

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 (1mg) introduced vaginally in term pregnancy for induction of labour as regard maternal and fetal outcome.

Methods

Three hundred pregnant women in full term (40- 41 weeks) pregnancy were randomly assigned for induction of labor either intra vaginal 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 1mg vaginally every 6 hourly, the both medications would not be repeated more than 3 doses. Outcomes were; expression of time interval of induction of labour, 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 score and final Bishop 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 no reassuring FHR, Uterine hyper stimulation and meconiumstained 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 labour 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 h $p < 0.04$. The vaginal deliveries, was 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 labour by misoprostol tablet vaginally was shorter than dinoprostone gel, associated with less requirement to augmentation of labor with oxytocin and more deliveries in the first 24 hrs of induction

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

Introduction

Labor induction at term is an 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 intra vaginal or intra cervical 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 (1mg) introduced vaginally in term pregnancy for induction of labor as regard maternal and fetal outcome.

Methods

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

Inclusion Criteria were

Singleton live fetus, Cephalic presentation, Gestational age 40-41 weeks, 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 cardiograph.

Exclusion Criteria

Previous uterine scar for c.s or else, 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/4h) vaginally was used for a maximum of (six doses) {Group 1} or dinoprostone gel 1mg 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 h and

5 h. If the active labor started, the membranes ruptured spontaneously or non reassuring FHR, transferee the patient to the labor room. Reassessment of Bishop Score, was conceded every 4h in misoprostol group or 6hr in dinoprostone group, If the cervix became favorable the oxytocin intravenous infusion augmentation was started 4 h after the insertion of last dose of any prostaglandin if the uterine contractions were insufficient and anatomy 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 that was 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

The both group 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 (\pm 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

Values expressed as mean \pm SD

P > 0.05 not significant

Percentage of non reassuring FHR, Uterine hyper stimulation and meconium stained amniotic fluid in both group had insignificant difference but spontaneous rupture of the membranes and uterine tachysystole tacked place more in G1 than G2with p value 0.02 and 0.01 respectively (Table 2).

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

The period between induction and delivery was 10.8 h vs. 14.7h 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 >0.05 with the same indications (Table 4,5).

Table 3: Intrapartum Events

	Misoprostol group {G1} N (150)	Dinoprostone gel { 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%	
Second	8%	23%	
Third	1%	2%	0.03
Delivery < 24 h	97%	90%	0.04
Required oxytocin augmentation	62%	75%	0.02

Data are presented as X (SD) mean differences. or number (percentage %).

Table 4: Mode of delivery

Mode of delivery	Misoprostol group { G1} N (150)	Dinoprostone gel group {G2} N(150)	P value
Vaginal (total)	90% 135	85.3 % 128	
Spontaneous vaginal	56% 84	60% 90	>0.05
Assisted via vacuum	34% 51	25.3% 38	
Caesarean section	10% 15	15.3% 23	>0.05

Data are presented as number (percentage %).

Table 5: Indications of Caesarean section

Indication	Misoprostol group { G1} N (10 %) 15	Dinoprostone gel group { G2} N (15%) 22	P value
Failed induction	2%	3%	>0.05
Non reassuring FHR	6%	8%	>0.05
Lack of labor progress	2%	4%	>0.05

FHR = fetal heart rate.

Data are presented as number (percentage %).

($p > 0.05$) not significant

The mean birth weight was 3262±280g in the misoprostol-induced group, 3164±320g the dinoprostone-induced group was no significant difference. Apgar score < 7 at 1min and at 5 min in both groups 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 group { G1} N (150)	Dinoprostone gel group { G2} 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

Values expressed as mean ± SD or number (percentage %).

$P > 0.05$ not significant

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 labour in uncomplicated term pregnancy. The mean time interval between inductions to delivery was less in the misoprostol group than dinoprostone group (10.8 hrs vs. 14.7 hrs and 97 % patients delivered in the first 24 hrs in misoprostol group versus 90 % patients in dinoprostone group. This is comparable to the study of Murthy Bhaskar Krishnamurthy [10]. Vaginal PGE1 50mg 6 hourly vs intracervical 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 met analysis [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. [9]. And Austin et al. [17]. But was disagreed with study was done by Liu [19]. Who accounted a higher vaginal birth percentage in <24 h for the Misoprostol group as regards safety, our work methodically analyzed maternal-fetal complications, and found no differences between both groups. Nevertheless, all the meta analyses 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 meta analysis [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 hyper stimulation, we found significant difference in both group with high rate of tachysystole 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 tachysystole uterine hyper stimulation. Papanikolaou et al. [15], to avoid uterine hyper stimulation and abnormal FHR tracings, used for first time in the literature, a 9 h interval between the prostaglandin doses. Although that they found 2.5% uterine hyper stimulation 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 intracervical 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]. Van Gemund et al. [23] 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. [24] 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 1mg. However, the sample size was restricted, and a small number of studies are accessible on the topic. Our recommendation; 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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