INDUCTION OF LABOUR WITH MISOPROSTOL VERSUS PROSTAGLANDIN E2 IN AN ALIVE TERM FETUS

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ABSTRACT
Objective: The objective of this study was to compare efficacy of misoprostol with PGE2 for induction of labor in an alive term fetus.
Materials And Methods: This study was conducted in Department of obstetrics and gynecology unit III, Nishtar Hospital Multan from 9th October, 2013 to 8th April, 2015. One hundred and fifty four patients at term were included in this randomized controlled trial. Final outcome i.e. successful vaginal delivery was confirmed at the end of 6 hours after giving the maximum dose of either medicine. Statistical analysis was performed using SPSS v17. P-value of ≤ 0.05 was taken as statistically significant.
Results: Mode of delivery in both groups revealed that 12.99% (n=10) in Group-A and 38.96% (n=30) in Group-B had cesarean delivery and 87.01% (n=67) in Group-A and 61.04% (n=47) in Group-B had normal vaginal delivery, p value was calculated as <0.001 which was significant. Efficacy in both groups revealed that in 12.99% (n=10) patients from Group-A and in 38.96% (n=30) patients from Group-B, the drug failed to show efficacy and in 87.01% (n=67) patients from Group-A and in 61.04% (n=47) patients from Group-B the respective drugs were efficacious, p value was calculated as <0.001.
Conclusion: The results of the study conclude that compared to PGE2, misoprostol has superior efficacy.
Keywords: Induction of labor, PGE2, Misoprostol.

INTRODUCTION
Induction of labour is the intentional initiation of labour before spontaneous onset, for the purpose of delivery of the fetoplacental unit.[1, 2] Induction accounts for approximately 20% of deliveries.[3] Induction of labour can be achieved by a variety of physical and biochemical stimuli designed for the purpose. Some studies of elective induction suggest higher rates of adverse outcomes, including prolonged first stage, failure to progress, intrapartum haemorrhage, admission to NICU and a higher incidence of assisted vaginal birth.[4, 5]

When the cervix is unfavorable, cervical ripening is recommended to increase the likelihood of successful induction. Prostaglandin E2 (PgE2), given vaginally or intracervically, has been shown to be effective for cervical ripening. Misoprostol, a prostaglandin E1 analogue manufactured for the prevention and treatment of gastric ulcers, has also been evaluated as a cervical ripening agent and has some potential advantages compared with PgE2. Misoprostol is inexpensive, stable at room temperature and easy to administer.[6-8] There is an increase in the rate of uterine hyperstimulation resulting in changes in fetal heart rate (FHR) pattern and staining of the amniotic fluid with meconium but without any apparent deleterious effect on the outcome.[9-10]

A recent study conducted in another tertiary health care center in Pakistan compared the use of misoprostol with PGE2 for induction of labour in term fetus. Induction was successful in 50% patients who received induction with prostaglandin E2 and 74% patients who received induction with prostaglandin E1. 25 (50%) patients of the former group and 37 (74%) patients of the latter group delivered by spontaneous vaginal delivery while 25 (50%) patients of the former group and 13 (26%) patients of the latter group required cesarean section. [11] Another local study found during literature search included 46 patients (23 in each group). Delivery within 10-12 h, after the first administration occurred more often in the misoprostol group than in the PGE2 [16 (69.56%) vs 2 (8.69%)].[12]However it was observed that the sample size was not adequate and

again the effect modifiers have not been controlled in either study.

Therefore despite the existing studies, there is a lack of evidence on the comparison between misoprostol and prostaglandin E2 for induction of labour in an alive term fetus as the available studies as mentioned earlier lack statistical value in some aspects. The purpose of this study was to evaluate the use of misoprostol compared with PGE2 for labour induction at term in terms of success of induction, mode of delivery and induction delivery interval.

MATERIAL & METHODS

This randomized controlled trial was conducted from 9th October, 2013 to 8th April, 2015 in the Department of obstetrics and gynecology unit III, Nishtar Hospital Multan. A specialized Performa was developed to record the findings of this study by the researcher. Permission from ethical committee of the institution was taken before the start of the study. Patients coming to the obstetrics and gynecology outpatient and emergency department Nishtar hospital fulfilling the inclusion and exclusion criteria were enrolled for the study. Informed consent was taken from all the patients. Subsequently the group allocation was done by lottery method to ensure randomization.

Patients from 18 to 36 years of age both primi and multigravida were included with gestational age from 37 to 41+6 weeks calculated by LMP. Women with previous cesarean section, uterine anomalies, multiple pregnancies or known sensitivity to prostaglandin analogues were excluded.

Misoprostol fifty micrograms was inserted in posterior vaginal fornix for every 6 hour till a maximum dose of three doses and the patients with misoprostol administration were termed group A. Prostaglandin E2 3mg pessary was inserted vaginally at 6 hour interval for a maximum of 3 doses and that group of patients with PGE2 insertion was called group B. Final outcome was confirmed by the researcher at the end of 6 hours after giving the maximum dose of either medicine.

Data analysis was done by SPSS software version 17. Mean +- SD was calculated for age, gestational age and bishop score. Frequency and percentages were calculated for efficacy and parity. Stratification with respect to age, gestational age, bishop score and parity was done. Post stratification chi square test was applied. P value less than or equal to 0.05 was considered as significant.

RESULTS

A total of 154 patients fulfilling the inclusion criteria were enrolled to compare the efficacy of misoprostol and PGE_2 for induction of labour in an alive term fetus unfavourable cervix (Bishop Score < 6).

Distribution of parity of the patients revealed 79.22% (n=61) in Group-A and 68.83% (n=53) in Group-B between P0-P2, 16.88% (n=13) in Group-A and 20.78% (n=16) in Group-B were between P3-P5 while 3.90% (n=3) in Group A and 10.39% (n=8) in Group B were >P5 (Table No. 1).

Distribution of Bishop Score of Patients revealed 38.96% (n=30) in Group A and 48.05% (n=37) in Group B had Bishop Score between 0-2 and 61.04% (n=47) in Group A and 51.95% (n=40) in Group B had Bishop Score between 3-5 (Table no. 2).

Mode of delivery in both groups revealed 12.99% (n=10) in Group-A and 38.96% (n=30) in Group-B had cesarean delivery and 87.01% (n=67) in Group-A and 61.04% (n=47) in Group-B had normal vaginal delivery, p value was calculated as <0.001. (Table No. 3)

Induction-delivery interval in both groups were compared in Table No. 5, where in Group-A 10.99±4.61 hours while 16.81±3.67 in Group-B, chi square test applied which shows a significant difference by calculating p value as <0.001. (Table No. 4)

Efficacy in both groups revealed that in 12.99% (n=10) patients from Group-A and in 38.96% (n=30) patients from Group-B, the drug failed to show efficacy and in 87.01% (n=67) patients from Group-A and in 61.04% (n=47) patients from Group-B the respective drugs were efficacious, p value was calculated as <0.001. (Table No. 5)

Table 1: Distribution of Parity of The Patients (n=154)

Parity	**Group-A (n=77)**		**Group-B (n=77)**		**Total**	
	No. of patients	**%**	**No. of patients**	**%**	**Frequency**	**%**
P0-P2	61	79.22	53	68.83	114	74.03
P3-P5	13	16.88	16	20.78	29	18.83
>P5	3	3.90	8	10.39	11	7.14
Total	**77**	**100**	**77**	**100**	**154**	**100**

Table 2: Distribution of Bishop Score of The Patients (n=154)

Bishop Score	Group-A (n=77)		Group-B (n=77)	
	No. of patients	%	No. of patients	%
0 – 2	30	38.96	37	48.05
3 – 5	47	61.04	40	51.95
Total	**77**	**100**	**77**	**100**
Mean± standard deviation	**2.47±1.438**			

Table 3: Frequency and Percentages for Mode of Delivery in Both Groups (n=154)

Mode of delivery	Group-A (n=77)		Group-B (n=77)	
	No. of patients (frequency)	%	No. of patients (frequency)	%
Cesarean delivery	10	12.99	30	38.96
Normal vaginal delivery	67	87.01	47	61.04
Total	**77**	**100**	**77**	**100**

Table 4: Induction-Delivery Interval in Both Groups (n=154)

Induction-delivery interval (in hours)	Group-A (n=77)		Group-B (n=77)	
	Mean	SD	Mean	SD
	10.99hrs	4.61hrs	16.81hrs	3.67hrs

P value= 0.000 t test

Table 5: Efficacy in both groups (n=154)

Efficacy	Group-A (n=77)		Group-B (n=77)	
	No. of patients	%	No. of patients	%
No	10	12.99	30	38.96
Yes	67	87.01	47	61.04
Total	**77**	**100**	**77**	**100**

P value= <0.001 (exact p value=0.000 Chi square test)

DISCUSSION

Induction of labor is a commonly performed obstetric practice and is carried out for a variety of indications all over the world. There is around 20 percent prevalence of induction of labor done in industrialized countries.[13] The methods used for induction of labor are either mechanical or chemical and what method is used is based clinical scenario and availability of the drug and physician preference. The superiority of one agent used for induction of labor over another has been evaluated in similar studies.

Our results reveal insignificant difference in demographics i.e. age, gestational age, bishop score and parity of the subjects in both groups. However, on comparison of mode of delivery in both groups reveals 12.99%(n=10) in Group-A and 38.96%(n=30) in Group-B had cesarean delivery and 87.01%(n=67) in Group-A and 61.04%(n=47) in Group-B had normal vaginal delivery, p value was calculated as <0.001 by chi square test, induction-delivery interval reveal that in Group-A 10.99$\pm$4.61 hours while 16.81$\pm$3.67 hours in Group-B, a significant difference in both groups was recorded.

These results were in accordance with another study carried out at Jinnah hospital Lahore where Misprostol (PGE1) was found more effective than Dinoprostone (PGE2) in producing cervical changes and induction of labour. In Group A (Dinoprostone), 59% patients delivered vaginally, while 70% in Group B (Misoprostol), showing high efficacy and successful induction. The cost of induction was remarkably less in group-B (PGE1) patients as compared to Group-A (PGE2).[14]

Ozkan S, Caliskan E, et al conducted a similar study where time interval from induction to vaginal delivery was found to be significantly shorter in misoprostol group when compared to PGE2 subjects (680 +/- 329 min vs. 1070 +/- 435 min, P < 0.001). Vaginal delivery rates within 12 h were found to be significantly higher with misoprostol induction [n = 37 (66%) vs. n = 25 (44.6%); P = 0.02]. More subjects required oxytocin augmentation in PGE2 group [n = 35 (62.5%) vs. n = 20 (35.7%), P = 0.005] and cardiotocography tracings revealed early decelerations occurring more frequently with misoprostol induction (10.7 vs. 0%, P = 0.03). Tachysystole and uterine hyper stimulation, mode of delivery, rate of cesarean sections due to fetal distress and adverse neonatal outcome were not demonstrated to be significantly different between groups (P = 1, P = 0.5, P = 0.4, P = 0.22, P = 0.5).[15]

Another study conducted in 2009 by Austin S and colleagues revealed similar results. Women who received misoprostol had a higher incidence of vaginal delivery within 12 and 24 hours of prostaglandin application, compared with dinoprostone. Both modalities had similar incidences of cesarean delivery, uterine hyperstimulation, and fetal tachysystole. There was an increased need for oxytocin augmentation in the dinoprostone group. No significant difference in neonatal outcomes was noted between the 2 groups.[16]

In a systematic analysis carried out by Aghideh FK, Mullin PM and colleagues in 2014, various methods used for induction of labor were compared. Among parous patients, the cesarean delivery rate varied significantly by induction method (p<0.001), being lowest among those receiving misoprostol (10%). Those receiving oxytocin and transcervical Foley catheter had cesarean rates of 22%, followed by PGE2 at 18%. The rate of failed inductions was 2% among those receiving misoprostol, compared to 7-8% among those in the other groups which included PGE2.(p<0.01) [17]

The current study shows that misoprostol is more effective than PGE2 for induction of labor in an alive term fetus. As it is relatively inexpensive and stable at room temperature, it is best suited for our setup where economic constraints are a main concern affecting patient management and hot climate and failure to maintain cold chain often results in reduced effectiveness of medication that require refrigeration like PGE2. As the use of misoprostol results in increased chances of a successful vaginal delivery compared to induction of labor with PGE2 while reducing induction to delivery interval, it can be safely used for the induction of labor in an alive term fetus in our setup.

CONCLUSION

The results of this study conclude that misoprostol has a significantly superior efficacy over PGE2 for induction of labor in an alive term fetus. A successful vaginal delivery with misoprostol is more likely to be achieved when compared with PGE2 and the induction to delivery interval is also significantly reduced when misoprostol is used.

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