ORIGINAL RESEARCH

Compare safety and efficacy of intravaginal misoprostol and intracervical dinoprostone in induction of labour

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ABSTRACT

Background: To compare safety and efficacy of intravaginal misoprostol and dinoprostone intracervically in inducing labour. **Materials & Methods:** A total of 50 patients with an indication for induction of labor were randomly assigned. Labour induction was considered successful if participant delivered within 36 hours of initiation of misoprostol or dinoprostone. A p-value less than 0.05 was considered significant. **Results:** The average time to delivery was notably shorter with misoprostol (1285) compared to dinoprostone (1501, $P < 0.01$). **Conclusion:** In inducing labor, intravaginal misoprostol proves to be a more efficient and cost-effective option than intracervical dinoprostone, while maintaining a comparable level of safety.

Keywords: Labour, Misoprostol, Intracervical.

INTRODUCTION

In the past decades there has been an increase in the incidence of induction of labor. Data from WHO Global survey on maternal and perinatal health has shown that all over the world 9.6% of deliveries required labor induction. [1] In the developed countries the incidence of labor induction is as high as 25%. [1]

Dinoprostone, a PGE2 analogue has long been used for cervical ripening and labor induction and is a very efficacious drug with a good safety profile. But it is costly and requires refrigeration for storage. Misoprostol, a PGE1 analogue has also been shown to be effective in cervical priming and labor induction. It is inexpensive, can be stored at room temperature and has few systemic side effects. Although, originally approved for use in prevention and treatment of peptic ulcer, in April 2002 FDA finally approved a new label for use of misoprostol during pregnancy. [2] This revises the contraindication and the precaution that misoprostol should not be used in pregnant women by stating that the contraindication is only for pregnant women who are using the medication to reduce the risk of NSAID-induced stomach ulcers. Misoprostol is now a part of the FDA approved regime for use with mifepristone to induce abortion in early pregnancy and is also recognized for its use for induction of labor.

Induction of labour is indicated frequently in modern obstetrics. But labour induction when performed in patients with unripe cervix is associated with a higher incidence of prolonged labour, instrumental delivery and caesarean delivery. To minimize these complications, a number of agents have been used to ripen the cervix before labour induction; this includes laminaria tents, oxytocin, prostaglandin and nitric oxide etc. [3-6] Labour induction with prostaglandins offers the advantage of promoting cervical ripening while stimulating myometrial contractility. Misoprostol a prostaglandin E1 analogue is one of the few drugs whose use has been taken up very enthusiastically by obstetricians. The most recent Medline database produced more than 200 publications using the subject heading ‘pregnancy’ and ‘misoprostol’. This is more unusual as misoprostol was developed by Searl in 1973 for treatment of peptic ulcer and its effect on the pregnant uterus was considered a major side effect. However in due course of time, use of this drug for medical termination of pregnancy and induction of labour has over shadowed its therapeutic value in gastrointestinal diseases. Labour induction with misoprostol is being investigated intensely all over the world. There are various studies that report on its excellent efficacy, minimal side effects and cost saving benefits. [7,8]

Hence, this study was conducted to compare safety and efficacy of intravaginal misoprostol and dinoprostone intracervically in inducing labour.

MATERIALS & METHODS

A total of 50 patients with an indication for induction of labor were randomly assigned. The subjects were divided into 2 groups as 25 in each. Induction with misoprostol, 50 micrograms intravaginally, or dinoprostone, 0.5 mg intracervically, every 4 hours until active labor was done. Once patients reached active phase of labour, same intra-partum guidelines were followed in each group. Labour induction was considered successful if participant delivered within 36 hours of initiation of misoprostol or dinoprostone. The results were analysed using SPSS software. A p-value less than 0.05 was considered significant.

RESULTS

The average time to delivery was notably shorter with misoprostol (1285) compared to dinoprostone (1501, P < 0.01). Achieving delivery within 24 hours of induction was significantly more common with misoprostol (80% of subjects vs 40%, P < 0.001). There was no variance in the cesarean delivery rate between misoprostol and dinoprostone (24% vs 20%, P < 0.6). Uterine hyperstimulation occurred more frequently with misoprostol (P < 0.006).

Table 1: Characteristics and mode of delivery

Variable	Misoprostol group	Dinoprostone group	P -value
Induction delivery interval (minutes)	1285	1501	<0.01
Vaginal delivery within 24 hours (%)	80%	40%	<0.001
Cesarean delivery rate (%)	24%	20%	0.6

Table 2: Intrapartum complications

Variable	Misoprostol group	Dinoprostone group	p-value
Uterine Hyperstimulation	8%	0%	<0.006
Scar dehiscence	-	-	-

Significant; P less than 0.05

DISCUSSION

The first drugs used for the induction of labor in PROM were oxytocin and prostaglandin E2.[9] After 37 WG, the American College of Obstetricians and Gynecologists (ACOG) recommends the use of oxytocin for induction of labor in PROM.[10] The National College of French Obstetricians Gynecologists (CNGOF) recommends the use of prostaglandins first line for an unfavorable cervix, as do the Royal College of Obstetricians and Gynaecologists (RCOG) and the National Institute for Health and Care Excellence (NICE) in the UK. [11]Because of its off-label use in obstetrics, misoprostol has been widely studied and compared with oxytocin, mechanical methods or placebos. All studies have concluded that misoprostol does not increase cesarean section rates or fetal or maternal morbidity. [11,12] Hence, this study was conducted to compare safety and efficacy of intravaginal misoprostol and dinoprostone intracervically in inducing labour.

In the present study, the average time to delivery was notably shorter with misoprostol (1285) compared to dinoprostone (1501, P < 0.01). Achieving delivery within 24 hours of induction was significantly more common with misoprostol (80% of subjects vs 40%, P < 0.001). A study by Blanchette HA et al, involved a retrospective analysis of 81 patients undergoing cervical ripening and induction of labor with prostaglandin E2 from May 1, 1996, to May 1, 1997. A comparison prospective analysis of 145 patients undergoing the same procedure with prostaglandin E1 from May 1, 1997 to May 1, 1998, was performed. The mean time to delivery was significantly shorter with misoprostol (19.8 +/- 10.4 hours) than with prostaglandin E2 (31.3 +/- 13.0 hours, P <.001). Delivery within 24 hours of induction was significantly more frequent with misoprostol (71.9% of subjects vs 31.3%, P <.001). There was no difference in the cesarean delivery rate with misoprostol (25.6% vs 22.2%, P <.67). The incidence of uterine hyperstimulation was higher with prostaglandin E2 (7.4% vs 0.7%, P <.007). There was no difference in neonatal outcome, with the exception of a fetal death related to uterine rupture in the misoprostol group. Compared with prostaglandin E2, misoprostol is more effective in cervical ripening and induction of labor, is as safe for patients who do not have a history of cesarean birth, may carry a higher incidence of uterine rupture, and should not be used for patients attempting vaginal birth after previous cesarean delivery. [13]

In the present study, there was no variance in the cesarean delivery rate between misoprostol and dinoprostone (24% vs 20%, P < 0.6). Uterine hyperstimulation occurred more frequently with misoprostol (P < 0.006). Another study by Kumar S et al, compared the safety and efficacy of intravaginal misoprostol versus existing hospital protocol of intracervical dinoprostone and oxytocin for cervical ripening and induction of labour. 200 patients with indication for induction of labour were randomly assigned to receive either intravaginal misoprostol or dinoprostone/oxytocin combination. In first group twenty five micrograms of misoprostol was placed intravaginally every 6 hours till the patient reached

active stage of labour. In second group dinoprostone gel 0.5 mg was placed in the endocervix at night and oxytocin induction was started in the early morning. The average interval from start to induction of vaginal delivery was shorter in misoprostol group (1315±811 minutes) compared to dinoprostone/oxytocin group (1512±712 minutes) ($p < 0.01$). There was no significant difference in route of delivery. 18% of misoprostol treated patients and 23% of dinoprostone/oxytocin treated patients required Caesarean section. Complications such as uterine tachysystole were significantly higher in misoprostol group ($p < 0.01$) but it was not associated with increased incidence of uterine hyperstimulation. Perinatal outcome was similar in both groups. [14] Liu A et al, investigated and compared the efficacy and safety of intravaginal misoprostol and intracervical dinoprostone for labor induction, including incidence of cesarean section, vaginal delivery rate within 24 h, uterine hyperstimulation, tachysystole, oxytocin augmentation, neonatal intensive care unit (NICU) admissions, and Apgar score of less than 7 at 1 and 5 min. Databases searched were MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials, up to July 2013. Randomized controlled trials comparing intravaginal misoprostol with intracervical dinoprostone in women with singleton pregnancy, intact membranes and unfavorable cervix (Bishop's <6) were included. Pooled relative risk, mean difference and 95% confidence intervals were calculated. The use of misoprostol was significantly effective in increasing the rate of vaginal delivery within 24 h and less oxytocin augmentation when compared with dinoprostone. However, the incidents of uterine hyperstimulation and tachysystole were significantly higher under the misoprostol protocol than dinoprostone protocol. Furthermore, we found similar efficiency in the rate of cesarean delivery, NICU admission and Apgar score at 1 and 5 min among the study groups. Intravaginal misoprostol appears to be more efficient for labor induction than intracervical dinoprostone; however, dinoprostone has been demonstrated to be safer because of the lower incidence of uterine hyperstimulation and tachysystole. Further high-quality studies assessing the possible effectiveness of misoprostol and dinoprostone in selected groups of patients are warranted. [15] Denguezli W et al, among 130 patients evaluated, 65 were allocated to the misoprostol group and 65 to the dinoprostone group. The proportion of vaginal delivery within 24 h was significantly higher in the misoprostol group (75%) than in the dinoprostone group (53.8%) (RR = 1.40, 95% CI [1.07-1.45], P = 0.02). There was no significant difference between the mean time interval of delivery in the misoprostol group and the dinoprostone group (14.9 vs.15.8 h) (P = 0.51). The Bishop score was significantly higher in the misoprostol group, 6 h after the onset of the study (1.38; relative risk, 95% CI [1.02-1.85], P = 0.03). The Caesarean delivery rate for fetal distress was higher in the dinoprostone group (21 vs. 10.8%, P = 0.15). The tachysystole (Misoprostol 6.1% vs. dinoprostone 4.6%, relative risk 1.15, 95% CI [0.6-2.24]) and hyperstimulation syndrome rates (Misoprostol 7.6% vs. dinoprostone 4.6%, relative risk 1.26, 95% CI [0.72-2.24]) were slightly increased in the misoprostol group than in the dinoprostone group without reaching the level of statistical signification. Misoprostol as used in this protocol is more effective than cervical dinoprostone gel application in the cervical ripening and labour induction. There is a tendency for an increase in the rate of tachysystole and hyperstimulation syndrome. [16]Kulshreshtha S et al, compared the safety and efficacy of intra-vaginal misoprostol (PGE1 analogue) with intra-cervical dinoprostone (PGE2) in progress and induction of labour, the maternal side effects and the foetal outcome. 40 pregnant women aged between 16-35 years with indication of induction of labour participated in the study. Twenty patients (control) were administered 0.5 mg dinoprostone intra-cervically, 12 hourly while 20 patients (study group) were given misoprostol 100 microg, 4 hourly, intravaginally. The mean induction of labour initiation interval was 2.08 +/- 1.46 hours in study group and 2.21 +/- 1.20 hours in dinoprostone group. The Induction delivery interval was 6.92 +/- 4.01 hours in misoprostol group and 12.54 +/- 7.73 in dinoprostone group, whereas vaginal route of delivery was 95% in misoprostol group and 85% in dinoprostone group. Average dosages required were 1.55 +/- 1.02 in misoprostol group and 1.30 +/- 0.46 in dinoprostone group. All these result were statistically significant. Very few maternal side effects were reported in study group. There was no significant difference in foetal out come in either group. Therefore, it can be concluded that misoprostol is easy to administer and is cheap, effective, safe and convenient drug for induction of labour.[17] Agarwal N et al, a total of 120 pregnant women requiring induction of labor were recruited. Cases were randomized to receive either 50 microg vaginal misoprostol 6 hourly (group 1, n = 60) or 0.5 mg intracervical dinoprostone 6 hourly (group II, n = 60). Outcome measures, such as change in Bishop's score, need of oxytocin, induction delivery interval; complications like tachysystoly, hyperstimulation, abnormal fetal heart rate, and meconium passage were compared between two groups. Statistical analysis was performed by Wilcoxan's Rank sum and Student's t-test. Bishop score rise, after 6 h of initiation of therapy was significantly higher in the misoprostol group than dinoprostone, 2.98 +/- 2.57 versus 2.05 +/- 1.83 (P = 0.04). The need of oxytocin augmentation was reduced in misoprostol versus dinoprostone group, 16.6% versus 78.3% (P = <0.001). Induction delivery interval was shorter in misoprostol; 12.8 +/- 6.4 h versus 18.53 +/- 8.5 h in dinoprostone group (P = <0.01). One case (1.6%) in misoprostol group, but none in dinoprostone had tachystole (P = 1.00).

Abnormal heart rate pattern was found more in misoprostol than dinoprostone 16.6% versus 4.9% (P = 0.14) and so was the incidence of cesarean section, 26.6 versus 15%, respectively (P = 0.47). Meconium passage was the same in both groups, 10% in each group. Vaginal misoprostol 50 microg 6-hourly is safe and effective for induction of labor with lesser need of oxytocin augmentation and shorter induction delivery interval. [18] Neiger R et al, compared the efficacy of intravaginal misoprostol (Cytotec) to intracervical dinoprostone (Prepidil) for pre-induction cervical ripening. Sixty-one patients admitted for induction of labor, whose cervices were unfavorable (Bishop score: 4), were randomly assigned to either intravaginal placement of a 50 micrograms misoprostol tablet or intracervical administration of dinoprostone gel. Eighteen women (56%) in the misoprostol group and five (17%) in the dinoprostone group achieved cervical ripening within 12 hours (P = 0.007). Fewer doses of misoprostol were required to achieve cervical ripening, and the interval from induction of labor to delivery was shorter in the misoprostol group. Sixteen patients (50%) in the misoprostol group required oxytocin, whereas 26 (90%) in the dinoprostone group required oxytocin augmentation (P = 0.008). There was no significant difference in mode of delivery or neonatal outcome between the two groups. Vaginal misoprostol appears to be a more effective cervical ripening agent than cervical dinoprostone. [19]

CONCLUSION

In inducing labor, intravaginal misoprostol proves to be a more efficient and cost-effective option than intracervical dinoprostone, while maintaining a comparable level of safety.

REFERENCES

1. WHO recommendations for Induction of labor. World Health Organization 2011. Available from: http://whqlibdoc.who.int/publications/2011/9789241501156_eng.pdf
2. ACOG committee opinion. New US Food and drug administration labeling of cytotec (misoprostol) use in pregnancy. . Int J Gynecol Obstet. 2003;82:137–38.
3. Wilson PD. A comparison of four methods of ripening of unfavourable cervix. Br J Obstet & Gynaecol. 1978;85:941–944.
4. Gower RH, Toraya J, Miller JM. Laminaria for preinduction cervical ripening. Obstet Gynaecol. 1982;60:617.
5. Normon JE, Thompson AJ, Greer IA. Cervical ripening after nitric oxide. Hum Reprod. 1998;13:251–252.
6. Riskin-Mashiah S, Willkins I. Cervical Ripening. Obstet Gynecol Clin North Am. 1999;26:243–257.
7. Chuck FJ, Huffaker BJ. Labour induction with intravaginal misoprostol versus intracervical prostaglandins E2 gel: randomized comparison. Am J Obstet Gynecol. 1995;173:1137–1142.
8. Sanchez-Ramos L, Kaunitz AM, Wears RL, Delke I, Gaudier FL. Misoprostol for cervical ripening and labour induction: a meta analysis. Obstet Gynecol. 1997;89:633–642
9. Carbonne B, Goffinet F, Cabrol D. Vaginal administration prostaglandin E2 in premature ruptured membranes at term with an unfavorable cervix. J. Gynecol. Obstet. Biol. Reprod. (Paris) 1996;25(8):783–791.
10. ACOG Practice Bulletin No 188 Prelabor rupture of membranes. Obstet. Gynecol. 2018;131(1):e1–14.
11. 1 Guidance | Inducing labour | Guidance | NICE [Internet]. [Retrieved Sept 5, 2019]. Available at: https://www.nice.org.uk/guidance/cg70/chapter/1-Guidance#induction-of-labour-in-specific-circumstances
12. Ngai SW, To WK, Lao T, Ho PC. Cervical priming with oral misoprostol in pre-labor rupture of membranes at term. Obstet. Gynecol. 1996;87(6):923–926.
13. Blanchette HA, Nayak S, Erasmus S. Comparison of the safety and efficacy of intravaginal misoprostol (prostaglandin E1) with those of dinoprostone (prostaglandin E2) for cervical ripening and induction of labor in a community hospital. Am J Obstet Gynecol. 1999 Jun;180(6 Pt 1):1551-9.
14. Kumar S, Awasthi RT, Kapur A, Srinivas S, Parikh H, Sarkar S. Induction of labour with misoprostol - A prostaglandin e1 analogue. Med J Armed Forces India. 2001 Apr;57(2):107-9.
15. Liu A, Lv J, Hu Y, Lang J, Ma L, Chen W. Efficacy and safety of intravaginal misoprostol versus intracervical dinoprostone for labor induction at term: a systematic review and meta-analysis. J Obstet Gynaecol Res. 2014 Apr;40(4):897-906.
16. Denguezli W, Trimech A, Haddad A, Hajjaji A, Saidani Z, Faleh R, Sakouhi M. Efficacy and safety of six hourly vaginal misoprostol versus intracervical dinoprostone: a randomized controlled trial. Arch Gynecol Obstet. 2007 Aug;276(2):119-24.
17. Kulshreshtha S, Sharma P, Mohan G, Singh S, Singh S. Comparative study of misoprostol vs dinoprostone for induction of labour. Indian J Physiol Pharmacol. 2007 Jan-Mar;51(1):55-61.
18. Agarwal N, Gupta A, Kriplani A, Bhatla N, Parul. Six hourly vaginal misoprostol versus intracervical dinoprostone for cervical ripening and labor induction. J Obstet Gynaecol Res. 2003 Jun;29(3):147-51.
19. Neiger R, Greaves PC. Comparison between vaginal misoprostol and cervical dinoprostone for cervical ripening and labor induction. Tenn Med. 2001 Jan;94(1):25-7.