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ORIGINAL ARTICLE

Maternal haemodynamics at elective caesarean section: a randomised comparison of oxytocin 5-unit bolus and placebo infusion with oxytocin 5-unit bolus and 30-unit infusion

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ABSTRACT
Background: Rapid intravenous injection of oxytocin is associated with marked hypotension secondary to decreased venous return. Reductions in dose and rate of bolus administration have reduced the incidence of cardiovascular side effects, but no study has yet investigated cardiovascular stability when oxytocin is infused for several hours after delivery. This study compared maternal haemodynamics during a 4-h 30-unit oxytocin infusion and during a placebo infusion following caesarean section.
Methods: Women booked for elective caesarean section were randomised to receive either oxytocin 5-unit bolus and placebo infusion or oxytocin 5-unit bolus and oxytocin 30-unit infusion. Before, during and for 4 h after surgery electrocardiogram, oxygen saturation, systolic and diastolic pressure and heart rate were monitored non-invasively and cardiac index (CI), left ventricular work index (LVWi) and systemic vascular resistance index (SVRi) by thoracic bioimpedance.
Results: A total of 74 women agreed to haemodynamic measurements. Heart rate, systolic and diastolic pressure, CI, LCWi and SVRi all fell following the onset of spinal anaesthesia, and, with the exception of SVRi, continued to decrease throughout surgery. After delivery of the baby, slow injection of oxytocin 5 units was associated with a temporary rise in CI, LCWi and heart rate, a decrease in SVRi and no change in systolic or diastolic pressure. Thereafter, haemodynamic measures returned to normal over 60 min with no adverse effects apparent from the additional oxytocin infusion.
Conclusions: An additional oxytocin infusion at elective caesarean section did not adversely affect maternal haemodynamics either during or after surgery.

Keywords: Maternal haemodynamics; Caesarean section; Oxytocin; Bioimpedance

Introduction

Oxytocin is routinely injected intravenously after delivery of the baby at caesarean section in order to reduce blood loss. Rapid bolus injection of oxytocin results in marked vasodilatation of arteries and capacitance vessels. Arterial vasodilatation increases cardiac output up to two-fold,[1] whereas vasodilatation of capacitance vessels decreases venous return, leading to a fall in blood pressure, increase in heart rate and, in some patients, myocardial ischaemia.[2]

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In response to a reported death following oxytocin administration, the 1997-99 Report on Confidential Enquiries into Maternal Deaths (CEMD) recommended that the i.v. bolus dose of Syntocinon should be limited to 5 units.[3] Despite widespread adoption of this dose,[4] side effects due to rapid i.v. injection have endured.

Attempts to reduce the haemodynamic side effects of oxytocin have focused on reduction in speed of injection and dose. In a single-blind study comparing rapid i.v. injection with a slow infusion over 5 min, rapid injection was associated with a greater incidence of tachycardia and hypotension,[5] while substitution of the 5-unit dose of oxytocin with 2 units provided the uterotonic benefits without cardiovascular side effects.[6]

Both the 2003-05 report on confidential enquiries into maternal deaths in the UK[7] (CEMACH) and the UK Obstetric Surveillance System[8] (UKOSS) 2007, have shown that obstetric haemorrhage remains a major cause of maternal morbidity and mortality. The most

recent recommendation from CEMACH is that i.v. oxytocin and/or ergometrine should be the treatment of first choice for uterine atony, followed by an oxytocin infusion over the next 2-4 h.

To date, the risks and benefits of oxytocin when given slowly as a bolus and continued as an infusion have not been fully investigated. Thus the primary aim of this study was to assess the effects of a slow 5-unit oxytocin bolus versus a slow 5-unit oxytocin bolus and 30-unit infusion at elective caesarean section.

Methods

This double-blind, single-site, randomised controlled trial was nested within a larger randomised controlled study,[9] designed to investigate the effect of oxytocin infusion on blood loss. This study focused on the haemodynamic effects of oxytocin when given as a slow bolus and infusion.

Ethics approval, European regulatory authority registration and local sponsorship were gained before starting the study. Women were recruited in the third trimester when arrangements were made for elective caesarean section. Women presenting for caesarean section between the ages of 18 and 45 years were included. Women were excluded if there was a placenta praevia, multiple pregnancy, known bleeding disorder or use of anticoagulant therapy, a history of major obstetric haemorrhage or if the surgeon felt that participation was not appropriate. In addition, women were excluded if there were technical problems in the time leading up to the administration of oxytocin.

After informed written consent, patients were randomised to receive one of two interventions to which they and staff were both blinded. The placebo group received a 5-unit i.v. oxytocin bolus over 3 min and a placebo infusion of Hartmann's solution 500 mL over 4 h. The oxytocin group received a 5-unit i.v. oxytocin bolus over 3 min and a 30-unit oxytocin infusion in 500 mL Hartmann's solution over 4 h. These doses were chosen because they were the two regimens used within our unit.

Coded and numbered ampoules containing either 30 units of oxytocin (Syntocinon) or the same volume of normal saline (placebo) were provided by the hospital pharmacy. The hospital-based clinical trials pharmacist prepared the packs and performed the randomisation. Drug packs were numbered and randomised in the pharmacy using the Table of Random Integers in Statistics for Pharmacists and were then stored on the labour ward and used in sequence.

Haemodynamic monitoring included electrocardiogram (ECG), oxygen saturation (SpO_2), non-invasive blood pressure (NIBP) standardised to the left arm and thoracic bioimpedance using a Physioflow thoracic bioimpedance machine. Measurements were made (i) in the preoperative assessment area: 5-min control period; (ii) in the operating theatre before spinal anaesthesia: 5-min control period; (iii) from the start of spinal anaesthesia until the end of surgery, and (i.v.) in the postoperative observational area for 4 h after the 5-unit injection of oxytocin.

Before each study period, the bioimpedance machine was calibrated by recording a series of 30 heart beats with the patient still, silent and breathing normally. The ECG, bioimpedance (Z), and first derivative of ECG (dECG/dt), and the first and second derivative of Z (dZ/dt) were calculated and displayed. After input of the calibration blood pressure, baseline results were computed. Thereafter, haemodynamic measurements were recorded every 5 to 15 s, except for the periods of patient transfer to and from the operating theatre. At all times the anaesthetist and obstetrician were blinded to the Physioflow measurements. The machine screen was turned away in the operating theatre and postoperative observations were conducted only by the research team.

Anaesthesia was standardised. Premedication consisted of oral ranitidine 150 mg 12 hourly started on the evening before surgery, and oral 0.3 M sodium citrate 30 mL given before the start of anaesthesia. After a 500-mL i.v. infusion of Hartmann's solution was started at an approximate rate of 25 mL/min, a 25-gauge Whitacre needle was inserted at the L3-4 interspace and once cerebrospinal fluid was detected, hyperbaric bupivacaine 11 mg and diamorphine 0.3 mg were injected with the patient in the sitting position. After spinal injection, the patient was placed supine with a 15° left lateral tilt. Anaesthesia to light touch $\geqslant$T 5 was considered adequate for caesarean section.

Surgery was standardised and specified blunt extension of the uterine incision, controlled cord traction for delivery of the placenta and two-layer closure of the uterine incision without exteriorisation. If the uterus remained atonic despite the trial intervention, the obstetrician could ask for an additional uterotonic agent, either replacing the trial infusion with a known infusion of oxytocin and/or use of a further agent.

Hypotension, defined as a fall of >10% below the preoperative blood pressure, was treated with i.v. boluses of phenylephrine 50 μg. The aim was to maintain blood pressure at preoperative values as recommended by Ngan Kee et al.[10] If the heart rate fell below 60 beats/min, a 0.3-mg i.v. bolus of glycopyrrolate was also administered. After delivery, the operating table tilt was removed and the patient placed in the full supine position. Blood loss at operation was replaced with colloid infusion or blood as deemed necessary by the anaesthetist. Postoperative pain relief was standardised to diclofenac 100 mg per rectum followed by oral diclofenac 50 mg 8-hourly and oral paracetamol 1 g with codeine 30 mg 6-hourly.