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The future of intrauterine contraception

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Abstract

In this review paper some guidelines for IUD use are presented that if followed should reduce the incidence of IUD-related complications. Recent IUD developments are discussed including the levonorgestrel-releasing T, a new variation of the Multiload, and IUDs designed for postpartum insertion. Since significant improvements in IUD safety will most likely result from a better understanding of IUD-related side-effects and adverse reactions, the paper includes recommendations for future IUD research that could enhance the safety, effectiveness and acceptability of available IUDs.

Over the past two and a half decades a considerable amount of research has been conducted to improve the effectiveness and safety of all contraceptive methods. Nevertheless, all methods of contraception, including intrauterine devices, are associated with side effects, complications and the failure to prevent pregnancy. In some countries, IUDs are not widely used (e.g. the United States), but in other countries they are in widespread use (e.g. Finland, Sweden) and in others (e.g. China, Indonesia) they are one of the mainstays of the national family planning programs. The variable worldwide pattern of IUD usage should not be taken as a reflection of the safety of IUDs relative to that of other methods of contraception. In fact, measured in terms of associated mortality, IUDs represent one of the safest forms of contraception.

Tietze [1] in 1978 suggested that death is the only common denominator that can be used for the comparative evaluation of the health risks associated with the use of different contraceptive methods. Table 1 gives age-specific death rates from causes due to the use of different contraceptive methods. These rates include deaths resulting from pregnancies

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due to contraceptive failures. The table shows that the risk of death at all ages is lower for IUD users than users of all other contraceptive methods. When evaluating the risks given in Table 1 for oral contraceptive users, it should be remembered that these risks are for women using "high" dose orals (greater than 50 μg of estrogen per tablet). Similar data on the risks for users of "low" dose orals have not been published. For the comparative evaluation of the safety of contraceptive methods, analyses based on the risk of death are inadequate since contraceptive-related deaths are exceedingly rare, as indicated by the rates in Table 1, for all methods of contraception.

Table 1 Death rates per 100 000 women attributable to the use of various contraceptive methods

Contraceptive method	Age (years)					
	15-19	20-24	25-29	30-34	35-39	40-44
None	5.6	6.1	7.4	13.9	20.8	22.6
Orals						
Non-smokers	1.3	1.4	1.4	2.2	4.5	7.1
Smokers	1.5	1.6	1.6	10.6	13.4	58.9
IUDs	0.9	1.0	1.2	1.4	2.0	1.9
Barrier methods	1.1	1.6	2.0	3.6	5.0	4.2

Source: Tietze [1]

Improving the safety of intrauterine contraception

Intrauterine devices (IUDs) provide a safe method of contraception. The primary medical reasons for IUD discontinuation are side effects such as bleeding and pain that resolve as soon as the IUD is removed, and are not associated with any long-term adverse health effects. IUD use has not been associated with any increased risk of cervical or uterine malignancy [2], toxic shock syndrome [3], or congenital malformations among the offspring of women who became pregnant with their IUDs in situ [4].

Current knowledge clearly indicates that the use of IUDs may be made even safer by adherence to the following:

(1) Screen women carefully for contraindications to IUD use.
(2) Adhere to the correct insertion technique.
(3) Inform women of the signs and symptoms of adverse effects associated with IUD use so that they may obtain prompt medical care.
(4) Advise women to report to their health care providers all adverse effects so that their IUDs can be removed and treatment initiated.

(5) Question the women about their method of contraception any time they are seen in an emergency room, clinic or physician's office. Too frequently the diagnosis of a contraceptive-related complication is missed simply because the health care provider was unaware of the woman's method of contraception.

Other strategies for reducing IUD-related complications and event rates include the fitting of IUDs. Preliminary data have indicated that IUD performance may be improved by using IUDs that are neither too large nor too small in relation to the size of the endometrial cavity. Hasson [5] reported that IUD event rates (pregnancy, expulsion, displacement, and removal for bleeding and/or pain) varied with the length of the endometrial cavity as measured by the Wing Sound [6] device. Higher event rates were experienced by women whose IUDs were either too small or too large in relation to the lengths of their endometrial cavities. Improved results with IUDs also have been obtained by others who have selectively fitted IUDs based on the size of the endometrial cavity [7].

Of the IUDs currently available, the Multiload is the only one that is available in multiple sizes. Favorable results have been obtained with the standard size devices (MLCu250, MLCu375), and the shorter (28 mm vs 36 mm) versions (MLCu250(s), MLCu375SL) of these devices [8]. The narrower version of the standard Multiload, the MLCu250(m), did not perform as well as the other Multiloads. This IUD was the same length as the standard size devices. Improved results with the MLCu250(m) for use by women with small uteri, may be obtained by reducing the length of the IUD. This approach was taken in the development of a small version of the Cu-7, in which both the length and width of the standard size Cu-7 were reduced. The results of a multiclinical trial of the small Cu-7 showed that the performance of this device was improved over that of the standard Cu-7 [9].

One safety concern related to all copper-releasing IUDs that contain filamentous copper is that there might be an increased likelihood of breakage of the copper wire the longer the IUDs remain in utero. In theory, this would lead to a reduction of the IUD's copper surface area and a reduction in its ability to prevent pregnancy. However, this has not been observed in clinical studies. One study [10] showed that intrauterine pregnancy rates for the MLCu250 did not increase more rapidly with increasing duration of use (up to 8 years). A study of the MLCu375 in which women were followed up for up to five years gave similar results [11]. The intrauterine life of either the MLCu375 or MLCu375SL is estimated to be at least five years. IUDs that have copper sleeves have an intrauterine life far in excess of five years.

Fragmentation of the copper wire does not pose any health risks to the IUD user. There are no known reports in the medical literature that have documented any adverse health effects resulting from the in utero fragmentation of the copper wire of an IUD.

Future IUD development

Some of the issues related to IUD use, such as the risk of infertility following IUD use and the risks of pelvic inflammatory disease, first should be resolved before serious efforts are made to develop new and improved IUDs. Solution of these issues might determine the future direction of IUD research and development. Future IUD development is likely to be conducted on a hit-or-miss basis unless answers to some of the basic questions regarding IUD use first can be answered. For example, to develop an IUD that reduces the incidence of menstrual bleeding and spotting requires some information of the mechanisms through which IUDs affect the hemostatic system.

Aside from the introduction in recent years of new copper-releasing IUDs, such as the Fincoid and Ombrelle, which only differ from other available IUDs in terms of the shape and dimensions of their plastic frames, there have been no significant developments in intrauterine contraception that have become available to consumers. During the past decade the use of nonmedicated IUDs has been replaced by the use of copper-releasing IUDs.

The most recent IUD development that is approaching various stages of regulatory approval in some countries is the levonorgestrel-releasing T. This IUD consists of a Nova-T device with the copper replaced by a Silastic rod impregnated with 50% levonorgestrel, and covered by Silastic tubing that releases an average of 20 μg levonorgestrel per day. Whether this device affords the user any significant advantages over copper-releasing IUDs such as the TCu380 and MLCu375 remains to be determined from the results of large clinical trials.

In one small randomized comparative trial of the levonorgestrel-releasing T and Nova-T, the performance of the Nova-T appeared to be slightly better in terms of IUD discontinuation rates [12,13]. After two years of observation the discontinuation rate for amenorrhea among the levonorgestrel-releasing T users was about 11.00 per 100 women. The corresponding rate for women using the Nova-T was 0.0. One advantage of the levonorgestrel-releasing T was that after about three months of use women reported fewer days of spotting/bleeding compared to women who used the Nova-T. Another approach to the slow release of steroids from an IUD is to wrap the vertical stem of a copper-releasing IUD with fibers that slowly release microgram amounts of the steroid. These IUDs were designed to reduce the incidence of IUD-related bleeding problems. One issue that remains to be clarified is the risk of ectopic pregnancy associated with the use of any progestin-releasing IUD, and in particular the levonorgestrel-releasing IUD.

Currently under development is the Multiload Mark II that was designed to optimize the insertion technique and to eliminate problems related to breakage of the arms during difficult removals. The Mark II device (Figure 1) has a copper surface area of 375 mm^2, and differs from the other Multiloads in the construction of the arms and lateral projections. Unlike insertion of the Multiload, the Mark II device is inserted with its arms contained within the inserter tube (Figure 2). The Mark II device is placed in the uterus by inserting the inserter tube to the uterine fundus and then extruding the IUD from the inserter tube. The

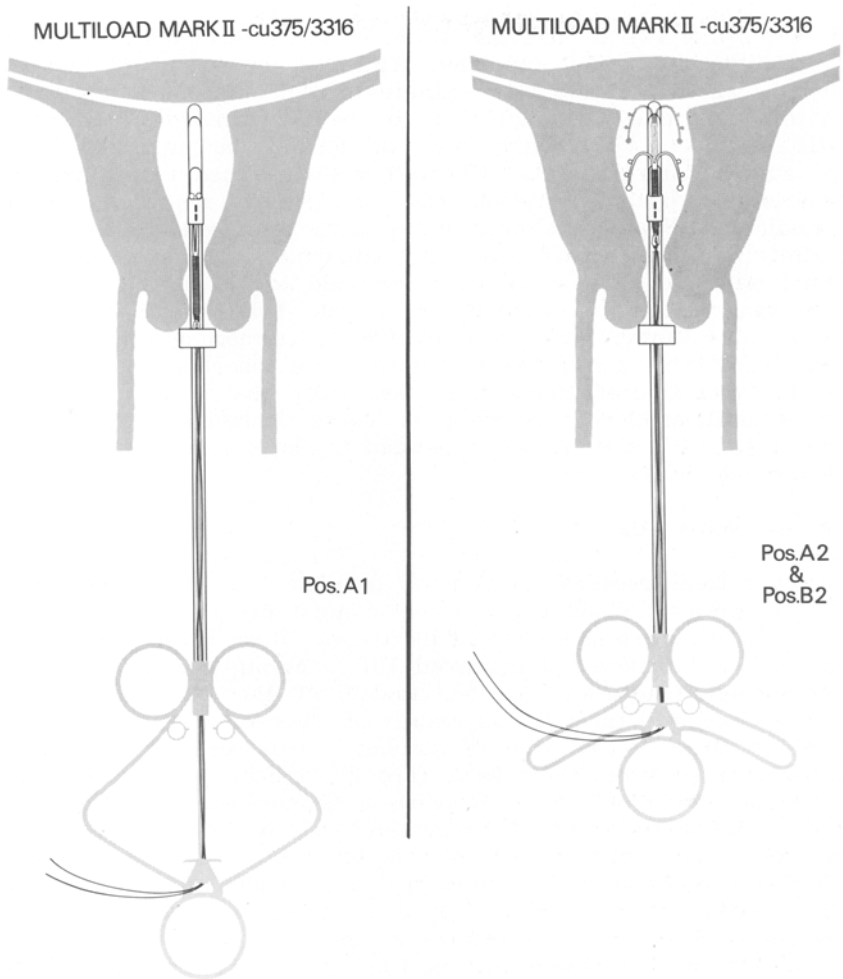

Figure 1 (left) The Multiload Mark II during insertion with its lateral arms contained within the inserter tube
Figure 2 (right) The Multiload Mark II after extrusion from the inserter

upper 3.5 cm of the inserter tube is half open and acts as a rail along which the IUD is pushed. The insertion mechanism is such that the Mark II cannot be pushed beyond the end of the inserter tube, thus limiting the risk of uterine perforation. The insertion technique insures that the IUD is correctly positioned. Clinical trials of the Multiload Mark II are in progress.

In many countries, especially in the developing world, the puerperium is the most convenient time for the initiation of contraception. Numerous studies have evaluated the postpartum insertion of IUDs [14], and have

found that if the IUD is inserted within seven days of delivery there is a relatively high risk of IUD expulsion. This risk appears to be lower if the IUD is inserted within about ten minutes of delivery of the placenta. Attempts to reduce this high expulsion rate have focused on modifications of the IUD design [14] through the addition of biodegradable (chromic catgut) suture material to the IUD that were designed to impinge against the anterior and posterior uterine walls and prevent expulsion. Studies of these modified IUDs did not indicate any advantages over unmodified IUDs, but they did demonstrate that postpartum IUD insertions could be performed safely if careful attention was paid to the insertion technique. The principal problem of immediate postpartum IUD insertions is the high expulsion rate. Current research directed at overcoming this problem has focused on modifications of the IUD design and insertion technique. Currently undergoing preliminary trials are IUDs that are retained in the uterus by small anchoring mechanisms. These mechanisms are attached to the top of the IUD and become embedded in the uterine fundus when the IUD is inserted [15].

Future research needs

Considerable basic research remains to be done to better understand the mechanisms through which IUDs protect against pregnancy and cause side effects such as increased menstrual blood loss. It is doubtful that this research will lead to new and improved IUDs. Among the IUDs that are in widespread use (Multiload, various models of the TCu, Progestasert), none were developed through the results of basic research directed at understanding their mechanisms of action. IUDs in current use were developed on a trial and error basis through clinical studies. For example, the optimum amount of copper on most copper-bearing IUDs and the average daily release rate of progesterone from the Progestasert were determined through clinical experimentation and not basic research. In view of this, the emphasis of future IUD research should be goal-oriented and be directed towards clinical experimentation to provide answers to some of the unknowns about intrauterine contraception.

The following are recommendations for future research that could enhance the safety, effectiveness and acceptability of IUDs currently available:

(1) Clinical studies to determine the maximum duration of IUD effectiveness for IUDs, such as the MLCu375, having large copper surface areas. These studies should also evaluate the incidence of fragmentation of the copper wire over time.

(2) Since the risk of PID is highest during the initial period after IUD insertion, randomized, comparative studies of the use of prophylactic antibiotics given at the time of IUD insertion need to be performed. An alternative study would be to evaluate the benefits of dipping the IUD in an antiseptic solution immediately before insertion. This latter study would be more practical for the rural areas of developing countries that have limited medical resources and where antibiotics are expensive and are not always immediately available.

(3) Some studies have suggested that there may be an increased risk of PID after prolonged use of IUDs. Long-term follow-up studies of IUD users should be conducted to determine the optimal time period for IUD replacement regardless of the IUD's demonstrated period of effectiveness.

(4) Evaluation of the risks, if any, associated with the continued use of IUDs by postmenopausal women. This might not be an issue in developed countries where women have immediate access to health care facilities and may have their IUDs removed at any time. However, this is not the situation in many developing countries.

(5) Additional studies on the return to fertility of women who either expelled an IUD or had it removed for any reason. Particular emphasis should be placed on evaluating the incidence of primary and secondary infertility, and the incidence of adverse pregnancy outcomes. These studies should be conducted in different populations and whenever feasible, comparison groups of users of other contraceptive methods also should be studied.

(6) Further investigation in large multiclinic studies of the complications asssociated with the use of IUDs by lactating women.

(7) Further studies to evaluate expulsion rates associated with the use of different types of IUDs for postplacental insertion, and identification of characteristics of the IUDs and users that are associated with low expulsion rates. These studies should be performed in different populations, especially in developing world countries where the postpartum period is an opportune time to start contraception.

(8) Since the use of low-dose progestins may be associated with an increased risk of ectopic pregnancy, extensive studies of progestin-releasing IUDs should be undertaken to evaluate their associated ectopic pregnancy rates.

(9) Studies of the relationship between lower and upper genital tract infections among users of different contraceptive methods, especially in developing world countries where cervical disease often is endemic.

(10) Additional studies to evaluate the effectiveness of the selective "fitting" of different Multiload models, based upon uterine measurements, such as uterine length using the measuring devices of Hasson [6] or Kurtz [7]. If necessary, Multiload IUDs of shorter/narrower dimensions might be developed and evaluated.

Conclusions

The need for additional clinical research on IUDs should not be interpreted to mean that the safety of intrauterine contraception is in question. Numerous studies conducted worldwide have demonstrated the safety

of this method of contraception. However, this should not prevent the continued development of even safer and more effective intrauterine devices.

The IUD provides women with one of the safest and most effective methods of contraception. This was reaffirmed in the following statement issued by The International Federation Of Fertility Societies at the XII World Congress Of Fertility And Sterility during their meeting in Singapore in October 1986: "IUDs are important methods of fertility control, have relatively low side effects, low failure rates and good patient acceptability. The XII Congress fully endorses their continued use in appropriately selected and informed women throughout the world".

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Resumen

En esta revisión presentamos una serie de directrices que si se siguiesen reducirían significativamente la incidencia de las complicaciones referidas al uso del DIU. Actualmente se evestionan los recientes descubrimientos en torno al DIU, incluido el Levonorgestrel-T, una nueva variación del Multiload y DIUs indicados para la inserción postparto. Desde que se efectuaron importantes modificaciones en su utilización, hemos observado un incremento de su inocuidad y un descenso de los efectos indeseables, gracias principalmente a una utilización más oportuna. Ademas nos ha permitido comprener mejor los efectos colaterales relacionados con su uso.Incluimos tambien recomendaciones, para futuros trabajos, que pueden cambiar las directrices seguidas hasta ahora, mejorando la seguridad, efectividad y aceptabilidad de los DIUs.

Résumé

Dans cette communication d'ensemble sont présentés des conseils généraux relatifs à l'utilisation des DIU, qui devraient permettre, s'ils sont suivis, de réduire l'incidence des complications que ces dispositifs peuvent entraîner. Y sont examinés de récents progrès réalisés sur les DIU, et notamment sur le modèle T libérant du lévonorgestrel qui est une variante du modèle Multiload et des dispositifs conçus pour leur insertion après l'accouchement. Etant donné que toutes les améliorations importantes qui seront apportées du point de vue de la sécurité des DIU résulteront probablement d'une meilleure compréhension des effets secondaires et des réactions adverses imputables aux DIU, cette communications inclut des recommandations pour les recherches à venir, qui pourraient rehausser la sécurité, l'efficacité et l'acceptabilité des dispositifs actuellement sur le marché.