

Safety and Efficacy of Misoprostol for Induction of Labour

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ABSTRACT

Background: Induction of labour is widely carried over the world in cases where continuation of pregnancy is hazardous to mother or fetus. Varieties of techniques are available for induction of labour. Prostaglandin is one of the most effective means for achieving cervical ripening and induction of labour. This study was carried out to see safety and effectiveness of Misoprostol for induction of labour.

Methods: This prospective study was carried out at Kathmandu University Hospital, Dhulikhel from Jan 2008 to Aug 2009. A total of 70 patients were included in this study. All patients received 50µg of Misoprostol in the posterior fornix with maximum dose up to 3 doses at interval of 6 hours. Bishops scoring was reviewed each time before application of Misoprostol. When favourable cervix along with good uterine contraction is noted then augmentation with Oxytocin was done holding Misoprostol. The measures used for the analysis of effectiveness and safety of Misoprostol were change in bishop score, total dose required, need for augmentation, side effects, duration of first, second and third stages of labour, duration from induction till delivery, mode of delivery and neonatal outcome. The primary outcome measures were induction to delivery interval and caesarean section rate.

Results: Out of 70 patients, 21 (30%) required augmentation. Among 70 patients, 46 (65%) underwent normal delivery, 6 (8.6%) underwent instrumental delivery and 18 (25%) patients underwent cesarean section for various indications ($p=0.00$). Total 31 (44%) patients delivered within 10 hours of induction, 16 (22%) within 15 hours and 4 (4.7%) took more than 18 hours. Duration of second stage of labour was also found to be shortened with use of Misoprostol for induction of labour. Duration of second stage of labour was less than 30 minutes in 42 (60%) cases and more than 30 minutes in 9 (17%) cases.

Conclusions: Misoprostol is an effective cervical ripening agent with favorable outcome and comparable with other inducing agents.

Key words: cervical ripening, induction of labour, misoprostol.

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INTRODUCTION

Initiation of labour before its spontaneous onset is known as induction of labour. Induction of labour is widely carried where continuation of pregnancy is hazardous to mother, fetus or both. Induction of labour in ripen cervix is not difficult but complication can increase significantly when cervix is not ripe. There are varieties of techniques available for induction of labour.¹ Prostaglandin is the most effective means of achieving cervical ripening and induction of labour, providing good clinical efficiency. The aim of this study was to see the effectiveness and safety of Misoprostol for induction of labour.

METHODS

A prospective study was carried out at Kathmandu University Teaching Hospital, Dhulikhel from Jan 2008 to Aug 2009. A total of 70 patients were included in this study. An informed consent was obtained before the procedure. All women who required induction of labour with singleton term pregnancy with live fetus with clear indication for induction of labour, cephalic presentation, unfavourable cervix, with or without rupture of membrane and intrauterine fetal death were included. Patients with previous cesarean section, preterm pregnancy, established labour, meconium stained amniotic fluid, contracted pelvis, mal-presentations and other contraindications for induction of labour and vaginal delivery were excluded.

Before induction all patients underwent ultrasonogram (USG) for amniotic fluid index (AFI), and non stress test. Bishops scoring was assessed before inserting Misoprostol. The entire patient received 50µg of Misoprostol in the posterior fornix with maximum dose up to 3 at interval of 6 hours. Bishops scoring was done each time before application of Misoprostol. Once favourable cervix along with good uterine contraction noted augmentation with syntocinon was done holding Misoprostol.

The measures used for the analysis were change in bishop score, total dose required for induction, need for augmentation, side effects, duration of induction till delivery, mode of delivery and neonatal outcome. The primary outcome measures were induction to delivery interval and caesarean section rate.

Statistical analysis was performed with the use software SPSS 10.

RESULTS

Out of 70 cases, 39 (56%) were primigravida and 31 (44%) were multigravida. The indications for induction were post dated pregnancy 27 (38%), decreased fetal movement at term 15 (21%), premature rupture of

membrane 10 (14%), pregnancy induced hypertension 7 (10%), intrauterine growth retardation 4 (5.7%), intrauterine fetal death 6 (8.6%) and bad obstetric history at term 1 (1.4%).

Bishop scoring is shown in table 1. Before induction, 32 (46%) patients had unfavourable cervix, 24 (34%) had favourable and 14 (20%) had highly favourable cervix.

Table 1. Bishops scoring and Drug dose

		Dose			Total
		1st	2nd	3rd	
Bishops scoring	<6	18 (56.3%)	13 (40.6%)	1 (3.1%)	32
	6-9	6 (25%)	16 (66.7%)	2 (8.3%)	24
	>9	8 (57.1%)	6 (42.9%)	-	14
Total		32 (45.7%)	35 (50%)	3 (4.3%)	70 (100%)

Table 2. Mode of delivery and Drug dose

		Dose			Total
		1st	2nd	3rd	
Mode of delivery	Normal	26 (56.5%)	19 (41.3%)	1 (2.2%)	46
	Cesarean section	6 (33.3%)	11 (61.1)	1 (5.6%)	18
	Vaginal delivery	-	5 (83.3%)	1 (16.7%)	6
Total		32 (45.7%)	35 (50%)	3 (4.3%)	70

Patients requiring augmentation is low 21 (30%). The most common side effect, foetal distress was seen in 13 (18.6%) patients with Misoprostol for induction. Among them foetal distress due to uterine hyperstimulation is 5 (7%). Nausea and vomiting was observed in 6 (8.6%), fever in 1 and pain abdomen in 2 cases.

Among all induced patients 46 (65%) underwent normal delivery, 6 (8.6%) instrumental delivery (VD) and 18 (25%) caesarean section for various causes listed in table 3.

Table 3. Indication of cesarean delivery

SN	Indication for cesarean delivery	Number	%
1	Fetal distress	9	50%
2	Uterine hyperstimulation with fetal distress	5	27.77%
3	Non progress of labour	3	16.66%
4	Deep transverse arrest	1	5.5%

Total 31 (44%) patients delivered within 10 hours of induction, 16 (22%) within 15 hours and only 4 (4.7%) took more than 18 hours (p=0.00).

Table 4. Total time taken from induction till delivery and Drug dose

	Dose			Total
	1st	2nd	3rd	
Total time < 10 hours taken	21 (67.7%)	10 (32.3%)	0	31
10 -15 hours	4 (25%)	12 (75%)	0	16
16 -20 hours	1 (33.3%)	1 (33.3%)	1 (33.3%)	3
> 20 hours	0	0	1 (100%)	1
Total	26 (51%)	23 (45.1%)	2 (3.9%)	51

Duration of 2nd stage was also found shortened with use of Misoprostol for induction of labour. Duration of 2nd stage was less than 30 minute in 42 (60%) cases and more than 30 minutes in 9 (17%) cases. Good APGAR score noted in 53 (76%) cases, and 10 (14%) had poor. No still birth noted.

DISCUSSION

Misoprostol is synthetic analog of Prostaglandin E1 [PGE1]. It increases the activity of collagenase in the cervix and helps in relaxation of smooth muscle which facilitates cervical dilation. Prostaglandins allow for an increase in intracellular calcium levels, causing contraction of myometrium.² Total systemic bioavailability of vaginally administered Misoprostol is three times greater than of orally administered Misoprostol.³ Misoprostol is stable at room temperature, is inexpensive and would be ideal agent for induction of labour.

Labour induction is a very important part of obstetric care. In recent years, there are significant interests in the use of Misoprostol for cervical ripening, induction and augmentation of labour. Result of present study showed that use of Misoprostol is associated with shorter induction to delivery interval and lower caesarean section rate with comparable safety profile.

Clinical trials indicate that the optimal dose and dosing interval is 25µg intravaginally every four to six hours.⁴ Higher dose and shorter dosing intervals are associated with a higher incidence of side effects like hyperstimulation syndrome and hypersystole.⁵ Lower dose of Misoprostol compared to higher dose were

associated with more need for oxytocin augmentation, less uterine hyperstimulation, less fetal distress and less admission to neonatal intensive care unit.^{6,7}

Uterine hyperstimulation with Misoprostol is a common denominator which leads to fetal hypoxia and subsequent hypoxic ischemic encephalopathy. Correct early identification of uterine hyperstimulation could prevent further addition of doses of Misoprostol and oxytocin in labour management.⁷ Other uncommon complications resulting from Misoprostol include nausea, vomiting, diarrhea, uterine rupture, fetal demise etc. Our study showed that with a 50µg dose given 6 hours apart maximum hyperstimulation noted with following 2nd dose (7%). We were able to achieve a lower hyperstimulation rate. Studies showed that the incidence of hyperstimulation varies between 1-10%.⁴ This proves the dose and interval we have taken is apparent and effective.

In our study we used 50µg Misoprostol every 6 hourly instead of 25µg every 4 hourly which is almost similar with the study done by Gondinjak Z et al. A 50µg Misoprostol every 6 hourly instead of 4 hourly is safe.⁸ The positive outcome of this study using entirely different dosage regimen suggests that more trials need to be conducted with different dosage regimen in different settings before final decision and consensus is made on it.

Study done by Oliver C Ezechi et al. showed that the incidence of hyperstimulation is related to doses.⁹ With 100µg given 12 hours apart, they were able to achieve low hyperstimulation rate compared to other doses regimes i.e. low dose with more frequent interval.^{10,11}

Sanchez-Ramos et al reported about hyperstimulation and suggested that even 50µg might be too large a starting dose. Perhaps 25µg would be more appropriate dose which might be difficult to obtain from 100µg tablet.¹²

Several studies have reported reduction in caesarean section rate following Misoprostol induction at term pregnancy.^{10,13} Present study showed slightly higher caesarean section rate (25%). The difference may be due to indication of induction as well as small sample size. Maximum (38%) of our patient induced were indicated for post dated pregnancy.

The start to delivery interval was shorter. The incidence of vaginal delivery after two doses was higher. 70% patients didn't require augmentation. This is similar with the study done by Chang et al and Sanchez-Ramos et al.^{12, 14}

CONCLUSION

The use of 50µg Misoprostol in posterior fornix per vaginally at interval of 6 hours is quite safe and effective for induction of labour. Though the outcome is very good, Misoprostol should be used with caution and frequent fetal monitoring should be done. Pre-induction assessment of fetal well being is of equal value.

REFERENCES

1. Arias F. Pharmacology of oxytocin and prostaglandins. *Clin Obstet Gynecol.* 2000; 43:455-68.
2. Jefferson H. Harman, Andrew Kim. Current Trends in Cervical Ripening and Labour induction. *AAFP.* 1999. [<http://www.aafp.org/aafp/990800ap/477.html>]. August 9, 2009.
3. Alisha B Goldberg, Deborah A Wing. Induction of labour. The Misoprostol controversy. *Journal of Midwifery & Women's Health.* 2003;4:244-48.
4. Wagner M. Adverse Events Following Misoprostol Induction of Labor. 2004 [Cited Dec 25, 2009]. Available from: URL:<http://www.midwiferytoday.com/articles/cytotecwagner71.asp>
5. Ezechi OC, Dalu BKE, Ndububa VI. Induction of labour by vaginal Misoprostol for Intrauterine fetal death. *Obstet Gynecol Ind,* 2004; 6:561-63.
6. Ezechi OC, Loto OM, Ezeobi PM. Safety and efficacy of Misoprostol in induction of laor in prelabour rupture of fetal membrane in Nigerian women: a multicenter study. *Iranian Journal of Reproductive medicine.* 2008; 6:83-7.
7. Norwitz E, Robinson J, Repke J. Labour and delivery. In: Gabbe SG, Niebyl JR, Simpson JL, eds. *Obstetrics: Normal and problem pregnancies.* 4th ed. New York: Churchill Livingstone, 2002:353-94.
8. Tenore JL. Methods of cervical ripening and Induction of Labour. *Am Fam Physician.* 2003. May 15;67(10)2123-8.
9. Hofmeyr GJ, Gulmezoglu AM. Vaginal Misoprostol for cervical ripening and induction of labour. *Cochrane Database Syst Rev.* 2003;1:124-5.
10. Li XM, Wan J, Xu CF, Zhang Y, Fang L, Shi ZJ, Li K. Misoprostol in labour induction of term pregnancy: a meta-analysis. *Chin Med J (Engl).* 2004 Mar;117(3):449-52.
11. Cheng SY, Ming H, Lee JC. Titrated oral compared with vaginal misoprostol for labor induction: a randomized controlled trial. *Obstet Gynecol.* 2008 Jan;111(1):119-25.
12. Sanchez-Ramos L, Kaunitz AM, Del Valle GO, Delke I, Schroeder PA, Briones DK. Labor induction with the prostaglandin E1 methyl analogue misoprostol versus oxytocin: a randomized trial. *Obstet Gynecol.* 1993 Mar;81(3):332-6.
13. A .Beigi, M Kabiri, F. Zarrinkoub. Cervical ripening with oral Misoprostol at term. *IJGO.* 2003; 83: 251-55.
14. Chang YK, Chen WH, Yu MH, Liu HS. Intracervical misoprostol and prostaglandin E2 for labor induction. *Int J Gynaecol Obstet.* 2003 Jan;80(1):23-8.