Outcome Analysis of Termination of Pregnancy in Second Trimester

Rijal H, Koirala P

Department of Obstetrics and Gynecology

Institute of Medicine,

Tribhuvan University Teaching Hospital,

Kathmandu, Nepal.

Corresponding Author

Hima Rijal

Department of Obstetrics and Gynecology

Institute of Medicine,

Tribhuvan University Teaching Hospital,

Kathmandu, Nepal.

E-mail: rizhima1234@gmail.com

Citation

Rijal H, Koirala P. Outcome Analysis of Termination of Pregnancy in Second Trimester. *Kathmandu Univ Med J.* 2023;83(3):315-9.

ABSTRACT

Background

Second-trimester abortions, constitute 10-15% of global annual abortions, leading to two-thirds of major abortion-related complications. Recognizing the elevated risk, the WHO recommends diverse methods for safe termination. Surgical and medical approaches, particularly using drugs like Mifepristone and Misoprostol, show promising success rates.

Objective

To analyze the outcomes of second-trimester termination using Mifepristone or PG analogues alone or in combination.

Method

This is a one-year retrospective study at Tribhuvan University Teaching Hospital analyzing second-trimester terminations, collecting data on demographics, medical history, period of gestation, doses of abotificient drugs, complications, and management.

Result

In a study of 66 second-trimester abortions, mean age was 28.8±4.96 years, gestational age 20.07±4.3 weeks. Mifepristone and Misoprostol combination succeeded in 66.7% of cases, while 42.2% required repeated Mifepristone doses. Misoprostol use was significantly higher in patients without medical comorbidities (p=0.018), but Mifepristone requirement didn't differ significantly based on medical conditions. Combined Mifepristone and Misoprostol were used more for fetal indications. Notably, the use of Mifepristone and Misoprostol didn't significantly differ for live and intrauterine fetal death cases.

Conclusion

Mifepristone and Misoprostol effectively terminate second-trimester pregnancies. In high-risk cases, cautious Prostaglandin use is crucial and Mifepristone alone, in divided doses, reduces complications with high success.

KEY WORDS

Abortion, Mifepristone, Misoprostrol, Second trimester, Termination

INTRODUCTION

Second trimester (13-28 weeks) is a critical period for(potential to be taken out) pregnancy termination due to significant changes in maternal and fetal physiology.[1] Second-trimester abortion is an important component of the comprehensive women's health care. About 10-15% of all induced abortions occur during the second trimester worldwide. Though the percentage of induced second-trimester abortion is low, its morbidity is higher than the first-trimester induced abortion. The abortion related mortality usually increases with the age of gestation. Overall, two thirds of all major complications of abortions are attributable to those performed in the second trimester.[2]

Besides various social, medical issues of women and fetal problems (deformed and not compatible to life), many a times various logistic and financial difficulties delays termination even after the decision to have it.[3] In addition, the stigma associated with second trimester abortion can cause further delay. These affect uneducated and underprivileged women threatening women health and life.[4] Different surgical and medical methods for abortion have been used since long. Introduction of prostaglandins and its analogues have increased the efficacy of medical methods of termination with lesser complications.[5]

Introductions of Prostaglandins and its analogues in medical abortion (MA) were made not so long. Further, Mifepristone was introduced for medical induced abortion since 1980s.[6-10] Medical abortion during early pregnancy was first approved in France in 1988. It was in 1999-2000 that both first and second trimester MA with Mifepristone and a Prostaglandins analogue were approved in many European countries.[11]

Mifepristone is an artificial steroid drug with anti-progesterone and anti-glucocorticoid actions. It affects the cervix and uterus favorably for termination and increases uterine sensitivity to Prostaglandins analogue.[12] Mifepristone, induces the labour by increasing the uterine contractility and the sensitivity of uterus to prostaglandins. Misoprostol, acts by softening and dilatation of the cevix.[13,14]

In Nepal, abortion was legalized in 2002 and since 2007 second trimester abortion services had been started with few specific indications. WHO and Royal Collage of Obstretrics and Gynaecology (RCOG) recommend pre-induction oral Mifepristone followed by Misoprostol (PG E1) 24-48 hours later, proving effective in shortening the induction to abortion interval.[15]

This protocol is considered as an effective regimen for second-trimester abortion with 91% efficacy within 24 hours of initiation of Misoprostol and with the lesser side effects than of Misoprostol alone.[3] Various time interval between administration of Mifepristone and Misoprostol is debated.[11] Maximal priming effects on the myometrium is achieved 36-48 hours after pre-treatment with Mifepristone.[16] About 0.2-0.4% of women had aborted with Mifepristone only.[17,18] While the dose of Mifepristone does not change, the dose of Misoprostol needs to be modified according to gestational age. Second trimester abortion is specially challenging in women with medical and surgical co-morbidities where one or the other drugs used for abortion should be used cautiously.

The aim of this study is to evaluate the outcome of second trimester terminations in women with/without comorbidities using regimens combining both the drugs that is highly effective and with the fewer side effects. In this study we have analyzed the demographic profile, total doses of drugs required, complications related to single agent or combination form among the subgroups based on parity, period of gestation, indications for abortion and co -morbidities.

METHODS

This was a descriptive retrospective type of study carried out in Department of Obstetrics and Gynecology, Tribhuvan University Teaching Hospital over the period of one year (January 2021 - January 2022). All data regarding terminations, with different maternal and fetal indications during the study period were collected from the record book of female surgical ward and patient file from hospital record section. The data were collected after the ethical clearance from Institute Research Committee. Women who had undergone pregnancy termination between 13 to 28 weeks period of gestation after admission, were included in the study. Termination of pregnancy performed beyond this period was excluded. Second trimester medical terminations were performed using Mifepristone and Misoprostol according to WHO recommendations. Mifepristone 200 mg followed by Misoprostol after 24-36 hours was given. However the women having multiple morbidities, medical termination was done with the use of Mifepristone only after the contraindications had been ruled out. The three repeated doses of Mifepristrone, 200 mg each at the interval of 24 hours were used. The patients who fail to expel were re-started with same doses and interval, failure to expel were managed with other methods such as mechanical methods or surgical evacuations. The following data such as age, parity, obstetrics history, medical and surgical history, period of gestation, method of induction a)medical-total dose of abortificent drugs used b) surgical c) mechanical methods, indication of termination, post-abortal complications, management of complications were recorded. The data were collected and entered into Microsoft excel and analyzed using statistical software SPSS 22. The descriptive statistics were mentioned using mean, frequencies and standard deviations. A p value < 0.05 was considered as statistical significance.

RESULTS

A total of 66 women had undergone termination in second trimester. The mean age was 28.8±4.96 (range=18-38) years. Mean gestational age for termination was 20.07±4.3 (13-28) weeks. Regarding parity, 66.6%(43) were multi-gravida, 34.8%(23) were primi-gravida

Table 1. Indication for Termination of Pregnancy

Indications	
Fetal	Maternal
46 (69.6%)	20 (30.3%)

Among the fetal indication, 37.8% (25) were for intra uterine fetal demise and 27.2% (18) had various fetal malformations. About 4.5% (3) had failed medical termination of pregnancy.

Table 2. Types of Fetal Malformation

Types of Fetal malformation	
Central Nervous System anomaly	6 (9%)
Cardiac/Lung Hypoplasia	5 (7.5%)
Renal anomaly	2 (3%)
Nasal Hypoplasia	2 (3%)
Musculoskeletal anomaly	1 (1.5%)
Fetal Hydrops	1 (1.5%)
Gastro Intestinal malformation	1 (1.5%)
Total	18 (27.2%)

The mean dose of Mifepristone was 370.2±274 mg (200 mg – 1400 mg), while the mean dose of Misoprostol was 379.2±366.5 mcg (50 mcg – 1600 mcg). Medical morbidities were found in 48.4% (32) women and 43.9% (29) had surgical comorbidities.

Mifepristone 200 mg or > 200 mg was used in 53.03% (35) patients with previous cesarean section and 33.3% (22) patients without previous cesarean section. In late second trimester, 47.7% (38) received single or repeated dose of Mifepristone.

Table 3. Maternal Indications for Terminations

Maternal Indications for terminations	
Per Vaginal Leak	6 (9%)
Antepartum Hemorrhage	3 (4.5%)
Connective tissue disorder	2 (3%)
Mental Health	2 (3%)
Malignancy	1 (1.5%)
Hepatitis	1 (1.5%)
Stroke	1 (1.5%)
Severe Preeclampsia with renal Impairment	1 (1.5%)
Total	20 (30.30%)

Table 4. Drugs Used

Drug Used	Fetal Indications	Maternal Indications	P value
Mifepristone Only	6	6	
Misoprostol Only	2	6	
Both	38	6	<0.05
Syntocinon High dose	0	2	

No correlation was found with individual abortificient drug Mifepristone and Misoprostol in patients with previous cesarean section, period of gestation and presence of any co morbidities (p value < 0.05).

Twenty-three percentage of patients (15) had post-abortion complications. Hysterotomy was required in 3.03% (2) for excessive per vaginal bleed pre-expulsion. Post termination PPH occurred in two of these patients and was managed medically in one while, the other required balloon tamponade. Retained product of conceptus was seen in 16.6% (11) and was managed with manual vacuum aspiration.

One patient with acute kidney injury under dialysis had medical termination with Mifepristone alone after 72 hours of intake. Seven percentage (4) out of total were admitted in Intensive Care Unit after termination due to their associated pre-existing morbidities.

Mifepristrol and Misoprostrol combination was successful in majority of patients (66.7%) for termination, while, 42.2% required repeated dose of Mifepristone.

Misoprostol was required in significantly higher number patients without medical comorbidities (p =0.018) while Mifepristone requirement was not significantly different among the patients with or without medical comorbidities.

Combined Mifepristone and Misoprostol were given in significantly higher number of patients with fetal indications compared to maternal indications. However, the use of Mifepristone and Misoprostol was not significantly different for live fetuses and Intra uterine fetal death.

DISCUSSION

Choosing the appropriate method for termination of pregnancy which is safe as well as accessible, is considered essential in women's health management.[3] The medical termination of pregnancy using Mifepristone and Prostaglandins and its analogues are effective abortificient drugs for clinical use and are gaining popularity due to their easy accessibility and safety.

For medical termination of pregnancy, comparative studies between 200 mg and 600 mg of Mifepristone in combination with 400 µg Misoprostol orally have found a slightly higher risk of continuing pregnancies with the 200 mg dose.[19]

Lievre et al. have compared 200 mg and 600 mg Mifepristone in combination with Prostaglandins for medical termination of pregnancy and concluded similar rates of complete abortion, however the substitution of 600 mg with 200 mg was likely to have chance of continuing pregnancy.[20] Contradicting to this report, in this present study we found no cases of pregnancy continuations despite single or repeated doses of Mifepristone. In addition to that, there were no differences in adverse events between different doses of Mifepristone or Prostraglandins.[20]

Use of combination of Mifepristone and Misoprostol were successful in terminating significantly higher number of women with fetal indications, however there was no significant difference ($p < 0.05$) in requirements of abortificents between live and intra uterine fetal death termination (IUFD). Few descriptive studies have reported a shorter time until delivery and lower required doses of Misoprostrol to obtain successful deliveries in cases of IUFD compared with live fetus.[21,22]

Mifepristone alone had expelled IUFD in about 60% of women within 72 hours following the first intake without use of Prostraglandins.[19] Cabrol et al. did a double-blind placebo controlled multicentric study in women with IUFD using Mifepristone 200 mg three times a day, to induce labour.[23] They found that labour occurred in 63% patients in the Mifepristone group compared to only 17.4% in the placebo group ($p < 0.001$). This study had 8% patients whose labour was induced only with Mifepristone, which may be due to different time interval protocol followed between use of Mifepristone and Prostraglandins for labour induction. Besides priming, with of single dose Mifepristone 200 mg, using repeated doses of Mifepristone, 600 mg in divided doses also can induce labour and had safe delivery without use of PGs where it is imprudent, such as in certain medical co morbidities or scarred uterus.[24]

Lelaidier et al. conducted a trial using Mifepristone 200 mg on day 1 and 2, to induce labour in women with previous cesarean section and found safe and efficient for induction in women with previous cesarean section.[25] Onset of labour occurred in 69% of patients in Mifepristone group compared to only 12% in placebo group ($p < 0.01$). However, in our study, 24% women with previous one cesarean section were successfully induced with combinations out of which 18% had received repeated dose of Mifepristone followed by Misoprostrol.

Goh et al. in their study, reported that combination of 200 mg Mifepristone and vaginally administered Misoprostol in early second trimester, with 97.9% and 99.5% aborting within 24 and 36 h, respectively.[26]

In this study, 21% of women had medical morbidities and Mifepristone had been used in more women for labour induction, though not statistically significant. And Misoprostrol was used in significantly higher number of patients without medical comorbidities ($p = 0.018$). Regarding the repetition of Mifepristrone, RCOG recommends the repetition of Mifepristone 200 mg same dose if the initial Mifepristone-Misoprostrol fail to induce labourl.[27] In present study, 42.42% delivered with repeated doses of Mifepristone followed by Misoprostrol.

The caesarean section rate is increasing globally. Ruptured uterus had been reported to occur with Misoprostol, with or without priming by Mifepristone.[28-30] The risk of uterine rupture among women with a prior cesarean delivery undergoing second-trimester abortion using only Misoprostol is reported to be around 0.3%.[31] The incidence of uterine rupture in women without previous scar is estimated to be 0.1-0.2% in the second trimester of pregnancy using Mifepristone.[32,33]

Dickinson et al. reported that patient with previous cesarean section had increased risk of uterine rupture with Misoprostrol use. In contrast, Arora et al. in their study used Mifepristone 200 mg orally, maximum six doses over a duration of 48 hours in women with IUFD in scarred uterus during second trimester. Patient were monitored and subsequent dose of drug was omitted if sufficient uterine contractions or improvement of Bishop score and further augmented with oxytocin wherever required. Spontaneous labour occurred in 74.3% women while operative (cesarean/ hysterotomy) delivery occurred in 17.9%. And the conclusion was that Mifepristone was found to be advantageous over prostaglandins and oxytocin, especially when oxytocics are contraindicated (i.e., scarred uterus). Thus, Mifepristone only regimen is quite safe and effective, inducing spontaneous labor in scarred uterus.[35]

However, no cases of ruptured uterus have been reported in the study, here as 85% cases had been induced with lower effective dose of Misoprostrol following Mifepristone and 42% had labour induction with repeated doses of Mifepristone. Thus, supporting the Mifepristone as effective in softening and dilating cervix and initiating induction of labour. It is noteworthy that dose of Misoprostol necessary to induce abortion was lower with pre-treatment and repeated doses of Mifepristone. However, comparison of our data with those published elsewhere is difficult because protocols varies widely with regard to administration mode, type and dosage.

This study's limitation is its small sample size, potentially limiting the generalizability of findings.

CONCLUSION

Both Mifepristrone and Misoprostrol have shown to be effective for termination of pregnancy during second trimester. In high-risk cases with medical or surgical morbidities, cautious use of Prostaglandin is essential. Administering Mifepristone alone or in divided doses is found to be effective, reducing complications and achieving a high success rate.

REFERENCES

1. Konar H. DC Dutta's Textbook of Obstetrics. 9th ed. Chapter 4.
2. Medical methods for termination of pregnancy. Geneva: World Health Organization; 1997 (WHO Technical Report Series No. 871)
3. The American College of Obstetricians and Gynecologists Women's Health Care Physicians Practice Bulletin Clinical Management Guidelines for Obstetrician-Gynecologists. Number 135. June 2013. Reaffirmed 2019.
4. Nepal Ministry of Health, National Safe Abortion Policy, Kathmandu, Nepal: Ministry of Health, 2002. http://www.mohp.gov.np/pdf/policy/National
5. Bygdeman M. The use of prostaglandins and their analogues for abortion. *Clin Obstet Gynaecol.* 1984 Dec;11(3):573-84. PMID: 6391777.
6. Silvestre L, Dubois C, Renault M, Rezvani Y, Baulieu EE, Ulmann A. Voluntary interruption of pregnancy with mifepristone (RU 486) and a prostaglandin analogue. A large-scale French experience. *N Engl J Med.* 1990 Mar 8;322(10):645-8. doi: 10.1056/NEJM199003083221001. PMID: 2304490.
7. Gottlieb C, Bygdeman M. The use of antiprogestin (RU 486) for termination of second trimester pregnancy. *Acta Obstet Gynecol Scand*. 1991;70(3):199-203. doi: 10.3109/00016349109006210. PMID: 1927296.
8. Bygdeman M, Swahn ML. Progesterone receptor blockage. Effect on uterine contractility and early pregnancy. *Contraception*. 1985 Jul;32(1):45-51.
9. Swahn ML, Bygdeman M. The effect of the antiprogestin RU 486 on uterine contractility and sensitivity to prostaglandin and oxytocin. *Br J Obstet Gynaecol*. 1988;95(2):126-34.
10. Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion. Evidence-based Clinical Guideline Number 7, 1997. revised edition Nov 2011.
11. Gemzell-Danielsson K, Lalitkumar S. Second trimester medical abortion with mifepristone-misoprostol and misoprostol alone: a review of methods and management. *Reprod Health Matters.* 2008 May;16(31 Suppl):162-72. doi: 10.1016/S0968-8080(08)31371-8. PMID: 18772097.
12. Sun Y, Fang M, Davies H, Hu Z. Mifepristone: a potential clinical agent based on its anti-progesterone and anti-glucocorticoid properties. *Gynecol Endocrinol.* 2014 Mar;30(3):169-73. doi: 10.3109/09513590.2013.856410. Epub 2013 Nov 11. PMID: 24205903.
13. Tang OS, Gemzell-Danielsson K, Ho PC. Misoprostol: Pharmacokinetic profiles, effects on the uterus and side-effects. *Int J Gynaecol Obstet.* 2007;99(Suppl 2):160-7.
14. Ho PC, Ngai SW, Liu KL, Wong GCY, Lee SWH. Vaginal misoprostol compared with oral misoprostol in termination of second-trimester pregnancy. *Obstet Gynecol*. 1997 Nov;90(5):735-73.
15. Thong KJ, Baird DT. A study of gemeprost alone, Dilapan, or mifepristone in combination with gemeprost for the termination of second-trimester pregnancy. *Contraception.* 1992;46:11-17
16. Heikinheimo O, Suhonen S, Haukkamaa M. One- and 2-day mifepristone-misoprostol intervals are both effective in medical termination of second-trimester pregnancy. *Reprod Biomed Online*. 2004;8(2):236-9.
17. Baird T, Castleman L, Hyman A et al. Clinicians' guide for second trimester abortion, 2nd ed. Chapel Hill, NC:Ipas;2007.
18. Tang OS, Thong KJ, Baird DT. Second trimester medical abortion with mifepristone and gemeprost: a review of 956 cases. *Contraception*. 2001 Jul;64(1):29-32.
19. New Zealand's abortion laws and regulations." Published in New Zealand Gazette on August 31, 2001. Available at: https//www.medsafe.govt.nz
20. Lièvre M, Sitruk-Ware R. Meta-analysis of 200 or 600 mg mifepristone in association with two prostaglandins for termination of early pregnancy. *Contraception.* 2009 Jul;80(1):95-100. doi: 10.1016/j.contraception.2009.01.011. Epub 2009 Mar 17. PMID: 19501223.
21. Dodd J, O'Brien L, Coffey J. Misoprostol for second and third trimester termination of pregnancy: a review of practice at Women's and Children's Hospital, Adelaide, Australia. *Aust N Z J Obstet Gynaecol.* 2005;45(1):25-9.
22. Srisomboon J Ponpisuttinum S. Efficacy of intracervicovaginal Misoprostrol in second trimester pregnancy termination :a comparison between and dead fetus. *J Obstet Gynecol*. 1998;24(1):1-5.
23. Cabrol D, Dubois C, Cronje H, Gonnet JM, Guillot M, Maria B. Induction of labor with mifepristone (RU 486) in intrauterine fetal death. *Am J Obstet Gynecol*. 1990;163(2):540-2.
24. Wildschut H, Both MI, Medema S, Thomee E, Wildhagen MF, Kapp N. Medical methods for mid-trimester termination of pregnancy. *Cochrane Database Syst Rev.* 2011 Jan 19;2011(1):CD005216. doi: 10.1002/14651858.CD005216.pub2. PMID: 21249669; PMCID: PMC8557267.
25. Lelaidier C, Baton C, Benifla JL, Fernandez H, Bourget P, Frydman R. Mifepristone for labour induction after previous caesarean section. *Int J Obstet Gynaecol*. 1994;101(6):501-3.
26. Goh SE, Thong KJ. Induction of second trimester abortion (12-20 weeks) with mifepristone and misoprostol: a review of 386 consecutive cases. *Contraception.* 2006 May;73(5):516-9. doi: 10.1016/j.contraception.2005.12.004. Epub 2006 Feb 23. PMID: 16627037.
27. Ashok PW, Templeton A, Wagaarachchi PT, Flett MMG. Midtrimester medical termination of pregnancy: a review of 1002 consecutive cases. *Contraception*. 2004;69(1):51-8.
28. Norman JE. Uterine rupture during therapeutic abortion in the second trimester using mifepristone and prostaglandin. Br J Obstet Gynaecol. 1995;102(4):332-3.
29. Chen M, Shih JC, Chiu WT, Hsieh FJ. Separation of cesarean scar during second-trimester intravaginal misoprostol abortion. *Obstet Gynecol*. 1999 Nov;94(5 Part 2):840.
30. Wiener JJ, Evans AS. Uterine rupture in midtrimester abortion. A complication of gemeprost vaginal pessaries and oxytocin. Case report. *Br J Obstet Gynaecol.* 1990;97(11):1061-62.
31. Goyal V. Uterine rupture in second-trimester misoprostol-induced abortion after cesarean delivery: a systematic review. *Obstet Gynecol.* 2009 May;113(5):1117-1123. doi: 10.1097/AOG.0b013e31819dbfe2.
32. Royal College of Obstetricians and Gynaecologists. The Care of Women Requesting Induced Abortion. Guidelines No. 7. London, 2004.
33. Atienza MF, Burkman RT, King TM. Midtrimester abortion induced by hyperosmolar urea and prostaglandin F2 alpha in patients with previous cesarean section: clinical course and potential for uterine rupture. *Am J Obstet Gynecol*. 1980;138(1):55-9.
34. Nayki U, Taner CE, Mizrak T, Nayki C, Derin G. Uterine Rupture during Second Trimester Abortion with Misoprostol. *Fetal Diagn Ther.* 2005;20(5):469–471. https://doi.org/10.1159/000087115.
35. Arora R, Patel BPD, Dabral A, Sachdeva M, Arya P. Use of Mifepristone for termination of intrauterine fetal demise in previously scarred uterus in the later half of pregnancy. *Int J Reprod Contracept Obstet Gynaecol*. 2018 Jul;7(7):2668-2671