Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing Caesarean section

J. S. Thomas*, S. H. Koh and G. M. Cooper

Department of Anaesthesia, Birmingham Women’s Hospital, Metchley Park Road, Edgbaston, Birmingham B15 2TG, UK

*Corresponding author: Department of Anaesthesia, Worcestershire Royal Hospital, Charles Hastings Way, Worcester WR5 1DD, UK. E-mail: jstgasman@btinternet.com

Background. The cardiovascular effects of oxytocin in animal models and women undergoing Caesarean section include tachycardia, hypotension and decrease in cardiac output. These can be sufficient to cause significant compromise in high-risk patients. We aimed to find a simple way to decrease these risks whilst retaining the benefits of oxytocin in decreasing bleeding after delivery.

Method. We recruited 30 women undergoing elective Caesarean section. They were randomly allocated to receive 5 u of oxytocin either as a bolus injection (bolus group) or an infusion over 5 min (infusion group). These women had their heart rate and intra-arterial blood pressure recorded every 5 s throughout the procedure. The haemodynamic data, along with the estimated blood loss, were compared between the groups.

Results. Marked cardiovascular changes occurred in the bolus group; the heart rate increased by 17 (10.7) beats min\(^{-1}\) [mean (SD)] compared with 10 (9.7) beats min\(^{-1}\) in the infusion group. The mean arterial pressure decreased by 27 (7.6) mm Hg in the bolus group compared with 8 (8.7) mm Hg in the infusion group. There were no differences in the estimated blood loss between the two groups.

Conclusion. We recommend that bolus doses should be used with caution, and further studies should ascertain if oxytocin is equally effective in reducing blood loss when given at a slower rate.

Accepted for publication: August 23, 2006

Oxytocin is given to women during Caesarean section to decrease blood loss. When given as a rapid i.v. bolus, it causes hypotension and tachycardia.\(^1\) Whilst its cardiovascular side-effects are widely known there is little agreement as to the mechanism by which they occur.\(^2-5\) Some studies suggest that the preservative, chlorobutanol, is the cause of these haemodynamic changes.\(^6\) The magnitude of these effects is dose-related.\(^7\) However, these effects are not widely appreciated by clinicians as highlighted in the Confidential Enquiry into Maternal Deaths (CEMD) published in 2001.\(^8\) The significant haemodynamic changes from administering 10 u of oxytocin could have contributed to the deaths of two women who were already cardiovascularly unstable. More recently, Pinder and colleagues\(^9\) studied the haemodynamic effects of i.v. boluses of oxytocin, 5 and 10 u, in women having Caesarean section under spinal anaesthesia. The dose-related effects of oxytocin were again confirmed.

Weis and colleagues\(^7\) showed that patients receiving an infusion were more haemodynamically stable; these workers used 10 u of oxytocin. We compared the effects of the recommended dose (i.e. 5 u) of oxytocin\(^10\) when given as an i.v. bolus or as an infusion over 5 min.

Methods

After approval and informed consent from the local Ethics Committee was obtained, we recruited women undergoing elective Caesarean section. They were randomly allocated to receive oxytocin either as an i.v. bolus or infusion. Women were excluded if they were known to have placenta praevia, hypertension, diabetes mellitus or pre-eclampsia as these could lead to cardiovascular instability during Caesarean section. Also women were excluded if there was cardiovascular instability or technical problems in the time leading up to the administration of oxytocin.
The monitoring and anaesthetic techniques were the same for all the women. They received ranitidine 150 mg and sodium citrate 0.3 M (30 ml) on the morning of surgery. On arrival at the theatre ECG and pulse oximetry monitoring were commenced, and a radial arterial cannula and a large bore i.v. cannula were sited under local anaesthesia. Hartmann’s solution 500 ml was infused, and thereafter, spinal anaesthesia was established in the sitting position at L3/4 using 24G pencil point needles. Hyperbaric bupivacaine 0.5% (2.4 ml) with fentanyl 25 μg were injected intrathecally. Block height was measured by temperature and fine touch bilaterally. Surgery was commenced once the block reached T4 or above to cold sensation, and to T6 to fine touch. Hypotension was treated with ephedrine 3 mg boluses aiming to restore mean arterial pressure (MAP) to within 20% of preoperative values.

Oxytocin was administered at delivery either as an i.v. bolus of 5 u diluted to 5 ml with normal saline given as quickly as possible (approximately over 1 s), or 5 u diluted to 15 ml with normal saline given over 5 min using a Graseby infusion pump.

A laptop computer was used to retrieve and record the data from a Datex anaesthetic monitor. MAP and heart rate (HR) were recorded every 5 s. The study period started 15 s before giving oxytocin, and it continued for a further 5 min. The first 15 s were taken to provide baseline data. The next 5 min allowed us to compare the haemodynamic changes between the two methods of administration of oxytocin. The study period of 5 min was set after a small pilot study.

The estimated blood loss during Caesarean section was recorded by the investigators. A difference in MAP of 10 mm Hg or above between the two groups was considered clinically significant. For the study to have 90% power at P<0.05, a sample of 13 patients per group was required. Data were analysed using SPSS 12.0.1. for unpaired t-test and generalized model for repeated measures test.

**Results**

Thirty women were successfully recruited. Two were excluded from analysis; one developed bigeminy during surgery before administration of oxytocin, and the other required vasopressors in addition to the study protocol for maintaining MAP after the onset of spinal anaesthesia.

The patient characteristics are shown in Table 1. A small (3.6 yr) but statistically significant difference was seen in the women’s ages in the two groups. Use of ephedrine, postoperative infusion of oxytocin (40 u over 4 h), and estimated blood loss were similar in both groups. Ephedrine was used during the study period.

Baseline MAP and HR were similar in both groups; mean MAP bolus group 89 mm Hg (sd 9.3), infusion group 87 mm Hg (8.7), mean HR bolus group 102 beats min⁻¹ (18.6), infusion group 93 beats min⁻¹ (13.4). A rapid increase in HR of [mean (sd) 17 (10.7)] beats min⁻¹ was seen at 35 s in the bolus group, with an apparent rebound bradycardia (<10 beats min⁻¹) at 120 s (Fig. 1). In contrast, the HR increased by 10 (9.7) beats min⁻¹ in the infusion group, a change which occurred slowly over the duration of the infusion. The MAP changes are shown in Figure 2. A decrease in MAP of up to 27 (7.6) mm Hg occurred at 35 s in the bolus group, with recovery to baseline at 110 s. The infusion group, in contrast, had a decrease in MAP of up to 8 (8.7) mm Hg during the study period. These cardiovascular changes in the two groups were statistically significant with P<0.01.

**Discussion**

Our study shows that slower injection of oxytocin can effectively minimize the cardiovascular side-effects of a bolus dose without compromising the therapeutic benefits. The cardiovascular effects of oxytocin have been described previously but the extent of physiological compromise had not been described using intra-arterial measurements. Our study demonstrated an average decrease in MAP of 27 (7.6) mm Hg in healthy women having an elective Caesarean section who received 5 u of oxytocin as a rapid bolus. Two women had decreases in MAP of 45 mm Hg. The women in our study took more than 90 s for their MAP to return to baseline after the bolus injection. Whilst this magnitude of decrease in MAP may be well tolerated normally, it may not be desirable if there is concomitant severe blood loss or when there is unsuspected myocardial disease. It is interesting to note that during this reduction in MAP there were no complaints of nausea or faintness. We have no explanation for this other than the short period of time that these women experienced the maximal reduction in MAP.

The changes in HR were significantly different in the two groups. The increase in the bolus group at 30 s could be expected. It was interesting that it decreased to below baseline at recovery of MAP. However, the gentler increase of HR in the infusion group is preferable clinically. It is reassuring to the anaesthetist who prefers to maintain cardiovascular equipoise that this physiological insult can be avoided simply by giving the oxytocin over 5 min. The decrease in MAP of 8 (8.7) mm Hg and the small increase in HR are certainly clinically preferable.
Pulse rate changes with oxytocin

Fig 1 Heart rate before and after oxytocin administration (time 0). The data points shown are the mean (2 SEM).

MAP changes with oxytocin

Fig 2 Mean arterial pressure recordings before and after oxytocin administration (time 0). The data points are mean (2 SEM).
Our study was designed to be single blinded with the analysis of data being separate from its collection to prevent bias. We had considered attempting to double blind the study but were unable to have sufficient investigators present to allow the administration of oxytocin to be a separate blinded process. We felt this would not have led to any bias as the investigator present was unable to influence the data collection via the laptop and no vasoactive agents were used during the study period.

Obviously there have been discussions within the obstetric anaesthesia community about the correct dose of oxytocin and its method of administration.\(^\text{11}\) Despite the controversy it seems more anaesthetists are using the lower dose of 5 u as recommended by the CEMD.\(^\text{12}\) This is supported by the work of Pinder and colleagues\(^\text{9}\) who showed dose-related haemodynamic effects, although they underestimated the potential reduction in MAP attributable to the use of non-invasive blood pressure measurements. Our study has further reinforced this trend to the use of lower dosage by showing greater haemodynamic stability when 5 u is administered over 5 min.

Whilst the cardiovascular results of this study are unequivocal, we have to accept that there are limitations in the estimations of blood loss. The prime reason for this estimation was to highlight any excesses that might have contributed to the haemodynamics being measured. As such the blood loss estimations were made by the investigator who was aware of the mode of oxytocin administration. A larger study with more accurate and independent measurement of blood loss is required to confirm the efficacy of both methods of oxytocin administration.

In summary this study supports the need for caution using oxytocin as a bolus in cardiovascularly unstable patients and offers relative reassurance of the effects when given as an infusion over 5 min.

Acknowledgement
We would like to thank all staff at the Birmingham Women’s Hospital for their help and support during this study.

References
12. Bolton TJ, Randall K, Yentis SM. Effect of the confidential enquiries into maternal deaths on the use of Syntocinon\(^\text{10}\) at Caesarean section in the UK. Anaesthesia 2003; 58: 277–9