CEOG Clinical and Experimental Obstetrics & Gynecology

A randomized controlled trial of intra-umbilical vein ergometrine as compared to intramuscular oxytocin for management of third stage of labor

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Summary

Aim: To compare the use of intra-umbilical vein injection (IUVI) of ergometrine, with the standard oxytocin intramuscular injection for management of third stage of labor. *Materials and Methods:* Two groups of women who delivered vaginally of a singleton were randomly assigned to receive 0.2 mg of ergometrine diluted in 10 cc of normal saline via the umbilical vein after clamping of the cord, or to receive oxytocin 5 IU intramuscularly, at delivery of anterior shoulder, plus 10 cc saline via umbilical vein for management of third stage of labor. The primary outcome was the amount of blood loss and the duration of third stage of labor. Secondary outcome included: postpartum hemorrhage (PPH), severe PPH (> 1,000 ml), retained placenta necessitating manual removal, and observed side effects. *Results:* A total of 1,035 women were recruited, 501 actually received 0.2 mg of ergometrine diluted in 10 cc of normal saline via the umbilical vein, group A, and 517 received oxytocin 5 IU at delivery of anterior shoulder plus 10 cc saline via umbilical vein, group B. Seventeen had no records available. No difference was observed between the two groups' demographic data. The amount of blood loss was slightly higher (270 *vs.* 230 cc, respectively) in the group of patients who received IUVI ergometrine of than those who received parenteral oxytocin (($p = 0.014$). There was no statistically significant difference in the number of PPH (both mild and severe) cases between the two groups. However blood transfusion was needed for only one patient who received oxytocin (group B) for PPH. Additional uterotonics were required in both groups with no significant difference ($p = 0.077$), between the two groups. Manual removal of the placenta was required for 12 retained placentae of group B, as compared to only nine in group A ($p = 0.66$). *Conclusion:* There was a minimal significant increase in the amount of blood loss, without increasing the prevalence of PPH. Local injection at the placental site showed a trend to decrease the need for operative intervention (manual removal of the placenta) than traditional use of oxytocin. Future studies are needed.

Key words: Intra-umbilical vein; Ergometrine; Third stage management; Uterotonics.

Introduction

Global estimates of maternal mortality rates (MMR) show that around 530,000 women die annually across the world because of complications during pregnancy and childbirth. Almost all of maternal deaths (99%) occur in the developing world [1]. Among the different causes of maternal death, hemorrhage alone is responsible for at least 25% of these deaths, with the majority due to postpartum hemorrhage (PPH) [2]. When blood loss after delivery is objectively measured, actively managed third stages following vaginal deliveries are associated with 3% to 5% prevalence of severe PPH (loss greater than 1.000 ml) [3, 4] and 14% of moderate PPH (loss greater than 500 ml) [3]. Without oxytocic's, incidences as high as 51% for moderate PPH and 17% for severe PPH were found in a randomized double-blind controlled trial in Guinea Bissau (compared to 45% and 11%, respectively, in those given prophylactic misoprostol) [5]. Active management is shown to be associated with a two-fold reduction in the risk of PPH and a reduction in the need for blood transfusion [6]. According to a survey of the WHO in 2003, in 15 countries, the overall use of the active management is low (25%), and there is a wide variation in the use of prophylactic oxytocics (overall usage 44% with a range of 0% to 100%) [7]. Umbilical or intra-umbilical vein injection (IUVI) for the treatment of retained placenta was first described in 1826. Large volumes (200-400 ml) had been used initially, but recent studies concentrated on smaller volumes of umbilical vein injection of 0.9% saline solution plus oxytocin, although most of these were uncontrolled [8]. Carroli and Bergel showed that IUVI of saline solution plus oxytocin was effective in the management of retained placenta [9].

Routine umbilical vein injection has been suggested as an alternative way of managing the third stage of labor, as it directs the treatment to the placental bed and uterine wall, resulting in an earlier uterine contraction and placental separation [8]. It also allows higher doses to be used, and a reduction of systemic side-effects. There is a wide variety of

Revised manuscript accepted for publication June 8, 2017

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLV, n. 4, 2018
doi: 10.12891/ceog4230.2018

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Table 1. — *Demographic data of women of both groups.*

Mean	Group A*	Group B*
Age (years)	26.6	26.1
Gravidity	2	2
Parity	1	1
Weight (kg)	71.1	70.8
Height (cm)	155.2	154.8
BMI (kg/m^2)	29.73	28.99
GAD (weeks)	39.5	39.3

NB: Group A: women received IUVERG 0.2 mg postpartum. Group B*: women received IUV saline plus routine intramuscular oxytocin 10 IU at delivery of anterior shoulder. BMI: body mass index. GAD: gestational age at delivery.*

Table 2. — *Comparison of primary and secondary outcomes between groups A and B.*

Outcome	Group A	Group B	*p* value	95% C.I.
Amount of blood loss (ml)	273.7	240	0.014	6.9-60.019
Duration of 3rd stage of labor (min)	7.82	6.8	0.567	-0.25- 4.57
PPH	51	47	0.596	
Severe PPH	14	6	0.072	
Manual removal of placenta	9	12	0.661	
Blood transfusion (cc)	0	1	1	
Use of other uterotonics	244	223	0.077	

IUVI methods [10]. To the present authors' knowledge, the use of IUVI ergometrine had not been tested before in a RCT.

Materials and Methods

Women delivered vaginally were recruited in the study. Randomization was by computer generated numbers. Inclusion criteria included: gestational age 37-42 weeks, singleton pregnancy, parity 1-5, and birth weight 2,500-4,500 grams. Exclusion criteria: blood pressure 140/90, H/O PPH, abnormal placentation, coagulation defects, and H/O previous cesarean section. Demographic data included age, parity, race, and H/O medical complications.

Cases were randomized to receive 0.2 mg of ergometrine diluted in 10 ml of normal saline injected into the umbilical vein just above the clamp after cord clamping, compared to giving oxytocin 5 IU intramuscularly as part of routine management of third stage of labor. This group also received 10 ml IUVI to decrease the effect of fluid on placental separation (placebo effect). The amount of blood loss was measured by collecting the blood in graduated containers. The blood was collected into a sterile bed pan after birth with the help of plastic bed linen. All gauze and pads were collected after the delivery of the placenta, but were not weighed and the amount of blood loss was estimated visually by the attending resident.

The duration of third stage was recorded in minutes. The mother's blood pressure was measured after delivery and after 15 minutes, and when normal, it was measured routinely, while the patient was still in the delivery room and during 4th stage of labor. If the placenta was retained for longer than 30 minutes, the placenta was removed manually.

The primary outcomes for the study were: amount of blood loss and duration of third stage of labor. The secondary outcomes included: mild and severe PPH (defined as clinically estimated blood loss greater than or equal to 500-1,000 ml respectively), Blood transfusion, manual removal of the placenta, and additionally therapeutic uterotonics. Randomization was done using computer generated numbers.

To achieve 50% reduction of the (PPH rate), 312 patients in each group were required with a probability of 95% and power of 80% and statistical significance, which was defined as $p < 0.05$. The statistical analysis was performed using SPSS version 16. Comparison was performed according to the intention to treat. Continuous variables were presented as mean and standard deviation, while categorical variables as frequency and percentage. Numerical variables were compared with *t*-test, while non-parametric variables were compared using Mann–Whitney test.

Results

The authors recruited a total of 1,035 women; 501 actually received 0.2 mg of ergometrine diluted in 10 cc of IUVI of normal saline, group A, and 517 women received oxytocin 5 IU at delivery of anterior shoulder plus 10 ml of normal saline injected into the umbilical vein to decrease the effect of fluid on placental. Separation, (placebo effect) group B. Seventeen were counseled but were not included, as their information could not be retrieved. No difference was observed between the two groups' demographic data (Table 1).

Manual removal of the placenta was performed for 12 retained placentae of patients of group B, as compared to only 9 in group A. Blood transfusion was needed for only one patient who received oxytocin for PPH; none was required for group A. Additional uterotonics use was not statistically significantly different between the two groups, (244 *vs*. 223 for group A and B, respectively, $p = 0.077$) (Table 2).

Although there was no significant difference in the duration of third stage of labor, the amount of blood loss, was significantly slightly higher when IUVI of ergometrine was used for management of third stage of labor ($p = 0.014$), although the increase was trivial (270 *vs*. 230 ml). The number of cases of PPH and severe PPH were not statistically different between the two groups (Table 2).

Discussion

Different methods of managing third stage of labor are still being explored to minimize the risk of PPH, as it is still a major contributor to maternal deaths worldwide [11]. Few studies compared the use of IUVI of oxytocin with saline with variable outcomes, and no previous studies of IUVI of ergometrine for management of third stage of labor.

This study showed that the use of IUVI of ergometrine was not associated with a statistically significant difference

in the number of cases of PPH (both mild and severe) as with the use of traditional uterotonics. There were no reported significant side effects. This study has also shown a trend that with the use of IUVI of ergometrine, manual removal of the placenta was required less often as compared to the use of saline alone.

A similar observation was noted by Nardin *et al.* [12] who compared IUVI of oxytocin solution compared to saline, and showed a reduction in manual removal of the placenta that was not statistically significant ($p = 0.661$). This the lack of significance could be explained by the relative infrequency of occurrence of retained placenta in this group (1.9%) and this compares well to the reported prevalence in the literature (3%) [13, 14].

Conclusion

This study has shown that the use of IUVI of ergometrine is as effective as oxytocin in the management of third stage of labor, with a trend for less need for manual removal of a retained placenta and without a significant increase in the risk of PPH or severe PPH, and manual removal of the placenta.

Acknowledgement

This project was funded by the Deanship of Scientific Research (DSR) at King Abdulaziz University, Jeddah, under grant number (493-140-1431). The authors, therefore, acknowledge with thanks DSR for technical and financial support.

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