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Original Article

Comparison of Vaginal Isosorbide Mononitrate with Prostaglandin E2 for Pre-Induction Cervical Ripening at Term

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Abstract

Background : To compare the efficacy of nitric oxide donor isosorbide mononitrate (IMN) with prostaglandin E2 (PGE2) on the cervical ripening and induction of labour at term.

Methods: In this descriptive study sixty patients were divided into two equal groups.Group A consisted of 30 patients to whom Prostaglandin E2 was given. Group B included 30 patients to whom isosorbide mononitrate was given. Three mg of prostaglandin E2 was placed in posterior vaginal fornix in group A patients and dose was repeated every six hours up to 2 doses. 40 mg of isosorbide mononitrate (Monis) was given vaginally in group B patients and dose was repeated every four hour up to 2 doses. During this procedure intermittent fetal heart rate and uterine contraction was noted. Time of first and second dose of tablet was noted and time at which patient delivers was also noted to know the induction-delivery interval. If Bishop Score improved more than 5 then amniotomy followed by augmentation, if necessary was performed. If Bishop score did not improve after 2 doses, it was considered induction failure and an indication for caesarean section. Possible side effects were also noted.

Results: Induction to delivery interval was longer in IMN group as compared to PGE2. There was no case of hyperstimulation in both groups. Side effects of IMN were mild and not clinically significant .

Conclusion: Like prostaglandin E2, the nitric oxide donor Isosorbide Mononitrate can be used for cervical ripening and induction of labour.

Key Words: Labour, Induction, Nitric Oxide Donors, PGE_2, Cervical Ripening.

Introduction

Degree of cervical ripening is of fundamental importance for successful induction of labour as it culminates in softening and distensibility of cervix. Normally labour starts spontaneously but in 10% to 20% cases it has to be induced. The mechanism of cervical ripening and labour is still not fully understood but is thought to involve different hormones including oestrogens, progesterone, prostaglandins and nitric oxide (NO). Induction of labour is the stimulation of regular uterine contractions before the spontaneous onset of labour & cervical ripening is the process that culminates in the softening and distensibility of cervix, thus facilitating labour and delivery.[1] Induction of labour is indicated when delivery is more beneficial for mother or fetus than continuation of pregnancy. [2] Various mechanical and pharmacological methods are used for induction of labour [3]. Indications for labour induction are postdates, pre labour rupture of membranes, medical disorders (PIH, diabetes, preeclampsia).[4] As 15% of all gravid women required aid in cervical ripening and labour induction there is widespread interest in demand for an effective and safe method.[5] Recently nitric oxide donor isosorbide mononitrate (IMN) has been evaluated for cervical ripening and induction of labour at term. [6] It produces cervical ripening without hyper stimulation of uterus and fetal heart rate abnormalities. [2, 7] Patient induced with isosorbide mononitrate have short in patient stay before delivery and short duration of labour without any serious side effects. It is cheap and widely available. [8-10]

Exogenous prostaglandins, particularly dinorostone (PGE2) are frequently used as cervical ripening agents but their use is associated with side effects, for example nausea, vomiting, diarrhoea, abdominal cramps, chills, shivering and uterine hyper stimulation more than isosorbide mononitrate. [11,12]

Patients and Methods

This descriptive study was conducted at Department of Gynae/Obs DHQ Teaching Hospital, Rawalpindi from June 2007 to November, 2007. Sixty women were divided into Group A: Prostaglandin E2 and Group B: Isosorbide Mononitrate. Sampling was convenience non-probability. Inclusion criteria were singleton gestation, Cephalic presentation, 37 weeks or more of pregnancy, reactive fetal heart rate pattern and obstetrical indication for labour induction. Exclusion criteria were Cervical dilatation more than 3 cm or Bishop more than 5cm, any contra indication for

induction such as placenta praevia, previous C-Section, evidence of cephalopelvic disproportion, evidence of chorioamnionitis, any contra indication to use of prostaglandin and isosorbide mononitrate.

Proper informed consent was taken from each woman. Initial evaluation was done by taking complete history, general physical examination, systemic and obstetric examination. Fetal assessment was done by Cardiotocography and Biophysical profile. A specially designed proforma was used for data collection. Three mg of prostaglandin E2 was placed in posterior vaginal fornix in group A patient and dose was repeated every six hours up to 2 doses, similarly 40 mg of isosorbide mononitrate (MONIS) was given in group B patients and dose was repeated every four hours up to 2 doses. During this procedure intermittent fetal heart rate and uterine contraction was noted. Time of first and second dose of tablet was noted and time at which patient delivers was also noted to know the induction-delivery interval. No further dose was given if patient went into labour or signs of fetal distress like tachycardia and bradycardia or moderate to severe decelerations in CTG are recorded or uterine hyper stimulations noted. If Bishop Score did not improve after 2 doses, it was considered failed induction.

Results

Both groups had minimum Bishop Score of 2 and maximum of 5 having no significant statistical value (Table 1). Primary outcome measure was induction delivery interval (Table 2). Mean induction delivery interval was 9.5 hours in PGE2 group and 13 hours in IMN group. Group A patients delivered approx about 4 hours earlier than patients in group B. There was no statistically valuable difference in mode of delivery between 2 groups as shown in (Table 3).

Table 1: Bishop Score

Group	Bishop Score				p-Value
	2	3	4	5	
A PGE2	4	5	10	11	0.704
B IMN	2	8	10	10	

Table 2: Induction to delivery interval (Hours)

Group	Range (Mean ± SD)	p-Value
A PGE2	5-16.5 (9.5 ± 2.46)	.000
B IMN	7-18 (18± 3.93)	

Thirty seven percent patients required 2 tablets in group A as compared to 73% in group B(Table 4).There were significant side effect (headache and palpitation) in group B. There were no cases of uterine hyper stimulation in both groups. Nausea vomiting was 23.3% in group A and 13% in group B and only 2 cases of shivering were recorded in group A and none in group B. (Table 5)

Table 3: Mode of delivery

Mode of delivery	A PGE2	B IMN
Spontaneous vaginal Delivery	**24 (80%)**	**22 (73%)**
LSCS due to failed progress	**3 (10%)**	**4 (13%)**
LSCS due to fetal distress	**2 (6.7%)**	**0 (3%)**
LSCS due to failed induction	**1 (3.3%)**	**4 (13%)**

Table 4: Number of tablets used

Number of Tablets	A PGE2	B IMN
1	**19 (63.3%)**	**8 (26.7%)**
2	**11 (36.7%)**	**22 (73.3%)**

Table 5: Side effects

	A PGE2	B IMN	p-VALUE
Headache	**1 (3.3%)**	**8 (26.6%)**	**.011**
Palpitation	**0**	**4 (13%)**	**.038**
Nausea and Vomiting	**7 (23.3%)**	**4 (13.3%)**	**.317**
Shivering	**2 (6.6%)**	**0**	**.15**
Hyper stimulation	0 (0)	0 (0)	0

Discussion

In a randomized comparison (PRIM study) it was found that mean duration of induction delivery was greater in IMN than PGE2 and no side effects were found in IMN group.[3] However, 7 % of patients in PGE2 group had abnormal fetal heart rate pattern. Although IMN was less effective, maternal satisfaction was greater. In present study, induction interval in IMN group was also greater (13 hours in IMN and 9.5 hours for PGE2). There was no significant difference in caesarean section rate between two groups. (20 % for PGE2 versus 26.6% for IMN). There was no case of hyperstimulation in both groups. Mild headache was 3.3% in PGE2 group and 26.6% in IMN group. There was no case of palpitations in group A as compared to

13% in group B. A slight increase in frequency of side effects in present study can be due to the use of two tablets of 40 mg of IMN in most patients with interval of 4 hours, while in PRIM study only single dose was used. [13]

PRIM study concluded that PGE2 was more effective than IMN in inducing change in modified Bishop Score and same is the case in present study (73% of patients required 2 tablets of 40mg of IMN as compared to 36% in PGE2 group). 63% of patients in PGE2 group as compared to 26% in IMN group. Our study also pointed out that IMN was not very much effective in inducing change in poor Bishop Score as caesarean section due to failed induction was 13% in IMN group as compared to 3% in PGE2 group.

Another study published in 2000 by Yuthika Sherma and Sunesh Kumar concluded that Nitric Oxide donors glyceryl trinitrate was also associated with lower episodes of tachysystoles (0% versus 9%) but medium Bishop Score after 12 hours was lower and headache and palpitations were more frequent with glyceryl trinitrate as compared t o PGE2 group.[14] Another randomized controlled study was carried out comparing use of IMN simultaneously with dinoprostone to dinoprostone alone and concluded that vaginally administred IMN does not play a role in promoting delivery in term pregenancy if given at the same time with dinoprostone. [15]

A randomized controlled trial was carried out to compare out patients vaginal administration of nitric oxide donor IMN for cervical ripening in labour induction using 40mg of IMN for post term pregnancies and concluded that it seems to be effective, safe and well tolerated procedure. [16] Present study concluded that induction of labour with IMN is a safe and well tolerated. Majority (86%) went into labour within 24 hours and there was no case of hyperstimulation and side effects were also mild.

As there are concerns on the use of prostaglandins for induction of labor on out door basis due to hyperstimulation leading to fetal hypoxia it is not recommended for use on outdoor basis. It is also not associated with fetal heart rate abnormalities.[17]

Conclusion

1.IMN is effective and cheaper alternative to PGE 2 for cervical ripening and induction of labour at term.

2.Induction delivery interval is prolonged but it is convenient to use and well tolerated.

3.It does not cause uterine hyper stimulation. Side effects like nausea, vomiting and palpitations are mild and not clinically significant.

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