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A COMPARATIVE STUDY OF COMBINATION OF MIFEPRISTONE WITH MISOPROSTOL OR MISOPROSTOL ALONE IN SECOND TRIMESTER ABORTION.

Medical Science

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ABSTRACT

INTRODUCTION : Over millions of pregnancies occur each year, approximately 210 million, out of this 22 % (i.e.,) 46 million are terminated by induced abortion

Although 'medications have been used to induce abortion for centuries, over the last five decades researchers developed safe and effective methods of medication based pregnancy termination.

Although a majority of abortions are done in early pregnancy, there is still an increasing need for mid trimester abortion. This is because of delay in the diagnosis of congenital anomalies, delay to recognize an unwanted pregnancy, financial difficulties in obtaining abortion services.

The Mifepristone-Misoprostol combination reduces the interval between induction and abortion significantly, side effects are lesser, with reduced misoprostol dose requirement. Therefore, wherever possible Mifepristone-Misoprostol combination regimen should be used. Routine post abortal curretage should be reduced.Comparative study of Mifepristone-Misoprostol combination and Misoprostol alone in second trimester abortion.

MATERIALS AND METHODS : This is the Comparative study of Mifepristone-Misoprostol combination and Misoprostol alone in second trimester abortion.

Data for the comparative study will be collected from labour ward and out -patient clinics of Govt. Raja Mirasuclhar Hospital, Thanjavur over a period of 10 months (October 2013 to July 2014)

Sample size was 100 pregnant women and divided in to two group A and B

Group A: 50 pregnant women were given 200mg of mifepristone Followed by vaginal Misoprostol 4001ncg alter 36h.rsfollowed by400rncg every 3hrs to a maximum of four doses.

Group B: 50 pregnant were women given 400n1cg of vaginal Misoprostol repeated every 3hrs up to five doses.

Intravenous antibiotics were administered to all patients after instilling Vaginal Misoprostol. Check ultrasonogram was done post abortion in both the group. Injection Anti-D immunoglobulin was administered to all patients with Rh negative blood within 72hrs of expulsion.

Patients selected for study by subjecting to

- History taking - age, parity, socioeconomic status, period of amenorrhoea, mode of delivery in previous pregnancy, marital history, menstrual history, history of any medical illness.
- General physical examination - pallor, pedal eodema
- Systemic examination - pulse rate, blood pressure, cardio vascular system examination, respiratory system examination.
- Per abdomen examination – for size of the uterus.
- Per speculum examination - to note any cervical lesions or bleeding through os.
- Per vaginal examination - for size of the uterus.
- Other Investigations

In both the groups, before repeating misoprostol, subjects were enquired about onset of painful contractions, vaginal bleeding or side-effects if any, and per vaginal examination done to note cervical dilatation.

After expulsion of products of conception, examination done to note if any excessive bleeding per vaginum is there, USG done to note for emptiness of uterine cavity.

OBSERVATIONS AND RESULTS

Inn this study, the mean age of the patients in combination regimen was 25.8yrs, the youngest was 19 yrs and the oldest was 35 yrs. The Mean age of patients in Misoprostal alone regimen was 26.7yrs, the youngest was 19 yrs and the oldest was 36yrs. In our study the maximum percentage of patient were in the age range of 21 to 25 yrs.

In our study there was a uniform distribution in parity between Mifepristone - Misoprosto1 group and Misoprostol alone group, most patients were multigravida. The mean gestational age in the Misoprostol alone group was @ l6.19wks the lowest was 13wks and the maximum was 20 wks. The mean gestational age in the combination group was l6.51wks the lowest was l4wks and the maximum was 20 wks.

Regarding distribution of gestational age among patients 56 of 100 patients were in the gestational age range of 13 to 16 weeks, 44of 100 patients were in the gestational age range of 16.1 to 20weeks.In the misoprostol alone group, majority of the patients 31 out of 50 were in 68 the gestational age range of 13m 16 wks.

In the combination group, 25 out of 50 in the gestational age of 13to l6wks and 25 were in gestational age of 16.1 to20 weeks. majority of the case were patients who needed and requested MTP in view of failed contraception and social causes, followed by patients with congenital anomalies and maternal conditions warranting termination of pregnancy. 72% and 40% of the patients did not have any side effects in the combination group and misoprostol alone group respectively. 28% (14 Patients) of the patients in the mifepristone - misoprostol group experienced side effects, the most common was abdominal cramps 28% (14) followed by nausea and chills. 60% (30) of the patients in the misoprostol alone group experienced side effects, the most common side effect was nausea 32.9% (25), followed by abdominal cramps l3.2.(l0), vomiting 11.8% (9), chills 6.6%, fever 5.3% and iarrhoea 3.9%. Overall the most common side effect in both the regimen was nausea.

The second most common was abdominal cramps, No grave complications like uterine rupture or maternal mortality were observed in both the groups. Complete abortion was achieved in 98% (49) of the patients in Mifepristone - Misoprostol group, one case (2%) ended in hysterotomy(failure). Complete abortion was achieved in 88% (44) of the patients in the misoprostol alone group, six cases (12%) required post abortal curettage for excessive bleeding per vaginum, or for USG evidence of retained products. Over all, complete abortion was achieved in 93 patients in our study.

CONCLUSION : The incidence of second trimester abortion has reduced significantly following PNDT act. But when the condition is not favourable (i.e) hazardous to the life of either the fetus or mother, the benefit of termination of pregnancy outweighs the risk of continuing pregnancy. This procedure is not only painful, but also has psychological impact. It is the obstetricians concern to reduce this stressful period to the shortest peiod as possible.

This study of pretreatment of mifepristone before misoprostol in second trimester medical abortion, offers a reliable, safe method with reduced interval between induction and abortion.

For medical second trimester termination termination of pregnancy, pre-treatment with oral mifepristone 200mg prior to vaginal misoprostol provides a non-invasive effective regimen with significantly reduced induction to expulsion interval, lesser side effects and good patient compliance.

KEYWORDS:

abortion, mifepristone, misoprostol

INTRODUCTION

Abortion is defined as 'Lennination of pregnancy by any means before the fetus is 'viable'. [1]Viability is now considered to be reached at 23-24 weeks of gestation. Second trimester, or mid trimester, is a period ranging from 13-28 weeks of gestation, which again is subdivided into an early period between 13 and 20 weeks and a late period between 20 and 28 weeks.

Over millions of pregnancies occur each year, approximately 210 million, out of this 22 % (i.e.,) 46 million are terminated by induced abortion (AlanGuttmacher Institute, 2009).[2,3]Though safe methods of contraception are available, abortion rate is high, especially in developing countries. Factors contributing to high incidence of unwanted pregnancies are lack of access to health facilities, lack of knowledge of effective contraceptive methods, high cost of certain contraceptives, incorrect usage of contraceptives and no method is 100 % effective.

Although 'medications have been used to induce abortion for centuries, over the last five decades researchers developed safe and effective methods of medication based pregnancy termination.

Although a majority of abortions are done in early pregnancy, there is still an increasing need for mid trimester abortion. This is because of delay in the diagnosis of congenital anomalies, delay to recognize an unwanted pregnancy, financial difficulties in obtaining abortion services.

In 1999 it was published by FIGO, [4,5]recommendations for induction of abortion. Those recommendations are "after proper counselling, a women has right to have access to medical or surgical methods for induced abortion and the health care services have an obligation to provide such services as safely as possible". The Technical and policy guidance on safe abortion was published in 2003 by World Health Organisation. The recommendations given by FIGO, WHO were supported by RCOG.

The MTP Act was approved in 197l, in Indian Parliament, came into force from April 1970, (From 1980 in Jammu and Kashmir), (Lakshadweep Union Territory has still a restrictive abortion law). [6,7]

The MTP act permits the termination of pregnancy up to 20wks, for a broad range of social and medical reasons :-

I) When pregnancy endangers life of the woman
ii) When continuing pregnancy affects physical health
iii) When continuing pregnancy affects mental health
iv) To terminate a pregnancy resulting from rape or incest.
v) Fetal impairment
vi) Contraceptive failure (UN 1993)

- Termination of pregnancy should be carried out by registered medical practitioners in approved places (Mathai 1998).
- For second trimester termination of pregnancy, opinion from two registered Medical Practitioners is necessary.
- Women must give consent prior to performing abortion. In the case of minors (Age < l8Yrs) and mentally retarded, written consent of guardian is necessary (UN 1993). [8,9]
- Safe abortions continue to be difficult to access. Illegal abortions (8.9%) continue to contribute to high maternal mortality rate (407 / 100000 live births, 2009).
- Two third of major complications related to abortion is contributed by second trimester abortion. For the past l0yrs, medical termination for second trimester of pregnancy has been made more accessible and safe.
- It is recommended that MTP, should be done in places where blood bank is functioning and emergency operative theatre is available. The major drawback for older methods was longer hospital stay and necessity of post abortal curettage. From l980s **MIFEPRISTONE** came into usage which improved medical methods of termination of pregnancy.

Now, the **MIFEPRISTONE-MISOPROSTOL** combination is considered as effective and safe for second trimester abortion. According to WHO, RCOG, the Mifepristone-Misoprostol combination reduces the interval between induction and abortion significantly, side effects are lesser, with reduced misoprostol dose requirement. Therefore, wherever possible Mifepristone-Misoprostol combination regimen should be used. Routine post abortal curretage should be reduced.

- In post caesarean pregnancy, termination should be done cautiously.
- Premedication antibiotics should be given at the time of induction with vaginal misoprostol.
- When needed, suitable analgesic shall be given.
- Advice regarding the contraceptive methods should be given and implemented.

Maternal indications:

Maternal conditions that may be considered as medical indication for an abortion include: renal failure, diabetic retinopathy, sickle cell disease, cardiac disease, neoplasia, and psychiatric problem. A cardiac anomaly with potentially greater mortality is the Eisenmenger syndrome with pulmonary hypertension, severe valvular stenosis. Other medical indications include intrauterine infections, chorioamnionitis and preterm premature rupture of membranes. Radiation, chemotherapy and live virus immunisation given inadvertently in early pregnancy are other reasons to opt for abortion.

Fetal indications:

Despite progress in prenatal diagnosis, most anomalies have to be terminated selectively. At present, fetal indications for induced abortion include those anatomic conditions [10,11] incompatible with life (e.g.anencephaly) and major congenital abnormalities (e.g.hypoplastic left heart, severe neural tube defects).

MATERIALS AND METHODS

Objectives of the study:

Comparative study of Mifepristone-Misoprostol combination and Misoprostol alone in second trimester abortion.

I) To compare the efficacy and safety of two regimens
ii) To study the induction to expulsion interval
iii) To study the completeness of abortion achieved in both

regimens.
iv) To study the dose of misoprostol requirement in both regimen for expulsion.

Aim of the study
To find a regimen combining the lowest doses of both drugs, that is highly effective, has 'fewer side effects, acceptable for women, with lesser induction to expulsion interval

Source of data:
Data for the study was collected from patients attending the outpatient clinic of the Department of Obstetrics and Gynecology Govt. Raja Mirasudhar Hospital, Thanjavur who needed MTP.

Method of Collection:
Data for the comparative study will be collected from labour ward and out -patient clinics of Govt. Raja Mirasuclhar Hospital, Thanjavur over a period of 10 months (October 2013 to July 2014)

- Sample size-100 pregnant women
- Group A: 50 pregnant women were given 200mg of mifepristone Followed by vaginal Misoprostol 4001ncg alter 36h.rsfollowed by400rncg every 3hrs to a maximum of four doses.
- Group B: 50 pregnant were women given 400n1cg of vaginal Misoprostol repeated every 3hrs up to five doses.
- Intravenous antibiotics were administered to all patients after instilling Vaginal Misoprostol.
- Check ultrasonogram was done post abortion in both the group.
- Injection Anti-D immunoglobulin was administered to all patients with Rh negative blood within 72hrs of expulsion.

Post abortal evacuation:
- surgical evacuation was not done as a routine.
- was performed only if there was evidence of incomplete abortion.
- If placenta is not expelled in 30 min, an infusion of 10 units of oxytocin in 500ml of NS is started, 1 - 2ml/min.
- After expulsion, placenta examined to see if any cotyledon is missing, if so post abortal curettage was done.
- After a period of l hr observation if placenta is not delivered even after oxytocin infusion or if the women bleeds excessively, surgical evacuation was carried out.
- After abortion, women were observed for at least 4hrs, with close monitoring of Vitals and the amount of bleeding per vaginum. If bleeding is excessive, speculum examination done to rule out lacerations of cervix and lower genital tract, surgical evacuation was considered to remove retained products of conception if any.

Selection of patients:
Patients selected for study by subjecting to

- History taking - age, parity, socioeconomic status, period of amenorrhoea, mode of delivery in previous pregnancy, marital history, menstrual history, history of any medical illness.
- General physical examination - pallor, pedalodema
- Systemic examination - pulse rate, blood pressure, cardio vascular system examination, respiratory system examination.
- Per abdomen examination – for size of the uterus.
- Per speculum examination - to note any cervical lesions or bleeding through os.
- Per vaginal examination - for size of the uterus.
- Investigations

- Hb%
- BT, CT
- Blood grouping
- PPTCT test
- Urine routine
- USG for gestational age, congenital a11omalies, fetal viability.

Inclusion Criteria:
All pregnant females between 12-20wks who needs Medical Termination of Pregnancy (Satisfying the criteria of MTP act, 1971, revised guidelines).

Exclusion criteria:
- Suspected ectopic pregnancy
- Previous history of sensitivity to prostaglandin and Mifepristone
- Patients with leaking or bleeding per Vaginum.
- HB < 8 g % (MTP done after anaemia correction)
- Presence of an intrauterine device.
- Medical conditions contraindicating the use of Mifepristone (adrenal disease)
- Medical conditions contraindicating the use of Misoprostol (eg. glaucoma, sickle cell anaemia)
- A history or evidence of Thromboembolism. Proper counselling done, advice regarding contraception given and written consent form obtained prior to starting the treatment.

During study, all subjects were given information about the study, informed consent was obtained, following which they were admitted in labour ward. Thorough history and clinical examination were done. Investigations including USG were done. In both the groups, before repeating misoprostol, subjects were enquired about onset of painful contractions, vaginal bleeding or side-effects if any, and per vaginal examination done to note cervical dilatation.

After expulsion of products of conception, examination done to note if any excessive bleeding per vaginum is there, USG done to note for emptiness of uterine cavity.

STATISTICAL TOOLS:
The information collected regarding all the selected cases were recorded in a Master Chart. Data analysis was done with the help of computer using **EPIDEMIOLOGICAL INFORMATION PACKAGE (EPI 2010)** developed by Centre for Disease Control.

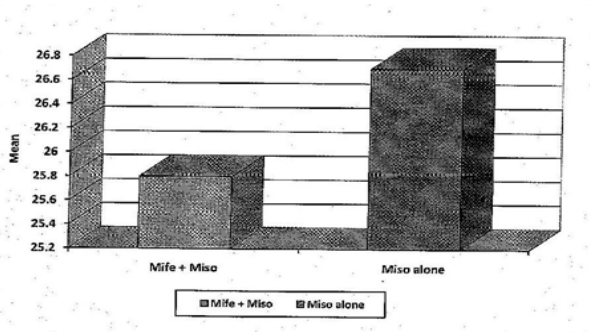
Using this software - range, frequency, percentage, mean, standard deviation, chi square and 'p' value were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATIONS AND RESULTS
Study Design
A comparative study to determine the efficacy of Mifepristone - Misoprostol combination over Misoprostol alone in the medical termination of second trimester pregnancy.

TABLE IA: Mean age distribution of Patients studied

Group	N	Mean age	Std Deviation	Minimum	Maximum
Mife +Miso	50	25.8	5.1	19	35
Miso alone	50	26.7	4.4	19	36

Graph 1A: Mean age distribution of the study group.

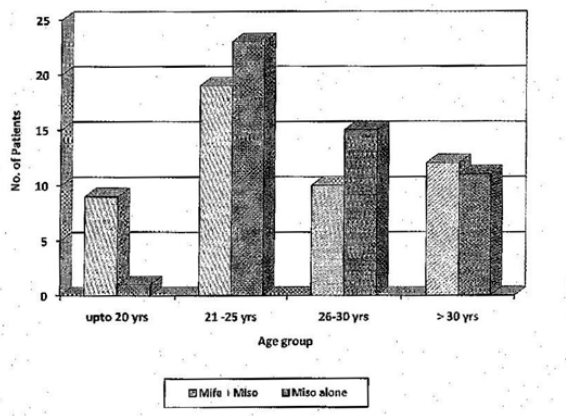


- The mean age of the patients in combination regimen was 25.8yrs, the youngest was 19 yrs and the oldest was 35 yrs.
- The Mean age of patients in Misoprostal alone regimen was 26.7yrs, the youngest was 19 yrs and the oldest was 36yrs.

Table 1B: Age distribution of the study group

Age Group	Mife + Miso		Miso alone	
	No	%	No	%
Upto 20 yrs	9	18	1	2
21 -35	19	38	23	46
26-30	10	20	15	30
>30 yrs	12	24	11	22
Total	50	100	50	100
Range	18-35 yrs		19-36 yrs	
Mean	25.8 yrs		26.7 yrs	
SD	5.1 yrs		4.4 yrs	
P	0.308 Not Significant			

Graph 1B: Age distribution of the study group.

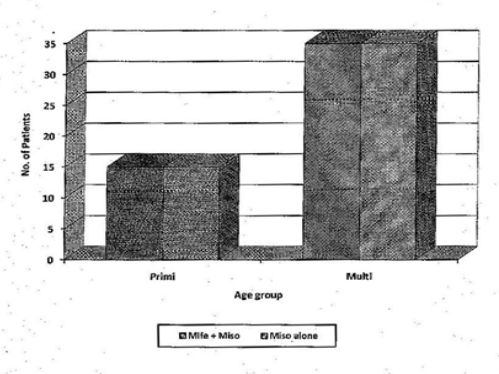


- In our study the maximum percentage of patient were in the age range of 21 to 25 yrs.

Table 2: Parity distribution of the study group

Gravidity	Miso + Mife	Miso alone	Total
Primi	15	15	30
	50%	50%	100%
Multi	35	35	70
	50%	50%	100%
Total	50	50	100
	50%	50%	100%

Graph 2: Distribution of the gravidity among the study group.

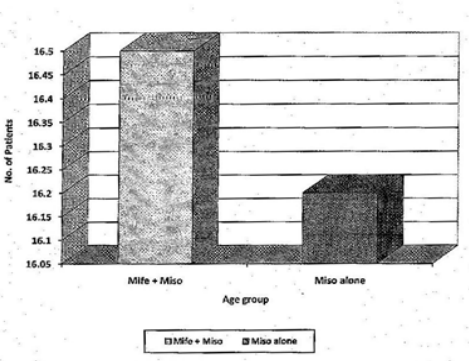


In our study there was a uniform distribution in parity between Mifepristone - Misoprosto1 group and Misoprostol alone group, most patients were multigravida.

Table 3A: Mean Gestational age in the study

Group	N	Mean GA	SD	Min	Max
Mife + Miso	50	16.510	1.4124	14.0	20.0
Miso alone	50	16.190	1.8039	13.0	20.0
Total	100	16.350	1.6198	13.0	20.2

Graph: 3A Mean Gestational age in the study

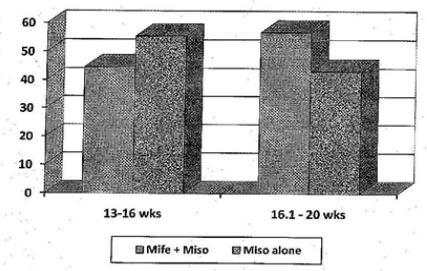


- In our study the mean gestational age in the Misoprostol alone group was @ l6.19wks the lowest was 13wks and the maximum was 20 wks.
- In our study the mean gestational age in the combination group was l6.51wks the lowest was l4wks and the maximum was 20 wks.

Table 3B: Distribution of Gestational age in the study

GA	Group		Total
	Mife + Miso	Miso alone	
13-16 wks	25	31	56
	44.6%	55.4%	100%
16.1 – 20 wks	25	19	44
	56.8%	43.2%	100%
Total	50	50	100
	50%	50%	100%
S.D	1.4124	1.839	
P	0.267 Not Significant		

Graph 3B: Distribution of Gestational age in the study



- In our study, regarding distribution of gestational age among patients 56 of 100 patients were in the gestational age range of 13 to 16 weeks, 44of 100 patients were in the gestational age range of 16.1 to 20weeks.
- In the misoprostol alone group, majority of the patients 31 out of 50 were in 68 the gestational age range of 13m 16 wks.
- In the combination group, 25 out of 50 in the gestational age of 13to l6wks and 25 were in gestational age of 16.1 to20 weeks.

Table 4: Indication for abortion according to etiology.

Indication	Mife + Miso	Miso alone
MTP Request	21	15
Severe pre eclampsia	3	2
Severe oligo	4	11
Fetal anomalies	17	13

PPROM	2	7
Maternal infections	1	1
NIHF	2	1

- In our study, majority of the case were patients who needed and requested MTP in view of failed contraception and social causes, followed by patients with congenital anomalies and maternal conditions warranting termination of pregnancy.

Graph4: Indication for abortions according to etiology.

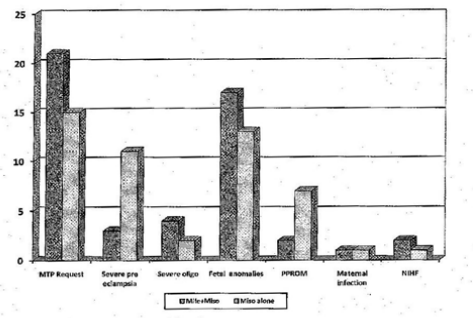


Table 5 : Risk Factors

Risk Factors	Mife + Miso Group		Miso group alone	
	No	%	No	%
Previous LSCS	11	22	5	10
Pregest DM	3	6	3	6
GDM	5	10	2	4
Hypothyroid	7	14	2	4
Hyperthyroid	0	0	1	2
Previous anomalous baby	0	0	2	4
Chronic HTN	1	2	2	4
ARF	0	0	1	2
Anaemia	1	2	0	0
Acute Spinal Injury	1	2	0	0
Cases with risk factors	29	58	18	36
Case with no risk factors	21	42	32	64

Graph 5: Risk Factors:

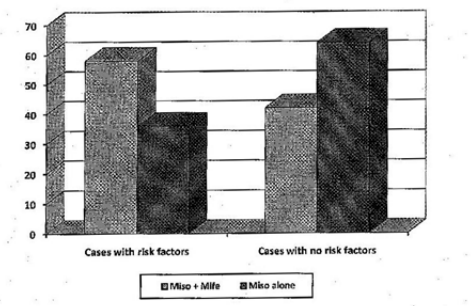


Table 6A: Side effect profile in the two regimens

Side effect	Group		Total
	Mife + Miso	Miso alone	
Abdominal cramps	14	10	24
Chills	4	5	9
Nausea	7	25	32
Diarrhoea	0	3	3
Fever	0	4	4
Vomiting	2	9	11
No side effect	36	20	56

Table 6B: Side effect profile in the two regimens

GA	Group		Total
	Mife + Miso	Miso alone	
0	36	20	56
	72.0%	40.0%	56.0%
1	3	13	16
	6.0%	26.0%	16.0%
2	9	8	17
	18%	16%	170%
3	2	9	11
	4%	18%	11%
Total	50	50	100
	100%	100%	100%

- In our study, 72% and 40% of the patients did not have any side effects in the combination group and misoprostol alone group respectively.
- 28% (14 Patients) of the patients in the mifepristone - misoprostol group experienced side effects, the most common was abdominal cramps 28% (14) followed by nausea and chills.
- 60% (30) of the patients in the misoprostol alone group experienced side effects, the most common side effect was nausea 32.9% (25), followed by abdominal cramps l3.2.(l0), vomiting 11.8% (9), chills 6.6%, fever 5.3% and diarrhoea 3.9%.
- Overall the most common side effect in both the regimen was nausea. The second most common was abdominal cramps,
- No grave complications like uterine rupture or maternal mortality were observed in both the groups.
- Complete abortion was achieved in 98% (49) of the patients in Mifepristone - Misoprostol group, one case (2%) ended in hysterotomy(failure).
- Complete abortion was achieved in 88% (44) of the patients in the misoprostol alone group, six cases (12%) required post abortal curettage for excessive bleeding per vaginum, or for USG evidence of retained products.
- Over all, complete abortion was achieved in 93 patients in our study.

Table 6: Side effect profile in the two regimens

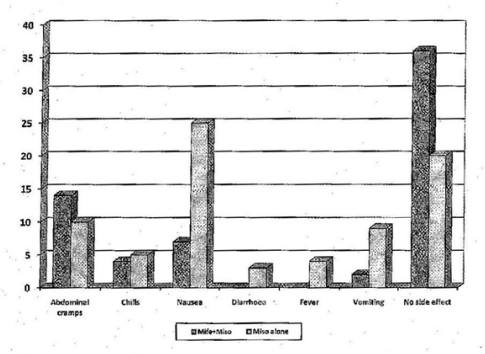


Table 7: Final outcome in our study.

Outcome	Group		Total
	Mife + Miso	Miso alone	
Complete Abortion	49	44	93
	98%	88%	93%
Failure	1	6	7
	2.0%	12.0%	7.0%
Total	50	50	100
	100%	100%	100%

Outcome:

1. Successful:

Complete expulsion of products of conception, without need for surgical intervention.

- History of onset of bleeding and expulsion of products of conception.
- USG done shows evidence of empty uterus with no retained products.
- No surgical intervention required.

2. Unsuccessful:

- Incomplete abortion-USG shows evidence of retained products.
- If placenta is not expelled in 2hrs, requiring post abortal curettage.

3. Failure:

- No response after administering 2000mcg misoprostol.
- Alternate methods needed to intervene.

4. Induction to expulsion(abortion)interval:

Defined us the interval from prostaglandin administration to expulsion of products of conception.

Graph 7: Distribution of outcome among study group.

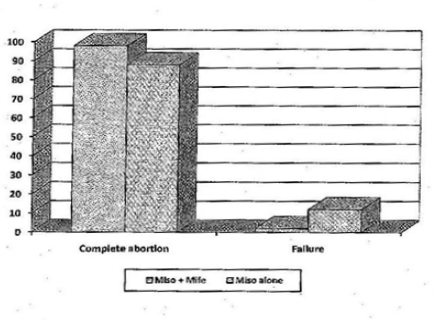
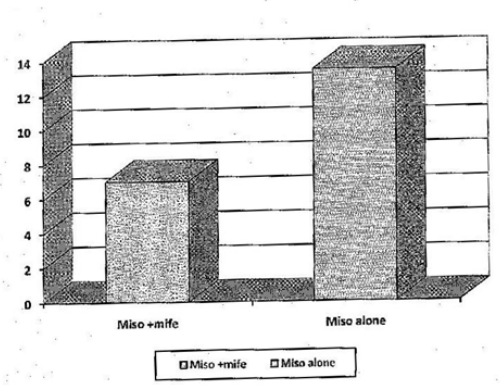


Table 8: Mean induction to abortion interval in study group:

	Miso + Mife	Miso alone
N	49	44
Mean	7.0	13.50
Median	7.115	14.114
SD	1.0171	3.1528
Min	6.0	9.5
Max	9.5	22.0
t value	212.605	
p value	0.0001 Significant	

Graph 8: Mean induction to abortion interval in study group.

Graph 9: Mean induction to expulsion interval according to gravidity (in hrs)



- Mean interval between induction and abortion in the misoprostol alone regimen was 13.5h.rs, the lowest was 9.5hrs and longest was 22.0 hrs.
- Mean induction to abortion interval in the Mifepristnne - Misoprostol group was 7.0hrs, the lowest was 6hrs, longest was 9.5 hrs.

In our study,

- In primigravida, mean interval between induction and abortion in the combination group was 7.0hrs, lowest was 6.0hrs and longest was 8.5hrs.
- In primigravida, mean interval between induction and abortion in the misoprostol alone group was l4.92hrs, lowest was 12.5hrs and longest was 22.0lu's.
- In multigravida, the mean interval between induction and abortion in the combination group was 7.l62hrs, lowest was 6.0hrs and longest was 9.5h.rs, while in the misoprostol alone group, the mean induction to abortion interval was]3.7h.rs, the lowest was 9.5hrs and longest was 22.0 hrs.

TABLE 9:Mean induction to expulsion interval according to gravidity

Gravidity	Primi		Multi	
Grup	Mife +Miso	Miso alone	Mife +Miso	Miso alone
No	15	15	35	35
Mean I-E interval in Hrs	7.0 Hrs	14.92 Hrs	7.16 Hrs	13.77 Hrs
Median (in Hrs)	7.0 Hrs	14.00 HRs	7.00 Hrs	13.50 Hrs
SD	0.8549	3.0472	1.0852	3.1829
Min (in Hrs)	6.0	12.5	6.0	9.5
Max (in Hrs)	8.5	22.0	9.5	22.0
t Value	87.484		130.31	
P value	<0.001 (Significant)		<0.001(Significant)	

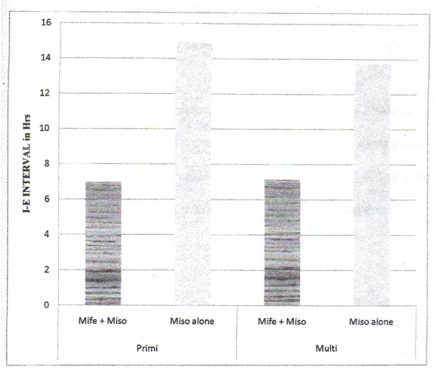
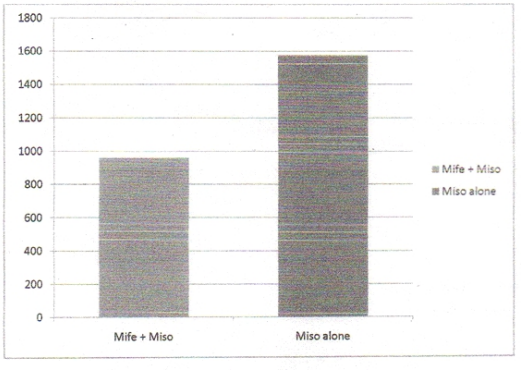


Table 10: Misoprostol Requirement in study group (in mcg)

Group	Min	Max	Mean	SD
Mife+Miso	400	1200	960	291.64
Miso alone	1200	2000	1576	320.20
P Value	0.0048 (Significant)			

Graph 10: Requirement of misoprostol in each group (in mcg)

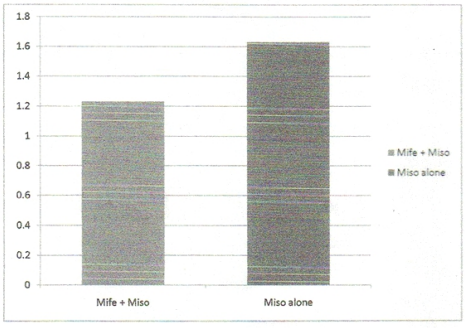


- The amount of blood loss was more with misoprostol alone group, compared with mifepristone-misoprostol group, but none of them required a blood transfusion. The amount of blood loss was assessed by post abortal fall in Hb%, which is significantly less in combination group than misoprostol alone group.
- No grave complications like uterine rupture or maternal deaths were observed in both groups,

Table 11: Post abortal fall in Hemoglobin

Parameters	Mife + Miso	Miso alone
Range	0.4-3	0.4-3.5
Mean	1.23	1.63
SD	0.62	0.74
P Value	0.0076 (Significant)	

Graph 11: Post abtortal fall in Hemoglobin



In our study,

- Mean dose of misoprostol required for complete abortion in Mifepristone - Misoprostol regimen was 960mcg ± 291.64mcg.
- Mean dose of misoprostol required for complete abortion in Misoprostol group was 1576mcg ± 320mcg.
- The difference in misoprostol requirement among the groups was significant,(p-0.0048).
- The maximum dose which was required to expel was l600mcg in combination group, and it was 2000mcg in misoprostol alone group.
- The amount of blood loss was directly proportional to the period of gestation, more with misoprostol alone group, compared with mifepristone - misoprostol group, but none of them required a blood transfusion.
- No grave complications like uterine rupture or maternal deaths were observed in both groups.

DISCUSSION

OUR STUDY comprises of 100 antenatal women in the gestational age range of 13 to 20 weeks, who for either maternal or fetal indications are admitted in our department for termination of pregnancy. These 100 women are randomly allotted to be either under mifepristone + misoprostol group or misoprostol alone group, to avoid selection bias.

Women who belong to mifepristone 4- misoprostol group – group A were given oral mifepristone 200mg followed by vaginal misoprostol 400mcg after 36l1rs, followed by 400mcg vaginal misoprostol every 3hrs up to next 4 doses or until abortion occurs, which- ever occurs early.

Women who belong to misoprostol alone group were given misoprostol 400mcg vaginally every 3hrs for up to live doses.

In our study, patients were studied from the age group ofl9yrs to 36yrs.

- Majority of the patients were in the age group of 20 to 25 yrs.
- The mean age of the patients in the mifepristone-misoprostol group was 25.8yr, the youngest was l9yrs and the oldest was 35yrs.
- The mean age of the patients in the misoprostol alone group was 26.7yrs the youngest was 19yrs and the oldest was36 yrs.
- In a study done by **M.Simseketul** in misoprostol in second trimester abortion with fetal anomalies, the mean age of the patients was 26.4yrs. [12,13]

In a study done by **Carbonellctal** in vaginal VS sublingual misoprostol with mifepristone for cervical priming in second trimester abortion by dilatation and evacuation, the mean age of patients was 26.6 yrs.

Regarding parity, **in our study** most of the patients were multigravida. In a study done by **Premila W. Ashoket** al in nonsurgical second trimester abortion, a review of 500 consecutive cases 51.8% were primigravida, 38.2% were multigravida.

Inourstudy: regarding mean gestational age:

- The mean gestational age in the combination regimen was 16.51 weeks, the lowest was 14weeks and the maximum was 20 weeks.
- The mean gestational age in the misoprostol alone group was 16.19 weeks the lowest was 13 weeks and the maximum was 20 weeks.

In a randomized clinical trial by **Carbonelletal,** [14,15] comparison between vaginal and sublingual administration of misoprostol, in mifepristone pretreated cases for cervical softening in second trimester abortion by dilation and evacuation, the mean gestational age was 15.1 ± 2wks for misoprostol alone regimen and l5.7 ± 2.4 wks for combination regimen.

In our study: regarding the distribution of gestational age among study group.

- 56 out of 100 were in the GA range of 13 to 16 wks.
- 44 out of 100 were in the GA range of l6 to 20wks.
- Majority of the patients, 31 out of 50 in the misoprostol alone group were in the GA range of 13 to l6wks.
- In the combination group, 25 out of 50 were in the gestational age range of 13 to 16wks and 25 in the GA range of 16.l to 20 wks.

Overall the majority of the patients were in the GA range of 13 to 16wks.

In the study done by **P.W.Asloket al** [16,17] in mid-trimester medical termination, a review of 1002cases, the median GA was l5wks (range13 to2lwks).75%(75l) were between 13 and l6wks and 25% were between 17 and 21wks gestation.

Regarding indications for abortion in our study, majority of the cases were patients who needed and requested For Medical Termination of pregnancy followed by congenital anomalies.

In a study done by **Bebbington MW** - A randomized controlled trial comparing two protocols for the use of misoprostol in midtrimester pregnancy termination (2002) 17,18 the most common indication for termination was structural anomaly followed by intrauterine death.

In a study done by **Nathaniee Parclmsilpchai et al** success rate of second trimester abortion,[19,20] the maternal indications commonly noted were HIV seropositivity (18.1%), rape (3.2%) and others 3 (3.2%). The common fetal indications were missed abortion (23.4%) followed by congenital anomalies incompatible with life (16%) such as multiple anomalies (7 of 15), anencephaly (5 of 15) and PPROM (3 of 15).

Inourstudy

- 72% and 40% of the patients did not have any side effects in the combination regimen and misoprostol alone regimen respectively.
- 28% of the patients (14) in the combination group experienced side effects, the most common was abdominal cramps 28% (14) followed by nausea and chills.
- 60% (30) of the patients in the misoprostol alone group experienced side effects, the most common was nausea 32.9% (25), followed by abdominal cramps 13.2% (10),vomiting ll.8% (9), chills 6.6.%, fever 5.3% and diarrhea 3.9%. Overall, the most common side effect in both the group was nausea, the second most common was abdominal cramps.
- In a study by **NatthinecParchasilpchaict al** [21,22] in second

trimester abortion, the most common maternal side effects were fever defined as temperature more than 37.8C (24.5%), abdominal pain (16%) and nausea, vomiting (5.3%)

- In a study by **Paul. A le Roux et al** [23,24] in second trimester termination of pregnancy, comparing mifepristone and misoprostol to gemeprostol, in the combination group of 39, 24 had pyrexia, 29 had gastrointestinal disturbances and live had shivering.

In our study, no grave complications like uterine rupture ormaternalmortality were observed in both the groups.

In our study:

- Complete abortion was achieved in 98% (49) of the patients in the mifepristone - misoprostol regimen, one case (2%) ended in hysterotomy (failure)
- Complete abortion was achieved in 88% (44) of the patients in misoprostol alone group, six cases (12%) required postabortal curettage for excessive bleeding per vaginum, retained products (unsuccessful)
- Over all complete abortion was achieved in 93 patients in our study.

In the study done by **NatthineeParchasilpchai et al**. in second trimester termination of pregnancy using misoprostol, the success rate of 48hrs was 89.4% (84 of 94) and 10.6% (10 of 94) did not abort within 48hrs.

In a study done by **P.W. Ashok et al**. second trimester medical termination of pregnancy, a review of 1002 consecutive cases by administering mifepristone, followed by misoprostol after 36-48hrs, 98.3% aborted within 12hrs, mean being 6.25 hrs.

In a study done by **Sin EeGohet al** [25,26,27] induction of second trimester abortion with mifepristone and misoprostol a review of 386 consecutive cases, success rate after 24hrs was 97.9% and surgical evacuation was needed in 2.1% cases.

In the study done by **Pramila W. Ashok et al** in medical methods of mid trimester abortion, a review of 500 consecutive cases -97.2% of women aborted successfully within five doses. [28,29] The median number of dosage of misoprostol was 1200ug, 1.4% aborted on the second day and the remaining 1.4% aborted on the third day. Surgical evacuation of the uterus was required in 9.4%.

In our study:

- Mean interval between induction and abortion interval in the combination regimen was7.0hrs, lowest was 6hrs and longest was 9.5 hrs.
- Mean interval between induction and abortion interval in the misoprostol alone regimen was 13.5hrs, the lowest was 9.5h.rs and longest was 22hrs.
- In primigravida, mean interval between induction and abortion in the combination group was7.0hrs, the lowest was 6.0hrs and longest was 8.5h_rs, in the misoprostol alone group, mean induction to abortion interval was 14.92h1s, lowest was 12.5hIs and longest was 22.0 hrs.
- In multigravida, mean interval between induction and abortion interval in the combination group was 7.162hrs, the lowest was 6.0hrs and longest was 9.5hrs, in the misoprostol alone group, mean induction to abortion interval was 13.7hrs, lowest was 9.5hrs and longest was 22.0 hrs.
- The mean misoprostol requirement in the combination group 960mcg ± 291mcg, compared to l576mcg ± 320mcg in the misoprostol only group, was less significantly.

S.No	Mean interval between induction and abortion (in hrs)	Regimens	References
1.	23.1	Vaginal misoprostol 100mcg q 6h for 36hr max	Nutilaetal.
2.	14	Vaginal miso 200mcg q 12h x 4	Jainetal.
3.	18.2	Vaginal miso 200mcg q 6h x 4	Dickensonetal.
4.	9	Mife 200mcg+vag.miso 200mcg q 3h x 5	Hopcetal
5.	8.7	Mife 200mcg+vag.miso 400mcg q 3h x 5	Hopcetal
6.	6.1	Mife 200mg + vag. Miso 800mcg + vag. Miso 400mcg q 3h x4	Bartley and baird.
7.	7.0	Mife 200mg+vag. Miso 400mcg + vag. Miso 400mcg q 3h x4	In our study

- In multigravida, mean interval between induction and abortion interval in the combination group was 7.162hrs, the lowest was 6.0hrs and longest was 9.5hrs, in the misoprostol alone group, mean induction to abortion interval was 13.7hrs, lowest was 9.5hrs and longest was 22.0 hrs.
- The mean misoprostol requirement in the combination group 960mcg ± 291mcg, compared to l576mcg ± 320mcg in the misoprostol only group, was less significantly.

SUMMARY

This study was conducted on 100 pregnant women in the gestational age of 13- 20wks to compare the efficacy of Mifepristone—Misoprostol combination with Misoprostol in second trimester termination of pregnancy, in terms of induction-expulsion interval, misoprostol requirement, completeness of abortion.

Complete abortion was achieved in 98% (49) of the patients in the **MIFEPRISTONE - MISOPROSTOL** group.

- Complete abortion was achieved in 88% (44) of the patients in Misoprostol group.
- **In our study**, over all complete abortion was achieved in 93 patients, out of 100.
- **In our study**, mean induction to expulsion interval in the combination group was 7.0hrs, the lowest was 6.0h.rs, longest was 9.5 hrs, failure in one case which ended in hysterotomy.
- **In our study**, mean induction to expulsion interval in misoprostol alone group was l3.5hrs, lowest was 9.5hrs and longest was 22.0hrs.
- Inprimigravida, mean induction to expulsion interval in the combination group was 7.0hrs,lowest was 6.0hrs and longest was 8.5hrs. In the misoprostol alone group it was 14.92 hrs., lowest was 2.5hrs and longest was 22.0hrs.
- In multigravida, mean induction to expulsion interval in the combination group was 7.l6hrs,lowest was 6.0hrs, longest was 9.5hrs, and in the misoprostol alone group it was l3.7hrs, the lost was 9.5hrs and longest was 22.0hrs.
- Mean close of misoprostol required in combination group 960mcg 291 .64mcg.
- Mean doseof misoprostol required in misoprostol alone group was I576mcg 320.20mcg.
- 72% and 40% of the patients did not have any side effects in the combination group and misoprostol alone group respectively. 28% (14) of the patients in the combination group and 60% (30) of the patients in the misoprostol alone group experienced side effects.
- No grave complications like uterine rupture or maternal mortality were observed in both the groups.
- Statistical analysis of the study showed that X2 test was positive i.e. the induction to abortion interval was significantly shorter in the study group, thereby decreasing the side effects of the drug.

CONCLUSION

The incidence of second trimester abortion has reduced significantly following PNDT act. But when the condition is not favourable (i.e) hazardous to the life of either the fetus or mother, the benefit of termination of pregnancy outweighs the risk of continuing pregnancy. This procedure is not only painful, but also has psychological impact. It is the obstetricians concern to reduce this stressful period to the shortest peiod as possible.

This study of pretreatment of mifepristone before misoprostol in

second trimester medical abortion, offers a reliable, safe method with reduced interval between induction and abortion.

For medical second trimester termination termination of pregnancy, pre-treatment with oral mifepristone 200mg prior to vaginal misoprostol provides a non-invasive effective regimen with significantly reduced induction to expulsion interval, lesser side effects and good patient compliance.

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