

Comparison of Mean Duration of Induction to Delivery in Isosorbide Mononitrate (Imn) plus Misoprostol between Misoprostol alone in Post-Term Pregnancies

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ABSTRACT

Objective: To compare mean duration of induction to delivery in patients induced with isosorbide mononitrate (IMN) plus misoprostol versus misoprostol alone, among women with post-term pregnancies.

Study Design: A Randomized Controlled Trial

Place and duration: Study was conducted at department of Gynaecology and Obstetrics, Peoples University of Medical and Health Sciences for Women, Nawabshah, Sindh, from 15 May 2018 to 15 November 2018.

Methodology: Total 102 pregnant women who were presented in outpatients and emergency department of hospital were recruited in this study. Study patients were divided into two equal groups by simple random method. In groups A patients IMN 40mg was used for induction of labor followed by 50 µg misoprostol and misoprostol (50 µg) alone in group B. Mean duration of induction to delivery were recorded from both groups. SPSS version 23 was used for data entry and analysis.

Results: Mean age, gestational age and parity of patients were 22.9±3.7 years, 40.22±2.3 weeks and 2.9±3 respectively. Overall 39 (38.23%) patients were diabetics, 30 (58.82%) patients were anemic in our study. Mean duration of induction to delivery of group A was 32.9±3.8 hours and duration of group B was 37.2±3.6 (p-value=0.0001).

Conclusion: Isosorbide mononitrate is a useful and effective medicine for artificial ripening of cervix having capability to reduce the interval of labor.

Keywords: Post-term pregnancy, duration of induction to delivery, isosorbide mononitrate (IMN), misoprostol alone.

INTRODUCTION

Post term pregnancy is defined as pregnancy that has extended to or beyond 2 weeks of gestation (294 days), or estimated date of delivery (edd) + 14 days. Post term pregnancy is associated with an increased risk of fetal and neonatal mortality and morbidity as well as an increased maternal morbidity.¹The incidence of post term pregnancy is ranged from 04% to 14%. Cause of perinatal mortality is prolonged gestation age which is ≥ 42 weeks. At 41 weeks of gestation the rate is 9 per 1000 live births, and it continues to rise there after².

Usually at term pregnancy patients have spontaneous onset but at some occasions natural course of labour may be altered and needs to be induced. Labor induction is increasing day by day from last few years³. Maternal indications of labor are pregnancy induced hypertension and pre-eclampsia and fetal include rupture membranes, post term dates, diabetes and growth retardation. Induction failure may be due to induction of labour without ripening of cervix, best agent should have properties of limited side effects regarding neonates like low Apgar score and mother like nausea vomiting. Numerous medical and non-medical methods are in practice for labour induction e.g prostaglandins. Although, prostaglandins has risk of hyper stimulation which hinders it's free use in outpatient department⁴.

Induction of labour and cervical ripening is usually achieved by means of prostaglandins (PG) administration. In recent years Nitric oxide (NO) and misoprostol are common in practice and evidences are found in cervical ripening. Many studies have been conducted on combine use of misoprostol and IMN⁵.

Among cervical ripening agents Nitric oxide (NO) is a free radical with very short half-life. Studies conducted before shown that NO reduction in cervix may cause post term pregnancy because of its role in collagen rearrangement. Collagen arrangement is responsible for softening of cervix without involvement of uterine contractions. Another agent used for cervical ripening is Isosorbide mononitrate (IMN) which is basically used in maintaining of blood pressure and relief from angina pectoris. Study conducted by Ekerhovd et al., reported that 40 mg IMN in cases of elective cesarean gives excellent results in

cervical ripening and dispensability⁶. A previous study also have evidence of self-administered IMN 40 mg per vaginally and end results of pre induction ripening of cervix⁷.

However we were conducted this study to determine the mean duration of induction to delivery in patients and also it is of increasing concern in low- and middle-income countries i.e. Pakistan, Bangladesh, Nepal, Sri Lanka, and India make about a quarter of the world's population and this region especially Pakistan has highest rate of the perinatal mortality. As there is limited local data available, therefore my research will provide the correct magnitude in our local population because of the different body habitus, environment and dietary habits and also help the government to allocate the sufficient budget in this regard and also it will be helpful for other healthcare provider.

METHODOLOGY

The current randomized controlled trial (RCT) study was conducted at department of Gynaecology & Obstetrics, Peoples University of Medical and Health Sciences for Women, Nawabshah, Sindh, from 15 May 2018 to 15 November 2018. Total 102 patient with post term pregnancy (gestational age > 40 weeks) were taken with demographics and clinical/maternal history. Initial Bishop's scores were determined by the researcher before vaginal tablets were inserted. These were divided into two equal groups A & B. Patients in group A were induced by using 40 µg IMN in posterior fornix of vagina and followed by 50 µg misoprostol. Patients in group B were induced by using 50 µg misoprostol only. In case progress of labor was not started or uterine contractions are not regular second dose of was given. Non establishment of uterine contractions was labeled if in duration of 10 minutes only 3 contractions of 35 to45 minutes were noted until 6 hours of 1st dose. Maximum of 4 doses were repeated at 6 hourly intervals until the patient goes into active phase & delivers. If patient does not deliver with maximum doses then patient were declared failure of induction and cesarean section were performed.

Duration of induction of delivery were access by Bishop score 3 to 6. Gestational age > 40 weeks (age were determined on the basis of the last menstrual period and sonography in the first

half of pregnancy i.e. assessed on ultrasound through femur length (built-in software calculate the age of fetus) were considered as post term pregnancy, age 18-34 years and women of any parity/gravida were included and patients with rupture of membrane, placenta previa with any type/grade and intrauterine growth restriction (IUGR) were excluded from study.

All data was compiled and analyzed using with SPSS version 23. Main variables like age, gestational age, parity, gravidity, duration of induction to delivery time were recorded from two groups and recorded on a pre-designed proforma. In all analysis p-value ≤0.05 was considered as significant.

RESULTS

A total of 102 patients, overall mean age, mean gestational age, BMI, mean gravidity and mean parity of patients were 22.9±3.7 years, 40.22±2.3 weeks, 23.9±2.9, 3.1±2.0 and 2.9±3 respectively. (Table. I). Majority of patients were un-booked 58 (56.9%), diabetes mellitus 39 (38.2%), anemic 65 (63.7%), and duration of induction to delivery 36.8±3.65 hours. (Table. I).

Comparison of mean duration of induction to delivery between both groups was stated, results showed significance difference between both groups mean duration of induction to delivery of group A was 32.9±3.8 hours and duration of group B was 37.2±3.6 (p-value=0.0001). Statistically significance results were seen when results of mean duration of induction to delivery compared between both groups like age groups, BMI groups, diabetes, anemia and booking status p value 0.004, 0.001, 0.001, 0.001, 0.001, and 0.001 respectively. (Table. II).

Table 1: Demographic variables of the study patients

Variables	Group-A	Group-B	Total
	Mean± SD	Mean± SD	Mean± SD
Age (years)	23.6±4.1	24.6±3.8	22.9±3.7
Gestational age(weeks)	40.69±2.1	41.0±2.5	40.22±2.3
BMI (kg/m ²)	23.3±3.2	24±3.2	23.9±2.9
Gravidity	2.9±2.1	3.1±1.9	3.1±2.0
Parity	2.3±2.5	2.8±2.2	2.9±3.1
Booking status			
Booked	21 (41.2%)	23 (45.1%)	44 (43.1%)
Un-booked	30 (58.8%)	28 (54.9%)	58 (56.9%)
Diabetes mellitus			
Yes	21 (41.2%)	18 (35.3%)	39 (38.2%)
No	30 (58.8%)	33 (64.7%)	63 (61.8%)
Anemia			
Yes	35 (68.6%)	30 (58.8%)	65 (63.7%)
No	16 (31.4%)	21 (41.2%)	37 (36.3%)
Duration of Induction to delivery (hours)			
	32.9±3.8	37.2±3.6	36.8±3.65

Table 2: Comparison of mean duration of induction to delivery between both groups

Variables	Group-A	Group-B	P-value
	Mean± SD	Mean± SD	
Age (years)			
≤25 in years	33.5±2.7	35.9±2.4	0.004
>25 in years	33.2±2.0	37.9±3.1	0.001
BMI			
≤25kg/m ²	31.2±2.2	36.9±3.2	0.001
>25kg/m ²	30.2±3.1	35.3±2.8	0.001
Diabetes			
Yes	33.1±2.8	36.7±2.6	0.001
No	32.3±2.5	35.9±2.5	0.001
Anemia			
Yes	31.5±2.6	36.1±2.7	0.001
No	32.6±2.8	36.7±2.9	0.001
Booking status			
Booked	31.0±3.5	36.4±2.9	0.001
Un-booked	32.3±3.2	35.3±2.95	0.001

DISCUSSION

Labour induction is an important component of maternity related practice and usually indicated for number of medical, social and obstetrical conditions. In our study two groups were compared in

terms of demographics, indications of induction of labour and pre induction Bishop Score.

We observed a statistically significant difference in post induction Bishop Score among the groups. In previous study conducted by Yazdizadeh et al., also reported similar findings as Bishop Score was 1.94 ± 1.3 before IMN and 6.7±2.2 after IMN⁹. But our results are different from studies conducted by Elsokary et al., who reported that per vaginal IMN administration does not give significant difference in promoting delivery when given at the time of dinoprostone³.

Studies conducted by Soliman et al. and Mohamad S. Abdellah⁹⁻¹⁰ concluded that misoprostol and IMN combination is found more effective as compare to misoprostol or IMN alone in cervical ripening or shortening of latent phase. This study reported 14.2 ± 2.7 hours delivery interval in IMN and misoprostol group and 20.8 ± 2.9 hours in misoprostol alone group (p<0.001).

Low induction at the delivery interval in the IMN and misoprostol group is explained by the synergistic effect on the cervix through the vaginal tract leading directly to the cervix through the cervical canal. A contrary study was conducted by Justin P. Collingham¹¹ reported that addition of IMN with misoprostol in induction of labour and cervical ripening is more beneficial as compare to both drugs in alone. This difference may be because of difference in administration route.

In our study we observed hemodynamic complications are more frequent in combination of misoprostol and IMN group as compare to misoprostol alone. Similar findings were reported by Kavita Agarwal et al., suggested that nitric oxide give vasodilatory effect that shows these findings. There was no significant difference was observed in Apgar score and birth weight among groups¹².

In this study it was suggested that both combination of misoprostol and IMN and misoprostol alone are effective and safe in all modes of administration but combination is more effective in terms of Bishop Score, post induction, induction to delivery time and shortening of active phase of labour.

Abnormalities of uterine contraction are not associated with isosorbide mononitrate but misoprostol is associated with hyper stimulation of uterus. Literature shows better Apgar score with misoprostol and isosorbide mononitrate at intervals of 1 and 5 minutes. That's why combination of nitric oxide and misoprostol is considered as main therapeutic advancement in cervical ripening in pre induction period of term pregnancy.

CONCLUSION

Isosorbide mononitrate is a useful and effective medicine for artificial ripening of cervix having capability to reduce the interval of labor. Further studies are needed to document the advantages of IMN in post term pregnancies.

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