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Intravenous oxytocin bolus of 2 units is superior to 5 units during elective Caesarean section

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Background. The optimal dose of oxytocin at Caesarean section is unclear. Oxytocin may cause adverse cardiovascular effects, including tachycardia and hypotension, whereas an inadequate dose can result in increased uterine bleeding. We compared the effects of two doses of oxytocin in a randomized double-blind trial.

Methods. Eighty patients undergoing elective Caesarean section received an i.v. bolus of either 2 or 5 units (u) of oxytocin after delivery, followed by an oxytocin infusion of 10 u h^{-1}. All received combined spinal–epidural anaesthesia with arterial pressure maintained by a phenylephrine infusion. We compared changes in heart rate (HR), mean arterial pressure (MAP), blood loss, uterine tone, the need for additional uterotonic drugs, and emetic symptoms.

Results. There was a greater increase in mean (SD) HR in patients who received 5 u of oxytocin [32 (17) beats min^{-1}] than in those who received 2 u [24 (13) beats min^{-1}] (P=0.015). There was a larger decrease in MAP in patients who received 5 u [13 (15) mm Hg] than in those who received 2 u [6 (10) mm Hg] (P=0.030). The frequency of nausea and antiemetic use was higher after 5 u (32.5%) than 2 u (5%) (P=0.003). There were no differences in blood loss, uterine tone, or requests for additional uterotonic drugs (17.5% in both groups).

Conclusions. In elective Caesarean section, a 2 u bolus of oxytocin results in less haemodynamic change than 5 u, with less nausea and no difference in the need for additional uterotonics.

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Although oxytocin is used to aid uterine contraction after delivery at Caesarean section, the optimal dose is unclear.[1–3] Oxytocin causes cardiovascular effects, including tachycardia, hypotension, and ST changes,[1 2 4] and the i.v. administration of 10 units (u) of oxytocin has been reported to cause cardiovascular collapse and death.[5] Although 5 u is the recommended dose in the UK and Australia,[6] the minimum effective bolus dose for 90% of patients (ED90) at elective Caesarean section has recently been estimated to be as low as 0.35 u.[7] However, it appears that many practitioners remain unconvinced. A recent UK survey of 365 obstetricians and anaesthetists found that nearly all gave an initial 'slow bolus' of at least 5 u,[8] followed by the selective use of an oxytocin infusion, most commonly at 10 u h^{-1}.

Our clinical impression has been that a smaller bolus of 2 u oxytocin, followed by a routine infusion, produces adequate uterine contraction with fewer adverse effects than a larger bolus. So in the present study, we compared the haemodynamic and adverse effects of 2 u, compared with 5 u of oxytocin, when both were followed by an oxytocin infusion of 10 u h^{-1}.

Methods

The study was approved by the ethics committee of the Cairns Base Hospital. After written informed consent, 80 women undergoing elective Caesarean section under regional anaesthesia received either 2 or 5 u of i.v. oxytocin after delivery in a randomized double-blind fashion. Patients at increased risk of uterine atony or excessive bleeding (more than two previous Caesarean sections, a history of previous post-partum haemorrhage, known placenta praevia or accreta, twin pregnancy, and polyhydramnios) or cardiovascular instability (pre-eclampsia or essential hypertension) were excluded.

All patients received famotidine 40 mg both the night before and the morning of surgery. In the operating theatre, i.v. access was secured, then pulse oximetry, ECG, and non-invasive blood pressure (NIBP) monitoring were commenced (Datex-Ohmeda S/5 Anesthesia Monitor). All patients received a combined spinal–epidural anaesthetic in the sitting position with hyperbaric bupivacaine 0.5% (2.3 ml) and fentanyl 10 μg given intrathecally. After securing the epidural catheter, patients were laid supine with a wedge under the right flank to achieve a leftward tilt of 15º. One litre of Hartmann's solution was then rapidly infused over 10–15 min, with further i.v. fluids given at the discretion of the anaesthetist. A phenylephrine solution 100 μg ml^{-1} was infused initially at 30 ml h^{-1} (3 mg h^{-1}) and titrated to maintain mean arterial pressure (MAP) within 10% of the level before anaesthesia.[9] Measurement of NIBP was taken at 1 min intervals from when the patient was laid supine until 10 min after delivery. Surgery was allowed once the neuraxial block height had reached T4 to cold perception using ice. Additional analgesic or anxiolytic medications were given at the discretion of the anaesthetist.

After delivery of the baby and cord clamping, the anaesthetist gave a 5 ml i.v. bolus of pre-prepared oxytocin (Syntocinon, Novartis), over 5–10 s. From a series of random numbers in sealed envelopes, either 2 or 5 u had been premixed in saline by a doctor not involved in the care of the patient or any data recordings, so that each anaesthetist and obstetrician was blinded to the oxytocin dose. Immediately after the bolus, a separate infusion of oxytocin 40 u in 1 litre of Hartmann's solution was commenced at 250 ml h^{-1} (i.e. 10 u h^{-1} for 4 h).

In addition to minutely measures of NIBP and heart rate (HR), the maximum HR after the oxytocin bolus was recorded (the Datex monitor displays a 10 s median HR, updated every second). The last measurement of NIBP and HR before giving oxytocin was recorded as a baseline for subsequent changes.

The placenta was delivered by controlled cord traction. Uterine tone was assessed by the obstetrician at 5, 10, 15, and 20 min on a five-point scale, where 1=atonic; 2=partial but inadequate contraction; 3=adequate contraction; 4=well contracted; and 5=very well contracted. Additional uterotonic drugs, if requested by the obstetrician, were administered in the following order: 5 u oxytocin, 10 u oxytocin, ergometrine 0.25 mg (all i.v.), then intramyometrial prostaglandin. Blood loss was estimated by visual assessment of suction bottles and drapes.

The occurrence of nausea or vomiting, both before and after the oxytocin bolus, was assessed by patient report and frequent direct questioning until the patient left the operating theatre, and recorded as a binary outcome (yes or no). Emetic symptoms were treated by correction of any hypotension, then if necessary with rescue antiemetics (one or more of i.v. metoclopramide 10 mg, ondansetron 4 mg, or droperidol 0.5–1 mg).

From previous studies,[1 2] it was predicted that changes in HR would be more reliable than changes in MAP when using non-invasive monitoring, so the primary outcome was the maximum change in HR after oxytocin. Sample size calculations were based on the data from Thomas and colleagues,[1] that is, a HR difference between the groups of 7 beats min^{-1}, with a standard deviation of 11. So at a power of 0.8 and $P<0.05$, 40 patients were required for each group for an unpaired Student's *t*-test. Additionally, Welch's *t*-test was used for parametric data with unequal variances; non-parametric data were analysed with a Mann–Whitney *U*-test; incident data were analysed with a Fisher exact test; and a paired *t*-test or Wilcoxon signed-rank test was used for comparing before-and-after changes within a group. Data were entered in an Access 2002 database and analysed using SigmaStat 3.5 and SigmaPlot 10.0.

Results

Eighty women were randomized and all completed the study. The patient characteristics of the two groups were similar, with no significant differences in vasopressor or antiemetic requirements before oxytocin was given (Table 1). The requirements for additional analgesia during surgery were equal (eight in each group).

After oxytocin, there was a significant increase from baseline in HR ($P<0.001$ for both groups). The greatest change in HR usually occurred <1 min after the oxytocin bolus,

Table 1 Patient characteristics and treatments before oxytocin bolus. Data are presented as number, mean (range) for age, mean (SD), or median (range)

	2 u (*n*=40)	5 u (*n*=40)	*P*-value
Age (yr)	30.8 (20–40)	30.9 (21–41)	0.889
Weight (kg)	79.3 (19.9)	77.6 (13.4)	0.679
Race: Caucasian	31	31	1.000
Parity	1.5 (0–6)	1.5 (0–7)	0.748
Nausea	5	8	0.546
Antiemetic treatment	2	3	1.000
Phenylephrine dose (μg)	1000 (300–2400)	800 (200–2100)	0.119
HR before oxytocin (beats min^{-1})	76 (14)	72 (14)	0.285
MAP before oxytocin (mm Hg)	93 (10)	91 (11)	0.432