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Low Doses of Vaginal Misoprostol versus Dinoprostone for Induction of Labor in Uncomplicated Term Pregnancy

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Abstract

Background: Prospective cohort observational study to compare the efficacy low doses (25 micrograms misoprostol) tablet with dinoprostone gel (1 mg) introduced vaginally in term pregnancy for induction of labor as regard maternal and fetal outcome.

Methods: Three hundred pregnant women in full term (40-41 weeks) pregnancy were assigned for induction of labor either intravaginal misoprostol tablet or dinoprostone gel. They were divided into 2 groups (A, B). Group A (150 ladies) obtained tablet misoprostol 25 micrograms vaginally 4 hourly and Group B (150 ladies) received dinoprostone gel 1 mg vaginally every 6 hourly, both medications were not to be repeated more than 3 doses. Outcomes were: expression of time interval of induction of labor, augmentation requirement, operative and instrumental rate, expenditure efficiency and neonatal outcome.

Results: The demographic criteria as regard the age, body mass index, gestational age, initial Bishop's score and final Bishop's score were analogous in both group (the misoprostol and dinoprostone groups), respectively with no significant differences but about parity there was significant difference between them with p value 0.4. No significant differences between both group as regard occurrence of non-reassuring FHR, uterine hyper stimulation and meconium stained amniotic fluid but there was significant differences in spontaneous rupture of the membranes and uterine tachysystole with p value 0.02 and 0.01, respectively. Time of labor induction was shorter in the misoprostol group with p<0.001. The need of more doses was fewer in G1 than G2 with p value 0.03. Also the need to oxytocin for augmentation was lesser in G1 than G2 with p value 0.02. In misoprostol group more deliveries within 24 hour, p<0.04. The vaginal deliveries were more in misoprostol group with lesser percentage of CS but with no significant difference. The fetal outcome in both group was similar according to birth weight, Apgar score and at 5, the requirement for neonatal resuscitation and neonatal intensive care unit admission.

Conclusions: The time interval for induction of labor by misoprostol tablet vaginally was shorter than dinoprostone gel, associated with fewer requirements to augmentation of labor with oxytocin and more deliveries in the first 24 hours of induction.

Keywords: Misoprostol tablet; Dinoprostone gel; Vaginal; Induction of labor; Term pregnancy

Introduction

Labor induction at term is a universal conventional obstetric interference with an objective to stimulate uterine contractions artificially to attain a spontaneous vaginal delivery [1]. The efforts must be done to make the cervix favorable. Introducing of intravaginal or intracervical prostaglandins has the main job of that [2].

A lot of studies have shown the benefits of using prostaglandins vaginally in priming of cervix and then induction of labor in terms with reduction of induction-delivery gap and subordinate operative rate [3]. Misoprostol is a prostaglandin E1 analogue originally registered as oral tablets for the management peptic ulcer.

Nearly all countries had extensive studies about its security, effectiveness, and dosage-reaction outcome in induction of labor at term pregnancies [4]. Until a moment ago, prostaglandin E2, or dinoprostone, has been the mainly broadly used one. On the other hand, it has many disadvantages like, instability at room temperature and its high price. Misoprostol, or prostaglandin E1 is cheap, stable at room temperature and could be taken vaginally , orally, or sublingually [5].

The World Health Organization, the International Federation of Gynecology and Obstetrics and the American College of Obstetrician and gynecologists introduced Misoprostol in the list of the important agents to be used for obstetrical require [6]. This current study was assumed to compare the efficacy of low doses (25 micrograms misoprostol) tablet with dinoprostone gel (1 mg) introduced vaginally in term pregnancy for induction of labor as regard maternal and fetal outcome.

Method

This was a prospective cohort study carried out on 300 ladies in the age group of 19-33 years with gestational age 40-41 weeks at the Department of Obstetrics and Gynecology, Zagazig University Hospital from the time period of January 2017 to July 2018.

Inclusion criteria

Singleton live fetus, Cephalic presentation, Gestational age 40-41weeks, with cervical Bishop's score ≤ 5 and no contraindications for vaginal delivery or utilize of prostaglandins. No uterine contraction which was proved clinically and by cardiotachograph.

Exclusion criteria

Previous uterine scar for c.s or else, previous orthopedic surgery in bone of the pelvis, any vaginal disorders interfere with labor, abnormal fetal lie, placenta previa, evidence of compromised fetus as intrauterine growth restriction or nor reassuring fetal heart rate monitoring.

Participants were engaged by non-probabilistic sampling of successive cases. Informed written consent was taken from all patients included in the study, after full explanation and discussion with them. The study protocol was approved by the Ethics Committee of the Zagazig University Hospitals.

In this protocol, Misoprostol Low-dose tablet (25 mcg/4 hour) vaginally was used for a maximum of six doses (Group 1) or dinoprostone gel 1 mg vaginally 6 hourly to a maximum of four doses (Group 2). A non-stress test (NST) was done to ensure the fetus well-being for each patient at the time of admission to the hospital before the application of the prostaglandin and was repeated after 1 hour and 5 hour. If the active labor started, the membranes ruptured spontaneously or non-reassuring FHR, transferee the patient to the labor room. Reassessment of Bishop's score, was conceded every 4 hours in misoprostol group or 6 hour in dinoprostone group, if the cervix became favorable oxytocin intravenous infusion augmentation was started 4 hour after the insertion of last dose of any prostaglandin if the uterine contractions were insufficient and amniotomy was carried out. If the cervix was still unfavorable, another dose of misoprostol or dinoprostone was given. When the last dose was inadequate for introducing spontaneous labor, oxytocin infusion was started as a trial of labor and if no progress the patient submitted to a CS.

Statistical analysis

The records were assembled, tabularized and investigated for different factors and were matched. The qualitative variables were presented in percentages, whilst the quantitative ones were presented as means and standard deviations (SD). A chi-square test was used to assess the relationship between the qualitative variables. A student's t-test was used to compare the cervical maturity method with the quantitative variables. All the variables those were statistically significant or clinically relevant in the univariate analysis. The level of significance used to compare all the hypotheses was 0.05. The statistical package employed was SPSS Windows 17.0.

Results

Both groups were analogous as regard the age of patient 20 years (19-30) *vs.* 21 years (20-32), p value was 0.06, parity; percentage of nullipara was 70% *vs.* 74% , multipara 30% *vs.* 26% with p value 0.4 ,body mass index 23.2 (21.7-25.2) *vs.* 24.1 (22.8-26.3) with p value 0.07, Gestational age 40 ± 3 *vs.* 40 ± 5 with p value 0.9, initial Bishop score 3.5 ± 1.3 *vs.* 3.6 ± 1.4 with p value 0.08, final Bishop score 6.1 ± 1.4 *vs.* 6.3 ± 1.5 in the misoprostol and dinoprostone groups, respectively (Table 1).

Character	Misoprostol (G1) Group N (150)	Dinoprostone gel (G2) Group N(150)	P value
Age (range)	20 (19-30)	21 (20-32)	0.06
Parity			
Nullipara	70% 105	74% 111	0.41
Multipara	30 % 45	26% 39	
Body mass index (BMI) (range)	23.2 (21.7-25.2)	24.1 (22.8-26.3)	0.07
Gestational age (± SD)	40 ± 3	40 ± 5	0.9
Initial Bishop score	3.5 ± 1.3	3.6 ± 1.4	0.08
Final Bishop score	6.1 ± 1.4	6.3 ± 1.5	0.06
Note: Values expressed as mean ± SD, P>0.05 not significant			

Table 1: Demographic characteristics.

Percentage of non-reassuring FHR, uterine hyperstimulation and meconium stained amniotic fluid in both group had insignificant difference but spontaneous rupture of the membranes and uterine tachysystole took place more in G1 than G2 with p value 0.02 and 0.01 respectively (Table 2) (Figures 1a and 1b).

Event	Misoprostol (G1) Group N (150)	Dinoprostone gel (G2) Group N (150)	P value
Nonreassuring FHR	16% 24	7.3% 11	>0.05
Rupture of membranes (spontaneously)	32% 48	15.3% 23	0.02

Uterine Hyperstimulation	3.3% 5	2% 3	>0.05
Uterine Tachysystole	10% 15	6% 9	0.01
Meconium stained Af	15.3% 23	6% 9	>0.05

Table 2: Intrapartum events.

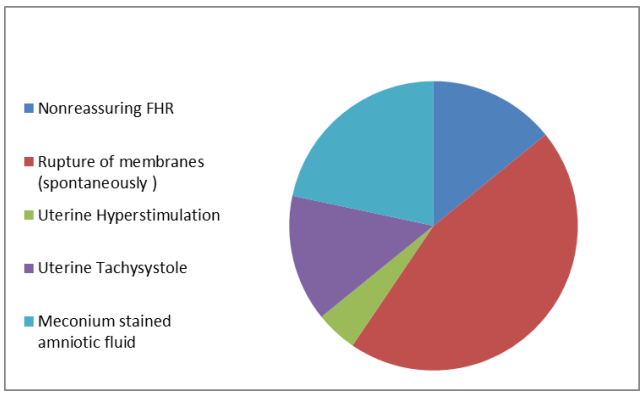

Figure 1a: Intrapartum events in misoprostol group.

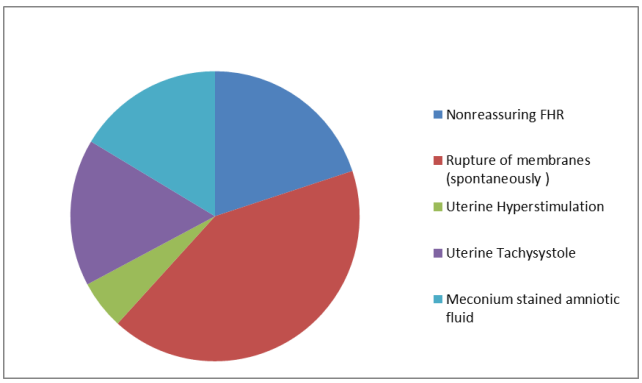

Figure 1b: Intrapartum events in dinoprostone group.

Event	Misoprostol (G1) Group N (150)	Dinoprostone (G2) Group N (150)	P value
Time from induction to delivery	10.8 ± 0.5	14.7 ± 0.8	0.001
Number of doses			
First	91%	75%	0.03
Second	8%	23%	
Third	1%	2%	
Delivery<24 h	97%	90%	0.04
Required oxytocin augmentation	62%	75%	0.02
Note: Data are presented as X (SD) mean differences or number (percentage %).			

Table 3: Intrapartum Events

The period between induction and delivery was 10.8 h *vs.*14.7 h which considerably shorter (p<0.001) in the misoprostol group, second or third dose were fewer in G1 than G2 with p value 0.03. Also the need to oxytocin for augmentation was less in G1 than G2 with p value 0.02. With misoprostol group further women delivered within 24 h, (97 % *vs.* 90%, p<0.04) (Table 3).

The greater part of participants in both groups had vaginal delivery, 90% in G1, and 85.3% in G2 either spontaneous or assisted by vacuum with no significant difference. Percentage of CS was lesser in G1 than G2 but with p value>0.05with the same indications (Tables 4 and 5) (Figures 2a and 2b).

Mode of delivery	Misoprostol (G1) Group N (150)	Dinoprostone (G2) Group N (150)	P value
Vaginal (total)	90% 135	85.3% 128	>0.05
Spontaneous vaginal	56% 84	60% 90	
Assisted via vacuum	34% 51	25.3% 38	

Caesarean section	10% 15	15.3% 23	>0.05
Note: Data are presented as number (percentage %).			

Table 4: Mode of delivery.

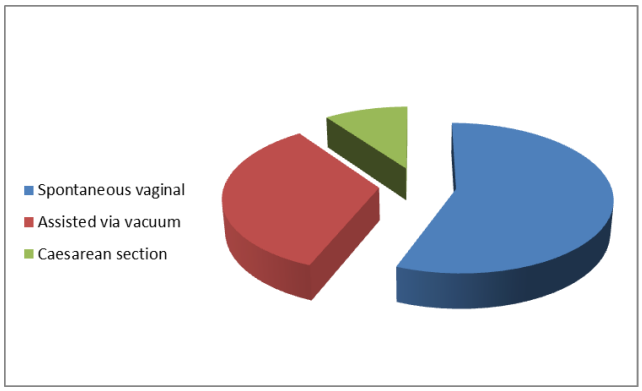

Figure 2a: Mode of delivery in misoprostol group.

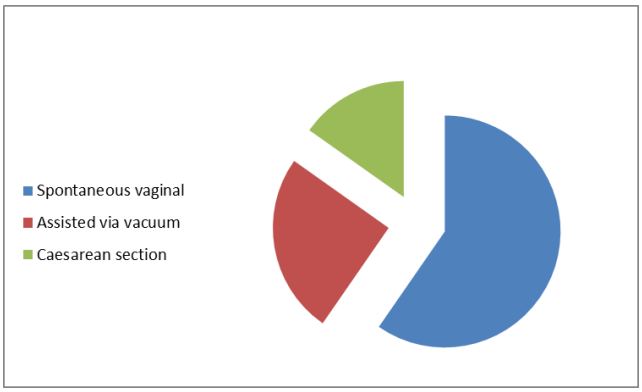

Figure 2b: Mode of delivery in dinoprostone group.

Indication	**Misoprostol (G1) Group N (10 %) 15**	**Dinoprostone gel (G2) Group N (15%) 22**	**P value**
Failed induction	2%	3%	>0.05
Nonreassuring FHR (fetal heart rate)	6%	8%	>0.05
Lack of labor progress	2%	4%	>0.05
Note: Data are presented as number (percentage %) and (p>0.05) not significant			

Table 5: Indications of Caesarean section.

The mean birth weight was 3262 ± 280 g in the misoprostol induced group, 3164 ± 320 g the dinoprostone induced group was no significant difference. Apgar score <7 at 1 min and at 5 min in both group the same. The requirement for neonatal resuscitation or neonatal intensive care unit admission in both groups was small with no significant difference. No cases of intrapartum fetal death or birth trauma (Table 6).

Outcome	**Misoprostol (G1) Group N (150)**	**Dinoprostone gel (G2) Group N (150)**	**P value**
Fetal birth weight (gram)	3262 ± 280	3164 ± 320	>0.05
Apgar score<7			
At 1min.	9%	7%	>0.05
At 5 min.	1%	1%	
Neonatal resuscitation			
O2 Supplementation	3	3	>0.05
Ambou ventilation	5	3	
Intubation in theater	1	1	

Birth trauma	0	0	>0.05
Intrapartum fetal death	0	0	>0.05
Neonatal Intensive Care Unit admission	2%	2%	>0.05
Note: Values expressed as mean ± SD or number (percentage %) and P>0.05 not significant			

Table 6: Neonatal outcomes.

Discussion

Currently, labor induction is broadly used than constantly before [7]. Women may practice grief once labor has not initiated by the predictable time [8]. Spanish Agency of Medicines approved misoprostol vaginally administered in 25 mcg tablets to induce at-term delivery, in 2008 in spite of dinoprostone which is the gold standard in many centers [9].

The present study is one of many those compared misoprostol and dinoprostone in small doses for induction of labor in uncomplicated term pregnancy. The mean time interval between inductions to delivery was less in the misoprostol group than dinoprostone group (10.8 h *vs.* 14.7 h and 97 % patients delivered in the first 24 h in misoprostol group versus 90 % patients in dinoprostone group. This is comparable to the study of Murthy Bhaskar Krishnamurthy [10].

Vaginal PGE1 50 mg 6 hourly *vs.* intracervial PGE2 gel was studied by Agarwal et al. [11] and Van Gemund et al. [12] studied 25 microgram misoprostol versus with dinoprostone vaginally, and had concluded that vaginal misoprostol is extra effective and secure for labor induction at term. About the need to LSCS our result did not agree with study of Sahu latika et al. [13] and the study of Patil Kamal et al. [14] as they found a smaller amount of LSCS in misoprostol group than dinoprostone group but we found no significant differences between both groups. But, Papanikolaou et al. [15] found the majority of women in the misoprostol group underwent either a CS or a vacuum operative delivery due to non-reassuring FHR, this agreed with findings of Cochrane metanalysis [16].

Our study achieved no differences in the percentage of "vaginal birth in less than 24h" from the initiation of induction in both groups. And this agreed with Wang et al. 2015 [9] and Austin et al. 2010 [17]. But was disagreed with study done by Liu et al. [18], who accounted a higher vaginal birth percentage in <24 h for the misoprostol group. As regards of safety, our work methodically analysed maternal-fetal complications, and found no differences between both groups. Nevertheless, all the metaanalyses accomplished that the studies were not large enough to evaluate any serious maternal-fetal complications [19]. Papanikolaou et al. [15] noticed a tendency on the way to a high rate of abnormal FHR tracings during induction with misoprostol and these findings, in agreement with the previous Cochrane metanalysis [16], which demonstrated that with misoprostol there was an increased possibility of meconium staining of amniotic fluid in addition to of uterine tachysystole and of abnormal FHR tracings.

As regard the tachysystole (defined as six contractions or more in 10 minutes on at least a 20 minute monitoring window) or uterine hyperstimulation, we found significant difference in both group with high rate of tachysystol in misoprostol group and this disagreed with Wing who reported low tachysystole rates for the misoprostol group and Harms [20] who showed no differences either in tachysystol uterine hyperstimulation. Papanikolaou et al. [15], to avoid uterine hyperstimulation and abnormal FHR tracings used for the first time in the literature, a 9h interval between the prostaglandin doses. Although that they found 2.5% uterine hyperstimulation in misoprostol and 1.2% in dinoprostone, Agarwal et al. [11] have concluded that vaginal misoprostol is more effective and safe for labor induction at term when use vaginal PGE1 50mg 6 hourly *vs.* intracervial PGE2 gel. Garry et al. [21] and Le Roux et al. [22] have reported an increased incidence of cesarean for fetal distress and tachysystole with 50 microgram of vaginal PGE1 when compared to vaginal dinoprostone [11,18]. It shows that the amplify in clinically related adverse effects is not only misoprostol interconnected but it may be dose dependent.

Van Gemund et al. [12] concluded that this lower dose of misoprostol is safer with lesser neonatal admissions in their study comparing 25 microgram vaginal misoprostol with dinoprostone, with adverse neonatal outcome as the primary outcome measure and Maydanli et al. [23] have concluded that 25 microgram vaginal misoprostol could be as efficient as 50 microgram for cervical ripening and labor induction. Consequently, 25 microgram which was used in the current study seems to merge effectiveness with security and could be the dose that can be assumed in clinical practice for induction of labor at term.

Conclusion

Induction of labor with low-dose misoprostol (25 mcg) vaginally proffers similar efficacy and security to induction by dinoprostone gel form 1 mg. However, the sample size was restricted, and a small number of studies are accessible on the topic. Our recommendation is that it is essential to achieve more clinical studies to weigh misoprostol against dinoprostone at the doses utilized here, and to embrace more outcomes like pregnant's satisfaction.

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