

# A retrospective study of the outcomes of second trimester pregnancy termination using vaginal misoprostol

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## Abstract

**Aim:** Misoprostol (Prostaglandin analogue) is the main method used for induction of abortion in the second trimester of pregnancy. The aim of this study was to assess the clinical outcomes and complications in women undergoing medical termination of pregnancy using vaginally administered misoprostol regimen.

**Methods:** One hundred and two consecutive women admitted to National University Hospital from 1st September 2005 to 31st August 2006 for medical termination with a gestational age ranging from 12+0 to 23+6 weeks of gestation were reviewed. Patients' characteristics, procedure outcomes and its complications were analyzed.

**Result:** A total of <80% of the patients aborted with one course of misoprostol (<24hours) which was comparable to other studies. The median initiation-to-abortion interval was about 12 hours. It was noted that 27.3% of the patient required evacuation of uterus to complete the abortion. There was no significant difference in treatment outcomes when taking maternal characteristics (eg parity, race, marital status, previous deliveries or medical problems) into consideration. The younger age group (<35years old) who were at an earlier gestation age (12 to 15+6weeks) are more likely to need evacuation of uterus to complete the termination. There appeared to be a longer initiation-abortion interval in those with fetal abnormalities. There was a high incidence of minor side-effects eg fever, pain and diarrhea in this misoprostol only regimen. But major complication eg blood transfusion or re-admission was rare.

**Conclusion:** Vaginally administered misoprostol only regimen is an effective and safe method for mid-trimester pregnancy termination. However, much could be done to reduce the abortion interval, rate of evacuation of uterus and the incidence of minor effects, and thus improved patients' satisfaction.

This research project was carried out in National University Hospital, department of obstetrics & gynaecology.

## INTRODUCTION

Various options exist for performing termination of pregnancy in the second trimester which include surgical dilation and evacuation, and medical induction of labor. Even in experienced hands, surgical evacuation is associated with significant rates of morbidity and mortality. In addition, the procedure requires specialized equipment and training. Thus, it has largely been given up by many centers.

Medical induction with prostaglandins has been recognized as a safe alternative to surgical termination of pregnancy. In fact, prostaglandins or their analogues have been used frequently as abortifacents for several decades (1,2).

Misoprostol (Cytotec, G.D. Searle and Co, Skokie) is a synthetic analogue of naturally occurring prostaglandin E1. It is marketed as an agent used for prophylaxis and treatment of gastroduodenal ulcers. Misoprostol is an effective and safe agent for cervical priming prior to surgical termination of pregnancy in the first trimester (3,4) and for labour induction at term (5,6). Several studies have also shown its efficacy for second trimester pregnancy termination (7,8,9). It is increasingly used in many countries because of the low cost, long shelf life and ease of storage and administration.

The purpose of this study is to report the effectiveness and safety of our hospital misoprostol regimen over one year period. The outcomes of this vaginally administered misoprostol regimen are examined, taking note of any significant complications of the procedure and side effects of

the medication.

## METHODOLOGY

One hundred and two consecutive women admitted to National University Hospital from 1<sup>st</sup> September 2005 to 31<sup>st</sup> August 2006 for pregnancy termination with a gestational age ranging from 12+0 to 23+6 weeks were studied. A database was developed to record the data of all women undergoing termination of pregnancy during this study period. All the terminations were performed under the conditions of the 1987 Singapore Abortion Act.

Ultrasound was performed for all the patients to determine the gestational age of the fetus. All patients were admitted to the hospital for the procedure, and the local protocol was followed: administering 400mcg doses of misoprostol vaginally, 3 hours apart, to a maximum of 5 doses. If abortion had not occurred by this time, the cycle was repeated 12 hours after the last dose of misoprostol. If the second cycle failed, then intra-amniotic injections of prostaglandins or repeat course of misoprostol was discussed with the women.

Analgesia (intramuscular pethidine 75mg 4 to 6 hourly) was given if required. Vomiting and diarrhea were healed with metoclopramide 10mg 8 hourly and codeine phosphate 30mg respectively.

The outcome of the procedure was measured by the interval from the administration of the drug to delivery of the foetus and/or placenta. Failure was defined as failure to expel the product of conception within 48hrs of starting the regimen. The expelled fetus and placenta were examined by the medical officer for completeness. Surgical evacuation of the uterus was carried out if there was clinical evidence of retained placenta tissue or suspicion of incomplete abortion. Side-effects including fever, pain (requiring analgesics), diarrhea and amount of vaginal bleeding were recorded.

The program SPSS version 13.0 for Windows was used for statistical analysis of continuous variables using the Mann–Whitney U test. Chi-square tests were used for the analysis of non-continuous variables. A  $p < 0.05$  was considered significant.

## RESULTS

### PATIENT CHARACTERISTICS

Table 1 shows the characteristics of the 102 women who underwent the pregnancy termination.

Majority of the patients are young, with a mean age of 25 years old. 74% of the patients are Malay. 65% (65/102) of the women are married with a mean parity of 1. And 61% (62/102) of them have previous vaginal deliveries. 45% (46/102) of the women have previous mid-trimester termination or surgical termination.

The median gestational age was 16 weeks. There was a higher proportion of termination due to fetal abnormalities (14%) as we are the regional referral centre. Although, almost all the terminations are for live fetuses, we have 2 cases of terminations due to early intra-uterine fetal demise.

**Figure 1**

Table 1

Characteristics	Total (N=102)
Parity	
-Nulliparous	40 (39.2%)
-Multiparous	62 (60.8%)
Median age in years (range)	25 years old (15-42)
Median gestational age in weeks (range)	16 (11 weeks to 24 weeks)
Race	
-Chinese	11
-Malay	74
-Indian	16
-Others	1
Number of women with previous vaginal deliveries	62 (60.8%)
Number of women with previous medical or surgical terminations	46 (45.0%)
Fetus	
Fetal abnormalities	14 (13.7%)
Status of fetus	
-Dead	2
-Alive	100

Characteristics of women who underwent mid-trimester pregnancy termination

### TREATMENT OUTCOMES

The treatment outcomes of the 95 women in this study were analyzed. 7 women were removed from analysis as they required 3<sup>rd</sup> course (3 women) of misoprostol or IAPG (4 women) to complete the abortion. 80% of the patients aborted within the 1<sup>st</sup> course of misoprostol ( $\leq 24$  hours). The median initiation-to-abortion interval is 12 hours (Range: 4 hours to 36 hours). It was noted that 27.3% (26/95) of the patient required evacuation of uterus to complete the abortion. There is no significant difference in treatment outcomes when taking maternal biodata (eg race, marital status, previous deliveries/terminations or medical problems) into consideration.

**Figure 2**

Age groups	Interval groups (n=95)		Require evacuation of uterus (n=26)	Statistical test
	<24hrs N=79	24-48hrs N=16		
15-24	39	7	9	No significant difference by Mann Whitney U test, p=0.235
25-34	35	6	14	
35-44	5	3	3	
<b>Gestational Age groups</b>				
12+0 to 15+6 weeks	28	8	14	No significant difference by Mann Whitney U test, p=0.134
16+0 to 19+6 weeks	23	6	7	
20+0 to 23+6 weeks	27	3	5	
<b>Parity</b>				
Nulliparous	32	6 (6/38=15.7%)	10 (10/38=26.3%)	No significant difference by Mann Whitney U test, p=0.977
Multiparous	47	10 (10/57=17.5%)	16 (16/57=28%)	
<b>Fetus status</b>				
Presence of FA (n=14)	10	4	2	

**MATERNAL AGE**

Following the administration of the first course of misoprostol, 79 (83%) patients aborted within 24hours. But a significant percentage of patients (20%) only aborted after 24 hours with the help of 2<sup>nd</sup> course of misoprostol. 26 patients out of 95 patients (27.3%) of the patients require evacuation of uterus to complete the abortion.

Interestingly, those (13/16=81%) who took a longer time to complete the abortion, and requiring evacuation of uterus, are in the younger age group (<35 years old)

**GESTATIONAL AGE**

The numbers in each of the gestational age group were evenly distributed. Most of the cases (14/26=54%) that require evacuation of uterus occur in the earlier (12+0 to 15+6 weeks) gestational age group.

**PARITY**

Multiparous women (28%) had a slightly higher incidence of surgical evacuation as compared to nulliparous women (26.3%). Initiation-to-abortion interval was shorter in multiparous than nulliparous. But both the incidence of surgical evacuation and the initiation-to-abortion were not statistically significant when taking parity into consideration.

**FETAL ABNORMALITIES**

There are 14 cases of termination that involved fetal abnormalities.

There appeared to be a trend of longer initiation-abortion

time (4/14=28.5% Vs 12/81=15% required >24hours), in those with fetal abnormalities. But the number is small to appreciate its significance.

There are only 2 cases of termination for early intra-uterine fetus demise. Both aborted within 24hours and did not require any surgical intervention.

**COMPLICATIONS**

Data on analgesic use and the side-effects of misoprostol such as fever and bleeding were recorded in all the 102 patients. (Table 2)

Almost 80% (82/102) will experience fever with a Tmax of 40 degrees with this misoprostol regimen. 53% (54/102) will require intra-muscular pethidine for pain relief. One patient has severe vaginal bleeding that requires blood transfusion.

There were 7 patients that did not abort after 2 courses of misoprostol regimen. They subsequently underwent 3<sup>rd</sup> course of misoprostol or intra-amniotic injection of prostaglandin that resulted in completion of the termination.

The average length of hospital stay was 3 days. 4 patients were re-admitted for problem of retained product of conception that required evacuation of uterus.

**Figure 3**

Table 2

Side-effects	N=102
Fever	82
Bleeding requiring transfusion	1
Analgesic use	54
Re-admission	4
Alternatives used eg IAPG	7 (4 IAPG, 3 required 3 <sup>rd</sup> course of misoprostol)

**DISCUSSION AND CONCLUSION**

The complete abortion rate (<24hours) for this study was 80%. This was comparable to previous studies using misoprostol only regimen. But the median initiation-abortion interval was about 12 hours, and this was longer than other earlier studies (average= 8 hours). This might be due to the fact that other studies used mifepristone or gemeprost prior to the initiation of misoprostol regimen. The uterus might have been primed by these pre-termination medication, thus was able to have a better response to the misoprostol. Use of pre-termination mifepristone/gemeprost probably served to shorten the initiation-abortion interval without affecting the complete abortion rate.

Our evacuation rate for this study was 27.3%. The range of evacuation rate quoted in the literature ranged from 5 – 80%.

This was probably due to the fact whether the diagnosis of retained POC was based upon on clinical grounds or ultrasound findings. We based our selection of cases for evacuation on the clinical grounds. Our rationale to perform evacuation of uterus was to avoid the potential risk of prolonged or major haemorrhage if any products of conception were retained.

In contrast to other reports, patient's biodata, for examples age, parity, and previous termination/deliveries seem to be poor predictors of the outcome of the termination in this study. Study by SE Goh (10) suggested that response from multiparous women was different from that of nulliparous women. However, in his study, he used mifepristone/misoprostol regimen, which was different from misoprostol only regimen. Although our study did not show any predictive value in the patient's biodata on the outcomes, we did achieve similar complete abortion rate (<24hours) as with other studies.

In this study, there appeared to be a higher evacuation rate if the termination is carried out in the early gestation (12 to 15+6 weeks). This was contrarily to the traditional belief that morbidity for termination is lower if it is carried out as early as possible. (7,8,9) The exact reason for this observation is unknown. One possible reason may be due to a higher response to the misoprostol at a later gestational age with the development of its receptors. (7,8)

As we are the tertiary centre in Singapore, we do get a higher number of referral for termination of fetal abnormalities. (11) This explained for the higher percentage of fetal abnormalities in this study. Again, there appeared to be a trend requiring longer initiation-abortion interval in this subgroup, although the complete abortion rate stayed the same. There was also no increase need for evacuation of uterus in this subgroup.

Minor side-effects eg fever and analgesic use were high in this study. This was probably due to the high dose of misoprostol (400mcg) used in this regimen. The dose of misoprostol could be reduced if there was additional priming prior to the start of termination.

Major complication eg transfusion or re-admission was rare in our study. This showed that misoprostol only regimen is safe, effective and non-invasive regimen for termination of

mid-trimester pregnancy. Mid-trimester pregnancy termination is an important problem in developing countries. If access to medical services and resources is limited, and skill and expertise to carry out safe dilatation and evacuation not available, the availability of a medical treatment such as misoprostol that do not incur a high cost in storage and transport makes provision of safe abortion feasible in the Third World countries.

The misoprostol only regimen described is a cost effective method for second trimester termination of pregnancy.

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