Recent Advances In Medical Methods Of Abortion

Dr. Geetha Balsarkar
Professor and Unit incharge
Nowrosjee Wadia Maternity Hospital
Seth G.S. Medical college, Parel, Mumbai
Secretary to the Editor, Journal of Obstetrics and Gynecology of India

More than one third of the approximately 205 million pregnancies that occur each year around the world are unplanned and about 20% of them end in induced abortions (1, 2). Most of these abortions take place during the first trimester of pregnancy, only 10%–15% of all induced abortions occur during the second trimester. Overall, two thirds of all major complications of abortions occur in those performed during the second trimester (3).

Over the past 30 years, there have been continuing efforts to improve abortion technology in terms of effectiveness, safety (lower complication risk), technical ease of performance and acceptability. The optimal method for abortions, whether medical or surgical continues to be debated (4). It is important to determine which is the best method in a particular set up to reduce abortion-related morbidity and mortality (3). The overall risk of death is 10 times higher with dilatation and evacuation abortion than with first trimester suction curettage (5), and the risk of mortality increases progressively with advancing gestational age (6). Any attempt to reduce mortality and morbidity from this procedure can bring significant benefits to the quality of life for the women undergoing this procedure.

The drugs are used to terminate pregnancy act by inhibiting the synthesis of progesterone, inducing myometrial contractions, antagonizing the action of progesterone, or inhibiting trophoblast development. Among the drugs used in medical abortion are epostane, prostaglandins (including misoprostol and gameprost), combined methotrexate and misoprostol, tamoxifen-misoprostol regimen, mifepristone and prostaglandin, and antiprogestin and prostaglandins. The efficacy, side effects, and contraindications of these drugs in the medical termination of pregnancy vary. In general, medical abortion is associated with higher rates of prolonged bleeding, nausea, vomiting, and pain as compared to surgical abortion. However, medical termination of pregnancy has a high rate of efficacy in women with early pregnancies. In addition, medical abortion is safe and acceptable to women, and it does not require anesthesia. Lastly, women who choose medical abortion must have access to a center where suction curettage is available, should heavy bleeding occur and blood transfusion is required.(2)

Medical abortion with mifepristone (RU 486) and a misoprostol tablets is now available in India, and reports suggest that it provides a safe and effective alternative to surgery in early pregnancy.(1) However, the demand for, and the acceptability of, medical abortion in Indian women is largely unknown. There is an increasing awareness among both the general public and the medical profession about the use of this non surgical technique. Mifepristone in combination with a prostaglandin analogue has been licensed for termination of pregnancy in the UK at up to 9 weeks amenorrhoea(1), and since 1995, beyond 13 weeks. In India,FOGSI recognises the universal evidence on the safety & effectiveness of mifepristone-misoprostol for MTP up to 49 days as approved for use by the Drug Controller of India. It is stressed that under existing laws these methods can only be administered by gynecologists & RMPs recognised for performing MTPs by the MTP Act of 1971. The form C of the MTP regulations needs to be filled even for medical abortions. FOGSI recommends close monitoring of distribution of these drugs & that the medical profession & the pharmaceutical industry exercise due diligence in their promotion & use. It is also vital that consumers be educated & counselled regarding its advantages,drawbacks, risks & limitations.

Currently most centres use a single dose of 600 mg of mifepristone followed 36 to 48 hours later by

either 200 mcg of oral misoprostol, 4 doses 12 hours apart or a single vaginal pessary of 8oo mcg ofmisoprost. There have now been extensive trials (chiefly under the auspices of the World Health Organisation) to investigate the optimal or minimum dose of antigestagen and prostaglandin and the route and research is also in progress to develop a 48 hour delayed release prostaglandin system to be given at the same time as the antigestagen. Avoiding the second visit for treatment would be of particular value in countries such as Britain where treatment for abortion must be administered only in a licensed clinic or NHS hospital. The patients must be convinced to accept surgical abortion in the event of failure-for fear of teratogenesis, though this has not been established in humans. Uterine bleeding lasts eight to 15 days, and in over 90% of cases no other treatment is needed. In the remainder a surgical curettage or suction procedure is still needed, either for heavy bleeding or because the combination treatment has failed to induce abortion (7).

Numerous protocols have been studied and are in use, but only 1 has been approved by the FDA. The FDA-approved regimen can be initiated up to 49 days after the first day of the LMP and consists of mifepristone 600 mg orally on day 1, misoprostol 400 mcg orally provided at the doctor's office on day 3, and a follow-up appointment on days 12-20. This protocol is 92% effective in inducing a complete abortion.(8,9) It is hoped that studies using different variations of the FDA-approved regimen will lead to expanded options that are safe and reduced costs.

It has been shown by the World Health Organization and others that a lower dose of mifepristone (200 mg) is just as effective as the 600-mg dose.(10,11) This is especially important for reducing the cost of medical abortions, as it would mean taking only one 200-mg tablet instead of three 200-mg tablets. Misoprostol inserted vaginally, rather than taken orally, has also been evaluated. The vaginal dose most frequently recommended is higher -- 800 mcg misoprostol -- compared with the 400 mcg taken orally. Given the very low cost of misoprostol, such variations do not substantially increase the cost of the regimen. A total of 95% of women who inserted 800 mcg misoprostol vaginally after taking 600 mg mifepristone up to 63 days post-LMP had complete abortions, as compared with 87% of women who took the lower oral dose of misoprostol.(7) This study and others confirmed that vaginal administration of misoprostol is superior to oral administration and that, for women initiating medical termination of pregnancy between 49 and 63 days after LMP, only vaginal misoprostol administration is recommended. Oral administration of misoprostol should not be used more than 49 days post-LMP. In at least 1 study, the incidence of gastrointestinal side effects from the misoprostol tends to be lower with vaginal administration.(12)

The FDA requires patients to return to the doctor's office on day 3 to obtain the misoprostol dose. Although many doctors have the patients wait in the office for 4 hours after administration of this dose (because this is a time of maximum cramping and bleeding and also when a majority of patients pass their pregnancies), misoprostol can also be self-administered by the patient in the privacy of her own home. This self-administered method, either orally or vaginally, is not only equally efficacious when compared with administration in the doctor's office, but it is also well accepted by both patient and physician.(6,10) Although the FDA-approved regimen allows for medical termination of pregnancy up to 49 days post-LMP, 1 study showed an efficacy rate of 98%, meaning complete abortion without surgical intervention, in a series of 2000 women up to 63 days post-LMP with 200 mg mifepristone orally, followed 2 days later by 800 mcg misoprostol vaginally. This demonstrates that the latter regimen has efficacy equal or superior to the FDA-approved regimen and suggests that medical abortion is safe for women who initiate termination at a later point in gestation.(11)

Another alternative regimen uses methotrexate 50 mg/m2 intramuscularly (IM) on day 1, followed by misoprostol 800 mcg vaginally 3 to 7 days later with repeated misoprostol dose every 48 hours for up to 3 doses until the pregnancy is terminated. This regimen seems to be 90% to 100% effective.(12,13) Efficacy decreases with increasing gestational age.(14)

Studies have also looked at using a standardized dose of methotrexate instead of basing the dose on the body surface area. Using 75 mg methotrexate IM followed by misoprostol 800 mcg vaginally 5 to 6

days later yielded an efficacy rate of 95% when used in pregnancies at gestational age of fewer than 49 days since LMP.(15) Methotrexate can also be administered orally and then followed 5-7 days later with misoprostol 800 mcg. Methotrexate, 25-50 mg taken orally, has been shown to be 90% to 91% effective when administered fewer than 56 days since LMP.(16)

Other protocols are being investigated, including one entailing administration of misoprostol alone,(17) which has been successful in second-trimester procedures when preceded by laminaria insertion, and one entailing use of tamoxifen and misoprostol. Cost and convenience and access to medications are important considerations driving this research.(18)

It was found that women attach a great deal of importance to the opportunity to choose their method of termination. The first stage of mifepristone is now a standard practice and an optimum dose has been determined. Several studies examined misoprostol used in the second stage of medical termination. Gestation and previous obstetric history is an important factor to take into account when determining optimal regimen.

More optimistic research is being conducted by WHO along with various NGOs to find out safer and cheaper alternatives for first and second trimester abortions for developing countries like India to reduce the morbidity due to induced abortions.

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