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Comparison of Mifepristone and Misoprostol Combination with Misoprostol Alone in Induction of Labor

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Abstract

There are various methods of induction of labor (IOL). One of the commonly used method is use of Misoprostol. However, with the use of Misoprostol alone, there are cases of failed IOL leading to operative deliveries. Another drug, Mifepristone has been shown to be effective in cervical ripening and induction of labor. So the aim of this study was to assess the effectiveness of Mifepristone as pre-treatment with misoprostol in induction of labor, thereby decreasing the rates of Caesarean section. This was a prospective comparative study where, one group receiving pre-treatment with Mifepristone 200mg orally 24 hours before Misoprostol and the other receiving only Misoprostol- 25mcg vaginally, maximum 2 doses 6 hours apart. The study was conducted in a period of 1 year at Patan Academy of Health and Sciences (PAHS), Nepal, which included 124 primigravidas. Fifty percent of women who underwent induction with Mifepristone+Misoprostol combination had vaginal deliveries, while 45% had emergency Lower Segment Caesarean section (LSCS) and 5% had instrumental deliveries. But, only 39% had vaginal deliveries in Misoprostol only group, with 56% LSCS and 5% instrumental deliveries. P value in the mode of delivery was not statistically significant ($p>0.05$). Failed IOL was commonly seen in Misoprostol only group (48%). The rate of failed IOL was 21% in Mifepristone+Misoprostol group, which was statistically significant ($p=0.026$). The mean induction-delivery time interval, was lower in Mifepristone+Misoprostol group (18.55 hours) than in Misoprostol only group (19.9 hours). Use of Mifepristone prior to Misoprostol decreases the caesarean section rates due to failed induction of labor.

Keywords: Induction of labor, Mifepristone, Misoprostol.

INTRODUCTION

Induction of labor (IOL) is indicated when continuation of pregnancy can cause potential harm to the fetus and the mother [1]. Although this is an unavoidable intervention for maternal and fetal safety, it can be associated with various complications like premature birth, increased operative interventions [1]. Prolonged pregnancy is one such condition that is associated with increased maternal and fetal morbidities. So induction of labor becomes an indication. Un-effaced cervix becomes a major hindrance in successful induction of labor. Both surgical and medical methods of induction can be used [2]. Misoprostol (PGE1 analogue) is commonly being used for inducing labor in patients with unripe cervix [3]. Misoprostol is effective in ripening the cervix and hence can be used to induce as well as augment labor process [4]. Mifepristone also called RU– 486, is 19 nor steroid with potent competitive anti-progesterone and anti-glucocorticoid activity [5]. It is used as a pretreatment to prime the cervix adequately. It produces a modification in the consistency of the cervix with an improvement in cervical dilatation [5]. Mifepristone is recognized as a component of safe abortion and is included in WHO list of essential medicines. The most commonly used approved indications include: termination of early pregnancy, cervical dilatation prior to surgical abortion, labor induction in IUFD [5]. Fewer studies have been done on effect of mifepristone on cervical ripening and induction of labor.

In our institute, induction is done using Tab.Misoprostol-25 mcg-2 doses 6 hours apart, vaginally. This is followed by use of Oxytocin 20 hours after the first dose of Misoprostol. Failed induction of

labor constitute a major indication for operative delivery. In our hospital, 20-25 % of caesarean sections are due to failed induction. If Mifepristone is added to Misoprostol, the load of operative delivery can reduce, which will be helpful.

So the aim of this study is to assess the effectiveness of Mifepristone in successful induction of labor, thereby decreasing the rates of caesarean section.

MATERIALS AND METHODS

A total of 124 patients planned for induction of labor from October 2018 to October 2019 in Patan Academy of Health and Sciences, Nepal (PAHS), who met the inclusion criteria of maternal Age< 35 years, primigravida, Singleton Pregnancy, gestational age: 40 weeks and 6 days, with intact membranes and BISHOPS Score <6were were enrolled in the study where as, maternal age > 35 years, multigravida, women not sure about LMP, Prelabor Rupture of Membranes (PROM), Multifetal gestation, women with any comorbidities and patients not willing to participate in the study were excluded from the study.

After taking the consent, patients were admitted at 40 weeks and 5 days of gestation and IOL was done the next day. Patients were divided into two groups based on simple random sampling. A box was made, which comprised of 62 mifepristone and 62 misoprostol written papers. The participants picked one from the lottery box. Whatever method they picked up, they were induced with that particular method.

First group were the patients getting pre-treatment with Mifepristone prior to Misoprostol. Second group were the patients getting Misoprostol alone.

Once the patient was admitted and consent was taken, a detailed history was taken and general physical examination was performed. Per abdominal examination and per vaginal examination was done. BISHOPs Score was calculated. Non Stress Test and Ultrasonography were done prior to induction for fetal wellbeing. Also, basic lab investigations like Hematocrit level, Platelets Count, PT/INR were done. Two pints of Blood was arranged. These were all done according to our hospital protocol.

Mifepristone and Misoprostol combination Group (Group A)

This group received 200 mg of Tablet Mifepristone orally at 10 am on Day 1 after abdominal and vaginal examination and BISHOP Score was recorded. After the administration of drug, maternal vital signs were monitored 4 hourly and fetal heart rate was monitored 2 hourly.

If they started having abdominal pain anytime following the drug administration, vaginal examination was done and Bishop's score was recalculated. If it was ≥6, augmentation with ARM and/or with 5 units of oxytocin in one pint of Ringers lactate (RL) at 10-60 drops/minute was started.

If there was no signs of labor, they were reassessed after 24 hours of Mifepristone. If the Bishops score < 6, they were induced with 25 microgram (mcg) of Tablet Misoprostol per vaginally and reassessment was done after 6 hours. If labor had started in between (BISHOP Score ≥6), second dose of Misoprostol was avoided. Otherwise second dose of 25 mcg of Misoprostol was administered per vaginally after 6 hours of first dose of Misoprostol. Once the patient went into labor, she was managed with ARM and/or oxytocin infusion if needed based on the contraction, as per hospital protocol. After each dose of Misoprostol, patient was kept in left lateral position for half an hour. FHR was monitored every 2 hourly and vitals 4 hourly.

If she failed to go into labor even after one dose of Mifepristone and 2 doses of Misoprostol, after 14 hours of 2nd dose of Misoprostol, induction/augmentation was done with 5 units of oxytocin in one pint RL at 10-60 drops/minute, followed by ARM.

Misoprostol alone group (Group B)

This group received 2 doses of 25 mcg of Misoprostol vaginally, 6 hours apart starting at 10 am in the morning on Day 1. Patient was kept in left lateral position for half an hour. Four hourly monitoring of maternal vitals and 2 hourly FHR monitoring was done.

If she had gone into labor after first dose, second dose was avoided. Once the Bishop score is ≥6, depending upon the contractions, labor augmentation was done by oxytocin and/or ARM. Oxytocin was started as 5units in one pint of RL at 10-60 drops/minute.

If patient had not gone into labor after getting two doses of Misoprostol, at 14 hours of 2nd dose, induction/augmentation was done with 5 units of oxytocin in 1 pint of Ringer Lactate, started at 10-60 drops per minute followed by ARM.

Rest of the labor was managed as per hospital protocol in other patients.

Both the groups were followed till delivery. The mode of delivery was noted. The induction to delivery time was calculated.

RESULTS

Table 1: Age groups in two groups

Age (in Years)	N	Mean
Group A	62	24.66
Group B	62	25.66

The age groups in both the induction groups were comparable

Table 2: Mode of Delivery between two groups

Mode of delivery	Group A	Group B	p-value
Vaginal Delivery	31	24	0.43
LSCS	28	35	
Instrumental delivery	3	3	

Fifty percent of women who underwent induction with Mifepristone+Misoprostol combination group had vaginal deliveries, while 45% had emergency LSCS for various indications and 5% had instrumental deliveries in our study. But, only 39% had vaginal deliveries in Misoprostol only group, with 56% LSCS and 5% instrumental deliveries. Although the rates of caesarean section were lower in combination group, the finding was not statistically significant. (P value 0.43).

In our study, group A, we found that 16 patients went into labor with Mifepristone alone

Table 3: Induction to Delivery time between two groups

Induction-Delivery time (In hours)	N	Mean	P-value
Group A	62	18.55	0.29
Group B	62	19.93	

Though the Induction to delivery time was lower in combination group than in Misoprostol alone group, the difference was not statistically significant

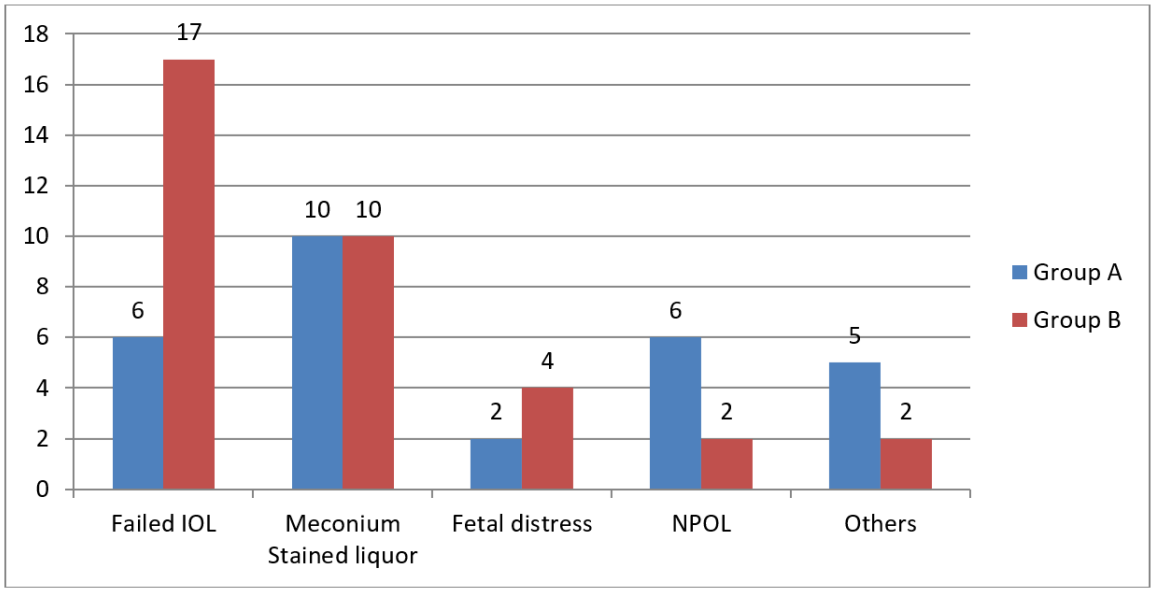

Figure 1: Indications of LSCS in two groups

Table 4: Comparison of Failed IOL to other indications

Indication of LSCS	Group A	Group B	P value
Failed IOL	6	17	0.026
Other Indications	22	18	

There was low rate of caesarean section due to failed IOL in Mifepristone and Misoprostol combination group in comparison to Misoprostol alone group, which is statistically significant.

Induction to delivery time was lower in Group A i.e. 18.55 hours than in Group B i.e. 19.93 hours. However, the finding was not statistically significant. (P-value=0.29)

DISCUSSION

This study compared the outcomes, induction to delivery time and the indications of Emergency caesarean sections, if performed, between two groups receiving Mifepristone and Misoprostol combination and Misoprostol alone for induction of labour. All the patients were primigravidas and induction was done for post-dated pregnancies. Thus, the patient characteristics in both the groups were comparable.

In our study, the mean age groups of the women undergoing IOL in two groups were 24.66 years and 25.56 years respectively. The difference in age was not statistically significant.

Similar to our study, study done by Athawale *et al* showed the mean age of women undergoing IOL with Mifepristone was 22.86±2.89 years which was comparable to our patients receiving Mifepristone prior to Misoprostol [6]. Similar findings were seen by Yelikar *et al* in which the mean age in mifepristone and misoprostol alone groups were 22.98±3 years and 23± 2.8 years respectively [7].

The above studies were done in our neighboring country, India. The geographical landmarks, socio-economic lifestyles and the age of marriage of the residents between India and Nepal are similar. This can relate to the similarity of age groups of patients included in the studies of both these countries.

Fifty percent of women who underwent induction with Mifepristone+Misoprostol combination group had vaginal deliveries, while 45% had emergency LSCS for various indications and 5% had instrumental deliveries in our study. But, only 39% had vaginal deliveries in Misoprostol alone group, with 56% LSCS and 5% instrumental deliveries. Although the rates of caesarean sections were lower in combination group, the finding was not statistically significant.

Yelikar *et al*. in their study showed that 86% patients achieved vaginal delivery and 12% underwent caesarean section in patients getting mifepristone prior to misoprostol [7]. Seventy 74% patients had vaginal delivery in misoprostol group and 16% underwent caesarean section. However the results showed no statistical significance. These results were similar to our study. The similarity can be attributed to the similar population in both studies as well due to inclusion of only postdated pregnancies.

Similar to present study, in a study done by Athawale R *et al*, 76% had vaginal deliveries and 24% had caesarean delivery in mifepristone group [6]. This demonstrates that mifepristone is efficacious in achieving vaginal delivery.

Though the rate of LSCS was high (32%) in Prostaglandin (Dinoprostone) group when compared to Mifepristone group (30%), the finding was not significant. This was the conclusion of Shah MK *et al*, which has resemblance to our study [8].

Failed IOL used to be the most common indication for doing caesarean section in our hospital, in most of the times. In our study, only 21% in combination group had to undergo caesarean section due to failed IOL as compared to 48% in Misoprostol only group. This was a significant finding of our study with p-value of 0.026. This finding of decreased caesarean section rates due to failed IOL when Misoprostol was preceded by Mifepristone in induction of labor supports the hypothesis.

The results of our study also had similarity with the one done by P. Sharma *et al*, which showed that the number of cases of Failed IOL was significantly higher in patients receiving only prostaglandins (Dinoprostone) when compared to those receiving Mifepristone prior to PGs(27.8% vs 14.1%) [9]. However the mode of deliveries were not seen statistically significant, as in our case.

In present study, the most common indication of LSCS in combination group was Meconium stained liquor. While in Misoprostol alone group, Failed IOL was the commonest indication followed by meconium stained liquor.

In a study done by Priyanka Sharma *et al*, on comparing the indications for LSCS, Failed IOL was the most common indication in Dinoprostone group while Meconium stained liquor in Mifepristone group.[9] Hence, the caesarean section rates due to failed IOL was significantly higher in patients not getting pretreatment with Mifepristone. This is similar to our study.

In contrast, Shah MK *et al* found that the most common indication for LSCS in both groups, whether receiving Mifepristone or not, was fetal distress.[10]

The mean induction-delivery time interval in Mifepristone+Misoprostol combination group was 18.5 hours which is lower than in Misoprostol alone group (19.9 hours), though the timing is not statistically significant.

CONCLUSION

This study has shown that use of Mifepristone prior to Misoprostol decreases the caesarean section rates due to failed induction of labor. This study has also shown that mifepristone can be used as a sole agent to induce labor.

Limitations

The limitations of this study would be small sample size. Despite having around 600 deliveries in a month, the sample size for the study is low, as we have included only pregnancies of 40 weeks and 6 weeks of gestation. We have not included other indications of IOL like gestational Hypertension, Gestational Diabetes mellitus, IUGR, etc. Another limitation of this study is the cost of Mifepristone. Mifepristone is slightly costlier than Misoprostol.

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