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Assessment of different routes of administration of misoprostol in first and second trimester abortions

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Abstract

Misoprostol can also be used to dilate the cervix in preparation for a surgical abortion, particularly in the second trimester (either alone or in combination with laminaria stents). Hence, the present study was carried out to compare the effectiveness of 400 µg of misoprostol through three different routes i.e. vaginal, sublihgual and oral for first and second trimester abortion as per MTP act.

The present study was planned in the Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital from Jan 2017 to Sept 2017.Total 75 females with a period of gestation between 12 and 20 weeks scheduled to have pregnancy termination as per MTP Act were included in the study. The all enrolled females were divided in three equal study groups based on the administration route of Misoprostol. The Group I, II and III were administered with the Misoprostol 400 mcg at 4-hourly interval by Sublingual, Vaginal and Oral route. The misoprostol was administered with 400 mcg at 4-hourly interval up to a maximum of four doses each.

The data generated from the present study concludes that Oral and sublingual routes of administration have shown to be more tolerable related to vaginal route of administration. But the effectiveness of oral administration is less. Thus, sublingual misoprostol has the advantage that it can evade the uncomfortable vaginal administration. Also absorption of the drug may be affected when the patient starts bleeding.

Keywords: misoprostol, second trimester pregnancy termination, sublingual route, vaginal route, abortion, abortion, etc

Introduction

Abortion is the ending of a pregnancy by removal or expulsion of an embryo or fetus before it can survive outside the uterus. An abortion that occurs without intervention is known as a miscarriage or spontaneous abortion. When deliberate steps are taken to end a pregnancy, it is called an induced abortion, or less frequently "induced miscarriage". The unmodified word abortion generally refers to an induced abortion. A similar procedure after the fetus has potential to survive outside the womb is known as a "late termination of pregnancy" or less accurately as a "late term abortion" [1].

When allowed by law and performed by trained personnel, abortion is one of the safest procedures in medicine. It is safer than carrying a pregnancy to term, which has a 14 times higher risk of death in the United States. Modern methods use medication or surgery for abortions. The drug mifepristone in combination with prostaglandin appears to be as safe and effective as surgery during the first and second trimester of pregnancy. The most common surgical technique involves dilating the cervix and using a suction device. Birth control, such as the pill or intrauterine devices, can be used immediately following abortion. When performed legally and safely on a woman who desires it, induced abortions do not increase the risk of long-term mental or physical problems. In contrast, unsafe abortions (those performed by unskilled individuals, with hazardous equipment, or in unsanitary facilities) cause 47,000 deaths and 5 million hospital admissions each year. The World Health Organization recommends safe and legal abortions be available to all women [2].

Around 56 million abortions are performed each year in the world, with about 45% done unsafely. Abortion rates changed little between 2003 and 2008 [16], before which they decreased for at least two decades as access to family planning and birth control increased. As of 2008, 40% of the world's women had access to legal abortions without limits as to reason. Countries that permit abortions have different limits on how late in pregnancy abortion is allowed [3]. Historically, abortions have been attempted using herbal medicines, sharp tools, forceful massage, or through other traditional methods. Abortion laws and cultural or religious views of abortions are different around the world. In some areas abortion is legal only in specific cases such as rape, problems with the fetus, poverty, risk to a woman's health, or incest. There is debate over the moral, ethical, and legal issues of abortion. Those who oppose abortion often argue that an embryo or fetus is a human with a right to life, and so they may compare abortion to murder. Those who favor the legality of abortion often hold that it is part of a woman's right to make decisions about her own body. Others favor legal and accessible abortion as a public health measure [4].

The MTP Act, 1971 has stipulated the conditions under which abortions can be done, the persons who can perform

the abortions and places where abortions can be done. According to the Act, only authorized Registered Medical practitioner having prescribed experience in OBG can perform the MTP. If the period of pregnancy is below 12 weeks a doctor does the abortion without consulting any other doctor. But if it is above 12 weeks then two doctors together must decide on the need for termination. The termination can be done by any one of the doctors. During emergency situation if the pregnancy is at 20 weeks or above, a single doctor can do the MTP without consulting the second doctor even in an unrecognized clinic or hospital. It is very important to take written consent of the women. If the women is the minor or in a state of shock or insane then written consent of guardian must be taken. Abortion under the MTP Act 1971 is considered as a personal matter and therefore strict confidentiality is to be maintained by the service providers, identify of the women is to be kept confidential. The doctor is protected from any legal action for any kind of problem cause or any problem, which is likely to occur because of termination, provided the doctor, and has taken all the precautions and proper care. But if any of the rules are violated, then the doctor is liable for punishment, which may include a fine up to Rs.1000. Termination of pregnancy on medical and Eugenic basis is good for both mother and child but no consider/use it as method for prevention of unwanted child especially the female child is unethical and antisocial and should be discouraged. Repeated abortions are harmful to mother's health and lead to high mortality and morbidity. Women should be explained about these and motivated for other methods of contraception [5].

Misoprostol is used either alone or in conjunction with another medication (mifepristone or methotrexate) for medical abortions as an alternative to surgical abortion. Medical abortion has the advantage of being less invasive, and more autonomous, self-directed, and discreet. It is preferable to some users because it feels more "natural," as the drugs induce a miscarriage. It is also more easily accessible in places where abortion is illegal. The World Health Organization provides clear guidelines on the use, benefits and risks of misoprostol for abortions [6]. Misoprostol is most effective when it is used with methotrexate or mifepristone (RU-486). Misoprostol alone is less effective (typically 88% up to eight-weeks gestation). It is not inherently unsafe if medically supervised, but 1% of women will have heavy bleeding requiring medical attention, some women may have ectopic pregnancy, and the 12% of pregnancies that continue after misoprostol failure are more likely to have birth defects and are usually followed up with a more effective method of abortion [7].

Most large studies recommend a protocol for the use of misoprostol in combination with mifepristone. Together they are effective in around 95% for early pregnancies. Misoprostol alone may be more effective in earlier gestation [26]. WHO guidelines recommend for pregnancies up to 12 weeks to use 12 tablets of 200 mcg (micrograms). The woman should put 4 tablets of misoprostol under the tongue or far up the vagina and let them dissolve for 30 minutes. She should wait 3 hours and repeat with 4 pills under the tongue or in the vagina for 30 minutes. She should wait 3 hours and repeat once more [8]. It works in 90% after first attempt and, in case of failure, the attempt may be repeated after a minimum of 3 days. Misoprostol can also be used to dilate the cervix in preparation for a surgical abortion, particularly in the second trimester (either alone or in combination with laminaria stents). Hence, the present study was carried out to compare the effectiveness of 400 µg of misoprostol through three different routes i.e. vaginal, sublihgual and oral for first and second trimester abortion as per MTP act.

Methodology

The present study was planned in the Department of Obstetrics and Gynaecology, Darbhanga Medical College and Hospital from Jan 2017 to Sept 2017.Total 75 females with a period of gestation between 12 and 20 weeks scheduled to have pregnancy termination as per MTP Act were included in the study. The all enrolled females were divided in three equal study groups based on the administration route of Misoprostol. The Group I, II and III were administered with the Misoprostol 400 mcg at 4-hourly interval by Sublingual, Vaginal and Oral route. The misoprostol was administered with 400 mcg at 4-hourly interval up to a maximum of four doses each.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study. Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Females with 12–20 weeks of gestation; and single live intrauterine pregnancy as determined by last normal menstrual period, Ultrasound confirmed clinical examination. Exclusion Criteria: Females with pregnancy less than 12 weeks and more than 20 weeks, any indication of serious past or present illnesses, severe anemia, any contraindications to use of misoprostol.

Results & Discussion

The data from all the three study groups patients were collected and presented as below. Medical abortion is becoming more popular now days as a method of termination of pregnancy in second trimester because it is effective and technically less demanding when compared to surgical methods [9]. Prostaglandin analogs are the mainstay of drugs used for this purpose. Among them, misoprostol is the most commonly used one, as it is cheap and stable at room temperature. It has been shown to be effective for second trimester termination of pregnancy [10].

Table 1: Background parameters of study group patients

Parameters	Group I	Group II	Group III
Route of Administration	**Sublingual**	**Vaginal**	**Oral**
Total Cases	25	25	25
Age (years)	23 – 30	24 – 32	21 – 28
No. of women with previous delivery	21	20	23
No. of women with previous abortions	9	7	9
BMI (kg/m2)	21.2 – 23.9	20.7 – 23.8	21.2 - 24.6
Gestational age(weeks)	13 – 17	14 – 18	14 – 19

Table 2: Treatment outcomes of study group patients

Parameters	Group I	Group II	Group III
Route of Administration	**Sublingual**	**Vaginal**	**Oral**
Total Cases	25	25	25
Abortion/success rate	21	20	15
Complete abortion (No. of Cases)	15	16	12
Failure rate (No. of Cases)	2	3	5
Mean induction–abortion interval in hours(range)	5.5 -18.3	6.5 – 18.6	6.5 – 19.6
Patients requiring surgical intervention (No. of Cases)	8	6	8

Table 3: Side effects observed

Parameters	Group I	Group II	Group III
Route of Administration	**Sublingual**	**Vaginal**	**Oral**
Total Cases	25	25	25
Nausea	3	3	5
Vomiting	3	2	4
Diarrhoea	6	2	7
Chills	8	7	7
Fever	6	8	3
Significant vaginal bleeding	2	3	1

Table 4: Subjective assessment of comfort

Parameters	Group I	Group II	Group III
Route of Administration	**Sublingual**	**Vaginal**	**Oral**
Total Cases	25	25	25
Comfortable	23	10	25
Not comfortable	2	15	0

Misoprostol has been used to induce medical abortion by various routes of administration. Vaginal misoprostol has been shown to be more effective than oral misoprostol. However, evidence that absorption through the vaginal route is inconsistent and that the patients find vaginal administration uncomfortable has led to the sublingual route as an alternative. Oral misoprostol reaches a high peak concentration in blood very quickly before a rapid fall in plasma level. After vaginal administration there is gradual rise up to peak level and then a slow fall of level [11-15].

Earlier studies by various authors [10-15] comparing oral with vaginal administration with the dose regimes varying from 400-800 µg at 3-hourly to 8-hourly interval have reported the success rate on vaginal administration to be in range of 56.8-99.26%.The induction-abortion interval observed was shorter than that observed in the other studies using misoprostol by various routes or by combination of routes for second trimester termination of pregnancy.

Ho *et al.* [16] in 1997 conducted a comparative study between oral and vaginal administration and concluded that oral administration is convenient and more acceptable to women and Ngai *et al.* [17] showed that oral administration of 400 µg of misoprostol 3 h before VA is as effective as a similar regimen of vaginal misoprostol. However, administration of oral drug with water 3 h before operation may cause problems especially if the patient requires general anesthesia for SE [18]. These, clinical studies have shown that the vaginal route is superior to oral misoprostol in termination of first trimester pregnancies. Sublingual misoprostol in medical termination of pregnancy has been studied [16]. The buccal mucosa being very vascular and misoprostol tablet being soluble in water dissolves within 10-15 min of administration [18]. This route is convenient to use, avoids vaginal administration and the ingestion of water before anesthesia (in case needed). A pilot study has shown that sublingual misoprostol with or without mifepristone is useful in first-trimester medical abortions [19].

Helena *et al.* [20] demonstrated that repeated administration of 400 µg Misoprostol either vaginally or sublingually is an effective and acceptable option. However vaginal administration appears to produce better results among multiparous women, but more women had fever >38C in Vaginal route. Shah *et al.* [21] studied role of vaginal Misoprostol for second trimester termination. They found it is effective and time saving drug for second trimester abortion. 96.6% women aborted within 20 hours. Mean Induction abortion interval was 9.43 hours with very low drug related side effects. Milani *et al.* [22] reported similar results as in our study. Dickson *et al.* [23] studied Oral, Vaginal and sublingual Misoprostol for second trimester abortion. They found that Vaginal or sublingual Misoprostol administrated after vaginal loading dose in second trimester abortion with Mifepristone is associated with a shorter time to pregnancy termination compared with an oral regime

Recently, it has been shown that misoprostol can be administered sublingually. A pharmacokinetic study has shown that after a single dose of sublingual misoprostol, the peak concentration is achieved in a shorter time than with vaginal misoprostol. The peak concentration and bioavailability were also higher with sublingual administration. Therefore, it was postulated that sublingual route of administration might be the most effective route for administration of misoprostol by Tang *et al.* [24]

The present study has few limitations as it was not a placebo-controlled trial, the number of patients was relatively less, repeat dose versus single dose, and pharmacokinetic parameters while comparing three routes were not studied, which are highly warranted to establish the comparative results of the present study. It can be concluded that sublingual misoprostol is an effective and favourable cervical ripening agent for first trimester abortion as compared to vaginal and oral dosage forms.

Conclusion

The data generated from the present study concludes that Oral and sublingual routes of administration have shown to be more tolerable related to vaginal route of administration. But the effectiveness of oral administration is less. Thus, sublingual misoprostol has the advantage that it can evade

the uncomfortable vaginal administration. Also absorption of the drug may be affected when the patient starts bleeding.

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