. In vitro studies with capacitated sperm exposed to concentrations of LNG similar to those issued by IUS showed a reduction in the number of sperm that interacts with the zona pellucida[33]. Moreover, after placing an IUS, endometrial A-Glicodeline, which is normally released 5-6 days after ovulation and throughout the luteal phase of the menstrual cycle, is also released during the fertile period (progesterone-dependent regulation). Since exposure to A-Glicodeline makes the sperm unable to bind to the zona pellucida, this could further reduce the chances of fertilization when a sperm is able to reach the oocyte. The reduction of mast cells in eutopic and ectopic endometrium[34] and of nerve growth factors (NGF, NGFR p75, TrkA) in the endometrium and myometrium[35] has positive effects on the treatment of endometriosis and adenomyosis pain. Low levonorgestrel-releasing devices (6 µg/day) cause changes in the cervical mucus that are similar to those of 20 µg/day levonorgestrel-releasing devices, while the endometrium is secretive[36].

2.3. If the patient is interested in intrauterine systems (IUS), what are the main features to be discussed during counselling?

1) Mechanism of action
2) Insertion procedure
3) Changes in the menstrual cycle
4) Post-insertion examinations

Informing women on all IUS aspects, answering questions and dissolving any doubts are the main goals of counselling.

2.3.1 Mechanism of action

Women should know that IUS are characterised by a local mechanism of action causing mucus thickening, thus preventing sperm penetration. Ovulation, however, is preserved since there is no systemic effect.

2.3.2. Information about the insertion procedure and possible complications

It is advisable to explain the insertion procedure, preferably with the aid of anatomical models, while emphasizing[37]:

-manoeuvring speed;
-the near absence of pain;
-that, usually, no analgesic and/or anesthetic premedication is required;
-that the risk of perforation of the uterine wall during insertion maneuvers is equal to about one in a thousand;
-that the possibility of a spontaneous expulsion is equal to 3-5%.

Also, before any insertion, all risk factors associated with pelvic infection should be discussed with the patient[38].

Women should be informed that, in rare cases, a vasovagal crisis may occur, most frequently in hypo-tense or epileptic patients.

The use of IUS of small size may reduce "discomfort".

It is important to inform women that the risk of unintended pregnancy (both intra-uterine and ectopic) with the IUS-LNG in place is very low, significantly lower than the risk reported in the general population.

Women with a history of ectopic pregnancy, tubal surgery or pelvic infection are at increased

risk of ectopic pregnancy. An ectopic pregnancy should be suspected in case of lower abdominal pain, especially if associated with menstruation absence or if bleeding occurs in amenorrhoeic women.

In case of undesired pregnancy with the LNG-IUS in place, there is a higher relative risk of ectopic pregnancy.

During the counselling session, women who are considering to use intrauterine systems should be informed of the signs and symptoms related to ectopic pregnancy.

Comments

Based on data from two large "managed care" databases in the United States, the estimated rate of ectopic pregnancies in women from the general population aged between 20 and 39 years (including users of contraceptive and not) ranged from 0.14 to 0.42 per 100 women/year[38-40].

In clinical studies on intrauterine systems, the overall incidence of ectopic pregnancy with LNG-IUS 13.5 mg was 0.11 per 100 women/year. Considering that the Pearl Index is 0.3 per 100 women/year, it is clear that about half of unintended pregnancies that occur while using IUS may be ectopic.

2.3.3. How does an IUS change the menstrual cycle in the first months after insertion?

In the first months after the insertion of the IUS, however, as it may happen with all hormonal contraceptives, it is very likely that the menstrual cycle may be subject to changes in terms of duration and quantity. In particular, in the first three months of use of an IUS, spotting and decreased blood loss and longer menstrual bleeding were observed.

Such possibility should not in any way frighten the patient, since it is part of a physiological uterine adaptation to a system which tends to improve and usually disappear after the first few months[18].

The local effect of LNG released by the IUS leads to a decrease in the menstrual flow that may be so significant that, in certain cases, within a year form the insertion, may lead to temporary amenorrhea. This circumstance, sometimes uncomfortable for women, is still more common when higher levels of progestin are used[18].

The use of LNG-IUS has, on the other hand, an effect on dysmenorrhoea[41].

2.3.4. Checks and tests required

Women should be informed that they will have to undergo at check-up a 4-6 weeks after insertion of an intrauterine system.

Women should know how to check the strings of an intrauterine contraceptive and addressed to a professional if they cannot feel the strings.

All women using IUS should still be informed of the possibility to return for a check anytime they want, to get all the answers they need or if they have noticed new symptoms.

Annual check-ups are recommended.

2.4 Frequently asked questions

Here is a list of frequently asked questions about this type of contraception:

2.4.1. Since this is a hormonal contraceptive, will I experience the same side effects of birth control pill?

Women should know that they will not experience the same side effects of birth control pill, because:

1) the mechanism of action of IUS is local and their systemic absorption is negligible;
2) intrauterine systems do not contain oestrogen, which means that certain side effects such as water retention, breast tenderness, or the risk of thrombosis are reduced or completely eliminated;
3) the most common side effects of IUS include headache, abdominal pain and changes in the menstrual flow. These effects tend to diminish over time.

Comments:

The typical side effects of combination hormonal contraceptives are reduced with 13.5 mg and 52 mg LNG-IUS and they also tend to diminish over time. LNG-IUS 13.5 and 52 mg have similar side effects (such as acne, breast tenderness/breast pain and headache). Furthermore, intrauterine system discontinuation rates due to side effects are comparable to those of copper devices[42].

2.4.2 Is weight gain one of the side effects I will experience?

The side effects of intrauterine systems do not include weight gain.

Comments

The minimum amount of hormone released by levonorgestrel-releasing intrauterine systems (LNG-IUS) does not cause significant weight gain or significant systemic side effects. For example, according to a large randomized controlled trial which compared the efficacy and safety of use of 13.5 mg 19.5 mg levonorgestrel-releasing intrauterine systems, the mean change in baseline

body weight after 36 months was 0.5 kg for 13.5 mg IUS and 0.6 kg for 19.5 mg IUS[43].

2.4.3. What are breast side effects?

During the first few months after insertion some women may experience breast tenderness, but not so intense and long lasting as the breast tenderness experienced when using SARC.

Comments

As for the risk of breast cancer, the evidence did not show any significant relationship between breast cancer and the use of preparations containing progestin only[44]. However, although the systemic exposure for IUS is absolutely reduced, non-hormonal contraception, such as that of IUDs, is more appropriate for women with a previous history of breast cancer.

2.4.4. Is foreign body sensation one of the side effects? Will my partner feel the IUS? May I use tampons or menstrual cups during my period?

Women do not experience foreign body sensation in their uterine cavity.

Sometimes you may feel the presence of the system strings, like a pinching sensation and your partner may also feel the strings during intercourse.

The use of tampons and menstrual cups is not associated with an increased risk of expulsion of the intrauterine system[45].

However, it is recommended to remove them gently so as not to inadvertently pull the strings, which will cause the expulsion of the intrauterine system.

2.4.5. How long after removing the IUS may I consider having a child?

Women should be informed that after removing the intrauterine system their fertility is immediately restored. This allows women to plan a pregnancy immediately in a responsible way.

Comments

It is useful to inform women that the use of LNG-IUS showed no significant changes in ovarian function (if not in the first year of use of 52 mg LNG-IUS) which means that ovulation continues to occur in the great majority of women. Clinical trials have showed that, during the first three years of use of 13.5 mg LNG-IUS, the ovulation rate is the same reported before the insertion of the system[36].

2.4.6. Is the insertion procedure painful?

Women should be informed that the insertion procedure is very quick, also considering the small size of the system, especially that of 13.5 mg LNG-IUS. Women usually feel something similar to menstrual pain but it lasts less and is usually well tolerated even by very young women who have never had a child.

You may experience cramping when the system arms are released by the insertion tube to be placed on the fundus.

The intensity of such cramps may vary from woman to woman but usually, when they occur, they last a few minutes and do not require the administration of pain killers and/or antispasmodics which however, if required, are not contraindicated.

2.4.7. Are intrauterine systems expensive?

Women should know that the initial cost of an LNG-IUS is higher if compared to daily, weekly or monthly hormonal contraception.

If, however, we consider that an LNG-IUS is used for 39/65 cycles, these systems are definitely less expensive than SARC and other LARC systems.

The cost of a three-year LNG-IUS is equivalent to the cost of SARC for one year.

Using a simple table (**Table 6**) can help physicians provide comprehensive information.

Table 6

Cost of an LNG-IUS compared to other hormonal contraceptives

	Cost (€)					
Use	LNG-IUS 13.5mg	LNG-IUS 52mg*	Pill**	Ring	Patch	Implant
1 year	173	220	221	240	199	183
2 years			442	480	398	183
3 years			663	720	597	183

**52 mg LNG-IUS has a duration of 5 years*

*** The price of the best-selling birth control pill*

2.5. What information should be provided to women during contraception counselling after voluntary termination of pregnancy?

Contraception counselling is a key part of programs for women who ask for termination of pregnancy.

The guidelines all emphasize how important it is that the staff of the clinics dealing with pregnancy termination services make sure that women receive adequate information on

contraception and all methods immediately available.

Women should know that, after voluntary termination of pregnancy, ovulation is immediately restored, with 83% of ovulatory cycles in the first month after surgery[46].

Comments

A detailed consideration of issues relating to counselling for women who chose pregnancy termination is available at the end of the document (**Background information 1**).

2.6. What information should be provided to women during contraception counselling after childbirth?

Contraception counselling should be included in childbirth programs, already during pregnancy or before discharge after delivery[47].

Puerperium and lactation must be taken into consideration when choosing a contraceptive, especially in relation to the increased risk of thromboembolism and possible interferences of contraceptives with milk production.

As for counselling addressed to women who just gave birth, please refer to paragraph 2.2, 2.3 and 2.4.

Comments

A detailed consideration of issues relating to counselling for women after childbirth is available at the end of the document (**Background information 2**).

Table 7

Four-step women's counselling model check list.

Counselling is a key tool to advise women on the contraceptive method that best suits their needs, through a shared and reasoned path, and provide them with important information.

1. UNDERSTANDING
Understanding if a woman needs to use a contraceptive method and what method better suits her needs is crucial.
• Do you **need** to use a **contraceptive method** now? • Are you **planning on having children** in the near future? • Are you **already using a contraceptive method**? If so, which one? • **Does it suit your needs**? • **Have you ever used** a hormonal contraceptive, or another contraceptive method **in the past**? • **Have you ever discontinued** a contraceptive method? If so, why? • Are there any **pre-existing medical conditions for which the use of some contraceptive methods is not recommended** (e.g. a history of deep vein thrombosis)?

2. EXPLAINING
You must explain in detail what are the differences between long-acting methods (LARC) and short-acting methods (SARC), including pros and cons.
Compared to SARC methods, LARC methods (intrauterine systems/devices and implantable systems): • **Free from contraceptive routine**, minimizing the need for compliance. • Have a better **efficacy, safety and tolerability profile**. • Intrauterine systems/devices, unlike other systemic methods, are characterised by a **local action**. They pose no risk of reduced efficacy due to drug interactions.

3. ARGUING
If your patient is going to use intrauterine systems, explain in detail the essential aspects and suggest her to schedule appointments for routine examinations.
• **Mechanism of action** of intrauterine systems: **local**, thanks to cervical mucus thickening that prevents the sperm penetration. • **Easy placement procedure** and any possible complications, though rare (perforation, expulsion, ectopic pregnancy) also due to patients' risk factors (history of ectopic pregnancy, tubal surgery or pelvic infection). • **Changes in the menstrual cycle**: reduction in flow, menstrual pain and spotting during the first months. • **Examination** required after placing the system/device. Answer any questions.

4. ORGANIZING
The insertion procedure must be properly planned and agreed with the patient, after dealing with questions or concerns.
Insertion scheduling criteria: • preferably within day 7 day of the menstrual cycle, • within the first 48 hours from delivery (or after uterine involution) or even after a caesarean section. • Emphasize: ▪ the rapidity of the procedure, ▪ the near absence of pain and/or risks, ▪ the absence of analgesic and/or anesthetic premedication (even it's not contraindicated). • Inform patients with hypertension or suffering from seizures of possible vaso-vagal crises.

Background information 1:

What information should be provided to women during contraception counselling after voluntary termination of pregnancy?

Contraception counselling is a key part of programs for women who ask for termination of pregnancy.

The guidelines all emphasize how important it is that the staff of the clinics dealing with pregnancy termination services make sure that women receive adequate information on contraception and all methods immediately available.

Women should know that, after voluntary termination of pregnancy, ovulation is immediately restored, with 83% of ovulatory cycles in the first month after surgery[46]. You must consider that, for some women, voluntary interruption of pregnancy could be a unique opportunity to access the health care system, therefore scheduling the following appointment to discuss contraception issues is a critical step that should not be skipped. In addition, women are more motivated to avoid unintended pregnancies after pregnancy termination.

Most women who decide to terminate their pregnancy have experienced contraception failure, due to incorrect use of contraception, including birth control pill and condoms. According to WHO, in fact, there is a significant difference in the effectiveness of barrier methods and hormonal methods (pill, ring, patch) between perfect use and typical use and high contraception discontinuation rates within 12 months after the first prescription[48,49].

LARC methods are the ideal solution for this group of patients, since their effectiveness does not depend on treatment adherence and also because, according to literature data, there is a high continuity of use at 12 and 36 months. In particular, a recent publication by the CHOICE group shows a three-year continuity of use of LARC methods of 67% versus 31% of non-LARC methods[50-52].

IUC systems can be placed during suction aspiration, without causing any discomfort to patients, since they are not required to schedule another appointment for the insertion procedure.

Their use immediately after an abortion procedure is recommended by the WHO document, Medical Eligibility for Contraceptive Use[48].

The effectiveness of LARC methods placed during a termination of pregnancy procedure was assessed by several studies that showed a significant reduction in repeated requests for termination of pregnancy in patients who chose these methods[51-53].

According to a study by the CHOICE group, women who have recently undergone termination of pregnancy are three times more likely to ask for the placement of an intrauterine device compared to women who do not have a history of abortion[54]. Therefore, counselling provided to women undergoing voluntary termination of pregnancy should include the most important information on highly effective contraceptive methods, able to guarantee adherence and ease of use.

Choosing an LNG-IUS can be even more advantageous, since it ensures both high efficacy and excellent clinical tolerability, as well as, compared to other LARC methods, a more favourable bleeding profile resulting in treatment adherence, which is crucial for this group of patients.

According to some studies, there is a lower risk of pelvic infections for LNG-IUS compared to copper IUDs, probably due to the changes in cervical mucus and the endometrium. The lower risk of pelvic infections related to the use of an LNG-IUS may become an important factor for a group of patients with an increased prevalence of sexually transmitted disease[55].

Women should know that, if they choose IUDs, the system can be inserted immediately after the end of suction aspiration, and that there are no particular health risks for women in this case. The simultaneous insertion is indeed recommended, since literature data show that usually women (about 40%) do not show up for the insertion procedure scheduled after abortion[56].

Women should also know that the insertion of intrauterine devices during surgical abortion is not associated with an increased risk of perforation or infection.

A greater risk of expulsion is only reported for advanced pregnancy, especially in the second trimester.

However, studies comparing simultaneous placement and post-abortion placement clearly show that the risk of expulsion is largely offset by the fact that many women do not show up for the scheduled procedure. According to a review by Cochrane, placing an intrauterine device during the abortion procedure is highly recommended[56].

If the patient chooses non-surgical abortion, on the other hand, the placement of an intrauterine device is delayed until the first post-abortion menstrual period[57].

Providing precise information on the checks to

be carried out after insertion, according to routine procedures, and system replacement is extremely important. Due to the possible increased risk of expulsion, women should know that a check is required after the first menstrual cycle, or not later than 6 weeks after the insertion procedure.

Background information 2:

What information should be provided to women during contraception counselling after childbirth?

Contraception counselling should be included in childbirth programs, already during pregnancy or before discharge after delivery[47]. Puerperium and lactation must be taken into consideration when choosing a contraceptive, especially in relation to the increased risk of thromboembolism and possible interferences of contraceptives with milk production.

After giving birth, women may have different needs and often ask for a long-acting contraceptive method.

According to WHO eligibility criteria, IUS/IUD systems are ideal during the postnatal period since they can be inserted immediately after delivery (<48 hours), without interfering with breastfeeding and ensure long-term effectiveness. Since these systems can be inserted immediately after delivery, women must be fully informed during pregnancy. Usually the insertion of an intrauterine system is discussed not earlier than 6 weeks before delivery or at least not before complete uterine involution. The insertion of IUDs after childbirth is associated with an increased risk of expulsion. However, according to the literature, the risk is reduced if the system is inserted immediately after the placenta is expelled, or within 48 hours after delivery[58,59]. The document Medical Eligibility for Contraceptive Use does not mention any restrictions (category 1) to the insertion of the intrauterine system within the first 48 hours or after 4 weeks or with uterine involution. The insertion is not recommended after 48 hours and earlier than 4 weeks after delivery (category 3). The system can also be inserted during Cesarean Delivery, with a lower risk of expulsion[48,60]. Women should also know that there is a slightly increased risk of perforation for systems inserted after delivery than for systems placed several weeks after delivery[60]. According to the SPC of 13.5 mg LNG-IUS[38], an intrauterine system must be placed after the involution of the uterus is complete and in any case not earlier than six weeks after delivery. If uterine evolution is delayed, the procedure should be scheduled not earlier than 12 weeks after delivery. The EURAS study (European Active Surveillance Study for Intrauterine Devices) showed that the factors associated with greater risk of perforation are breastfeeding and placement earlier than 36 weeks after delivery. The incidence of uterine perforation during insertion of the IUC is, however, very low and equal to 1 in 1,000. The risk is 5.6 times greater for placement procedures performed earlier than 36 weeks after delivery for breastfeeding women and 1.7 times greater for non-breastfeeding women. According to the conclusions of the Study Group, however, the benefits of intrauterine contraception outweigh the risks of perforation, therefore there is no reason to discourage the use of intrauterine systems after delivery[60]. However, patients should be informed of the symptoms of a possible perforation, that is when after-placement pain is very intense, much more intense than menstrual pain, or in case of heavy bleeding associated with pain persisting for several weeks after insertion, pain during intercourse or inability to feel the strings of the IUD in the vagina[60].

However, women should know that they can use LNG-IUDs while breastfeeding. According to evidence-based literature, indeed, there are no particular risks concerning the use of progestin-only contraception while breastfeeding. A large-scale review by the Cochrane Collaboration involved three studies comparing IUDs and medicated IUS. One study reports an earlier suspension of breastfeeding for women who use medicated IUS, while two more recent studies showed no difference between the two groups. Therefore, World Health Statistics 2015 includes the use of medicated IUS during breastfeeding in Category 2 (benefits of using IUS usually outweigh the risks)[61-64].

In conclusion, the staff assisting women during pregnancy and childbirth should know how important it is that contraception counselling is included in childbirth programs, already during pregnancy, so that women can choose an effective and safe method. Intrauterine devices, and in particular LNG-IUS can be used by most women who are breastfeeding, provided that the placement procedure is performed immediately after delivery or six weeks after delivery. The slightly increased risk of uterine perforation in breastfeeding women and in case of placement earlier than 36 weeks after delivery should not limit the use of this safe and effective method.

3. Practical aspects of intrauterine system placement

3.1. What are the necessary requirements for the clinic where the IUC placement procedure is performed?

IUC placement procedures can be performed at any clinic or doctor's office meeting the requirements set forth by the region where the clinic is located or by local health authorities.

In Italy, outpatient services provided by the National Health Service are defined by Ministerial Decree of 22/07/1996 (Ministerial Decree of 22 July 1996 "Outpatient services provided by the National Health Service and related fees"), clearly stating that this procedure (code ICD 9CM: 69.70) can be performed by any clinic.

IUC placement procedures should be performed in a comfortable environment where all safety and sterility requirements are met. The clinic should also be equipped with all the instruments required (such as specula, forceps, hysterometer, swabs to clean the cervix, scissors).

3.2. What are the main "steps" for a gynecologist who approaches the IUC placement procedure for the first time?

Gynaecologists should receive adequate training[42].

The main steps are reported below[65,66]:

-perform a bimanual vaginal examination, to evaluate the mobility, the position and size of the uterus;
-use a speculum, possibly short and wide; this improves the visibility of the cervix and makes it easier to grab it with forceps;
-the use of forceps blocks the cervix and possibly straighten the angle of the uterus;
-use a hysterometer, with perfectly visible centimetre graduation, possibly conical;
-during the insertion carefully follow the procedure required for the type of IUC used.

3.3. What is the best time for the placement of intrauterine systems?

IUC systems can be placed after excluding pregnancy[37].

The placement procedure should be performed within 7 days from the first day of the menstrual cycle to ensure greater contraceptive effectiveness.

IUC systems can also be placed immediately after a miscarriage or voluntary termination of pregnancy[37].

3.4. Is the placement of intrauterine systems recommended for nulliparous women?

IUC systems can be used by and are recommended for nulliparous women of all ages[67].

IUC systems are well tolerated by most nulliparous women, although pain during the procedure is more frequent.

The availability of small IUC systems, such as 13.5 mg LNG-IUS, facilitates insertion in nulliparous women[68].

Comments

According to a retrospective study, the rates of insertions of 52 mg LNG-IUS judged as "simple" by the operator were similar for nulliparous women (80.8%) and women who have given birth (82.2%), while dilation of the cervical canal was required mainly for nulliparous women (7.7% nulliparous women vs. 3.1% multiparous women[69]). Similarly, a US study which involved 1,177 adolescents aged between 13 and 24 years showed that for 1,132 of them the IUD or 52 mg LNG-IUS system was placed on the first attempt with a success rate of 95.8% for nulliparous women (665 out of 694) and 96.7% for women who had already given birth (467 out of 493). Only in 1.8% of cases auxiliary measures were required (the help of another colleague in 5 cases, ultrasound in 10 cases, mechanical dilation in 10 cases, use of misoprostol in 8 cases, paracervical block in 8 cases). The success rate for young women (169 women aged 13 to 17 years) was 95.5%, while for older women (963 women aged 18 to 24 years) it was 96.3%. The only significant differences between the 2 groups were parity and the length of the uterine cavity[70].

In the phase III trial[71] of 13.5 mg LNG and another LNG system not yet on the market, but of the same size, 39.2% of 2,884 women were nulliparous (had never given birth) and 12.4% of them had undergone a Caesarean section: the insertion success rates and pain experienced was essentially similar for the two groups.

There is no evidence that nulliparous women can benefit from premedication with misoprostol: two randomized controlled trials found an increase in adverse effects without a reduction in pain and difficulty when inserting the system in nulliparous women treated with such premedication[72]. In particular, when treating nulliparous women, the physician must be prepared to administer

a local anesthetic if the woman is experiencing moderate or severe pain or if dilation of the cervix is required[73].

3.5. How to manage the system insertion after childbirth? What is the best time for the placement of the intrauterine system?

According to WHO guidelines, IUC systems can be placed 4-6 weeks after giving birth[48].

IUS can be inserted from the 6th week after delivery and, in any case, after the involution of the uterus is complete, according to the summary of product characteristics (SPC).

According to WHO guidelines, if a woman is breastfeeding, progestogen-only contraceptives can be used safely[48]: progestogen-only birth control methods, indeed, do not seem to affect the quantity or quality of breast milk.

In case of puerperal infections, the use of IUC systems is not recommended[74].

3.6. Is post-partum insertion more difficult for women who have undergone a Caesarean section?

A Caesarean section is not a contraindication to the insertion of IUC systems, even though the procedure can be more difficult due to the presence of an isthmocele[75].

3.7. Is the presence of an isthmocele a contraindication to the insertion of intrauterine systems?

For patients who undergone a Caesarean section, who may suffer from cesarean-induced isthmocele, a proper clinical evaluation will allow the physician to place the IUC system.

The presence of an isthmocele is not a contraindication to the insertion of IUC systems, but it is a condition that must be recognized by the gynaecologist, who will have to carefully follow the insertion procedure (examination, forceps, detorsion of the uterus, hysterometry) to ensure that the device is correctly positioned and avoid complications, such as perforation.

In case of difficult insertion, hysteroscopy will allow you, during the same session, to assess the presence of the isthmocele and place the device properly.

Comments

Uterine isthmocele represents a possible consequence of one or more cesarean deliveries. This is due to the presence of a diverticulum on the anterior wall of the uterine isthmus or of the cervical canal at the site of a previous cesarean delivery scar. It may cause pathological changes which have an impact on the reproductive system and clinical symptoms such as abnormal post-menstrual uterine bleeding, heavy menstrual bleeding and suprapubic pain, but also peritonitis and secondary infertility. Uterine isthmocele can be diagnosed with transvaginal ultrasound or diagnostic hysteroscopy, but in most cases the symptoms reported by the patient are enough to diagnose this condition. Cesarean-induced Isthmocele is reported for 40-70% of patients undergoing such surgery but is symptomatic in only 10% of cases[76].

3.8. What is the procedure to follow in case of insertion after voluntary termination of pregnancy?

When women, who must undergo voluntary termination of pregnancy, are admitted to the hospital, they should also be informed of the possibility to use a reliable contraception method (including IUC systems) immediately after surgery.

IUC systems should be placed immediately after suction aspiration.

After medical abortion, IUC systems can be placed when the gynaecologist is absolutely sure that the woman is no longer pregnant.

A check after the next menstrual cycle should be recommended, as well as protected intercourse until a check is performed, due to the increased risk of expulsion during the days immediately following voluntary termination of pregnancy.

IUS are better for teenagers and nulliparous women: in fact, its use seems to be associated with a reduced risk of PID compared to IUDs[77].

3.9. Is the hysterometer required for all procedures?

The hysterometer can be used to assess patency, direction and length of the cervical canal and the uterine cavity. This will help you to properly place the IUC system.

Comments

A historical study performed by Hasson[78] showed how there were 11 different combinations of cervical length and endometrial cavity length in 55 women with a total hysterometry of 7 cm.

3.10. Is ultrasound required before the insertion procedure?

A pelvic examination to assess the position, the size and morphology of the uterus and hysterometry is always required before any insertion procedure.

An ultrasound evaluation is not required prior

to the insertion of IUC systems since, in most cases, this procedure does not provide additional information compared to a pelvic examination and hysterometry[79].

However, if available, ultrasound can help if bimanual examination is difficult, as in the cases of obesity or major uterine fibromatosis[73].

An ultrasound evaluation before the insertion procedure may also be useful in case of abnormal uterine bleeding to exclude the presence of uterine intracavitary pathologies.

3.11. Should the cervix always be grasped?

Grasping the front lip of the cervix prior to the insertion of an IUC system helps you to secure the uterus and to straighten it, thus facilitating the insertion.

If the uterus is retroverted, the posterior lip of the cervix should be grasped.

3.12. Should I disinfect or cleanse the cervix?

Before placing IUC systems, the cervix should be cleansed to remove mucus, blood or vaginal secretions, to better see the cervical canal.

3.13. Follow up: when should I schedule the first examination? Should I use ultrasound?

It is recommended to schedule the first follow-up examination 4-6 weeks after insertion to check the strings and verify the correct position of the IUC. If possible, an ultrasound should be performed.

3.14. What should I do in case of cervical stenosis?

The use of a hysterometer, after grasping and straighten the uterus, may help you to detect the presence of stenosis and to solve the problem.

After positioning the speculum and cleansing the area, you may also use some small tools such as Bengolea forceps, Hegar dilators, micro Klemmer forceps and so on, so as to dilate the external uterine orifice with minimum discomfort for your patient.

However, we must always consider that most of these conditions occur due to retroflexed or severely anteverted uterus; proper clinical and anatomical assessment of the bowel position, therefore, is one of the most important moments to avoid assessment errors.

If the outcome of the procedure is not as expected and cervical stenosis persists, it is recommended to use other diagnostic tools such as ultrasound and/or outpatient diagnostic hysteroscopy.

Moreover, the box containing the IUC should be opened only after assessing the cervical canal and verifying its accessibility.

Comments

Cervical stenosis affects 3-8% of women. Stenosis may be affect one or more sections of the cervical canal as a result of endocervical inflammation. It is usually caused by a trauma of the endocervical mucosa resulting in fibrotic reactions with stenosis and subsequent alterations. The procedures that may cause this situation include iatrogenic injuries, such as traumatic outcome of curettage, endocervical polypectomy, Hegar dilatation, endocervical biopsies, assisted conception treatments. Cervical stenosis may also be caused by acquired diseases such as compression by a uterine myoma. Cervical stenosis is undoubtedly one of the most difficult moments of intrauterine manoeuvers. It can be both acquired and congenital. The presence of fibrous and inelastic tissue requires mechanical expansion, to be performed according to guidelines[80].

3.15. Is the use of medications for cervical preparation or post-insertion painkillers required?

There is no evidence suggesting the effectiveness of medications for cervical preparation[81].

After the procedure, women can use the same painkillers that are usually used for menstrual pain (e.g.: NSAIDs, paracetamol).

3.16. Vasovagal crisis: is it common? What are the consequences? How can I treat or prevent it? How to handle it?

Vasovagal crises can be associated with the most common gynecological procedures (such as pelvic examination, pap test, trans-vaginal ultrasound etc.), and it is difficult to predict them[73], this is why you are supposed to know how to handle it.

Cervical stimulation during insertion of an IUC system can cause a vasovagal reaction with more or less serious cardiovascular events. In healthy women vasovagal reactions are usually handled with simple stimulation maneuvers; rarely bradycardia persists or requires treatment with intramuscular or intravenous atropine[42].

A preparation of 0.5 mg sublingual atropine can also be used.

The mechanical stimulation of the upper lip sulcus (Chinese medicine) may help you prevent and treat a vagal episode.

3.17. Is IUC placement supposed to be perfect?

IUC systems should be placed lower down in the uterine cavity.

If the ultrasound reveals that the IUC is dislocated, you need to investigate any related symptoms as pain, intermenstrual spotting or metrorrhagia[82].

If the patient has symptoms, the IUC should be removed and a new IUC can be placed on the same occasion.

There are limited data suggesting how to behave in case of malpositioning of an IUC device in asymptomatic women. The FSRH working group, which drafted the guidelines on intrauterine contraception, suggests to emphasize that the contraceptive efficacy of an IUC not placed on the fundus cannot be guaranteed. Furthermore the decision to remove and then replace the device should be discussed with the woman, also considering the age of the patient, prior expulsions and the type of IUC placed[42].

Replacing a poorly placed IUC device is always recommended.

Comments

There is little evidence on the management of IUC which have not been perfectly placed. Usually the position of the device on the fundus of the uterus is associated with maximum effectiveness, while if the device is not placed on the fundus this may increase the risk of expulsion. Data from a large study showed no difference in pregnancy rates between women with 20 micrograms/24h LNG-IUC placed in the endocervix and women with 20 micrograms/24h LNG-IUC properly placed[84]. As a general rule, if the IUC is in the lower uterine segment or near the fundus, it is recommended to leave it in place as it will not be expelled[85]. If, on the other hand, the device is located in the cervix, it should be removed, since the risk of expulsion is high. In general, contraceptive efficacy cannot be guaranteed, if the IUC is located at a distance from the fundus of the uterus of more than 2 cm, as measured by ultrasound[11].

3.18. What should I do if strings are not detected?

In 5-15% of women with an IUC device strings are not visible.

If speculum examination does not show IUC strings, there can be several explanations[86,87]:

-the IUC is in place, but the strings are located in the cervical canal or in the uterine cavity (98% of cases). An enlargement of the uterine cavity due to growing fibroids or the rotation of the spiral may cause the retraction of the strings;

-the IUC was expelled (about 1% of cases);

-the IUC has perforated the uterus and is located in the myometrium or in the abdomen (<1% of cases).

The first thing to do is ruling out pregnancy.

If the patient is pregnant, an ultrasound is required to assess the position of the IUC and date the pregnancy. How to manage the situation will depend on the position of the IUC, pregnancy date and the desire to continue pregnancy.

If the patient is not pregnant, you can use a cytobrush in the cervical canal to pull out the strings out of the cervical canal; if the strings are finally visible, no further action is required[88]. If, on the other hand, strings are still not detected but the ultrasound shows the correct placement of the IUC device[89], the patient can continue to use the IUC as a contraceptive method[86].

The risk of expulsion for IUC devices is low (about 2%) in women with no visible strings and properly placed IUC. However, the patient must be informed of the typical symptoms associated with the expulsion or incorrect placement of IUC devices, such as changes in bleeding pattern or pain[86].

If the IUC must be removed (to replace it or to stop contraception), outpatient hysteroscopic removal is recommended. You may also try to retrieve the strings with mechanical tools, such as Klemmer forceps or other instruments, however these methods can be painful and cause endocervix and endometrial lesions[37].

If the ultrasound examination does not show the position of the IUC, anteroposterior (AP) and lateral radiographs of the entire abdomen and pelvis may show what is missing. If the IUC position is not detected, an expulsion can be reasonably suspected.

3.19. Can intrauterine systems affect Pap test results?

Some publications dating back to the early 2000s showed that Pap test results for women using intrauterine systems were not affected by the devices compared to women who were not using them[90].

SPECIAL THANKS

Thanks to Fabio Parazzini for the comments to the methodology and to the manuscript.

REFERENCES

1) Buhling KJ, Zite NB, Lotke P, Black K, Group IW. **Worldwide use of intrauterine contraception: a review.** Contraception. 2014;89(3):162-73.

2) **United Nations DoEaSA, Population Division**,. **World Contraceptive Use 2012 (POP/DB/CP/Rev2012)**. (pubblicato 2012; consultato: 31/3/2016). Disponibile all'indirizzo:http://www.un.org/esa/population/publications/WC 2012/MainFrame.html. 2012.

3) Buhling KJ, Hauck B, Dermout S, Ardaens K, Marions L. **Understanding the barriers and myths limiting the use of intrauterine contraception in nulliparous women: results of a survey of European/Canadian healthcare providers.** Eur J Obstet Gynecol Reprod Biol. 2014;183:146-54.

4) Trussell J. **Contraceptive failure in the United States.** Contraception. 2011;83(5):397-404.

5) **American College of Obstetrics and Gynecologist Practice Bulletin.** (pubblicato 2011; consultato: 31/3/2016). Disponibile all'indirizzo: http://www.acog.org/-/media/List-of Titles/PBListOfTitles.pdf. 2011.

6) **Faculty of Family Planning and Reproductive Health Care Clinical Effectiveness Unit. Emergency Contraception**. http://www.fsrh.org.uk/admin/uploads/449_EmergencyContraceptionCEUguidance.pdf [Consultato 31/3/2016]. 2006.

7) Sufrin CB, Postlethwaite D, Armstrong MA, Merchant M, Wendt JM, Steinauer JE. **Neisseria gonorrhea and Chlamydia trachomatis screening at intrauterine device insertion and pelvic inflammatory disease.** Obstet Gynecol. 2012;120(6):1314-21.

8) Steenland MW, Zapata LB, Brahmi D, Marchbanks PA, Curtis KM. **Appropriate follow up to detect potential adverse events after initiation of select contraceptive methods: a systematic review.** Contraception. 2013;87(5):611-24.

9) Grimes DA, Lopez LM, Schulz KF. **Antibiotic prophylaxis for intrauterine contraceptive device insertion.** Cochrane Database Syst Rev 2010;1–16

10) **American College of Obstetrics and Gynecologist Practice Bulletin. Long-acting reversible contraception.** N.121. (pubblicato 2011; consultato: 31/3/2016). Disponibile all'indirizzo: http://www.acog.org/~/media/Practice%20Bulletins/Committee%20on%20Practice%20Bullet ns%20--%20Gynecology/Public/pb121.pdf?dmc=1. 2011.

11) Faculty of Sexual and Reproductive Healthcare Clinical Guidance. **Intrauterine Contraception.** (pubblicato 2007; consultato: 31/3/2016). Disponibile all'indirizzo: http://www.fsrh.org/pages/clinical_guidance_Archive.asp 2007.

12) Mansour D, Gemzell-Danielsson K, Inki P, Jensen JT. **Fertility after discontinuation of contraception: a comprehensive review of the literature.** Contraception. 2011;84(5):465-77.

13) Foster DG, Rostovtseva DP, Brindis CD, Biggs MA, Hulett D, Darney PD. **Cost savings from the provision of specific methods of contraception in a publicly funded program.** Am J Public Health. 2009;99(3):446-51.

14) **Ten Pregnancy Strategy** https://www.gov.uk/government/publications/teenage pregnancy-past-successes-future-challenges

15) Backman T, Huhtala S, Blom T et al. **Length of use and symptoms associated with premature removal of the levonorgestrel intrauterine system: a nation-wide study of 17,360 users.** BJOG 2000; 107: 335-9

16) Godfrey EM, Folger SG, Jeng G, Jamieson DJ, Curtis KM. **Treatment of bleeding irregularities in women with copper-containing IUDs: a systematic review.** Contraception. 2013;87(5):549 66.

17) Ronnerdag M, Odlind V. **Health effects of long-term use of the intrauterine levonorgestrel releasing system. A follow-up study over 12 years of continuous use.** Acta Obstet Gynecol Scand. 1999;78(8):716-21.

18) Gemzell-Danielsson K, Schellschmidt I, Apter D. **A randomized, phase II study describing the efficacy, bleeding profile, and safety of two low-dose levonorgestrel-releasing intrauterine contraceptive systems and Mirena.** Fertil Steril. 2012;97(3):616-22 e1-3.

19) Arisi E. **Flussi mestruali abbondanti: le raccomandazioni della SIGO.** Gyneco AOGOI 2007;1:18.

20) Rosenberg MJ, Waugh MS. **Oral contraceptive discontinuation: a prospective evaluation of frequency and reasons.** Am J Obstet Gynecol. 1998;179(3 Pt 1):577-82.

21) Moos MK, Bartholomew NE, Lohr KN. **Counseling in the clinical setting to prevent unintended pregnancy: an evidence-based research agenda.** Contraception. 2003;67(2):115 32.

22) Madden T, Mullersman JL, Omvig KJ, Secura GM, Peipert JF. **Structured contraceptive counseling provided by the Contraceptive CHOICE Project.** Contraception. 2013;88(2):243-9.

23) Winner B, Peipert JF, Zhao Q, Buckel C, Madden T, Allsworth JE, et al. **Effectiveness of long acting reversible contraception.** N Engl J Med. 2012;366(21):1998-2007.

24) Blumenthal PD, Voedisch A, Gemzell-Danielsson K. **Strategies to prevent unintended pregnancy: increasing use of long-acting reversible contraception.** Hum Reprod Update. 2011;17(1):121-37.

25) Parazzini F, Ricci E, Cipriani S, Motta T, Chiaffarino F, Malvezzi M, et al. **Temporal trends in adolescent pregnancies in Lombardy, Italy: 1996-2010.** Eur J Contracept Reprod Health Care. 2013;18(2):88-94.

26) Stoddard A, McNicholas C, Peipert JF. **Efficacy and safety of long-acting reversible contraception.** Drugs. 2011;71(8):969-80.

27) American College of O, Gynecologists. ACOG Committee Opinion No. 392, December 2007. **Intrauterine device and adolescents.** Obstet Gynecol. 2007;110(6):1493-5.

28) Larsson B, Ljung B, Hamberger L .**The influence of copper on the in vitro motility of the human Falloppian tube.** Am J Obstet Gynecol 1976; 125(5): 682-690

29) Ortiz MA, Croxatto HB. **Copper-T intrauterine device and levonorgestrel intrauterine system: biological bases of their mechanism of action.** Contraception 2007; 75: S16 S30

30) Lewis RA, Taylor DS, Natavio MF et al. **Effects of the levonorgestrel-releasing intrauterine system on cervical mucus quality and sperm penetrability.** Contraception 2010; 82 : 491–496;

31) Natavio MF, Taylor DS, Lewis RA et al. **Temporal**

changes in cervical mucus after insertion of the levonorgestrel-releasing intrauterine system. Contraception 2013; 87: 426–431
32) Gomes MKO, Rosa-e-Silva JC, Garcia SB et al. **Effects of the levonorgestrel-releasing intrauterine system on cell proliferation, Fas expression and steroid receptors in endometriosis lesions and normal endometrium.** Hum Reprod 2009; 24 (11): 2736 2745
33) Munuce MJ, Nascimento JAA, Rosano G et al. **Doses of levonorgestrel comparable to that delivered by the levonorgestrel-releasing intrauterine system can modify the in vitro expression of zona binding sites of human spermatozoa.** Contraception 2006;73:97–101
34) Mandelin E, Koistinen H, Koistinen R et al. **Levonorgestrel-releasing intrauterine device-wearing women express contraceptive glycodelin A in endometrium during midcycle: another contraceptive mechanism?** Hum Reprod 1997;12: 2671– 5)
35) Labied S, Galant C, Nisolle M et al. **Differential elevation of matrix metalloproteinase expression in women exposed to levonorgestrel releasing intrauterine system for a short or prolonged period of time.** Hum Reprod 2009; 24 (1): 113–121
36) Apter D, Gemzell-Danielsson K, Hauck B et al. **Pharmacokinetics of two low-dose levonorgestrel-releasing intrauterine systems and effects on ovulation rate and cervical function: pooled analyses of phase II and III studies.** Fertility and Sterility 2014; 101(6): 1658-82
37) Arisi E., Bruni V, Di Spiezio A, Dubini V, Gubbini G, Parazzini F **Linee Guida Italiane sull'utilizzo efficace ed appropriato della contraccezione intrauterina.** Gynecol & Obstet , Vol 26 N° 4. 2014.
38) Bayer HealthCare Pharmaceuticals Inc. Jaydess **Summary of Product Characteristics** (pubblicato 2012; consultato: 4/4/2016). Disponibile all'indirizzo: (http://www.jaydess.com/faq-bleeding-profile#) 2012.
39) Trabert B, Holt VL, Yu O, Van Den Eeden SK, Scholes D. **Population-based ectopic pregnancy trends, 1993-2007.** Am J Prev Med. 2011;40(5):556-60.
40) Van Den Eeden SK, Shan J, Bruce C, Glasser M. **Ectopic pregnancy rate and treatment utilization in a large managed care organization.** Obstet Gynecol. 2005;105(5 Pt 1):1052-7.
41) Kelekci S, Kelekci KH, Yilmaz B. **Effects of levonorgestrel-releasing intrauterine system and T380A intrauterine copper device on dysmenorrhea and days of bleeding in women with and without adenomyosis.** Contraception. 2012;86(5):458-63.
42) Faculty of Sexual & Reproductive Healthcare **Clinical Guidance Intrauterine Contraception Clinical Effectiveness Unit April 2015** (Updated October 2015) disponibile all'indirizzo: http://www.fsrh.org/pages/Clinical_Guidance_2.asp
43) Nelson A, Apter D, Hauck B, Schmelter T, Rybowski S, Rosen K, et al. **Two low-dose levonorgestrel intrauterine contraceptive systems: a randomized controlled trial.** Obstet Gynecol. 2013;122(6):1205-13.
44) Shapiro S, Rosenberg L, Hoffman M, Truter H, Cooper D, Rao S, et al. **Risk of breast cancer in relation to the use of injectable progestogen contraceptives and combined estrogen/progestogen contraceptives.** Am J Epidemiol. 2000;151(4):396-403.
45) Wiebe ER, Trouton KJ. **Does using tampons or menstrual cups increase early IUD expulsion rates?** Contraception. 2012;86(2):119-21.
46) **World Health Organization Safe abortion: technical and policy guidance for health systems.** World Health Organization, Department of Reproductive Health and Research. 2101 2011
47) **NICE Clinical Guideline. Postnatal care: Routine postnatal care of women and their babies** (pubblicato 2006; consultato: 5/4/2016). Disponibile all'indirizzo: https://www.nice.org.uk/guidance/cg37). 2006.
48) WHO. **Medical Eligibility Criteria for Contraceptive Use. 4th Edition.** WHO Library Cataloguing-in- Publication Data. (pubblicato 2009; consultato: 5/4/2016). Disponibile all'indirizzo: (http://www.spdc.pt/files/publicacoes/5_11292_2.pdf). 2009.
49) Trussell J. Contraceptive efficacy. In: (Hatcher RA, Trussell J, Nelson AL, Cates W, Stewart FH, Kowal D. eds). **Contraceptive technology: nineteenth revised edition.** New York NY: Ardent Media. 2007.
50) Diedrich JT, Zhao Q, Madden T, Secura GM, Peipert JF. **Three-year continuation of reversible contraception.** Am J Obstet Gynecol. 2015;213(5):662 e1-8.
51) Secura GM, Allsworth JE, Madden T, Mullersman JL, Peipert JF. **The Contraceptive CHOICE Project: reducing barriers to long-acting reversible contraception.** Am J Obstet Gynecol. 2010;203(2):115 e1-7.
52) McNicholas C, Madden T, Secura G, Peipert JF. **The contraceptive CHOICE project round up: what we did and what we learned.** Clin Obstet Gynecol. 2014;57(4):635-43.
53) Rose SB, Lawton BA. **Impact of long-acting reversible contraception on return for repeat abortion.** Am J Obstet Gynecol. 2012;206(1):37 e1-6.
54) Madden T, Secura GM, Allsworth JE, Peipert JF. **Comparison of contraceptive method chosen by women with and without a recent history of induced abortion.** Contraception. 2011;84(6):571-7.
55) Andersson K, Odlind V, Rybo G. **Levonorgestrel-releasing and copper-releasing (Nova T) IUDs during five years of use: a randomized comparative trial.** Contraception. 1994;49(1):56 72.
56) Okusanya BO, Oduwole O, Effa EE. **Immediate postabortal insertion of intrauterine devices.** Cochrane Database Syst Rev. 2014;7:CD001777.
57) Shimoni N, Davis A, Ramos ME, Rosario L, Westhoff C. **Timing of copper intrauterine device insertion after medical abortion: a randomized controlled trial.** Obstet Gynecol. 2011;118(3):623-8.
58) Lopez LM, Bernholc A, Hubacher D, Stuart G, Van Vliet HA. **Immediate postpartum insertion of intrauterine device for contraception.** Cochrane Database Syst Rev. 2015;6:CD003036.
59) Sonalkar S, Kapp N. **Intrauterine device insertion in the postpartum period: a systematic review.** Eur J Contracept Reprod Health Care. 2015;20(1):4-18.
60) Levi EE, Stuart GS, Zerden ML, Garrett JM, Bryant AG. **Intrauterine Device Placement During Cesarean Delivery and Continued Use 6 Months Postpartum: A Randomized Controlled Trial.** Obstet Gynecol. 2015;126(1):5-11.

61) Lopez LM, Grey TW, Stuebe AM, Chen M, Truitt ST, Gallo MF. **Combined hormonal versus nonhormonal versus progestin-only contraception in lactation.** Cochrane Database Syst Rev. 2015;3:CD003988.
62) Heikkila M, Luukkainen T. **Duration of breast-feeding and development of children after insertion of a levonorgestrel-releasing intrauterine contraceptive device.** Contraception. 1982;25(3):279-92.
63) Shaamash AH, Sayed GH, Hussien MM, Shaaban MM. **A comparative study of the levonorgestrel-releasing intrauterine system Mirena versus the Copper T380A intrauterine device during lactation: breast-feeding performance, infant growth and infant development.**
64) Stuart GS, Lesko C, Stuebe A, Bryant A. **Breastfeeding and postpartum insertion of the levonorgestrel intrauterine system: a randomized trial.** Obstetrics and Gynecology 2014;123 (Suppl 1):15s.
65) National Institute for Health and Care Excellence (NICE). **Long acting reversible contraception (update), issued September 2014.** NICE Clinical Guideline 30, guidance.nice.org.uk/cg30; http://www.nice.org.uk/guidance/cg30
66) Millar S, Cameron S. **Intrauterine Contraceptives.** Glob. libr. women's med., (ISSN: 1756 2228) DOI 10.3843/GLOWM.10394. 2015.
67) **Committee on Adolescent Health Care Long-Acting Reversible Contraception Working Group**, The American College of Obstetricians and Gynecologists, 2012; Committee on Adolescence, 2014)
68) Gemzell-Danielsson K, Buhling KJ, Dermout SM, Lukkari-Lax E, Montegriffo E, Apter D. **A Phase III, single-arm study of LNG-IUS 8, a low-dose levonorgestrel intrauterine contraceptive system (total content 13.5mg) in postmenarcheal adolescents.** Contraception. 2016.
69) Bahamondes MV, Hidalgo MM, Bahamondes L, Monteiro I. **Ease of insertion and clinical performance of the levonorgestrel-releasing intrauterine system in nulligravidas.** Contraception. 2011;84(5):e11-6.
70) Teal SB, Romer SE, Goldthwaite LM, Peters MG, Kaplan DW, Sheeder J. **Insertion characteristics of intrauterine devices in adolescents and young women: success, ancillary measures, and complications.** Am J Obstet Gynecol. 2015;213(4):515 e1-5.
71) Gemzell-Danielsson K, Apter D, Hauck B, Schmelter T, Rybowski S, Rosen K, et al. **The Effect of Age, Parity and Body Mass Index on the Efficacy, Safety, Placement and User Satisfaction Associated With Two Low-Dose Levonorgestrel Intrauterine Contraceptive Systems: Subgroup Analyses of Data From a Phase III Trial.** PLoS One. 2015;10(9):e0135309.
72) Ward K, Jacobson JC, Turok DK, Murphy PA. **A survey of provider experience with misoprostol to facilitate intrauterine device insertion in nulliparous women.** Contraception. 2011;84(6):594-9.
73) Bahamondes L, Mansour D, Fiala C, Kaunitz AM, Gemzell-Danielsson K. **Practical advice for avoidance of pain associated with insertion of intrauterine contraceptives.** J Fam Plann Reprod Health Care. 2014;40(1):54-60.
74) Kapp N, Curtis KM. **Intrauterine device insertion during the postpartum period: a systematic review.** Contraception. 2009;80(4):327-36.
75) Tower AM, Frishman GN. **Cesarean scar defects: an underrecognized cause of abnormal uterine bleeding and other gynecologic complications.** J Minim Invasive Gynecol. 2013;20(5):562-72.
76) Bij de Vaate AJ, van der Voet LF, Naji O, Witmer M, Veersema S, Brolmann HA, et al. **Prevalence, potential risk factors for development and symptoms related to the presence of uterine niches following Cesarean section: systematic review.** Ultrasound Obstet Gynecol. 2014;43(4):372-82.
77) Grimes DA, Lopez LM, Schulz KF, Stanwood NL. **Immediate postabortal insertion of intrauterine devices.** Cochrane Database Syst Rev. 2010(6):CD001777.
78) Hasson HM. **Uterine geometry and IUCD design.** Br J Obstet Gynaecol. 1982;89(Suppl 4):1 10.
79) Kaislasuo J, Heikinheimo O, Lahteenmaki P, Suhonen S. **Predicting painful or difficult intrauterine device insertion in nulligravid women.** Obstet Gynecol. 2014;124(2 Pt 1):345-53.
80) Christianson MS, Barker MA, Lindheim SR. **Overcoming the challenging cervix: techniques to access the uterine cavity.** J Low Genit Tract Dis. 2008;12(1):24-31.
81) Lopez LM, Bernholc A, Zeng Y, Allen RH, Bartz D, O'Brien PA, et al. **Interventions for pain with intrauterine device insertion.** Cochrane Database Syst Rev. 2015;7:CD007373.
82) Braaten KP, Benson CB, Maurer R, Goldberg AB. **Malpositioned intrauterine contraceptive devices: risk factors, outcomes, and future pregnancies.** Obstet Gynecol. 2011;118(5):1014-20.
83) Benacerraf BR, Shipp TD, Bromley B. **Three-dimensional ultrasound detection of abnormally located intrauterine contraceptive devices which are a source of pelvic pain and abnormal bleeding.** Ultrasound Obstet Gynecol. 2009;34(1):110-5.
84) Pakarinen P, Luukkainen T. **Five years' experience with a small intracervical/intrauterine levonorgestrel-releasing device.** Contraception. 2005;72(5):342-5.
85) Morales-Rosello J. **Spontaneous upward movement of lowly placed T-shaped IUDs.** Contraception. 2005;72(6):430-1.
86) Marchi NM, Castro S, Hidalgo MM, Hidalgo C, Monteiro-Dantas C, Villarroeal M, et al. **Management of missing strings in users of intrauterine contraceptives.** Contraception. 2012;86(4):354-8.
87) Tugrul S, Yavuzer B, Yildirim G, Kayahan A. **The duration of use, causes of discontinuation, and problems during removal in women admitted for removal of IUD.** Contraception. 2005;71(2):149-52.
88) Ben-Rafael Z, Bider D. **A new procedure for removal of a "lost" intrauterine device.** Obstet Gynecol. 1996;87(5 Pt 1):785-6.
89) Peri N, Graham D, Levine D. **Imaging of intrauterine contraceptive devices.** J Ultrasound Med. 2007;26(10):1389-401.
90) Kazerooni T, Mosalaee A. **Does contraceptive method change the Pap smear finding?** Contraception. 2002;66(4):243-6.


SOCIETÀ ITALIANA DI OSTETRICIA E GINECOLOGIA
IVNONI LVCINAE
MDCCCXCII