

## Randomized Trial to Compare of Combination of Mifepristone Plus Misoprostol Versus Misoprostol Alone for Induction of Labour In Subject of IuFd Between 20 to 32 Weeks of Pregnancy.



### Medical Science

**KEYWORDS :** IntrauterineFetalDeath,Mifepristone,Misoprostol,InductionofLabour

**Dr. Parth M. Shah** Third year resident, Dept. of obst & gynaec.

**Dr. Anjani shrivastava** Associate professor, Dept. of obst & gynaec.

**Dr. Nilam Prajapati** Assistant professor, Dept. of obst&gynaec.

**Dr. Jagruti Anavadia** Assistant professor, Dept. of obst&gynaec

### ABSTRACT

*Objective: To compare efficacy, safety and tolerance of combination of mifepristone and misoprostol versus misoprostol-only in induction of intrauterine fetal death (IUFD) between 20 to 32 weeks of pregnancy.*

*Materials and methods: This prospective study included a consecutive series of 100 women with IUFD between 20 – 32 weeks of gestation from January 2013 to October 2014. Women were divided into two groups. First group of women received a single oral dose of 200mg mifepristone, and 100µg of intravaginal misoprostol was administered, followed by intravaginal 100µg misoprostol at four hourly intervals if required. Second group of women received 100µg misoprostol at four hourly interval per vaginally (maximum 4 doses). Oxytocin was given for augmentation if needed.*

*Results: The induction-to-delivery time was shorter with the combination regimen ( $p < 0.001$ ) group. The total dose of misoprostol needed was lower in the group pre-treated with mifepristone ( $p < 0.001$ ).*

*Conclusion: Both regimens, misoprostol-only and the combination of mifepristone and misoprostol are safe in induction of labor after intrauterine fetal death (IUFD). Pre-treatment with mifepristone is more effective in terms of reducing of induction delivery interval, requirement of lesser dose of misoprostol.*

### INTRODUCTION

• When fetal death occur in utero after 20 weeks of gestation, spontaneous expulsion may take several weeks. Such retention of the fetus is associated with emotional distress and grief reaction, which may be severe to the extent of depression.

• When the rupture of fetal membranes occur the risk of intrauterine infection increase and if the dead fetus is retained in the uterus for long duration there is a time related risk of consumptive coagulopathy.

• In modern obstetric practice medical induction of labor is recommended provided it can be undertaken safely. Prostaglandins are used for induction of labor in cases of intrauterine fetal death.

• Misoprostol, a synthetic analogue is widely used because of its low cost, stability at room temperature and ease of administration.

• Mifepristone is a steroid compound, which competes with progesterone at receptor level and is widely used for first and second trimester termination of pregnancy.

• Mifepristone administration before misoprostol increases the sensitivity of the uterus to prostaglandins and ripens the cervix, thereby allowing lower doses of misoprostol to induce expulsion of fetus.

• Research work continues for the dose intervals between mifepristone and misoprostol for maximal efficacy and minimal adverse effects.

• Therefore we conducted the efficacy of simultaneous use of Mifepristone-misoprostol combination to misoprostol alone for induction of labour in subject of IUFD between 20 -32 weeks of pregnancy.

### Objectives:

• To compare the induction delivery interval and the dose required of misoprostol in mifepristone-misoprostol induced

group versus misoprostol induced group.

• To compare the side effects and complication in both groups.

### MATERIALS AND METHODS:

The study was conducted on selected 100 subjects came for induction of intrauterine fetal death (IUFD) between 20 to 32 weeks of pregnancy. From January 2013 to October 2015.

**Inclusion Criteria:** 1) The woman with intrauterine death confirmed by ultrasound. 2) Woman who are not in labour. 3) Those patients who understood the medical regimen and gave informed written consent for induction.

**Exclusion criteria:** 1) Multiple pregnancies with one intrauterine death. 2) Major degree of cephalo-pelvic disproportion. 3) Previous history of caesarean deliveries, hysterectomy and myomectomy. 4) Any contraindication to Mifepristone and Misoprostol.

• A detailed history and general and systemic examination were done in all subjects. Routine hematological investigations were done in all subjects.

• Written informed consent was taken and confidentiality was maintained.

• Gestational age was estimated by LMP, clinical examination and confirm by USG scan.

• All the subjects were randomly divided in two groups of 50 each.

• Study group received 200mg of Mifepristone orally followed by 100µg of misoprostol vaginally immediately and thereafter 100µg every 6 hr until the delivery occurred or up to a maximum of 4 doses.

• Control group received 100µg misoprostol vaginally only in the same dose schedule.

• The subjects were closely monitored for side effects, compli-

cations if any, the onset of contraction, cervical dilatation each time before insertion of each misoprostol.

- Induction delivery interval, the time period between instillation of first intravaginally misoprostol tablet to delivery of fetus, was noted down.
- The process was considered failed if delivery failed to occur even after maximum 4 misoprostol instillations.
- In event of failure, endocervical Dinoprostone gel or oxytocin infusion was attempted.

**Observations and discussion:**

**Table-1. Epidemiological factor. [Age, gestational age]**

Epidemiological factor	Study group	Control group
Mean age (years)	24.02	23.97
Mean gestational age (weeks)	26.16	26.92

**Table-2.No. of misoprostol instillation required:**

No of misoprostol instillation	Dose of misoprostol (µg)	Study group (n=50)	Control group (n=50)	P-value
Once	100	9	1	0.00358
2 times	200	34	10	0.00001
3 times	300	7	24	0.00007
4 times	400	0	15	0.00061

- Mean misoprostol instillation of group-A was 1.96 times and 3.06 times in group-B which was statistically significant. (p<0.001)
- Majority of the subjects in group A (34/50) needed two doses of misoprostol whereas majority in group B (24/50) needed three doses.
- Mean dose requirement of misoprostol in group-A was 196 µg and that of group-B was 306 µg, which was statistically significant..(p<0.001)

**Table-3. Induction delivery interval:**

Induction delivery interval (hrs)	Study group (n=49/50)	Control group (n=47/50)	P value
<=6	07(13.2%)	01(1.69%)	0.0003
6-12.	34(67.1%)	10(18.1%)	0.0002
13-18	08(15.4%)	24(46.3%)	0.0003
19-24	00	12(23.1%)	-----
Failure	01(1.8%)	03(5.46%)	0.3087
Mean[hours]	9.79	17.35	0.0001

- All subjects who responded in group A had delivered within 18 hours of misoprostol instillation while those in group B delivered within 24 hours.
- Majority of subjects (82%) in group A delivered within 12 hours, whereas majority of subjects (70%) in group B delivered within 18 hours, which is more important for emotional wellbeing of patient.

(As shorter induction delivery interval reduce the chances of emotional trauma to the patient)

- Mean IDI in group A was 9.79 hours which was significantly shorter than that of group B which was 17.35 hours which was statistically significant.(P<0.001)
- The difference in number of subjects delivering less than 6 hours, between 6 to 12 hours and 13 to 16 hours between two

groups was statistically significant.(p- values were 0.0003, 0.0002 and 0.0003 respectively)

**Table-4. Side effects:**

Side effects	Study Group n=31(62%)	Control Group n=42(84%)	p value
Nausea	11(35.4%)	21(50%)	0.0321
Vomiting	7(22.5%)	9(21.4%)	0.2927
Fever	0	2(4.7%)	0.2375
Need for analgesics	12(38.7%)	17(40.4%)	0.1384
Shivering	8(25.8%)	14(33.5%)	0.0748
Headache	1(3.2%)	2(4.7%)	0.2799
Total no. of patients	31(62%)	42(84%)	0.0068

- Most common side effect was nausea in both groups.
- All the side effects were more in control group as compared to study group due to prolonged induction delivery interval and exposure of higher dose of misoprostol.

**Table-5. Complication:**

Complication	Study Group	Control Group
Hemorrhage(PPH)	0	3
Shock	0	0
Hypertonic Uterine contraction	0	0
Uterine Rupture	0	0
Retained products	0	0

- There were no any complication in study group while only complication in the control group was hemorrhage noted only in 6% of cases which was controlled by oxytocics only, no need for any blood transfusion.

**Conclusion:**

- Pre-treatment with mifepristone adds to the effectiveness of misoprostol and reduces the amount of prostaglandins required and also reduce the induction delivery interval and also reduce the side effects and complication. So, ultimately improves subject's compliance and satisfaction.