

# Comparison of Isosorbide Mononitrate (IMN) Plus Misoprostol Versus Misoprostol Alone in Post-Term Pregnancies

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## ABSTRACT

**Objective:** compare mean induction to delivery interval in patients induced with isosorbide mononitrate (IMN) plus misoprostol versus misoprostol alone in post-term pregnancies.

**Methodology:** To conduct this Randomized Controlled Trial at Social Security Hospita, MNCH, Lahore, we enrolled 150 patients (75 patients in each group) and randomly separated them into two groups of similar size. Group A had IMN (40mg) injected into the posterior fornix of the vagina, followed by misoprostol (50ug), while Group B received misoprostol (50ug) alone was induced. After the initial dose, second doses were only administered if labour was not started or regular uterine contractions had not been started within six hours of the first dose. A maximum of four doses were administered at six-hour intervals until the patient entered the active phase and gave birth. A pre-designed proforma was added to record the average time from induction to delivery. Patients' age, parity, and number of doses of misoprostole were stratified to adjust for possible effect moderators.

**Results:** In our study, 62.67% of the cases (n=47) in A Group and 56% (n=42) in B Group were in range of 18 and 25, while 37.33 percent (n=28) in A Group and 44 percent (n=33) in B Group were in range of 26 and 35, with mean+sd calculated as 24.4+5.06 and 25.25+5.53 years, respectively. Mean time of induction to delivery was 19.28+1.75 in A Group and 23.75+2.47 mins in B Group.

**Conclusion:** Patients induced with isosorbide mononitrate (IMN) and misoprostol had a considerably shorter induction-to-delivery time than those treated with misoprostol alone.

**Keywords:** Post-term pregnancies, mean induction to delivery interval, isosorbide mononitrate (IMN) plus misoprostol, misoprostol alone

## INTRODUCTION

A pregnancy is considered to be prolonged if it continues for > 42 weeks/ 294days, after the first day of the menstrual cycle, it is also known as 'post-term pregnancy'.<sup>1</sup> In UK every year, nearly 60,000 women give birth postdates.<sup>2</sup> Post-term pregnancy is linked to an increased risk of intrapartum and postpartum obstetric complications, as well as higher rate of perinatal morbidity and mortality, and it continues to be a challenging and contentious issue in contemporary obstetrics.<sup>3</sup> The incorrect dating of pregnancy accounts for around two thirds of all these pregnancies. In addition, when compared with babies who were born on their due date, babies who were born after the due date have a higher chance of being hospitalised within the first three years of their lives and have a higher risk of developing conditions such as epilepsy, neuro developmental deviation, and Asperger's syndrome later in life.<sup>4</sup>

Induction methods are available in a wide variety.<sup>5</sup> The best way to induce labour is still a long way off. Prostaglandins are commonly used for labour induction when the cervix is in an unfavourable position. This has been the only method of administering prostaglandins and their analogues since 1960. While many other substances, such as oxytocin, corticosteroids, oestrogen, relaxin, and alike, have been used to induce labour, whereas nitric oxide donor (NO donor) is a relatively a new addition.<sup>6</sup> Cervical reaping is assumed to be mediated mostly by nitric oxide, a short-lived free radical gas.<sup>7</sup>

Abdellah MS and colleagues<sup>8</sup> in a prevuis trial revealed (19.56+3.96 in Isosorbide Mononitrate (IMN) plus misoprostol vs. 23+2.6, misoprostol alone, P 0.001), hours duration of induction to labour, however, local data was generated by Uzma Shafique<sup>9</sup> only. We planned this study to generate local magnitude for further help for obstetricians and patients as well.

## METHODOLOGY

In this Randomized Controlled Trial, at the Department of Gynecology and Obstetrics (Unit-II) at at Social Security Hospita, MNCH, Lahore, we enrolled 150 women, with 75 in each group. The women had to be at least 18 years old, have post-term

pregnancies longer than 40 weeks (as determined by a dating scan), singleton pregnancy, Bishop score of 3 to 6 (which is good for induction). A random number table was used to divide these 150 pregnant women into two equal groups. In Group A, IMN (40 mg) was applied to the posterior fornix of the uterus, and then misoprostol (50 ug) was given. In Group B, misoprostol (50 ug) was given alone. Second doses were only given if labour hadn't started or if the uterus hadn't started contracting regularly (3 or more 35-45 second contractions in 10 minutes) within 6 hours of the first dose. Up to four doses were given every six hours until the patient went into active phase and gave birth. On a pre-made form, the average time from induction to delivery was written down. Data was stratified for age and parity and number of misoprostole doses of the patients to control the effect modifiers.

## RESULTS

Patients in Group-A (n=47) and Group-B (n=42) were aged between 18-25 years of age, whereas 37.33 percent (n=28) and 44 percent (n=33) in Group-A (n=28) were between 26-35 years of age, respectively, and their mean+sd was computed at 24.4+5.06 and 25.25+5.53 years. More than 84% of patients in Group A and 78.67% of patients in Group B were between 40 and 41 weeks of gestation, while 12% in Group A had a gestational age of 42 weeks and a mean+sd of 40.37+1.32 weeks, respectively, for the two groups. A parity distribution showed that 52 percent (n=39) of patients in Group A and 46.67 percent (n=35) of patients in Group B had >3 paras, whereas 48 percent (n=36) of patients in Group A and 53.33 percent (n=40) of patients in Group B had mean+sd of 2.64+1.21 and 2.52+1.33, respectively. (Table 1)

Comparison of the mean duration of induction to delivery in both groups was done, which shows that the mean duration of induction to delivery in Group-A was calculated to be 19.28+1.75 minutes, while the mean duration of induction to delivery in Group-B was calculated to be 23.75+2.47 minutes. The p value for this comparison was calculated to be 0.000, indicating a significant difference. (Table 2)

Table 1: Demographics of the Patients (n=150)

Variables		Group-A (n=75)	Group-B (n=75)
Age(in years)	18-25	47(62.67%)	42(56%)
	26-35	28(37.33%)	33(44%)
Gestational Age (in weeks)	40-41	63(84%)	59(78.67%)
	42	12(16%)	16(21.33%)
Parity	1-3	39(52%)	35(46.67%)
	>3	36(48%)	40(53.33%)

Table 2: Comparison of Mean Duration of Induction to Delivery in Both Groups (n=150)

Mean duration (minutes)	Group-A (n=75)		Group-B (n=75)		P value
	Mean	S.D.	Mean	S.D.	
	19.28	1.75	23.75	2.47	

**DISCUSSION**

Practitioners disagree on the optimal strategy for cervical ripening; nonetheless, vaginal administration of isosorbide mononitrate (IMN) is regarded a low-risk method for inducing labour in full-term pregnant women. This study was designed to assess the mean length of induction until delivery in patients induced with isosorbide mononitrate (IMN) with misoprostol versus misoprostol alone in post-term pregnancies in order to generate local magnitudes, as there is a paucity of data locally.

According to the results of our research, out of a total of 150 cases (75 in each group), 62.67 percent of those in Group-A (n=47) and 56 percent of those in Group-B (n=42) were between the ages of 18-25, and 37.33 percent of those in Group-A (n=28) and 44 percent of those in Group-B (n=33) were between the ages of 26-35, with the mean and standard deviation being calculated as 24.4+5.06. Comparison of the mean duration of induction to delivery in both groups was done, which shows that the mean duration of induction to delivery in Group-A was calculated to be 19.28+1.75 minutes, while the mean duration of induction to delivery in Group-B was calculated to be 23.75+2.47 minutes. The p value for this comparison was calculated to be 0.000, indicating that there is a significant difference between the two groups. The results of our research are consistent with the results of a study that was carried out by Abdellah MS and his co-workers. 8 For the purpose of cervical ripening and labour induction, this study compared the efficacy and safety of intravaginal administration of isosorbide mononitrate (IMN) in combination with misoprostol to intravaginal administration of misoprostol alone. The duration of time from the induction to the delivery was documented by the researchers (19.56+3.96 vs. 23+2.62, p:0.001) hours.

Misoprostol, isosorbide mononitrate (IMN), and combination therapy for cervical ripening prior to induction of labour at term were all evaluated by Ahmed T Soliman and colleagues,<sup>10</sup> who found that combination therapy was superior to IMN or misoprostol alone in terms of efficacy, safety, and tolerability. Misoprostol (60 percent) and combination therapy (62.1 percent) had considerably greater rates of successful induction (vaginal birth within 24 hours of initiation of cervical softening) than the IMN (27.7 percent) group (P 0.0001). The IMN group had a significantly longer time from treatment initiation to delivery than the misoprostol and combination medication groups (P 0.0001). Just in the IMN group did the IMN group require oxytocin (93.8%), compared to the misoprostol (21.5%) and combination therapy (25.6%) group, which required only 25.8%. Misoprostol and combination therapy were shown to be less effective and less safe when compared to IMN. This study found no significant differences in the rates of caesarean delivery between groups; however, there were significant differences in the most common causes of caesarean delivery, including dystocia (54.5 percent) in the IMN group versus a persistent nonreassuring foetal heart rate pattern in the misoprostol and combination therapy groups (57.1 percent). Preinduction cervical ripening at term was shown to be more effectively treated with a combination of IMN and misoprostol than with either agent alone, the researchers concluded. A better option

was found in the form of intramuscular neuropathic medication (IMN).

When isosorbide mononitrate was combined to oral misoprostol for cervical ripening and labour induction, Collingham JP and others<sup>11</sup> investigated if the time to vaginal delivery was reduced. According to the researchers, a total of 156 women were randomly assigned to the study, although three were later deemed ineligible. Misoprostol was administered to 78 women, whereas the remaining 78 received isosorbide mononitrate in addition to misoprostol. The demographics of the two groups were nearly identical. In the case of isosorbide mononitrate with misoprostol, the time to delivery was not decreased. The rates of caesarean deliveries, as well as anomalies in contractions and foetal heart rate, were comparable between groups, which is in line with our own findings.

The findings of this study and other studies<sup>8,10</sup> justify the hypothesis of the study that **“Misoprostol when administered with IMN shorten the duration of induction to delivery than Misoprostol alone”**, is justified. However, the findings of our study are primary and others studies are required to further strengthen the current findings.

**CONCLUSION**

We concluded that mean induction to delivery interval in patients induced with isosorbide mononitrate (IMN) plus misoprostol is significantly shorter than misoprostol alone in post-term pregnancies.

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