Randomized double blind prospective trial of active management of the third stage of labor

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Abstract

Introduction: To determine if timing and mode of administration of prophylactic oxytocin influences duration of the third stage of labor, amount of blood loss, and incidence of third stage complications.
Material and methods: A randomized double-blind prospective trial in singleton vaginal deliveries comparing oxytocin intravenous injection after infant delivery versus infusion after placental delivery. Vials of medication oxytocin/saline were prepared by the hospital pharmacy. Results were analyzed after study completion, using the Student's t test.
Results: Ninety-nine patients were recruited; 64 completed the study, 32 in each group. The study group received oxytocin after second stage. Drop out occurred due to rapid labor, and due to cesarean deliveries. The two groups were comparable for age, parity, gestational age, and birth weight. Mean (± SD) subjectively estimated blood loss (EBL) showed a statistically significant difference (315.53±91.97 vs. 384.38±116.7, p=0.01). Hematocrit drop and duration of third stage showed a trend to be less in the study group. No cases or controls had retained placenta, hypotension, cardiac arrhythmias, or post partum hemorrhage.
Conclusions: Intravenous injection of oxytocin after the second stage is safe and effective compared with common practice of oxytocin infusion after placental delivery. Future larger studies may show larger benefits.

Key words: oxytocin, second stage, blood loss.

Introduction

Prevention of excessive blood loss in the third stage of labor significantly reduces morbidity and mortality for the obstetric patient. Excessive blood loss can be controlled by the use of oxytocic agents and/or ergot alkaloids during the third stage. The timing and route of administration, i.e., before or after delivery of the placenta, is variable. Active management of the third stage of labor, with administration of oxytocin immediately after delivery of the baby, is practiced in the UK, Australia, and New Zealand. In the United States, the patient commonly receives rapidly infused oxytocin as a dilute solution after delivery of the placenta, due to the widespread belief that administration of oxytocin prior to placental separation can result in retained placenta.

The Cochrane collaboration stated that routine 'active management' is superior to 'expectant management' in terms of blood loss, post partum hemorrhage and other serious complications of the third stage of labor [1]. Canadian obstetricians were surveyed via a questionnaire and responded that 52% of them administered oxytocin before delivery of the placenta [2]. On the contrary, only 14.9% of Texan obstetricians

administered oxytocics before delivery of the placenta compared to 92.1% who gave oxytocics after delivery of the placenta [3]. Thus there is a "significant intracountry and intercountry variation in the practice of the active management of the third stage of labor ...which confirmed the existence of a large gap between knowledge and practice" [4]. Therefore we decided to proceed with this randomized double-blind trial to compare active management of the third stage of labor (prophylactic use of oxytocin) with expectant management.

Material and methods

The study was performed between January and March, 2006, at New York Downtown Hospital, New York. It was a Chief Resident Graduation Project, and was approved by the Institutional Review Board of the hospital. Private attending physicians agreed to permit their patients to participate in the trial. Patients signed informed consent upon admission to Labor and Delivery (L & D). All patients at term gestation, service and private, who were expected to deliver vaginally, were eligible to participate in the study. Exclusion criteria included history of coagulopathy, planned cesarean delivery, and multiple gestations.

Study vials were prepared by the hospital pharmacy. All staff on L & D, including nurses and physicians, were blinded to the contents of the vials. For each patient, a Ziploc pack, made in the pharmacy, contained two vials labeled Vial A and Vial B. Each vial contained 11 milliliters (ml) of clear fluid, with normal saline only in one vial and normal saline 10 ml plus 1 ml of 10 units oxytocin in the other vial. Randomization was performed by the chief pharmacist, with either Vial A or B being the one containing oxytocin. The packs were then stocked on labor and delivery and one was randomly picked for each consenting patient by her nurse.

As is standard practice in our L & D, all patients had an intravenous line inserted upon admission to L & D, with a crystalloid run at 125 ml/hour. A sample for complete blood count was drawn at the time of IV insertion. Each study participant was injected intravenously over 30 s with the contents of vial A, given through the IV line immediately after the delivery of the baby. Each patient also had the contents of vial B added to her mainline IV bag of crystalloid and then run as fast as possible after delivery of the placenta. Therefore, the timing of oxytocin administration, which could have been in either vial A or vial B, was unknown to the patient's nurse and physician. The rest of the third stage process was completed as usual, i.e., the placenta was delivered by cord traction when signs of placental separation were apparent. After the bag of fluid infused with contents of vial B was completed, all patients received an infusion of one liter IV fluid with 20 units of oxytocin at 125 ml/hour. This was also routine practice in our L & D unit. On postpartum day one, all patients had a specimen drawn for complete blood count.

Records of the subjectively estimated blood loss at delivery and duration of third stage of labor were routinely noted in the patients' charts. These data were recorded by the physician present at the time of delivery. The differences in hematocrit between antepartum and postpartum levels were recorded on postpartum day number one. We recorded maternal and neonatal outcomes including morbidity. Other parameters that were considered significant contributors to the blood loss at delivery included parity, gestational age, birth weight, duration of second and third stages of labor, use of epidural anesthesia, use of any analgesia, any perineal lacerations, chorioamnionitis and whether labor had been induced or augmented. All of these records were maintained by the involved physicians.

At the conclusion of the study, the vial code was broken. The patients who received oxytocin after infant delivery comprised the study group, and those who received oxytocin after placental delivery (expectant management) comprised the control group. The above parameters were then analysed for the two groups.

Statistical analysis was performed using two-tailed Student's t test (ref-http//statpages.org/).

Results

Between January 7 and March 4, 2006, ninety-nine patients were recruited for consent for the study and 79 consented. Of these, 64 completed the study, 32 in each group.

Fifteen out of the 79 patients that consented were not able to complete the study. Seven of these needed to be delivered by emergency cesarean section and no longer met the inclusion criteria. Eight patients were excluded due to rapidity of labor and mistakes on the part of the involved L & D staff, such that the study drug was incorrectly given.

Table I shows that the two groups were comparable for parity, age, gestational age, birth weight, duration of 1st and 2nd stages of labor, and labor induction or augmentation rates. The study group received oxytocin after delivery of the infant, the control group received oxytocin after placental delivery.

Table II shows that subjectively estimated blood loss was significantly less in the study group. Measured outcomes including duration of 3rd stage of labor, and change in hematocrit showed a trend to be less in the study group than the controls, but the difference did not reach statistical significance. Two cases in the standard protocol group were not included in the final calculations as their change in

Table I. Comparison between the two groups for parity, age, gestational age, birth weight, duration of 1st and 2nd stages of labor and labor induction or augmentation rates

Group	Parity		Age (years)	Birth weight (gr)		GA (weeks)	1st stage (hours)	2nd stage (min)	Induction/ augmentation
	nullip	multip		mean	>3500 g				
Study (n=32)	14	18	28.5±4.5	3255.3 ±285.34	6	39.3±1.22	4.5±3.45	47.47 ±41.91	21
Control (n=32)	18	14	27.2±4.9	3288.2 ±391.96	10	39.35 ±1.07	4.32±2.85	48.72 ±43.82	15
P value	NS	NS	NS	NS	NS	NS	NS	NS	NS

hematocrit was at far extremes compared to the average range. One patient had an increase in hematocrit in the postpartum period by a value of 5.1% and the other had a drop by 18.8% secondary to IV access infiltration in the 3rd stage. These were considered to be outliers. Including them would cause a greater drop in hematocrit in the control group, and thus a larger difference between the two groups.

The calculations apart from EBL did not show a statistically significant difference, most likely because our numbers were very small. We present them as pilot data. No cases or controls had retained placenta requiring manual removal. There were no incidences of hypotension, or cardiac arrhythmias. There were no cases of PPH, no patient needed blood transfusion, misoprostol or ergot alkaloids. No patient had significant perineal lacerations. There were no instances of febrile morbidity or neonatal NICU admissions.

Table II. Primary outcomes of the two groups for duration of 3rd stage of labor, estimated blood loss and change in hematocrit between intrapartum and postpartum values

	Study group (n=32) mean ± SD	Control group (n=32) mean ± SD	P value
Duration of 3rd stage (min)	6±4.55	6.7±4.26	0.52
EBL (ml)	315.53±91.97	384.38±116.70	0.01
Change in HCT (%)	4.16±2.63	4.57±2.76	0.55

Discussion

In women considered to be at low risk for third stage complications, postpartum hemorrhage is still a very important preventable cause of morbidity and mortality, especially in the third world. The commonest cause of postpartum hemorrhage has been shown to be uterine atony. Recent surveys show that there are still wide practice variations in management of the third stage of labor around the world. Active management advocates giving oxytocin immediately at the beginning of third stage whereas with expectant management, which is widely used in the US, oxytocin is administered after placental delivery.

Oxytocin has been thought to cause transient hypotension or cardiac arrhythmias when injected intravenously. No such complications were noted in any of our thirty-two patients who received oxytocin as an IV push in vial A. This may be because the drug was diluted in 10 ml of NS and was injected via the IV line rather than directly into the vein in a nondiluted form. Larger studies may be needed in the future to demonstrate absolute safety of this mode of administering oxytocin. In published literature, oxytocin has been given intravenously without any adverse side effects [1, 5].

Our study showed a trend towards a shorter third stage and significantly decreased blood loss using active management Ascertainment bias is excluded by the double blind study design. A similar study by Jackson et al. [6] had shown no difference in the incidence of PPH with the timing of oxytocin administration. The physiologic basis of reduced blood loss at delivery is the fact that the uterus should already be contracting firmly as the placenta is delivered. This is only possible if a large amount of a uterotonic agent is delivered to the uterus coincidental with placental separation. In Jackson's study, oxytocin was administered in a dilute form over a 15 to 30 min duration in both arms whereas in our study the administration of 10 units oxytocin in the study group was rapid, lasting approximately 30 s, immediately after delivery of the baby. This could have accounted for the advantage noted in the study group with reduced blood loss.

In conclusion IV injection of oxytocin at the start of the third stage is a safe and effective alternative to the usual US practice of oxytocin infusion after placental delivery. We noted a significantly decreased estimated blood loss as well as a trend towards a shorter third stage and a lesser drop in hematocrit. Future larger studies may show benefits.

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