World Journal of Health and Medicine (ISSN: 2584-0223)

Shah SR, et al. W J Heal Med. 2024;2(2):1-6

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Review Article

Comparison of Induction of Labour with Mifepristone and Misoprostol at Term *V/S*. Induction with Misoprostol Alone

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Received Date: April 05, 2024; Accepted Date: April 18, 2024; Published Date: April 22, 2024

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Citation: Shah SR and Vhora H. Comparison of Induction of Labour with Mifepristone and Misoprostol at Term V/S. Induction with Misoprostol Alone. W J Heal Med. 2024;2(2):1-6.

Abstract

This study was carried out in Dr. M.K. Shah Medical college and SMS Multi-speciality Hospital, Tertiary care medical centre, catering to Lower middle class and middle-class community.

Objective: To study the Efficacy and outcome of Oral Mifepristone and sublingual misoprostol *vs* sublingual misoprostol only for Induction of labour in Term Pregnancy.

Methodology: Prospective study has been carried out in the Department of Obstetrics and Gynaecology, Dr. M.K Shah medical college and Research Centre, SMS multi-speciality hospital, Chandkheda, Ahmedabad, Gujarat, India, for a period of 12 months: January 2023 to December 2023. Consent of Ethical committee of the hospital and Written consent of the Patient was taken. An attempt is made in one group to use oral Tab Mifepristone (200 mg) followed 24 hr Low dose sublingual Tab Misoprostol (25 microgram) and in other group only sublingual Tab misoprostol (25 microgram).

Results: 15 patients were included in the MIFE/MISO group and 15 patients, in the MISO group. Median time to expulsion was significantly lower in the MIFE/MISO group than the MISO group (10.0 h and 16.4 h respectively; $P < 0.001$). Adverse effects were reported in 30% and 36% of patient records, respectively. Complication rates were similar between 2 groups.

Conclusion: As induction is always planned delivery for various indications, priming the cervix 24 hours before by tab Mifepristone 200 mg significantly reduces induction delivery interval. Further study in the way this study has been carried out, will help in adding Mifepristone 200 mg 24 hours before induction by misoprostol.

Keywords: Mifepristone; Misoprostol; Induction of labour; Normal delivery; Caesarean section; Bishop score

Abbreviations and Acronyms

LSCS: Lower Segment Caesarean Section

ART: Artificial Reproductive technique

BMI: Body Mass Index

NSAIDS: Non-Steroidal Anti-inflammatory Drugs

MISO: Misorprostol

MIFE: Mifepristone

Introduction and Review of Literature

Induction of labour is defined as initiation of uterine contractions after the period of viability by any methods medical, surgical, or combined, for the purpose of vaginal delivery. The success of induction, depend upon pre-induction cervical status i.e. cervical ripening which is a series of complex biochemical changes in the cervix, mediated by hormones altering both cervical collagen and ground substance [1].

Different primary methods of induction of labour are mechanical and pharmacological. Cervical ripening agents are utilized primarily when the bishop score is unfavourable (less than six). Mechanical cervical ripening of the cervix can be done using a Foley catheter or double-balloon device (i.e., Cook catheter) placed through the endocervical canal [2].

Osmotic dilators, Laminaria, and synthetic dilators are also used for cervical ripening and placed in the cervical os. Pharmacological forms of IOL include synthetic prostaglandins and synthetic oxytocin [3]. Prostaglandins are used for cervical ripening. Misoprostol, prostaglandin E1 (PGE1), and dinoprostone, prostaglandin E2 (PGE2), are used in various doses and routes of administration [4].

The sequential use of mifepristone, an antiprogesterone agent that has been shown to mature and dilate the cervix in pregnant women, and a prostaglandin has been extensively researched for termination of pregnancy in all trimesters, for cervical preparation prior to surgical termination of pregnancy, and for induction of labour in late pregnancy in cases of intrauterine death [5].

Notably, prostaglandins should be used with caution in women with a history of a low transverse cesarean section due to concerns for uterine rupture. Oxytocin is administered intravenous infusion in varying dosing regimens. Amniotomy is often used in combination with both mechanical and pharmacological labour induction methods [6].

The most common indications include preterm or early rupture of membrane without labour, gestational hypertension, oligohydramnios, non-reassuring fetal status, post-term pregnancy, and various maternal medical conditions such as chronic hypertension and diabetes and in recent times due to availability of ART has increased the incidences of induction of Labour [7].

Several Factors Contribute to the ability of labour induction to achieve vaginal delivery. Favourable factors include younger age, multiparity, normal BMI, favourable Bishop score. Favourable cervix is a major contributor for successful labour When delivery is necessary, and ripening has not had time to occur this natural process has to be accelerated with Cervical Ripening agents [3]. The status of cervix can be assessed by Bishop scoring system. Bishop score of less than 6 usually requires cervical ripening agent [8].

Methodology

Prospective study has been carried out in the Department of Obstetrics and Gynaecology, Dr. M.K Shah medical college and Research Centre, SMS multi-speciality hospital, Chandkheda, Ahmedabad, Gujarat, India, for a period of 12 months: January 2023 to December 2023. Consent of Ethical committee of the hospital and Written consent of the Patient was taken.

Inclusion Criteria

Singleton pregnancy with:

- cephalic presentation
- term pregnancy
- maternal or fetal indications for labour induction
- Women in whom labour induction could be deferred for 48 hours.
- unfavourable cervix with Bishop's score < 6

Exclusion Criteria

- Non vertex presentation
- Multiple pregnancy

- >1 previous caesarean section
- Contraindication to vaginal delivery
- Renal failure, hepatic disorder, adrenal insufficiency
- Blood clotting disorders
- Known hypersensitivity to prostaglandins or Mifepristone.
- Women on anticoagulant therapy or corticosteroids

Preliminary Procedure

All eligible women with obstetrical or medical indication for labour induction were enrolled in the study taking inclusion and exclusion criteria in consideration. Participants were briefed about the nature of the study; details of the treatment and written consent was obtained after being explained about the risks and benefits of the study.

A thorough history including patients' menstrual history, obstetric history and any significant past/family/treatment history was taken and recorded. Complete systemic and obstetric examination was done in all patients. Baseline complete blood count, liver function test and renal function test along with fetal ultrasound with doppler were done in all patients. Per magnum examination was done to assess the modified bishops score and pelvis.

Method of Study

A total number of 30 females with Singleton term Gestation planned for Induction of Labour with a Bishop Score of less than 6 at presentation were selected for the Study. 15 patients were given Tab Mifepristone 200 mg orally and after interval of 24 hour; Misoprostol 25 microgram sublingual was given 4 hourly, maximum up to 4 doses and 15 patients were induce with misoprostol 25, microgram 4 hourly, maximum up to 4 doses without priming of cervix by mifepristone. Patients going in labour after administration of drug were noted. Patients were closely monitored for vitals and progress of Labour. Fetal Heart monitoring was done. 4 Hourly P/V examination was done, and Bishop score was assessed.

Active stage of labour was monitored partographically. Mode of delivery was noted down. Apgar score was recorded.

Result

In group A patients are between 23 years to 31 years of age with parity of Primigravidas are 60% (9 patients) and multigravidas are 40% (6 patients).

In group B patients are between 20 years to 34 years of age with parity of primigravidas are 53.3% (8 patients) and multigravidas are 46.6% (7 patients).

Bishop's score of group A before induction; <4 (n=10) and 4-6 (n=5). Bishop's score of group B induced patients before induction are (n=11) and (n=4) respectively. All patients are in prelatent or latent phase of labour.

Induction delivery time interval in group A was between 6.4 hours to 15.5 hours, mean induction delivery time is 10.95 hours. Induction delivery time interval in patients group B were between 12.5 hours to 20.4 hours, mean induction delivery time interval is 16.45 hours. This difference between group B and group A is statistically significant ($p<0.001$).

Mode of delivery in group A; LSCS are 5 (25%) and vaginal delivery are 10(75%). In group B patients LSCS are 4 (27%) and Vaginal delivery are 11 (73%). Rate of delivery by LSCS in both group is not significant (p value >0.001).

Fetal distress in Group A induced patients are 3 cases and group B induced patients are 3. Failure of induction are 2 cases in mifepristone misoprostol and 1 cases misoprostol.

In group A cervical tear were 2 and MSL were 7 cases. In group B cervical tear were 5 and MSL were 6 cases.

In group A baby weight were between 1.9 kgs to 3.2 kgs. Mean weight being 2.75 kg. In group B baby weight were between 2.0 kg to 3.4 kg, mean weight being 2.56 which is comparable.

Observation

15 patients were included in the MIFE/MISO group and 15 patients, in the MISO group. Median time for induction delivery interval was significantly lower in the MIFE/MISO group than the MISO alone group (10.0 and 16.4 h respectively; $P < 0.001$). Adverse effects were reported in

30% and 36% of patient records respectively. Complication rates were similar between 2 groups.

As induction is always planned delivery for various indications, priming the cervix 24 hours before by tab Mifepristone 200 mg significantly reduces induction delivery interval. Further study in the way this study has been carried out, will help in adding Mifepristone 200 mg 24 hours before induction by misoprostol.

Very few inductions are carried out by oxytocin drip, this study has not included it as induction drugs.

Description

A. Age wise Distribution

26 (86.6%) patients where in age group 18 to 30 which is peak reproductive age in our country. Only 4(13.33%) where in age group more than 30 (Table 1: Age wise distribution).

Table 1: Age wise Distribution.

AGE	Group A	Group B	TOTAL
18-25	8(26.7%)	5(16.7%)	13(43.3%)
26-30	4(13.3%)	9(30%)	13(43.3%)
>30	3(10%)	1(33.3%)	4(13.4%)
TOTAL	15(50%)	15(50%)	30(100%)

B: Parity wise Distribution

In group A patients, parity of Primigravidas is 60% (9 patients) and multigravidas are 40% (6 patients).

In group B patients, parity of primigravidas is 53.3% (8 patients) and multigravidas are 46.6% (7 patients) (Table 2: Parity wise distribution).

Table 2: Parity Wise Distribution.

Gravida	Group A	Group B	TOTAL
Primi	9(30%)	8(26.7%)	17(56.7%)
Multigravida	6(20%)	7(23.3%)	13(43.3%)
G2P1L1	5(16.7%)	6(20%)	
>G2L1	1(3.3%)	1(3.3%)	
TOTAL	15(50%)	15(50%)	30(100%)

C: Indication of Induction Labor

There is marked difference in indication for induction of labour in the group eg: for postmaturity/postdatism for group A there were 7 patients (23.33%) whereas in group B there were 3(10%) patients (Table 3: Indication of Induction Labor).

Table 3: Indication of Induction Labor

Causes Of Induction	Group A	Group B	Total
Post Dated /Postmaturity	7(70%)	3(30%)	10(100%)
PROM	3(33.3%)	6(66.6%)	9(100%)
IUGR	3(42.8%)	4(57.1%)	7(100%)
Oligohydroamnios	2(50%)	2(50%)	4(100%)
Total	15(50%)	15(50%)	30(100%)

D: Bishops Score

In both the group percentages of patients having bishops score less than 4 where almost equal. This applies to bishops score more than 4 (Table 4: Bishops Score).

Table 4: Bishops Score.

Bishop Score	Group A	Group B	Total
<4	10(33.3%)	11(36.67%)	21(70%)
>4	5(15.67%)	4(13.33%)	9(30%)
Total	15(50%)	15(50%)	30(100)

E: Induction delivery time

As seen from table there is marked difference in mean induction delivery interval in group A and B. Group A was having 5.5 hours less in mean induction delivery time. These is statistically very significant as verified by p value which is less than 0.001 which is significant.

In Subrat P et al, induction delivery time of group A and group B were 8.46 hours and 15 hours. Which is statically significant. Subrat P, et al. and our study correspond very well. (Table 5: Induction delivery time) [10].

Table 5: Induction delivery time

	Maximum	**Minimum**	**Mean**	**SD**	**P Value**	**Subrat P et al 10 Mean**	**P value**
Group A	15.5 hr	6.4 hr	10.95 hr	3.4 hr	0.0006 (<0.001)	8.46 hr	(<0.001)
Group B	20.4hr	12.5 hr	16.45 hr	4.3 hr		15 hr	

F: Mode of delivery

In both the groups rate of successful vaginal delivery almost equal which is verified by p value. LSCS rate (combine in both groups) is 30% which is less than my institute which is 45-50%. Which is statistically significant (p value <0.001) (Table 6: Mode of delivery).

Table 6: Mode of delivery.

Mode of delivery	**Group A**	**Group B**	**TOTAL**
Vaginal delivery	10(33.3%)	11(36.7%)	21(70%)
LSCS	5(16.7%)	4(13.3%)	9(30%)
TOTAL	15(50%)	15(50%)	30(100%)

G: Indication Of LSCS

Major indication for lscs was meconium-stained liquor (20%). We don't have facility for scalp P^H so we have taken all patients with meconium stained liquor as fetal distress. It is observed that patients induced with prostaglandin derivatives are having more incidence of meconium-stained liquor. Whether this is because of fetal distress or meconium-stained liquor in absence of fetal distress. This needs to be verified by fetal scalp PH study (Table 7: Indication Of LSCS).

Table 7: Indication of LSCS.

Indication of cs		**Group A**	**Group B**	**TOTAL**
Fetal Distress		3(27.3 %)	3(27.3 %)	6(54.5 %)
	IUGR	1(9%)	-	1(9%)
	Oligohydroamnios	-	1(9%)	1(9%)
Failure of Induction		2(18.2 %)	1(9%)	3(27.3 %)
Total		6(54.5 %)	5(45.5 %)	11(100 %)

H: Complications

Cervical tears present in 23% which required suturing, but it was not life threatening.

MSL was significant complication, but it is suggestive of fetal distress or not which needs to be authenticated by fetal scalp P^H (Table 8: Complications).

Table 8: Complications.

Complication	**Group A**	**Group B**	**Total**
Cervical tear	2(6.66%)	5(16.66%)	7(23.33%)
MSL	7(23.33%)	6(20%)	13(43.33%)
Total	9(30%)	11(36.6%)	20(66.66%)

I: APGAR score

7 babies having APGAR score less than 7 at 1 minutes which decreased to 3 patients with APGAR score at 5 minutes. Out of these 3 patients only 1 patient required C-PAP for 24 hours (Table 9: APGAR Score).

Table 9: APGAR Score.

	Apgar Score	**Group A**	**Group B**	**TOTAL**
At 1 minute	<8	3(10%)	4(13.33 %)	7(23.33 %)
	>8	12(90%)	11(36.66 %)	23(76.67 %)
At 5 minute	<8	1(3.33%)	2(6.67%)	3(10%)
	>8	14(46.67 %)	13(43.33 %)	27(90%)
		15(50%)	15(50%)	30(100%)

J: Baby weight

There are no significant changes in birth weight in both the groups. 18 (60%) patients have birth weight from 2.5 kg to 3 kg (Table 10: Baby weight).

Table 10: Baby weight

Baby Weight	Group A	Group B	Total
<2.5 kg	7(23.3%)	5(16.7%)	12(40%)
2.5-2.9 kg	7(23.3%)	9(30%)	16(53.3%)
>3.0 kg	1(3.3%)	1(3.3%)	2(6.7%)
Total	15(50%)	15(50%)	30(100%)

K: NICU admission

2(6.67%) patients in group A and 4(13.33%) patients required NICU admission.

Out of these 6 patients (group A and B), only 1 baby required NICU admission for C-PAP for 24 hours. Rest of 5 babies were admitted in NICU for observation (Table 11: NICU admission).

Table 11: NICU admission

NICU admission	Group A	Group B	Total
Yes	2(6.67%)	4(13.33%)	6(20%)
No	13(43.33%)	11(36.66%)	24(80%)
Total	15(50%)	15(50)%	30(100%)

Conflict of Interest

We declare that the research was conducted in absence of any commercial or financial relationships that could be constructed as a potential conflict of interest.

Author Contributions

Research study was carried out jointly by Author 1 and 2. Record keeping was done by Author 2 under supervision of Author 1.

Funding

No funding was taken from anyone.

Acknowledgement

We are thankful to Superintendent of Dr M.K Shah Medical College and Research Centre. Last but not the least, we are greatly thankful to patients for giving their consent and allowing us to study, without support of them this study would not have been possible.

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