JOURNAL OF PHARMACEUTICAL AND BIOMEDICAL SCIENCES

Sharma N, Jhanwar A. **To Study The Effect Of Mifepristone-Misoprostol Combination For First Trimester Abortion In Cases With Previously Scarred Uterus.** *J Pharm Biomed Sci* 2014;04(11):930-935.

Journal of Pharmaceutical and Biomedical Sciences (***J Pharm Biomed Sci.***), **Member journal. Committee of Publication ethics (COPE) and Journal donation project (JDP).**

JPBMS
Journal of Pharmaceutical and Biomedical Sciences

ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

Original article

To Study The Effect Of Mifepristone-Misoprostol Combination For First Trimester Abortion In Cases With Previously Scarred Uterus

Neelam Sharma[1,*], Anshul Jhanwar[2]

Affiliation:-
[1]Assistant Professor, Department of Obstetrics & Gynecology, Jhalawar medical college, Jhalawar, Rajasthan, India
[2]Assistant Professor, Department of Pharmacology, Jhalawar medical college, Jhalawar, Rajasthan, India

The name of the department(s) and institution(s) to which the work should be attributed:
Department of Obstetrics & Gynecology, J.L.N. medical college, Ajmer, Rajasthan, India

Address reprint requests to
Dr. Anshul Jhanwar.
III/2,Doctor's residence, Medical College Campus, Jhalawar, Rajasthan, India (Pin-326001) or at dranshul123@gmail.com

Article citation:
Sharma N, Jhanwar A. **To study the effect of Mifepristone-Misoprostol combination for first trimester abortion in cases with previously scarred uterus.** *J Pharm Biomed Sci* 2014; 04(08):930-935. Available at www.jpbms.info

ABSTRACT

Introduction: In India to deal with unwanted pregnancy in the scarred uterus is thorny situation, since the caesarian section rate is increasing. Although most widely used method for terminating pregnancy is dilatation and evacuation but it increases morbidity and mortality by causing uterine perforation, serious hemorrhage and shock. Therefore medical abortion offers an advantageous alternative to surgical abortion.

Material and methods: Total one hundred and fifty patients were selected for the present prospective study and were divided randomly into two equal groups after fulfilling the inclusion and exclusion criteria. Both groups were given 200 mg Mifepristone followed by 800 µg Misoprostol after 48 hours. Group 1 consist of patients with previously scarred uterus. Group 2 consisted of patients with previously non-scarred uterus.

Results: Mean period of gestation in group 1 was 43.48 days and in group 2 was 43.81 days. Mean gravidity in group 1 was 3.24 and in group 2 was 3.17.Mean parity in group 1 was 2.2 while in group 2 was 2.14.Efficacy of procedure which was determined by the number of complete abortions in the group (92% in group 1 and 93.3% in group2.Minor side effects were seen in 21 % patients of group 1 as compared to 28% in group 2.

Conclusion: Both the groups who underwent medical abortion with mifepristone-misoprostol combination were found to be comparable in terms of efficacy, safety and acceptability for termination of pregnancy of gestational age upto 49 days.

KEYWORDS: Mifepristone, Misoprostol, Scarred uterus, Lower segment cesarean section.

INTRODUCTION

In recent year, the cesarean section rate is increasing gradually in almost all countries of world, which leads to one of the long term problem in dealing with unwanted pregnancies[1]. During the same time period termination of pregnancy has also become more common procedure due to intensive development of medicine and increasing demand for such procedures. Consequently, a specific group of patients has emerged, namely those with a

PBMS
Journal of Pharmaceutical and Biomedical Sciences
ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

previous uterine scar who require termination of pregnancy[2]. Worldwide an estimated 26 million pregnancies are terminated legally each year, and 20 million are terminated illegally with more than 78 thousands deaths[3]. Although most widely used method for terminating pregnancy is dilatation and evacuation but it increases morbidity and mortality by causing uterine perforation, serious hemorrhage and shock[4]. Therefore medical abortion offers an advantageous alternative to surgical abortion. More than 3 million women worldwide had medical abortion in past decade alone[5]. Medical abortion regime using Mifepristone and Misoprostol are highly effective and safe protocol without having any surgical intervention and anaesthesia hazards and have been widely used for termination of early pregnancy, especially in France, China and several other countries[6,7].

As to pregnant women with scarred uterus however the published data's about safety and efficacy of such medical abortion still remains few upto now. It was thought earlier that this kind of abortion regimen is contra-indicated for cicatrical uterus but there is no evidence in experimental and clinical research to confirm this[8].

Moreover medical termination of pregnancy in early gestational period ≤ 49 days is more preferable for the patient as it maintains the privacy and convenience of the patient as well as it alleviates the anxiety for surgical intervention and reduces hospital stay. In previously scarred uterus the use of medical abortion regimen could avoid severe complications such as uterine perforation,cervical laceration and other physical and psychological trauma which are caused by surgical termination of pregnancy[9].

Mifepristone along with misoprostol offers a safe and acceptable non surgical alternative to women seeking early pregnancy termination Mifepristone, synthetic antiprogesterone is used to competitively block the effects of progesterone and weaken the attachment of an early pregnancy on the endometrium[10-12]. Misoprostol a synthetic prostaglandin used 36–48 hours after Mifepristone to induce cervical softening, dilatation and utrine contractions to assist the expulsion of products of conception[13].

AIMS AND OBJECTIVES

- To compare the abortificient outcome of medical abortion in previously scarred and non-scarred uterus in termination of early pregnancy (≤ 49 days).
- To study the efficacy, safety of medical abortion in termination of early pregnancy (≤ 49 days) in previously scarred uterus.

MATERIAL AND METHODS

The present prospective study was carried out in department of Gynaecology and Obstetrics of J.L.N. Medical College and Associated group of hospitals, Ajmer from March 2009 to November 2010.

Total one hundred and fifty patients were selected for the prospective study and were divided randomly into two equal groups after fulfilling the inclusion and exclusion criteria. Both groups were given 200 mg Mifepristone followed by 800 µg Misoprostol after 48 hours. Group 1 consist of patients with previously scarred uterus. Group 2 consisted of patients with previously non-scarred uterus.

The study was approved by the Medical Ethical Committee of J.L.N. Medical College, Ajmer. The study was performed in accordance with Good Clinical Practice (GCP) guidelines. All patients provided written informed consent prior to any study-related procedures.

INCLUSION CRITERIA[14]

- Early pregnancy of ≤ 49 days with confirmed dates and regular menstrual cycle (28-33 days)
- Patients who are not sure of her menstrual dates, had conceived in lactational amenorrhoea or within 3 month of discontinuation of oral contraceptive pills or where there is disparity between menstrual dates and pelvic findings the pregnancy was confirmed and accurately dated by TVS.
- Routine positive urine hCG presented.
- The size of uterus on pelvic examination is compatible with the estimated duration of conception.
- Routine transabdominal USG confirming uterine pregnancy.

EXCLUSION CRITERIA[15]

- Suspected ectopic pregnancy/undiagnosed adnexal mass.
- Inherited porphyrias.
- Known coagulopathy or concurrent anticoagulant therapy.
- Contraindication to use of Mifepristone including chronic systemic corticosteroid administration or adrenal disease.
- Pregnancy > 49 days.
- Hemoglobin < 8 gm%.

PBMS
ournal of Pharmaceutical and Biomedical Sciences
ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

- Uncontrolled hypertension with blood pressure > 160/100 mm of Hg.
- Severe cardiovascular or renal diseases.
- Pelvic infections.
- Uncontrolled seizure disorder.

METHODOLOGY

Before starting the abortificient medication, a detailed history was taken with emphasis on menstrual history, last menstrual period, period of gestation and obstetric history specially regarding first and last lower segment cesarean section (LSCS), or any other surgeries like myomectomy. All patients were subjected to detailed general physical and systemic examination followed by complete gynecological examination.

First visit (Day 1)

- A careful history and examination and informed written consent was obtained.
- Tab. Mifepristone 200 mg was administered orally.
- Anti-D (50µgm) given to Rh negative patient with pregnancy > 6 weeks.

Second visit (Day 3)

- History of any bleeding or side effect should be noted.
- Vaginal Misoprostol 800 µgm was given and then patient was observed for 4 hours.
- The time of start of bleeding and expulsion of products is to be noted by the patient.
- During this time patient had hourly pulse, blood pressure, temperature charting.
- Patients were observed for any passage of products of conception, excessive bleeding per vaginum, any signs of drug reaction, flushing, nausea, vomiting, diarrhea, cramps, and fever.
- Patient was instructed to take adequate rest and abstain from intercourse for 15 days.

Third visit (Day 4)

- Patient was advised transabdominal USG to check the integrity of previous uterine scar and find out the completeness of abortion.
- A repeat dose of Misoprostol 800 µgm was inserted per vaginally if there was no bleeding PV even after 24 hours of 1st day or the USG shows presence of retained product of conceptus(RPOC's).
- Patients were observed for passage of products of conception or excessive bleeding per vaginum.

Fourth visit (Day 14)

- A clinical history regarding postabortal fever, duration and amount of bleeding p.v., passage of products of conception, pain abdomen.
- USG was required if the history and examination do not confirm expulsions of products of conception and whose day 4 USG showed presence of RPOC's or presence of gestational sac.
- Patient has informed that her next periods may be delayed but she should come for check up if she doesn't get period in 6weeks.

Follow up and post abortion contraception counselling.

- Contraception should be offered to all patient seeking medical abortion.
- Oral combined pills or DMPA can be started on Day 15 after the abortion process appears to be complete.
- Copper-T must be inserted after one normal period.
- Condom should be used otherwise abstinence is preferred.

RESULTS

Mean age in group 1 was 28.86 year and Group 2 was found to be 28.13 as shown in Table 1.

Table 1.Age groups of patients.

Age(years)	Study Group (Group I) Number	%	Control Group (Group II) Number	%
20 – 24	11	14.6	13	17.3
25 – 29	37	49.3	37	49.3
30 – 34	19	25.3	18	24
> 34	8	10.6	7	9.3
Total	75	100	75	100

Mean period of gestation in group 1 was 43.48 days and in group 2 was 43.81 days as shown in Table 2. Mean gravidity in group 1 was 3.24 and in group 2 was 3.17 (Table 3). Mean parity in group 1 was 2.2 while in group 2 was found to be 2.14 (Table 4). Efficacy of procedure which was determined by the number of complete abortions in the group (92% in group 1 and 93.3% in group 2 shown in Table 5. Minor side effects were seen in 21 % patients of group 1 as compared to 28% in group 2) as shown in Table 6. There were no incidences of major complication like myocardial complication, stroke, bronchoconstriction in the

PBMS
ournal of Pharmaceutical and Biomedical Sciences
ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

entire study. The mean fall in hemoglobin in group 1 and group 2 was 0.29gm% and 0.19gm% respectively. Acceptability of both groups was judged on the basis of five parameters i.e. discomfort, anxiety, amount of bleeding, length of bleeding and overall satisfaction which was found to be comparable in both groups.

Table 1.Age groups of patients.

Age (years)	Study Group (Group I)		Control Group (Group II)	
	Number	%	Number	%
20 – 24	11	14.6	13	17.3
25 – 29	37	49.3	37	49.3
30 – 34	19	25.3	18	24
> 34	8	10.6	7	9.3
Total	75	100	75	100

Table 2.Period of gestation in days.

Period of Gestation(days)	Study Group (Group I)		Control Group (Group II)	
	Number	%	Number	%
< 40 days	20	26.6	19	25.3
41 – 45	25	33.3	26	34.6
46 – 49	30	40	30	40
Total	75	100	75	100

Table 3.Gravidity of patients.

Gravidity	Study Group (Group I)		Control Group (Group II)	
	Number	00	Number	%
Primigravida	00	24	02	2.6
2nd gravida	18	42.6	18	24
3rd gravida	32	20	30	40
4th gravida	15	13.3	15	20
5th gravida	10	100	10	13.3
Total	75	00	75	100

Table 4.Parity of patients.

Parity	Study Group (Group I)		Control Group (Group II)	
	Number	%	Number	%
Nullipara	00	00	02	2.6
Primipara	20	26.6	18	24
Second Para	30	40	32	42.6
Third para	15	20	13	17.3
Fourth para	10	13.3	10	13.3
Total	75	100	75	100

PBMS
ournal of Pharmaceutical and Biomedical Sciences
ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

Table 5.Efficacy of medical termination of pregnancy.

Efficacy	Study Group (Group I)		Control Group (Group II)	
	Number	%	Number	%
Complete Abortion	69	92	70	93.3
Incomplete Abortion	5	6.6	4	5.33
Failed Abortion	1	1.3	1	1.3
Total	75	100	75	100

Table 6.Incidence of minor complications.

S.No.	Complications	Study Group (Group I)		Control Group (Group II)	
		Number	%	Number	%
1	Nausea	12	16	14	18.6
2	Vomiting	4	5.3	6	8
3	Diarrhea	4	5.3	5	6.6
4	Fever	2	2.6	2	2.6
5	Headache	7	9.3	8	10.6
6	Flushing	5	6.6	4	5.3
7	Pain requiring oral analgesics	8	10.6	10	13.3
8	Pain requiring parentral analgesics	Nil	Nil	Nil	Nil

DISCUSSION

The mean age in study group was comparable to that in study conducted by WHO task force (2000) where the mean age of patients was 27.3 years. The mean gestational age for the study conducted by JXU, H.Chen et al. in 2016 on 192 patients with 35 patients of previous scarred and 157 patients with previous non-scarred uterus was comparable to our present study.

In 1991, Norman et al. reported enhanced uterine activity after the administration of Misoprostol, a prostaglandin E1 analogue alone or in combination with mifepristone.

El Refaey et al. (1995) conducted a study in United Kingdom where the oral route of Misoprostol was compared with its vaginal administration in terms of efficacy and side effects. The subjects were 270 women who were seeking abortion within 63 days of onset of. They were given 600 mg of mifepristone followed 48 hrs later by misoprostol 800 µg either vaginally or orally and kept under observation for 4 hrs. They were asked to come for follows up after 14 days. The entire therapy ended in complete abortion in 87% of women who received oral misoprostol and 95% of women who received vaginal misoprostol.

The role of misoprostol in inducing abortion in previous cesarean section its safety & efficacy was studied in a descriptive study conducted by Razia Iftikhar at the Department of Obstetrics & gynaecology, Baqrai Medical University and private clinics, from January, 2007 to January, 2009. Fifty patients were selected for the study having previous caesarean section for the termination of pregnancy having nonviable pregnancy between 14–20 weeks gestation, an embryonic gestation (Slighted ovum) and fetal anomalies. All pregnant women of gestational age > 24 wks, hypersensitivity to prostaglandin, those with the history of bronchial asthma, were excluded. They received 400 µgm of misoprostol tablets moistened with 2 – 4 days of water intravaginally. Effectiveness was determined by the number of women who expelled fetus/product of conception without the need for surgical

PBMS
ournal of Pharmaceutical and Biomedical Sciences
ISSN NO- 2230 – 7885
CODEN JPBSCT
NLM Title: J Pharm Biomed Sci.

intervention in a previously scarred uterus. Patients in the study group underwent termination of pregnancy for missed abortion (n 32), foetal anomaly (n 14) and foetal demise (n 4). The median induction abortion interval was 16 hours (range 10–21 hours). They found misoprostol to be safe in their cases of post caesarean women and there was no case of scar rupture or dehiscence, hemorrhage and shock.

CONCLUSION

1.Both the groups who underwent medical abortion with mifepristone-misoprostol combination were found to be comparable in terms of efficacy, safety and acceptability for termination of pregnancy of gestational age upto 49 days.
2.Patients undergoing medical abortion with previously scarred uterus experienced minor bleeding that was comparable in duration as well as amount to patient with previous non-scarred uterus.
3. The efficacy of medical abortion was not affected by previous number of LSCS and none of the patients were found to have disruption of scar.
4. No medical emergency was encountered which required immediate surgical intervention or blood transfusion.

Thus early medical abortion with Mifepristone-Misoprostol combination represents an important new method in previous scarred uterus patients having unwanted pregnancy. These regimens offer the prospect of a more private, less intrusive form of abortion that is both safe and effective.

REFERENCES

1.Norman JE et al. Uterine contractility and induction of abortion in early pregnancy by misoprostol and mifepristone. Lancet 1991; 338:1233-1236.
2.Abraham Debby et al. Mid trimester abortion in patients with a previous uterine scar. European Journal of Obst & Gyne 2003.
3.Maitre SC,Bouchard P,Spitz IM .Medical termination of pregnancy.N Engl.J Med 2000;342:946-56.
4.Wu Y,Medical progress in China-Family planning.Natl Med J China 1995;75(12):749-75.
5.Creinin MD. Medical abortion regimens. Historical contest and overview. Am J Obstet & Gynecol 2000; 183:53-59.
6.Belfort P,Pinotti JA,Eskes Tkab.Fertility,sterility and contraception. Caterton Hall, Carnforth, UK: The Parthenon Publishing Group.1989; 28-31.
7.Bygdeman M. Termination of pregnancy upto 8 or 9 weeks-Modern methods of inducing abortion. Black-well science:Oxford;1995:39-53
8.Sun H,Wu S,Xu H et. Al.The potential of Ru 486 for medical termination of pregnancy: An acceptability and feasibility study. J Repro Med (China). 1995; 4(3):749-75.
9.Coyaji K,Etul B,Krishna U,Otiv S, Ambardekar S,Bopardikar A: Mifepristone abortion outside the urban research hospital setting in India.Lancet,2001;357:120-22.
10.Brogden RN, Goa KL, Faulds D. Mifepristone: A review of its pharmacodynamic and pharmacokinetic properties, and therapeutic potential. Drugs 1993; 45:384-409.
11.Renee M, Hart S. Mifepristone: Annuals of pharmacotherapy 2001;35:707-15.
12.Robbins A,Spitz IM. Mifepristone clinical pharmacology. Clin Obstet Gynecol 1996;39:436-50.
13.Berghella V,Airoldi J. Misoprostol for first trimester pregnancy termination in women with prior cesarean;a systemic review. BJOG;May 2009.
14.Muhammad Fawzy. Mid trimester abortion using vaginal misoprostol for women with 3 or more prior cesarean deliveries. JJOG 2010 March.
15.Premila W,Prabath T. Factors affecting outcome of early medical abortion: A review of 4132 consecutive cases; BJOG: Nov 2002;109:1281-89.
16.J Xu, Chen H. Termination of early pregnancy in scarred uterus with mifepristone and misoprostol. IJOG.72 (2001):245-51.

Competing interest / Conflict of interest

The author(s) have no competing interests for financial support, publication of this research, patients and royalties through this collaborative research. All authors were equally involved in discussed research work. There is no financial conflict with the subject matter discussed in the manuscript.

Disclosure forms provided by the authors are available with the full text of this article at jpbms.info