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IPPF *Medical Bulletin*

Contents

IMAP Statement on contraception for women over 35

The statement below was revised by the IPPF International Medical Advisory Panel (IMAP) during 1997.

Introduction

Women over the age of 35 constitute at least 20% of contraceptive users. They need special consideration because pregnancy in this age group carries greater health hazards for mother and baby. Characteristics that may affect their choice and use of contraceptive methods include a higher prevalence of obesity, diabetes and hypertension, the particularly dangerous effect of smoking and the general decline of fertility with age. The choice of method is also affected by the woman's previous contraceptive experience, and her habits and lifestyle. The incidence of menstrual disorders increases with age and this too is relevant to selection of a method of contraception. All methods can be considered after proper health screening and discussion of their benefits and risks.

Choice of methods

Surgical sterilization

Older couples who do not want to have any more children are more likely to choose sterilization than younger couples. They need adequate information and counselling before they can make such a decision. As a general rule, vasectomy is safer than female sterilization. For older women, it may be important to weigh the risk of the surgical procedure against the number of years for which the contraceptive protection will be needed. Recent studies do not support the clinically held impression that female sterilization causes menstrual problems. Before operating, service providers should exclude the possibility of uterine disease or other gynaecological disorders that might necessitate further surgery in the future. Hysterectomy should not be performed for the sole purpose of sterilization. A recent study in the United States of America suggests that the risk of tubal sterilization failure, while low, may be higher than was previously thought, particularly with certain techniques (spring-clip application and bipolar coagulation). Pregnancies can arise even many years after tubal sterilization and a high proportion of these are ectopic. Both the risk of pregnancy in general and the risk of ectopic pregnancy are lower among women who have the sterilization procedure at an older age.

Intrauterine devices

The IUD is a good method for many older women. It is a long-acting, effective method with no systemic effects. Contra-indications to its use that are present more often in the over–35 group are fibroids which distort the uterine cavity so as to prevent proper placement of an IUD, and abnormal vaginal bleeding which requires diagnosis. Pelvic inflammatory disease may be less frequent with the use of IUDs at this age, because women are more likely to be in a mutually monogamous relationship. Women who reach the menopause while using an IUD should have it removed one year after the final menstrual period. In women with heavy menstrual periods, the levonorgestrel-releasing IUD can be a good alternative to a copper-bearing device because it may decrease the amount of bleeding.

Barrier methods and spermicides

Barrier methods and spermicides have no known significant side-effects. Although in general the effectiveness of barrier methods is lower than that of hormonal methods and intrauterine devices, when used consistently and correctly barrier methods can be reasonably effective, especially the condom. When counselling clients, it should be emphasized that improper use of these methods is associated with high failure rates. Older couples may be better motivated to use barrier methods properly; but their decisions regarding contraception should take account of the particularly adverse consequences of pregnancy at older ages. Where national laws permit, the availability of back-up abortion may increase the acceptability of these methods.

Spermicides, because of their low effectiveness, should be used mainly in conjunction with other barrier methods. The lubricating effect of spermicides may be an advantage to women in this age group for whom dryness of the vagina may cause discomfort during sexual intercourse.

Periodic abstinence

Despite their relatively low use-effectiveness, methods based on periodic abstinence may be more acceptable to women over 35 than to younger women. Older couples are more likely to follow the instructions for identifying the fertile phase of the cycle and to abstain from intercourse when necessary. In pre-menopausal women with irregular menstrual cycles, periodic abstinence techniques are unsuitable, whether based on changes in cervical mucus (interpretation of which becomes more difficult towards the end of fertile life) or basal body temperature (because in anovulatory cycles biphasic changes will be absent). If they are relying on the basal body temperature method, long periods of abstinence will be necessary.

Hormonal contraception

Combined hormonal contraception

The risk of cardiovascular disease increases with age and may also increase with combined oral contraceptive (COC) use in women over 35 years of age. However, if these women do not smoke and have no other risk factors for cardiovascular disease, such as hypertension or diabetes, the increased risk is very small. Low-dose COCs may be used by women over 35, but before COCs are started, and periodically thereafter, women in this age group must be screened to exclude the presence of cardiovascular risk factors.

Recent studies show that current users of COCs are more likely to have breast cancer diagnosed; however, the cancers diagnosed are less advanced clinically than the cancers diagnosed in never users. The reported increased risk disappears gradually over time after discontinuation of COCs with no excess risk after 10 years. For the above reasons the increased risk observed is believed to represent either enhanced early detection of existing tumours or a late-stage promotion of tumours. Although the relative risk is slightly greater among younger women, it translates into a very small number of excess breast cancer cases because of the low incidence of this disease in young women.

However, in older women the background incidence of breast cancer is relatively high and therefore any increase in risk has a greater impact, especially in areas where breast cancer is common. The advantages and disadvantages of COCs for older women should be set against those of other contraceptives available and the risks associated with unwanted pregnancy.

Combined once-a-month injectable contraceptives (CICs) are becoming available and may be an option for healthy women over 35. Laboratory studies have shown that they have no or very little effect on coagulation factors and metabolism. However, there are no epidemiological data on the effect of CICs on the risk of cardiovascular disease. By extrapolation from the COC studies, any possible increased risk, among women who do not smoke and have no other risk factors (eg, hypertension or diabetes), is expected to be slight.

Progestagen-only contraception

Progestagen-only contraceptives offer the advantage of freedom from oestrogen-related side-effects which may occur with COCs or combined injectables. Bleeding problems may occur which could mask or simulate bleeding caused by gynaecological disease. The high and long-term effectiveness of injectables and implants may be especially attractive to women over 35. A possible hypo-oestrogenic effect of progestagen-only may result in accelerated loss of bone tissue. Although more research is needed to confirm this, in the case of women who are at risk of developing osteoporosis CICs may be a suitable alternative to progestagen-only injectables.

Progress with early medical abortion

David Paintin

Early medical abortion induced with the progesterone receptor blocking agent mifepristone (RU486) followed by a prostaglandin analogue is an option that has been available in a few countries for several years. Many thousands of women in France, Great Britain, Sweden and China have used this method successfully. The gestation limit in Britain is 63 days from the first day of the last menstrual period but is 49 days elsewhere. In the European countries, the manufacturer's instructions stipulate that 600 mg of mifepristone is given by mouth and, 48 hours later, a 1 mg tablet of the prostaglandin E_1 analogue gemeprost is placed high in the vagina. Various regimens have been used in China, where mifepristone is produced by the government under licence and where the usual prostaglandin has been the $F_{2\alpha}$ analogue carboprost. Mifepristone and gemeprost are expensive, and gemeprost deteriorates if not distributed and stored while refrigerated (virtually precluding its use in developing countries). Most of the unpleasant side-effects – pain, vomiting and diarrhoea – are associated with the prostaglandin. Research has continued, particularly into the optimum amount of mifepristone and the most suitable prostaglandin analogue.

The baseline criteria against which changes in the mifepristone/gemeprost treatment regimen must be assessed are those derived from the two large multicentre studies conducted in France and Britain in the late 1980s.[1,2] The principal outcomes are shown in Table 1.

TABLE 1: MULTICENTRE STUDIES OF EARLY MEDICAL ABORTION WITH 600 MG MIFEPRISTONE ORALLY AND 1 MG GEMEPROST VAGINALLY

Study	Gestation limit (days)	No. of women	Complete abortion (%)	Uterine evacuation		Continuing pregnancies (%)
				Urgent (acute bleeding)	Delayed (retained products)	
UK Multicentre Study[1]	63	957	94.8	0.4	4.9	0.3
Ullman et al[2] (France)	49	1211	96.5	0.8	2.3	0.4
Both studies (95% confidence interval)		2168	95.5 (94.6–96.4)	0.6 (0.3–1.1)	3.4 (2.7–4.3)	0.4 (0.2–0.7)

Can misoprostol be used instead of gemeprost?

Misoprostol is an orally active analogue of prostaglandin E_2 that is licensed in many countries for the treatment of gastric and duodenal ulceration. No life threatening side-effects have been reported after very extensive use. It is inexpensive and has an acceptable shelf life at room temperatures. A study from France of 878 women with up to 49 days' amenorrhoea reported that 600 mg mifepristone followed 48 hours later by 400 µg misoprostol by mouth resulted in complete abortion in 97%, with a continuing pregnancy rate of only 0.8%.[3] In Edinburgh, 800 pregnant women with up to 63 days' amenorrhoea had 600 mg mifepristone and, 48 hours later, were randomly allocated to gemeprost 0.5 mg vaginally or misoprostol 600 µg orally.[4] The complete abortion rates were about 95% in both groups but the continuing pregnancy rates were 0.2% and 2.3%, respectively. An important observation was that eight of the nine pregnancies that continued were at gestations of 50 to 63 days. In Aberdeen, 266 women with up to 63 days' amenorrhoea who had had 600 mg mifepristone were allocated at random to misoprostol 800 µg orally or 800 µg vaginally.[5] The complete abortion rates in this small study were 87% and 95%, respectively, with continuing pregnancy rates of 7% and 1%. Abortion occurred within 4 hours significantly more frequently after

the vaginal misoprostol. These studies show that misoprostol can be as effective as gemeprost, that oral administration of 400–600 µg is satisfactory up to 49 days of amenorrhoea, but that 800 µg by the vaginal route is more effective from 50 to 70 days. Misoprostol tends to cause less pain than gemeprost, but vomiting and diarrhoea, while similar when the tablets are taken by mouth, are less frequent when administration is vaginal.

Can the dose of mifepristone be reduced to 200 mg?

The World Health Organization coordinated a multicentre study in which 1182 pregnant women with amenorrhoea of up to 56 days were allocated at random to have 200 mg, 400 mg or 600 mg of mifepristone by mouth, followed 48 hours later by a 1 mg vaginal pessary of gemeprost.[6] Overall 95.5% had a complete abortion and from 0.3% to 0.5% had pregnancies that continued. There were no significant differences in any outcome between the three groups. A study from Edinburgh suggests that the results would have been similar had misoprostol been used instead of gemeprost.[7] 220 pregnant women with amenorrhoea of up to 63 days were allocated at random to either 200 mg or 600 mg mifepristone, followed 48 hours later by 600 µg misoprostol by mouth. The complete abortion rates were identical in the two groups (93.6%) and there was only one continuing pregnancy in the whole study. The complete abortion rates between the groups did not differ significantly with gestation but, when the groups were combined, complete abortion rates were significantly greater at up to 49 days than at 50–63 days (97.5% *versus* 84.4%) – additional evidence that 600 µg misoprostol by mouth is unsatisfactory when the gestation exceeds 49 days. Further evidence that 200 mg of mifepristone is adequate is provided by the randomized study from Edinburgh in which both groups had 200 mg mifepristone and the effects of gemeprost and misoprostol were compared.[4] From these several studies it can be concluded that 200 mg mifepristone is effective for medical abortion at up to 63 days' amenorrhoea.

Is methotrexate an acceptable alternative to mifepristone?

Mifepristone is not available for routine clinical use in the United States and Canada. A sequence of careful studies has shown that early medical abortion can be induced with the folate antagonist methotrexate followed 7 days later by vaginal misoprostol – but with results that are inferior to those obtained in other countries with mifepristone/misoprostol. In a multicentre observational study, 300 pregnant women with amenorrhoea of up to 56 days were given an intramuscular injection of methotrexate (50 mg/sq m) followed, 7 days later, by 800 µg misoprostol vaginally, the misoprostol being repeated the next day if abortion did not occur.[8] There was complete abortion in the 24 hours following the first or second dose of misoprostol in only 67%, and in a further 28% after a mean delay of about 24 days, giving an overall complete abortion rate of 88%. Vacuum aspiration was performed in all women in whom the method failed. Vomiting and diarrhoea followed both medications in some women but were no more prevalent or severe than would have been expected with mifepristone/misoprostol. No serious side effects resulted from the use of methotrexate. 75% of the women found the method acceptable and 83% said they would prefer this method to vacuum aspiration if the need arose again. However, methotrexate in repeated doses is capable of inducing fatal suppression of the bone marrow, and a single dose has some teratogenic potential for continuing pregnancies. This is a method that requires close medical supervision. It could be an alternative but only in countries where mifepristone is not available. Poorly regulated use would result in unacceptable risks to the abortion-seeking woman and to any children born after continuing pregnancies.

The acceptability to women of early medical abortion

There have been several studies of the acceptability of early medical abortion.[9] In developed countries, when offered a choice between early medical abortion and vacuum aspiration, 60–70% of women chose the medical method. The perceived advantages were closer personal control over the abortion process, greater privacy and the avoidance of anaesthesia and of the intrusion into their body of instruments. After the experience, women were rather less satisfied with the medical method than with vacuum aspiration – particularly with regard to pain, the number of visits to the providing agency, and the time taken to confirm that the abortion was complete. Nevertheless, most said they would choose the medical method again if this became necessary. A recent study with centres in China, Cuba and India suggests strongly that the mifepristone/misoprostol regimen has the potential to combine effectiveness with accessibility in developing countries.[10] The barriers to its widespread use in countries in which clandestine unsafe abortion is frequent relate to social and political factors rather than effectiveness and safety.

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Evolution of IUD performance

T M M Farley

The intrauterine device (IUD), used by an estimated 100 million women for the prevention of pregnancy, is the most common reversible method of contraception.[1] The clinical performance of IUDs for the prevention of pregnancy has improved[2] from annual pregnancy rates between 2% and 3% seen with the early non-medicated and copper-bearing devices to less than 0.5% with newer devices including 375 and 380 sq mm copper. The most recent hormone-releasing device (releasing 20 µg levonorgestrel per day) also has a very low annual pregnancy rate (figure 1). Ectopic pregnancy rates have likewise declined with the more recently introduced devices, though the rates were highest with the progesterone-releasing progestasert device. Annual expulsion rates within the first year of use with the medicated devices lie in the range 3% to 10% depending on age and parity and other characteristics of the users.

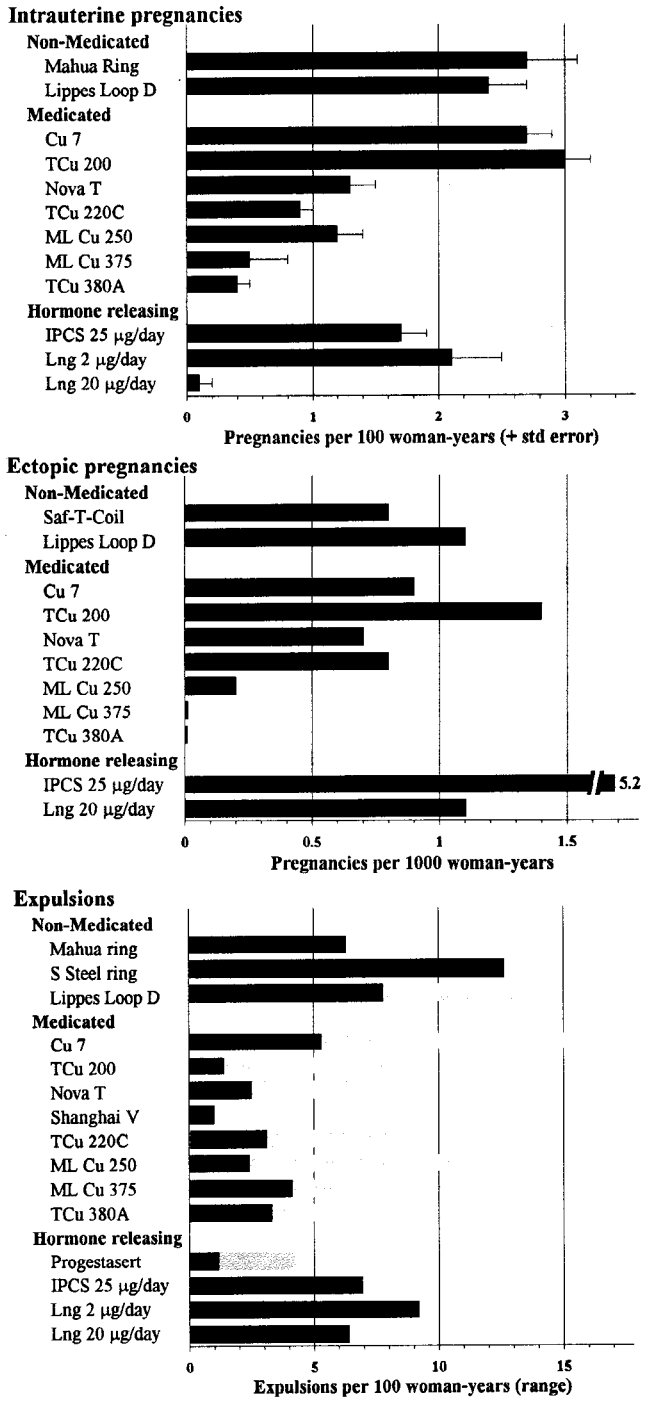

Figure 1: Performance of various IUDS

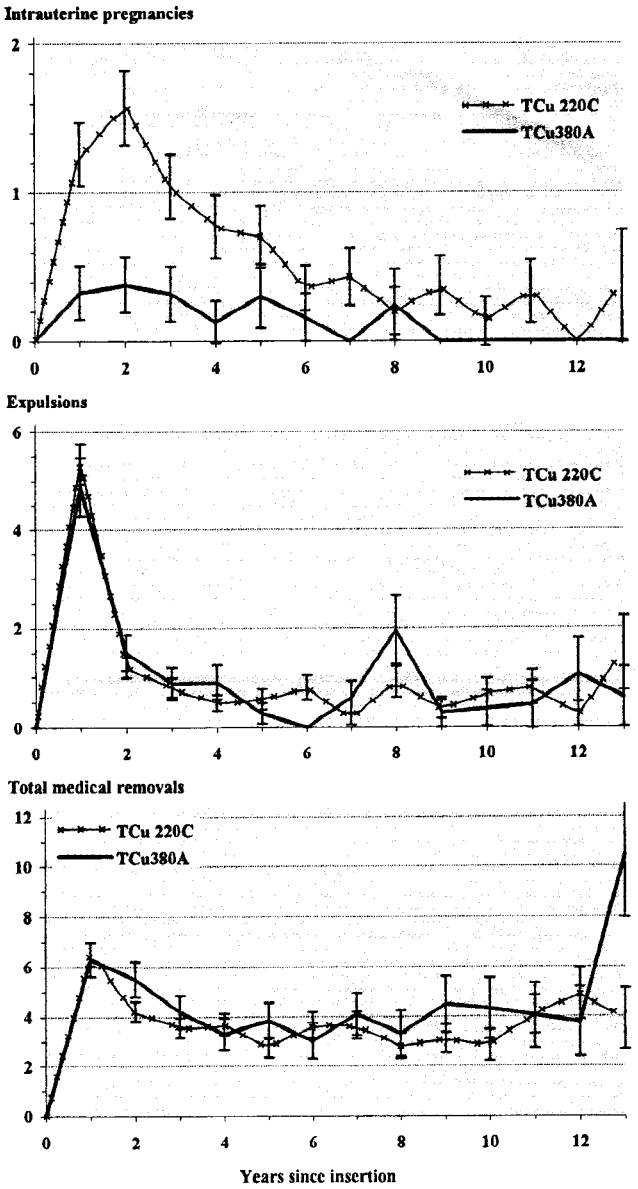

Figure 2: Annual discontinuation rates (+standard error) in percent

Randomized trials of the TCu 220C and TCu 380A devices conducted by the UNDP/UNFPA/WHO/World Bank Special Programme of Research, Development and Research Training in Human Reproduction have shown that the effectiveness of these devices extends up to 13 years of use with very low annual pregnancy and expulsion rates after the second year of use (figure 2).[3] Removals for medical reasons (primarily increased menstrual pain and/or bleeding) remain at approximately 4% per year and represent the area where improvement in IUD performance is most required. Nevertheless, the high contraceptive efficacy up to 12 years after insertion means that the TCu 380A can be regarded as a non-surgical, potentially reversible, alternative to tubal ligation for women seeking long-term fertility regulation.

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