HJOG An Obstetrics and Gynecology International Journal

Review

First trimester medical abortion: The several merits of combination mifepristone - misoprostol

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Abstract

Abortion is a very common procedure among women of reproductive age. Medical abortion is an alternative to surgical evacuation, especially in the early first trimester. Following the introduction of mifepristone, the number of medical abortions has rapidly increased. Mifepristone is used at doses of either 600mg or 200mg in combination with misoprostol and is regarded as a safe and effective method, though clinicians need also to be aware of its limitations in order to appropriately select cases and adequately inform their patients. In this review we present the current data on the use of mifepristone for medical abortion in first trimester, as well as of mifepristone in combination with misoprostol, as concerns the different doses of both regimens, the rates of treatment failure and possible complications.

Keywords: Mifepristone; misoprostol; abortion; medical abortion; first trimester; pregnancy

Introduction

It is estimated that every year round the world approximately 40 million abortions are performed, legal and illegal, resulting in an abortion rate of 3.5%[1].

While in the past surgical abortion was the method of choice, the introduction two decades ago of mifepristone resulted in a rapidly growing number of medical abortions being performed worldwide. Today, mifepristone is registered for this use in more than 50 countries (www.gynuity.org).

The approved regimen in most countries advises the use of 600 mg mifepristone, but in practice the standard dose worldwide varies, the most common dose being 200 mg[2, 3]. In order to enhance the success rate, misoprostol (prostaglandin) is administered after mifepristone. The World Health Organization (WHO), the International Federation of Obstetrics and Gynecology and the Royal College of Obstetricians and Gynecologists recommend vaginal, buccal or sublingual misoprostol administration at doses up to 800 mcg 24 - 48 hours after mifepristone intake[4, 5].

In this review we present the current data on the use of mifepristone in the first trimester for medical abortion. The published data clearly demonstrate the effectiveness and safety of mifepristone in conjunction with misoprostol, while in addition the use of the lower dose of 200 mg mifepristone is suggested without incurring any significant failure rates or complications.

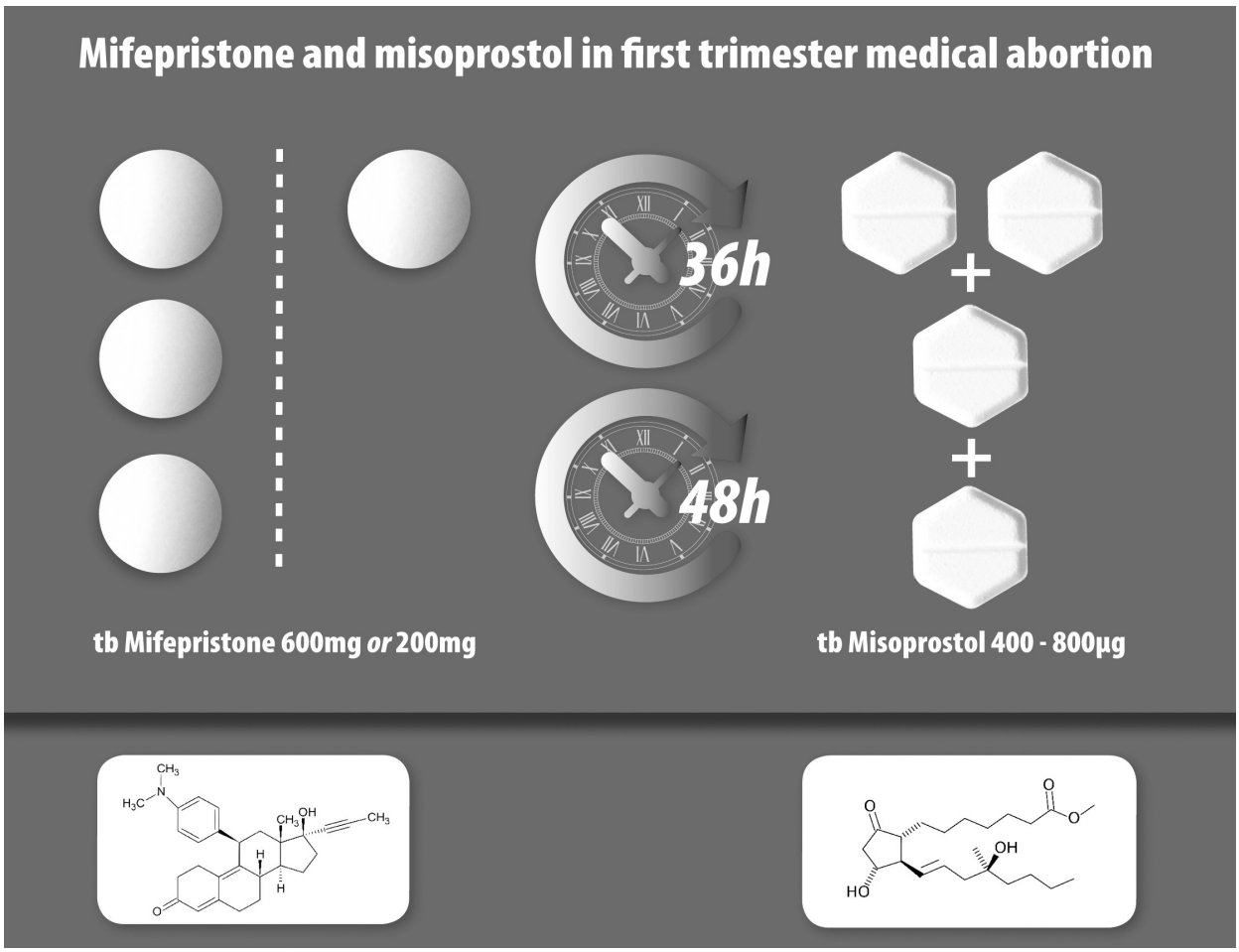

Figure. A two - step medical abortion procedure: Oral administration of 600 or 200 mg mifepristone is followed by oral or transvaginal 400 - 800 mcg misoprostol 36 - 48 hours later. The chemical structure of both drugs is illustrated

Mifepristone

Mifepristone is an antiprogesterone, a synthetic steroid that binds to the progesterone receptor, inhibiting the effect of endogenous progesterone[6, 7]. The binding of mifepristone to the receptor is indeed very strong, being almost five times greater than that of endogenous progesterone[5].

Administration of mifepristone results in cervical ripening while additionally hindering progesterone's decidualisation effect on the endometrium[5, 8]. It has also been found that uterine contractility is significantly increased 24 - 36 hours after the administration of mifepristone, while the sensitivity to exogenous prostaglandins is five times higher after its administration[5, 6].

Though during the first years after its introduction mifepristone was used as a single regimen, the reported effectiveness was not sufficient, and the significant failure rates that were documented eventually led worldwide to the standard use of mifepristone in combination with prostaglandin[9-12].

Meanwhile, clinicians should also be made aware of mifepristone's contraindications. Thus, women with severe asthma or a history of cardiovascular disease and heavy smokers over 35 years should not use this drug[13]. Moreover, mifepristone cannot be applied in breastfeeding women because of the risk of a potential teratogenic effect on the infant[13].

Although the approved mifepristone dose regimen is 600 mg, the regimen of 200 mg is in wide use[3, 9]. A

Cochrane review of seven Randomized Control Trials concluded that the efficacy of the 200 mg dose is the same, while it is suggested that the dose can be reduced to 200 mg without any decrease in efficacy or safety[14].

A multicenter trial was conducted by the WHO which evaluated the efficacy of an even lower dose[15]. However, this study examining the use of 50 mg of mifepristone showed a significant increase in treatment failure and complications rate as compared to the 200 mg regimen, consequently this very low 50 mg dose is not recommended. As regards the dose of 100 mg, there is not at present enough data to support its use in routine practice, further research being needed[16].

Misoprostol

At the present time, the use of misoprostol in combination with mifepristone is the gold standard for medical abortion due to its achievement of higher success rates[12]. France was the first country to establish the use of mifepristone together with a single dose of 400mcg misoprostol orally[17]. The success rates were 95-97% at 49 days' gestation with no reported further need for misoprostol administration.

For women at up to 63 days' gestation, the success rates of mifepristone - misoprostol are, however, decreased, a higher misoprostol dose therefore being suggested. Ashok et al. have documented the use of 800 mcg of misoprostol vaginally that resulted in a complete abortion rate of 97.5% and had significantly better efficacy after 49 days' gestation as compared to lower doses[18]. These data are in agreement with another review which showed that use of misoprostol doses higher than 400 mcg lowers the risk of abortion failure even in pregnancies of more than 63 days[9].

Misoprostol has the additional advantage that it can also be taken at home, i.e. in an environment that is familiar and convenient for the woman. This is a common policy in the USA where a very high efficacy and acceptability rate is reported[19, 20]. Another review corroborated the benefits of this practice, reporting no evidence of increased failure rates or complications in women taking misoprostol at home[9]. On the other hand, there are many countries where it is mandatory for women to pay a second visit to the physician for misoprostol administration[21]. In our opinion, women should be offered the opportunity of receiving misoprostol at home, based of course on certain criteria regarding the selection of cases.

Success rates and complications

The existing data show that medical abortion in the first 63 days of gestation with the combination of mifepristone - misoprostol has very satisfactory results. More specifically, a recent systematic review including more than 45,000 cases over the last two decades showed that surgical intervention was necessary in less than 5% of all cases[9, 22]. An even lower proportion was noted, namely 1% of cases, of required surgical intervention for ongoing pregnancies at follow - up examination at up to 49 days, this being increased with gestational age[9, 14, 22]. Of all the above cases, only 0.4% of the women suffered a serious complication and required either hospitalization or transfusion.

The main factors that increase the success rate were clearly set out in a recent review[9]. First, an interval of at least 24 hours is required between mifepristone and misoprostol administration. Furthermore, doses of misoprostol higher than 400 mcg, irrespective of the route of administration, result in a significantly lower complication rate in ongoing pregnancies[14].

Gestation age is another factor that should be taken into consideration for 1st trimester medical abortion. For women in the 9th week of gestation the failure rate was very high (25%), although the ongoing pregnancy rate was not different[9, 14, 22]. All these cases were treated with surgical evacuation, without any further complications.

Genital tract infection is another possible complication of medical abortion, occurring in up to 10% of cases[14]. The severity varies from a simple vaginitis to pelvic inflammatory disease; in these cases, the use of prophylactic antibiotics and exclusion of an exist-

ing lower genital tract infection before the abortion is recommended.

Analgesia intake

A major concern for many clinicians and women with respect to medical abortion is the adverse effect of abdominal pain after misoprostol administration. It has been found that younger women, with a longer induction to abortion time-interval and of a higher gestational age, require higher doses of analgesics[15]. In contrast, multiparous women are less likely to ask for analgesia[23]. The need for analgesia is independent of the misoprostol administration route. Nevertheless, it is suggested that all women undergoing medical abortion should be supplied with analgesics, a strategy that increases women's acceptability.

Follow - up

The final issue as regards women undergoing medical abortion is the follow - up visit. This follow - up is necessary in order to confirm that the abortion has been completely successful and, if not, to identify early possible complications. Although after misoprostol intake the products of conception are very often seen, a transvaginal ultrasound of the uterus is mandatory.

The follow - up examination should ideally be performed within 2 weeks of abortion[11, 14], although there are no existing data showing any significant association between failure rates and the time of the follow - up evaluation.

It is essential to give all women simple instructions and explain all the possible complications and how they may promptly detect them. This could be in selected cases an alternative to a follow - up examination. On the other hand, in women in whom the conception products were not identified, a transvaginal ultrasound is mandatory, while additionally they should be more closely followed up for possible abortion failure or complications.

Conclusion

Today, medical abortion is regarded worldwide as a safe and effective option, especially for the first 63 days of gestation. This is an attractive alternative for many women who wish to avoid a surgical procedure and its attendant likely complications, while they also have the option of taking misoprostol in the comfort of their own home. Of course, patients should be fully informed as to the possible complications and limitations of this choice, as well as about the small likelihood of the need for an additional surgical evacuation.

Another important aspect is the lower cost for the National Health Systems of a medical abortion in contrast to a surgical evacuation, this issue being of particular import in countries such as Greece where, due to the present economic crisis, resources are severely lacking. Meanwhile, on a personal level, medical abortion provides a safe option for uninsured women who, in its absence, may well resort to alternatives that put their health at risk.

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