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CLINICAL ARTICLE

Oral misoprostol vs. intravenous oxytocin in reducing blood loss after emergency cesarean delivery

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Abstract

Objective: To compare the effectiveness of oral misoprostol and intravenous oxytocin in reducing blood loss in women undergoing indicated or elective cesarean delivery (CD) under spinal anesthesia. *Methods:* In this prospective, double-blind pilot study, 56 parturients who received 5 IU of intravenous oxytocin after cord clamping were randomized to further receive either misoprostol orally and a placebo infusion intravenously or placebo orally and an oxytocin infusion intravenously. *Results:* After adjustment was made for the sonographically estimated amniotic fluid volume, there was no statistical difference in blood loss between the 2 groups (mean ± S.D., 1083 ± 920 mL in the oxytocin group vs. 970 ± 560 mL in the misoprostol group; $P = .59$). *Conclusion:* Oxytocin followed by oral misoprostol is as effective as an oxytocin injection followed by an oxytocin infusion in reducing postoperative blood loss after CD, and the protocol may be a safe, valuable, and cost-effective alternative to oxytocin alone. Visual estimation of intraoperative blood loss undervalues the effective value of misoprostol use by 30%.

1. Introduction

Postpartum hemorrhage (PPH) is the leading cause of maternal morbidity and mortality worldwide, and the number of maternal deaths due to PPH is estimated to exceed 100,000 each year [1]. Post-

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partum hemorrhage is defined as a blood loss of more than 1000 mL in the first 24 h following delivery [2]. Active management of the third stage of labor, use of uterotonic agents, and early cord clamping with controlled cord traction [3] have contributed to reducing the incidence of PPH by 40% [4,5]. However, oxytocin, ergot preparations, and prostaglandins such as sulprostone, which have been traditionally used to control postpartum bleeding, are associated with adverse effects and complications when administered within a dose range likely to be effective in cases of PPH. The effectiveness of misoprostol, a prostaglandin E1 derivative, in preventing PPH after vaginal delivery has been well established [6]. A low-cost drug that can be taken orally and remains stable even when stored at elevated temperatures, misoprostol appears to be particularly suitable for use in developing countries. The present study was designed to compare the effectiveness of oral misoprostol as an uterotonic drug with that of intravenous oxytocin in patients undergoing indicated or elective or cesarean deliveries (CDs). Intraoperative and postoperative blood loss, a quantitative parameter of postpartum hemorrhage, was compared for the 2 drugs, as well as drug-related adverse effects in women treated by the same surgical and anesthesiological team in one institution.

2. Materials and methods

2.1. Study design

This prospective, double blind, placebo-controlled pilot study was approved by the Basel Women's University Hospital institutional review board, and written informed consent was obtained from all participants. The trial was posted on the Clinical Trials Web site (available at: www.clinicaltrials.gov).

A total of 56 pregnant women at low risk for PPH who underwent indicated or elective CD after the 37th week of pregnancy were included in the study whether or not labor had begun. Indications for CD were breech presentation, malposition, intrauterine growth retardation, placenta previa marginalis, twin pregnancy, previous CD, maternal disease, and failure of labor to progress. Exclusion criteria were emergency CD within 30 min of admission, fetal distress, fetal malformations, pre-eclampsia, or HELLP (hemolysis, elevated liver enzymes, and low platelet count), hypersensitivity to prostaglandins, coagulopathy, severe systemic disorders, an American Society of Anesthesiologists physical status of 3 or greater, severe asthma, prior myomectomy, and fever (>38.5 °C). The resident and attending physician were responsible for the enrollment of the participants. The hospital pharmacy performed the 1:1 computer-generated randomization that assigned the participants to their group. The pharmacy also provided the study drugs and placebos in unidentifiable form. Numbered containers held either 800-μg tablets of misoprostol (Cytotec; Pfizer, Zurich, Switzerland) to be taken orally plus a syringe filled with a normal saline solution supplemented with placebo, or a placebo tablet to be taken orally plus a syringe filled with a normal saline solution supplemented with 20 IU of oxytocin (Syntocinon; Novartis Pharma, Berne, Switzerland).

Preoperatively, an ultrasonographic evaluation was performed to estimate the amniotic fluid volume, which was calculated as an amniotic volume index (AFI) [7]. One AFI centimeter was estimated to be equivalent to an AF volume of 30 mL [8]. Postoperatively, following cord clamping and as soon as written informed consent was received, 5 IU of oxytocin were administered intravenously. When the membranes had ruptured before the CD procedure, the amount of intraoperative and postoperative blood loss was calculated by determining the difference in weight of cloths and pads used to absorb blood during surgery and postoperatively in the intermediate care unit. When the membranes had not ruptured preoperatively, the amount of blood loss was assessed by collecting the blood in suction bottles and subtracting the estimated amniotic fluid volume. A 100-g increase in cloth and pad weight was considered equivalent to 100 mL of blood or amniotic fluid. The women participating in this study remained at least 6 h in the postoperative care unit for control of vital parameters. A questionnaire was used by obstetricians and anesthesiologists to record the volume of administered perioperative fluid, blood loss, and urine, as well as any adverse effect and complication. Hemoglobin levels were assessed preoperatively and postoperatively after 24 h and 48 h. All CSs were performed using a transperitoneal approach and transverse lower uterine segment incision under spinal anesthesia. All participants received a 5-IU bolus of oxytocin intravenously. Afterwards, they were randomized to receive immediately after cord clamping either (A) 800 μg of misoprostol orally plus an infusion of normal saline solution (1000 mL over 8 h) supplemented with placebo, or (B) an oral placebo plus an infusion of normal