Termination of Pregnancy in First Trimester - Medical Option

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Abstract

Background: The objective of this study was to confirm the effectiveness and safety of methotrexate and misoprostol or misoprostol alone for abortion up to 12 weeks of gestation.

Methods: A group of volunteer patients desiring MTP with gestations up to 84 days (12 weeks) were studied. The patients were divided into 2 groups. Group 1 patients with gestation up to 56 days were further subdivided as (a) Patients who received methotrexate 50 mg IM + misoprostol 800 gms intravaginal and (b) patients who only received 800 gms of misoprostol. Group 2 included the patients who were 8-12 weeks pregnant and they received same treatment as group 1 (b). Outcome measures assessed included successful abortion (complete abortion without need for surgery), side effects, decrease in hemoglobin and mean duration of vaginal bleeding.

Results: Complete abortion occurred in 36 (90%) of 40 patients in group 1 (a), 10 (67%) of 15 patients in group 1(b) and 29 (83%) of 35 patients in group 2. There were only 2 patients with clinically significant decrease in hemoglobin, but none required transfusions. Vaginal bleeding lasted 15 ± 6 days in group 1 (a), 16 ± 6 days in group 1(b) and 16 ± 5 days in group 2. All the patients stopped bleeding when endometrial thickness was ≤ 5 mm. Five percent women had stomatitis after methotrexate and 44% patients had fever with chills after misoprostol administration.

Conclusion: Considering the low cost and availability of methotrexate and misoprostol, these drugs constitute a good alternative for medical abortion. They are safe and effective.

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Key Words : Methotrexate; Misoprostol; MTP; Induced abortion

Introduction

Termination of pregnancy has been practiced since the time immemorial. Most widely used methods for terminating pregnancy in first trimester are surgical, primarily suction evacuation. An estimated 26 million pregnancies are terminated legally throughout the world, and 20 million are terminated illegally, with more than 78,000 deaths [1]. In India alone 10-12 million abortions take place annually, resulting in 15-20 thousand maternal deaths, mainly due to illegal abortions [2]. Non availability of trained medical help and the unwarranted secrecy surrounding the unwanted pregnancy often force women to go for illegal abortion which may be fatal at times. The availability of safe drugs for termination of pregnancy would be of great value to the patients and medical profession and may save many lives. A number of drugs, considered safe for termination of pregnancy, have been tried recently. Some like mifepristone are expensive and not so easily available. In this article we focused on trial of easily available and cheaper alternatives like misoprostol and methotrexate for termination of pregnancy. Methotrexate has long been

used for the treatment of ectopic pregnancy with excellent results. Its use for termination of intra-uterine pregnancy is the natural outcome. The Food and Drug Administration, USA has approved misoprostol for prevention of gastric ulcer disease with the warning that it may lead to abortion in pregnant patients. This particular side effect of the drug is now being used for therapeutic effect. This study has been undertaken to assess the efficacy and safety of misoprostol and methotrexate as abortifacient.

Material and Methods

This is a retrospective study of 90 patients who opted for non-surgical methods of MTP from Jan 2002 to Oct 2002. All the patients were ≤ 12 weeks (84 days) pregnant. The group 1 included patients having pregnancy ≤ 56 days (eight weeks) and the group 2-the patients with pregnancy 57 days to 84 days (8 weeks to 12 weeks). Informed consent was taken from all patients.

Treatment Protocol

Group 1

(a) Methotrexate + Misoprostol (patients who were not

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Table 1**Relation between type of medical regimen, gestational age and success rate**

Gestational age	Treatment regimen	No. of patients	Complete abortion No (%)	Patients needing D & E No (%)	On going pregnancy
56 days or less Group 1(a)	Methotrexate 50 mg IM + Misoprostol 800 g intra vaginal	40	36 (90)	4 (10)	Nil
56 days or less Group 1 (b)	Misoprostol 800 g intra vaginal	15	10 (67)	5 (33)	Nil
57 days to 84 days Group 2	Misoprostol 800 g intra vaginal	35	29 (83)	6 (17)	Nil

breast feeding the baby)

Day 1 - Hb, TLC, DLC, Blood Urea, LFT, USG (Ultrasound examination) for gestational age, Methotrexate 50 mg IM.

Day 4 - Misoprostol 800 g, intravaginal. Detained in the ward for two hours.

Day 7 - Hb, USG for complete / incomplete abortion, 2nd dose of misoprostol if required.

(b) Misoprostol alone (methotrexate was not given to the patients who were breast feeding the baby)

Day 1 - Hb, TLC DLC, USG for gestational age, misoprostol 800 gm intravaginal. Detained in the ward for two hours.

Day 4 - USG, 2nd dose of misoprostol if gestational sac present.

Day 7 - Hb, USG for complete / incomplete abortion.

The patients in group 1 were treated on OPD basis. The patients were advised to report to hospital in case of severe pain abdomen or severe bleeding per vaginum. They were also advised to call gynaecologist on phone for advise in case of any doubts.

Group 2 - same as group 1(b). All the patients in this group were hospitalized.

Hemoglobin (Hb) was also repeated at completion of abortion process if it took more than 7 days. Significant fall in Hb was defined as fall of Hb more than 2 gm%. Methotrexate was not given to lactating mother or the patients having liver or renal disease. Bronchial Asthma was the only contraindication for misoprostol therapy. Rh-negative patients who were unsensitized to Rh antibodies, were given Rh₀ (D) immune globulin 50 gm intramuscularly at the time of insertion of misoprostol. In case of excessive bleeding P/V due to incomplete abortion, suction evacuation was performed under sedation / general anaesthesia. Successful abortion was defined as a complete termination of pregnancy (Absence of gestational sac on USG) within seven days after the first or second administration of misoprostol. For each woman, we evaluated the amount and duration of vaginal bleeding, and the occurrence of nausea, vomiting, diarrhea or any other side effects after the administration of methotrexate or misoprostol.

Results

A total of 90 women underwent medical abortion. 75 of these women had successful abortion. Success rate varied with the type of regimen used and gestational age of the

Table 2**Induction abortion interval among the women with successful abortion**

*Introduction abortion interval in hours	Group 1(a) n=36	Group 1(b) n=10	Group n=29
< 6	12	2	10
6-12	14	4	14
12-24	6	1	2
25-72	1	Nil	Nil
3 days to 10 days	3	3	3

*From time of administration of 1st dose misoprostol to expulsion of products of conception

fetus (Table 1). 15 patients (17%) required additional surgical procedure for completion. In each of these 15 patients cervical dilation was not necessary up to insertion of 6 mm suction canula. USG examination in all four cases in group 1 (a) indicated an absence of further growth or crumpling of gestational sac, reduction in size of fetal pole, or disappearance of previously identified cardiac activity. After administration of misoprostol no patient had pain or vaginal bleeding in less than 2 hours. On the basis of patients report 72% in group 1 (a), 60% in group 1 (b) and 82% in group 2 aborted within 12 hours of administration of misoprostol (Table 2). This was later confirmed by USG. Only nine patients, three in each group required 2nd insertion of misoprostol. Table 3 indicates duration of bleeding. The duration of bleeding after abortion was quite variable and was difficult to quantify therefore divided in two groups-flow of blood like menstrual bleeding or spotting only. Only 2 patients one in group 1 (b) and one in group 2 had fall in Hb more than 2 gm% but none required blood transfusion. Table 4 shows side effects attributable to methotrexate and misoprostol. One patient had severe stomatitis and oral ulcers after giving methotrexate; the symptoms subsided after giving B complex for a week. 44% patients had fever ranging from 99-102°F within 2 hours of administration of misoprostol. All the patients were regularly monitored with USG. Some of the patients had collapsed and crumpled sac few days after administration of misoprostol which looked like thickened endometrium. It was observed that post-abortion bleeding completely stopped when endometrial thickness reduced to 5mm or less.

Discussion

Methotrexate and misoprostol are the drugs being

Table 3**Peri-abortion bleeding**

Group	Duration of bleeding	Duration of spotting	Total bleeding days mean $\pm$ SD	Fall in Hb > 2 gm% mean $\pm$ SD	Blood transfusion mean $\pm$ SD
Group 1 (a)	6 $\pm$ 4 days	8 $\pm$ 4	15 $\pm$ 6	Nil	Nil
Group 1 (b)	7 $\pm$ 5	7 $\pm$ 3	16 $\pm$ 6	1	Nil
Group 2	8 $\pm$ 3	7 $\pm$ 3	16 $\pm$ 5	1	Nil

Table 4**Side effects of drugs**

Side effects	Methotrexate No. of patients (%) n=4	Misoprostol No. of patients (%) n=90
Nausea	2 (5%)	2 (2.2%)
Vomiting	1 (2.5%)	2 (2.2%)
Stomatitis/oral ulcers	2 (5%)	Nil
TLC count <5000/cumm	Nil	Nil
Transient fever with chills	Nil	40 (44%)
Broncho spasm	Nil	Nil

increasingly used for termination of pregnancy. Methotrexate is a folic acid antagonist and is especially effective against trophoblast. Misoprostol is a synthetic prostaglandin E1 compound which acts by increasing the uterine contractions and softening the cervix. There are questions about risk of possible teratogenic effects related to misoprostol and methotrexate if pregnancy continues to 3rd trimester [3,4]. All the patients in our study were informed before the start of treatment about the possible harmful effects of the drugs on the fetus if they decide to continue pregnancy after administration of drugs. Therefore, no patient continued pregnancy after exposure to these drugs. In event of failure of drug treatment in certain patients, suction evacuation of uterus was done.

Methotrexate and misoprostol either in combination or alone have been tried with varying degree of success. Success rate varying from 84% to 96% has been reported with methotrexate and misoprostol combination for termination of pregnancy less than 56 days [5]. 90% success rate in our study in this group is in agreement with other studies. Caronell et al [6] reported 92% success with misoprostol alone in pregnancies less than 63 days, on the other hand Ozeren et al [7] reported only 58% success rate with misoprostol alone compared to 89% success rate with combination of methotrexate and misoprostol. Our success rate in this group (group 1 (b) was 63% comparable with later study. Complete abortion with misoprostol alone was higher when gestational age of the fetus was between 8-12 weeks (83%). Induction abortion interval was higher when misoprostol was used alone in pregnancies up to 56 days ($P > .05$). Majority of patients in group 1 (a) (72%), and

group 2(82%) aborted within 12 hours of administration of misoprostol compared to 60% in group 1 (b). It appears that misoprostol alone is more effective when gestational age of the fetus was more than 56 days. It is a known fact that the uterine sensitivity to misoprostol increases with gestational age of fetus. It is also seen in patients with term pregnancy where only 25 gm of the drug induced uterine contractions compared to 800 gm in early pregnancy [8].

There was no significant difference in duration of peri-abortion bleeding in any of the groups ($P > 0.1$). Most of the patients had some form of bleeding for about 2 weeks. Mean duration of bleeding varying between 11 $\pm$ 3 days to 17 $\pm$ 8 days have been reported in literature [1]. Majority of patients (97%) did not have any substantial fall in Hb, indicates that the procedure is safe as far as hemorrhage is concerned. Post abortion bleeding in absence of gestational sac in the uterus was one of the irritating problems of medical abortion. Some of the patients had collapsed and crumpled sac few days after administration of methotrexate or misoprostol which looked like thickened endometrium or decidua. It was observed that post-abortion bleeding completely stopped when endometrial thickness reduced to 5mm or less. The side effects of methotrexate were minimal and were limited to nausea, vomiting, stomatitis and oral ulcers. All these side effects were self limiting. Crenin et al [9] have also reported only 5% incidence of side effects in form of stomatitis and oral ulcers. Misoprostol was associated with higher incidence of side effects. The following incidence has been reported [1]-nausea 3-66 percent, vomiting 2-25 percent, diarrhea 3-52 percent and fever with chills 8-60 percent. Fever with chills within few hours after insertion of misoprostol was the most common side effect in our study. Symptomatic treatment in form of paracetamol was generally adequate. Diarrhea, one of the common side effect of prostaglandins, occurred in only 4.4% patients.

Medical treatment of pregnancy is acceptable to majority of women in both developed and developing country [10]. Among the women who had successful abortions with methotrexate and misoprostol, 90% said that they would prefer medical abortion to surgical abortion if facing the choice again. Women who refused the medical abortion did so because it required too much

time and too many visits to the hospital. It is natural to compare medical abortion with suction evacuation. Ashok et al [11] compared the two and found no significant difference in the success rate, though minor complications and bleeding days were more with medical abortion. Ours was not a comparative study but we do feel medical abortion is an effective option though it may not completely replace suction evacuation.

To conclude, medical termination of pregnancy with methotrexate and misoprostol is a safe, simple and effective approach. It permits greater privacy to the patients. A woman has the opportunity to make an unpressured and personal decision about unwanted pregnancy [12]. Wide spread use of medical abortion may reduce number of deaths due to traumatic illegal termination of pregnancies.

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