

## INDUCTION OF LABOUR IN POSTDATE PREGNANCIES A COMPARATIVE STUDY BETWEEN ISOSORBIDE MONONITRATE PLUS MISOPROSTOL VS MISOPROSTOL ALONE AS A METHOD OF INDUCTION OF LABOUR

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### ABSTRACT

**BACKGROUND:** Postdate pregnancies are the pregnancies beyond the expected date of delivery, postterm pregnancies are also included in the classification of postdate pregnancies which lasts more than 42 weeks or 294 days calculated after the first day of last menstrual period. Intrapartum and postpartum obstetric complications are enormous in post term pregnancy and is associated with higher perinatal morbidity and mortality rates. Postdate pregnancy is one of the major indication of induction of labour. There is plethora of techniques available for labour induction.

### OBJECTIVES:

To compare the efficacy of intra vaginal use of Isosorbide Mononitrate (IMN) plus Misoprostol versus Misoprostol alone for induction of labour in postdates pregnancies.

**DESIGN:** Randomized Controlled Trial

### PATIENTS AND METHODS:

This study was done at obstetrics and Gynaecology Department unit 3 Lady willingdon Hospital / king Edward medical university Lahore for a period of six months from 1.7.2014 to 31.12.2014. 100 pregnant postdate women were divided equally in two groups randomly. Group A was induced with IMN (40mg) applied in posterior fornix of vagina followed by Misoprostol (50ug) and Group B, was induced by Misoprostol (50ug) alone. Efficacy of both methods of induction was compared.

### RESULTS:

In this study mean age in group-A and group-B was  $24.53 \pm 4.65$  years and  $24.98 \pm 4.87$  years respectively. A total of 42(84%) in group-A and 38(78%) in group – B had had gestational age 40-41 weeks while 42 gestational age was calculated in 8(16%) of group-A and 11(22%) of group-B. Efficacy of both treatments were compared using Chi-square test, so in group-A efficacy was higher (68%) as compared to group-B (34%), p-value = 0.001.

**CONCLUSION:** The results of the study revealed that intravaginal administration of IMN plus Misoprostol is more effective than Misoprostol alone for labour induction in post term pregnancies.

**KEY WORDS:** Post term pregnancy, induction of labour, intravaginal administration IMN plus Misoprostol, Misoprostol alone, efficacy.

### INTRODUCTION

Induction of labour is a procedure which is designed to stimulate uterine contractions when it does not starts spontaneously.<sup>1</sup>

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Sometimes it is necessary to bring on labour artificially because of the safety concerns for the mother or baby<sup>2</sup>. The induction currently occurs for almost 24% of infants between 37 & 41 weeks of gestation<sup>3</sup>. There is a wide range of fetal complications due to postterm pregnancy, which includes oligohydramnios, fetal birth injury, meconium aspiration syndrome and increase incidence of caesarean section.<sup>4</sup> In order to reduce the risk of these complications induction of labour is planned, success of this procedure depends upon the degree of cervical ripening.<sup>5</sup> Labour induction is also associated with few complications like pyrexia, fetal distress, uterine hyper stimulation and increase risk of caesarean sections, but with the modern methods for induction of labour, these risks appeared to be diminished<sup>6</sup>. There is plethora of techniques available for labour induction.<sup>7</sup> Among the pharmacological methods, Misoprostol, a methyl analogue PgE<sub>1</sub> has become the choice prostaglandin of more recent studies, for many reasons: it is cheaper, easy to store because of thermo stability, can be used many ways with efficacy. As for the main undesirable effect, uterus hyper stimulation, the use of low doses (25 mcg) every four hours has been determined to be safe, reducing this effect.<sup>8</sup> The use of vaginal nitric oxide donor isosorbide mononitrate for cervical ripening has been reported in few publications<sup>9</sup>. Nitric oxide donors by increasing the expression of cyclooxygenase 2 in the cervix improve cervical distensibility without causing uterine contractions. Potential benefits include its potential use in the outpatient setting, low cost, and ease of administration. A recent RCT comparing self-administered isosorbide mononitrate with placebo did not detect a difference in admission to delivery interval despite a clinical effect on cervical ripening<sup>10</sup>. Furthermore, the addition of Misoprostol or dinoprostone to the isosorbide mononitrate does not reduce the time to vaginal delivery<sup>11</sup>. Therefore, at present, isosorbide mononitrate should not be used for cervical ripening except in clinical trials. Many foreign studies have been conducted to use IMN<sup>12</sup>, but locally in Pakistan rarely any data is available to use IMN plus Misoprostol in post

term pregnancies. Keeping in mind these facts, this study was designed to evaluate the additive effects of two drugs locally, so that perinatal and maternal outcome can be improved by reducing the complications of post term pregnancies, to shortened induction delivery interval, hospital stay and economical burden on patients should be reduced in low resourced country, and also to compare the efficacy of intravaginal administration IMN plus Misoprostol versus Misoprostol alone for labour induction in post term pregnancies.

### PATIENTS AND METHODS

This randomized study was done at the obstetrics and Gynaecology Department unit 3 Lady Willingdon Hospital / King Edward medical university Lahore for a period of six months from 1.7.2014 to 31.12.2014. Non-probability purposive sampling technique was used. 100 patients who fulfill the inclusion criteria from emergency and OPD department of unit III of Lady Willingdon Hospital Lahore were included in the study. All patients aged Age  $\geq 18$  years, post date pregnancies  $\geq 40$  weeks (calculated by dating scan), Women of any parity, Bishop score 2 to 4 and Vertex presentation (accessed on USG) were included in this study. Females with rupture of membranes (accessed on per speculum examination), placenta previa, IUGR (accessed on USG), severe pre-eclampsia (accessed by B.P  $\geq 160/110$  + proteinuria measured with dipstick with or without symptoms) were excluded from study.

These 100 pregnant women were divided equally in two groups randomly by lottery method. One group (Group A) was induced with IMN (40mg) applied in posterior fornix of vagina followed by Misoprostol (50ug) and the other group (Group B) was induced by Misoprostol (50ug) alone. Second doses were administered only in subjects where the bishop score was not improved i.e. ( $>8$ ) or there were no uterine contractions (3 or more contractions of 35-45 sec in 10 mins) within 6 hrs of first dose. Maximum of 4 doses were repeated at 6 hrly intervals until the patient goes into active phase & delivers. If patient does not deliver

with maximum doses then she was declared failure of induction and caesarean section was performed. Data was collected for the no. of doses required for the delivery of patients within 24 hrs. Data was stratified for the no. of doses to address the effect of modifiers.

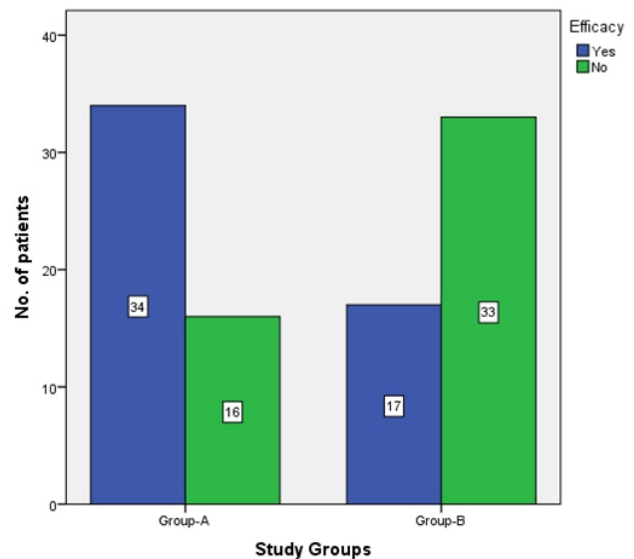
The data was analyzed by using SPSS-16 software. Efficacy (qualitative variables) was presented as frequency tables and percentages. All metric (quantitative) variables like age (in years) and gestational age was presented in form of mean  $\pm$  S.D. Chi-square test ( $X^2$ ) was applied to compare the efficacy in both groups. A P value of  $\leq .05$  was taken as statistically significant.

## RESULTS:

In this study mean age in group-A and group-B was  $24.53 \pm 4.65$  years and  $24.98 \pm 4.87$  years respectively. The most frequent age group was 26-30 years preceding by 18-25 years, 31-35 years and > 35 years. A total of 42(84%) in group-A and 38(78%) in group - B had gestational age 40-41 weeks while 42 gestational age was calculated in 8(16%) of group-A and 11(22%) of group-B.(table 1) Efficacy of both treatments were compared using Chi-square test, so in group-A efficacy was higher (68%) as compared to group-B (34%), p-value = 0.001.

**Table-1: Comparison of maternal and gestational age in both study groups**

		Study groups	
		Group-A	Group-B
Age groups	18-25 years	11 (22%)	14 (28%)
	26-30 years	23 (46%)	21 (42%)
	31-35 years	10 (20%)	11 (22%)
	> 35 years	6 (12%)	4(8%)
Mean age [mean $\pm$ S.D]		24.53 $\pm$ 4.65	24.98 $\pm$ 4.87
Gestation age (weeks)	40-41	42(84%)	39 (78%)
	42	8 (16%)	11 (22%)



P value= 0.001

## DISCUSSION

Post term pregnancy, is one that lasts longer than 42 weeks or 294 days after the first day of last menstrual period. In the UK every year around 60,000 women deliver postdate.<sup>13</sup> Post term pregnancy remains constantly a difficult and controversial problem in modern obstetrics, there are many intrapartum and postpartum obstetric complications which are associated with these pregnancies and cause higher perinatal morbidity and mortality rates<sup>14</sup>. Mistaken dates account about two third of the prolonged pregnancies<sup>15</sup>. In comparison with the babies delivered at term, babies delivered postdates are more likely to be hospitalized during the first 3 years of life and are at greater risk of developing conditions including neurodevelopmental deviation, epilepsy, and Asperser's syndrome in later life<sup>16</sup>. Bishop's score is a deciding factor for determining the choice of the method of induction<sup>17</sup>. Many studies advocate the use of Misoprostol for successful induction of labour<sup>18</sup>.

The result of the study revealed, majority of the patients i.e. 46%(n=23) in Group-A and 42%(n=21) in Group-B were between 26-30 years of age, the mean age was recorded as  $24.53 \pm 4.65$  years in Group-A and  $24.98 \pm 4.87$  years in Group-B. The majority of the patients in these groups are due to the reason that in

Pakistan early marriages trend is settled.

While comparison of efficacy in both groups was done which shows 68 % (n=34) in Group-A and 34 % (n=17) while 32 % (n=16) in Group-A and 66% (n=33) in Group-B were not recorded as effectively treated, these findings show a significant difference, p value was calculated as 0.00.

The results of our study were in agreement with a study conducted in Egypt which showed that by using IMN plus Misoprostol for labour induction 73.1% patients delivered vaginally as compared to 37.9% by inducing with Misoprostol alone within 24hrs<sup>19</sup>.

Another study done by Abdellah MS, and co-workers evaluated the safety and efficacy of intravaginal administration of isosorbide mononitrate (IMN) plus Misoprostol versus Misoprostol alone for labour induction and as an agent for cervical ripening, they recorded that in the women in which IMN plus Misoprostol was used to cause cervical ripening showed significant changes in the Bishop score 6 h after application as compared to Misoprostol plus placebo ( $8.57 \pm 1.46$  vs.  $7.6 \pm 1.39$  h,  $P = 0.001$ ), intervals from the beginning of the induction to the start of the active phase of labour was also shorter ( $10.97 \pm 2.87$  vs.  $13.91 \pm 2.16$  h,  $P = 0.0004$ ) furthermore, the induction to the time of delivery was alone reduced ( $19.56 \pm 3.96$  vs.  $23 \pm 2.62$   $P \leq 0.001$ ) and concluded that combination of IMN and Misoprostol is more effective than Misoprostol alone for rapid cervical ripening and shortening of induction-labour interval<sup>12</sup>. Though the success regarding vaginal delivery was not recorded in the above study but the study revealed the efficacy regarding obstetrical outcome.

Our study revealed better improved Bishop's score in the IMN group compared to Misoprostol alone group. Chanrachakul et al<sup>20</sup> concluded after a small trial in which they compared 40 mg of IMN with 50 ug of Misoprostol and used maximum of three doses 6 hours apart. The baseline Bishop's score was three in both the groups. After the three doses, the overall increase in the score was 1.5 U in IMN group and 3 U in the Misoprostol group. In comparison to our trial, this trial examined either of both

agents alone and, though Bishop Score was not included in our data analysis of the study, but on behalf of this variable also, the efficacy of IMN plus Misoprostol group was evident.

Our study had few limitations; it was lacking to address the maternal satisfaction rate at the end. It was observed that IMN group complained headache (although it was not severe in most of cases). Therefore, in the future trials, maternal satisfaction questionnaire should be included in the studies.

### CONCLUSION:

The results of the study revealed that intravaginal administration of IMN plus Misoprostol is more effective than Misoprostol alone for labour induction in postdate pregnancies.

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A FOOL'S MIND IS AT THE MERCY OF HIS TONGUE AND A WISE MAN'S  
TONGUE IS UNDER THE CONTROL OF HIS MIND.

***Hazrat Ali (Karmulha Wajhay)***