Dinoprostone vaginal insert versus intravenous oxytocin to reduce postpartum blood loss following vaginal or cesarean delivery

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Summary

Objective: To compare the impact of a dinoprostone vaginal insert and intravenous oxytocin in reducing blood loss of women undergoing vaginal or cesarean delivery. *Methods:* This study was conducted among term singleton pregnancies delivered vaginally or by elective cesarean section. In the vaginally delivered cases, active management of the third stage of labor was conducted. During cesarean delivery, 20 IU of intravenous oxytocin was administered. Women, who either delivered via the vaginal or abdominal route, were then randomly allocated to receive 10 mg vaginal dinoprostone insert for 12 hours (group I, n: 100) or intravenous oxytocin (group II, n: 100), respectively. *Results:* Mean blood loss and need for additional uterotonics and postpartum hemoglobin and hematocrit levels at 24 and 36 hours after delivery did not differ between the two groups. Women allocated to the dinoprostone vaginal insert arm experienced more nausea and vomiting. *Conclusion:* Dinoprostone vaginal insert was as effective as intravenous oxytocin in the prevention of postpartum blood loss.

Key words: Postpartum blood loss; Dinoprostone vaginal insert; Vaginal delivery; Cesarean delivery.

Introduction

Postpartum hemorrhage remains in the top five causes of maternal deaths in both developed and developing countries [1]. The period following the birth of baby and first hours postpartum are crucial in the prevention, diagnosis and management of postpartum hemorrhage (PPH). The injection of the most commonly used uterotonic drug, oxytocin, has proven to be very effective in reducing the incidence of PPH [1, 2]. Misoprostol, a new PGE1 analogue, has been suggested as an alternative for routine management of the third stage of labor [3]. Moreover, it has been mainly used by different routes of administration for the prevention of PPH, results of which have showed promising results, indicating similar efficacy in comparison to oxytocic agents [4-7]. Given its low cost, ease of administration, and stability misoprostol use was a good option for the prevention of PPH [8, 9].

Dinoprostone (PGE2 analogue) vaginal insert has been recently implemented as an alternative agent for labor induction with high efficacy in achieving cervical ripening and succesful labor induction [10-14]. Controlled-release dinoprostone, delivered over 24 h from a vaginal insert, results in cervical ripening within 12 h in most women. It is marginally more effective than immediate release formulations and has a comparable efficacy to misoprostol [15].

However, there is paucity in the literature regarding the use of the controlled-release dinoprostone vaginal insert in the prevention of postpartum blood loss. Within this context, this study represents the first attempt in the literature to investigate the efficacy of dinoprostone in the prevention of PPH.

Materials and Methods

Approval for this study was obtained from the Institutional Ethical Board of the University Hospital. All the patients were informed and consented to take part into the study. This prospective, randomized study enrolled 200 term singleton pregnancies undergoing spontaneous vaginal (n: 56) and elective cesarean delivery (n: 144) from December 2007 to May 2008. Exclusion criteria were known sensitivity to prostaglandins, excessive postpartum hemorrhage with hemodynamic instability that necessitated blood transfusion, assisted vaginal delivery, use of epidural anesthesia and cases with labor induction. All the women enrolled to this study met the inclusion and exclusion criteria. Intrapartum blood loss was not taken into consideration in any case.

In the vaginal delivery, active management of the third stage of labor was implemented, consisting of early cord clamping, 10 IU intravenous oxytocin infusion (Synpitan fort®, 5 IU ampoule, Deva, Istanbul) following the delivery of the anterior shoulder of the baby and controlled cord traction. In cases undergoing cesarean section, 20 IU intravenous oxytocin infusion was given after the delivery of the placenta.

Following the vaginal or cesarean delivery, 100 women (group I) were randomly allocated to controlled-release PGE2 vaginal insert with a constant delivery of 0.3 mg/hr (Propess®, Vitalis Sağlık Urunleri Danismanlık ve Tic Ltd., Turkey) for 12 hours following the insertion instead of oxytocin. An equal number of women (group II) were assigned to intravenous oxytocin infusion in balanced solution (10 IU oxytocin for vaginal as described above for active management of the third stage of labor and 20 IU oxytocin for cesarean delivery, infused 24 hours pospartum, respectively). Randomization was done independ-

Revised manuscript accepted for publication February 26, 2009

ently through the hospital pharmacy by random allocation. All deliveries were attended by an experienced obstetrician and a senior resident.

Patient demographic characteristics such as age, number of gravidity, parity, living children, mode of delivery, gestational age at birth and neonatal birthweight were determined in both groups. Estimated amount of postpartum blood loss was assessed via a gravimetric method by counting the blood-filled pads within 24 hours of postpartum. Dry weight of the pads was assessed prior to delivery and found to be equivalent to 30 ml. Main outcome measures were the amount of bleeding, need for additional oxytocins, hemoglobin and hematocrit level changes during the postpartum period and drug-related side-effects such as nausea, vomiting, shivering, pyrexia and diarrhea and postpartum vaginal or endometrial infections in groups I and II, respectively.

Statistical analysis was performed using SPSS 10.0 (SPSS 10.0, Chicago IL, USA). Results are presented as the mean ± SEM. Test of normality was performed by the one-way Kolmogorov-Smirnov test. Patient demographic characteristics and main outcomes were analyzed by the Student's t-test and the chi-square test, and Fisher's exact test or Wilcoxon log-rank test, where applicable. A two-sided p value of < 0.05 was set to be statistically significant.

Results

Demographic characteristics such as age, number of gravidity, parity, abortions, gestational age at delivery, and mode of delivery did not differ between group I and group II, respectively (Table 1). Hemoglobin (g/dl) and hematocrit (%) levels before and 24 and 36 hours after delivery were not significantly changed in the two groups (Figure 1). Number of pads and estimated blood loss (ml) did not differ between the two groups, even the cases that were sub-analyzed in terms of mode of delivery (Table 2). Women allocated to dinoprostone vaginal insert arm experienced more nausea (9% vs 2%; $p < 0.05$) vomiting (5% vs 0%). Moreover, diarrhea (n: 1), pyrexia (n: 1) and shivering (n:1) were only seen in group I cases. Days of hospitalization (5.5 ± 3.2 days vs 5.2 ± 3.3 days) did not differ between group I and II, respectively. There were 12 cases in the dinoprostone group who felt unconfortable during the 12 hours of insertion. There were no cases of vaginal or endometrial infection in the two groups during postpartum follow-ups.

Table 1. — *Demographic characteristics of women in group I (controlled-release dinoprostone vaginal insert) and group II (intravenous oxytocin infusion), respectively.*

Clinical parameters	Group I (Dinoprostone) (n = 100)		Group II (Oxytocin) (n = 100)	
	VD (n: 28)	CS (n: 72)	VD (n: 28)	CS (n: 72)
Age (years)	28.8 ± 5.1	29.7 ± 5.6	29.7 ± 5.9	29.9 ± 6.0
Gravidity (n)	2.1 ± 1.1	2.1 ± 1.2	2.1 ± 1.1	2.1 ± 1.1
Parity (n)	0.8 ± 0.7	0.8 ±.08	0.7 ± 0.8	0.7 ± 0.9
Abortion (n)	0.3 ± 0.7	0.3 ± 0.8	0.4 ± 0.8	0.4 ± 0.7
Living children (n)	0.7 ± 0.7	0.7 ± 0.8	0.6 ± 0.8	0.6 ± 0.7
Gestational age (weeks)	37.6 ± 2.4	37.8 ± 2.6	37.3 ± 2.9	37.4 ± 3.1
Birth weight (g)	2990 ± 660	2882 ± 652	2914 ± 770	2920 ± 780

VD: vaginal delivery, CS: cesarean section; p value was non significant for all comparisons.

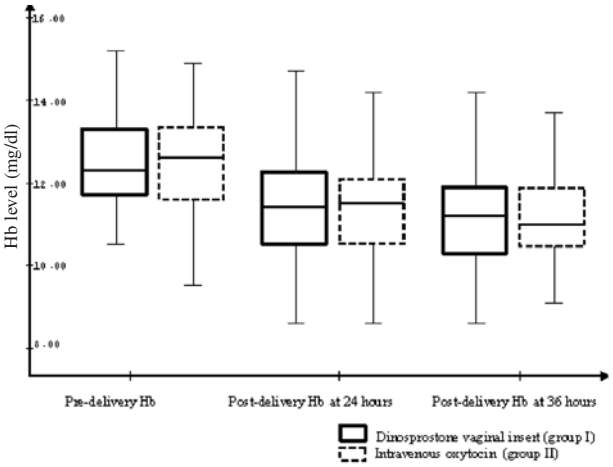

Figure 1. — Pre- and post-delivery (at 24 hours and 36 hours postpartum) hemoglobin (Hb) levels within 95% confidence intervals in groups I and II, respectively.

Table 2. — *Pre- and post-delivery hemoglobin (Hb, g/dl) and hematocrit (Hct %) levels, number of pads, amount of estimated blood loss (ml) and need for additional oxytocin injection in groups I and II, respectively. Data are presented as mean ± SEM.*

Clinical parameters	Group I (Dinoprostone) (n = 100)		Group II (Oxytocin) (n = 100)	
	VD (n: 28)	CS (n: 72)	VD (n: 28)	CS (n: 72)
Pre-delivery Hb	12.4 ± 1.3	12.4 ± 1.2	12.3 ± 1.2	12.2 ± 1.2
Pre-delivery Hct	36.2±1.2	35.1±3.2	35.2 ± 2.3	36.3 ± 2.4
Post-delivery Hb*	11.5 ± 1.5	11.2 ± 1.4	11.2 ± 1.3	11.1 ± 1.2
Post-delivery Hb * *	11.3 ± 1.3	11.2 ± 1.2	11.1 ± 1.1	11.0 ± 1.1
Post-delivery Hct*	35.1 ± 2.7	34.2±1.1	33.1 ± 1.2	34.9 ± 1.7
Post-delivery Hct**	34.4 ± 1.3	33.8±1.3	33.8 ± 2.1	33.9 ± 1.3
Estimated blood loss (ml)	170 ± 54	173 ± 45	169 ± 37	171 ± 34
Number of pads	5.8 ± 1.5	5.8 ± 1.4	5.6 ± 1.2	5.7 ± 1.1
Need of additional oxytocin	–	2	–	–

*24 hours postpartum, ** 36 hours postpartum , VD: vaginal delivery, CS: cesarean section; p value was non significant for all comparisons.

Discussion

Based on the results of the current study, the 10 mg dinoprostone vaginal insert was as effective as intravenous oxytocin in terms of postpartum blood loss in both vaginal and cesarean deliveries. Several studies and meta-analyses have suggested that prostaglandin analogues, especially PGE1, were effective in reducing postpartum hemorrhage but were associated with more side-effects [16, 17].

The dinoprostone vaginal insert has not yet been used prophylactically to reduce postpartum blood loss in women with different modes of delivery [3, 5, 18, 19]. Hence, our study constitutes the first one in the literature that enables physicians to discuss PGE2 analogue use in this setting. In contrast to PGE2 analogues, PGE1 analogues (misoprostol) have a range of potential benefits including ease of use with different route of administra-

tion (rectal, buccal), low cost and stability at room temperature, the latter of the two were found to be drawbacks of the PGE2 analogues [11, 20-22]. Dinoprostone vaginal insert application per se is much more expensive (92.9 ± 2.3$ vs 5.8 ± 2.1$, $p < 0.05$) and needs to be stored in cold temperatures (between -10 and -20°C) based on our experience. Although there is no apparent study in the literature comparing the cost of dinoprostone in the setting of postpartum blood loss prevention, in the context of labor induction, Ramsey *et al*. [23] stated that misoprostol is more cost-effective than comparable commercial dinoprostone prostaglandin preparations.

In general, despite its comparable effectiveness to oxytocin, PGE1 or PGE2 analogues should be considered as a useful option in settings where women receive no uterotonic agents [3]. The dinoprostone vaginal insert was as effective as intravenous oxytocin for the prevention of PPH. However, this approach has a high cost and is not easy to store. Hence, in most parts of Turkey, other PG analogues like PGE1 preparations seem to be a good option for postpartum blood loss prevention in settings where injectable oxytocic agents are not available [25]. However, none of the prostaglandins of different routes of administration and dosage are comparable to conventional injectable uterotonics like oxytocin or methylergonovine maleate [24].

To conclude, the dinoprostone vaginal insert was shown to be effective in the prevention of postpartum blood loss. However based on the current study, this approach is not cost-effective in terms of postpartum blood loss as compared to PGE1 preparations. This basic knowledge should be considered in the decision-making process regarding which drug to use for the prophylaxis of PPH.

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