Minimum effective bolus dose of oxytocin during elective Caesarean delivery

Editor—We read with interest the study by Butwick and colleagues\(^1\) on minimum effective bolus dose of oxytocin during elective Caesarean delivery and wish to make a few comments. We appreciate that their findings indicate that adequate uterine contraction may be achieved in some patients with doses of oxytocin of 0.5–3 units but feel that this does not justify their conclusion that the routine use of 5 units oxytocin during elective Caesarean section be abandoned.

The authors study showed that supplemental oxytocin was required for 20% of patients in both the 0.5 unit group and the 1 unit group. Even in the 5 unit group, 13% of patients ultimately required further boluses of oxytocin to achieve clinically satisfactory uterine contraction. This surely indicates that a significant proportion of the patients who were underdosed initially and also that there is a significant group of patients who require more than 5 units of oxytocin post-delivery to achieve adequate uterine contraction.

It is well recognized that the major risk period for massive blood loss is immediately after delivery of the fetoplacental unit. During this period, underdosing of oxytocin could potentially contribute to significant haemorrhage secondary to uterine atony. We are concerned that failure to be proactive in administering adequate doses of oxytocin during this period may put some women at risk of massive haemorrhage.

Unfortunately, we cannot predict which patients will have adequate uterine contraction with low-dose (or even no) oxytocin. If we recommend reducing the dose for all patients, we may disadvantage a subset of patients who require a larger dose to prevent serious post-partum haemorrhage.

It has been appreciated for some time that bolus dosing of 5 units oxytocin post-delivery can lead to marked cardiovascular changes which can precipitate haemodynamic collapse in those with pre-existing cardiovascular compromise.\(^2\) Recent work has shown that slowing the rate of delivery of the bolus of 5 units oxytocin\(^3\) or giving the 5 units as an infusion\(^4\) leads to more cardiovascular stability without increasing blood loss. We share the authors’ concern that bolus dosing of 5 units oxytocin may produce potentially serious cardiovascular side-effects but suggest that slowing the rate of delivery rather than reducing the dose may be more appropriate.

Conflict of interest
None declared.

M. Lohit*
P. Slater
Northampton, UK
*E-mail: lohitm69@googlemail.com

Editor—We read with interest the study\(^1\) investigating the minimum effective bolus of oxytocin during elective Caesarean delivery. We are grateful that it addresses the important topic of the optimal dose of oxytocin maximizing uterine contractility while minimizing the well-known adverse effects of the drug. However, given the chance for a potential substantial change in clinical practice, we would like to draw attention to a few issues regarding this paper.

After a Caesarean delivery, uterine tone is dependent on a number of factors including parity and previous Caesarean deliveries, both of which were not controlled for in this study. In addition to this, the practice of uterine massage and uterine exteriorization, both important determinants of uterine tone, was performed to varying degrees at the discretion of the obstetrician and this was not controlled for either.

While oxytocin bolus dosing was initially controlled for, the introduction of ‘rescue’ boluses of oxytocin to counter inadequate uterine tone as early as 2 min post-delivery is a major confounding factor to uterine tone. Additionally, the practice of initiating an oxytocin infusion was not standardized as it was dependent on the achievement of adequate uterine tone, as assessed by the obstetrician. This therefore led to variable time intervals between delivery and the commencement of oxytocin infusions across all groups. In essence, standardization of oxytocin dosing was lost after 2 min.

Uterine tone as a subjective marker of uterine contractility in response to oxytocin bolusing was the primary endpoint in this study. While we appreciate that the two are directly related, we feel that the more relevant clinical endpoint in this situation ought to have been a more objective marker, for example, blood loss. Further to this, postoperative uterine atony, a major contributor to post-partum haemorrhage, was not accounted for as uterine tone was only assessed up until 9 min after delivery and postoperative haematocrit (HCT) was measured within 30 min of completion of surgery. A further confounding factor within this study was the intraoperative fluid management which was carried out to the anaesthetist’s discretion and would therefore have impacted on postoperative HCT values.

In summary, further studies investigating oxytocin dosing after elective Caesarean sections ought to focus on the clinical endpoint of haemorrhage and aim to seek an optimal bolus and infusion regime that will promote ongoing uterine contractility extending well into the post-partum period.

Conflict of interest
None declared.

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Editor—The authors wish to thank Drs Lohit, Slater, Woo, and McGlennan for their interest in our study.1 We wish to emphasize that our primary study aims were to investigate the ED50 and ED95 of oxytocin. Therefore, our results support those of Carvalho and colleagues5 who reported that the ED90 of oxytocin = 0.35 units. In addition, no previous studies have attempted to investigate the ED50 and ED95 oxytocin incorporating a placebo group into the study design, which adds further value to our results. Our study was not powered to investigate differences in the number of rescue oxytocin rescue doses and rates of uterine atony between 3 and 9 min post-injection. We commented on the sample sizes as a limitation for assessing differences in secondary outcomes in the paper. As highlighted in our previous response,6 we hope that commentary of our secondary outcomes does not lessen the importance of the results of our primary study aims. We accept that our findings apply only to healthy patients undergoing uncomplicated elective Caesarean delivery (CS), and that high-risk or labouring patients7 are likely to have different oxytocin requirements for prophylaxis. Nonetheless, we are also unaware of any scientific evidence base to substantiate the empirical use of 5 units oxytocin for prophylaxis for patients undergoing elective CS. We feel that our study adds to the current evidence to justify a reduced bolus dose of oxytocin for the initial achievement of adequate uterine tone during elective CS.

It is important to differentiate the overall rates of inadequate uterine tone from the rates of inadequate tone at 2 min after oxytocin injection. As stated in our paper, the rates of adequate uterine tone at 2 min were high in all oxytocin groups, therefore we do not agree that a significant proportion of patients were underdosed initially. The authors feel that there should be an important distinction made between (i) oxytocin dosing needed for the initial achievement of adequate uterine tone and (ii) oxytocin dosing for maintaining adequate uterine tone after initial bolus dose administration. These regimens are commonly used as prophylaxis to prevent uterine atony. As this was a dose-finding study, it was necessary to incorporate rescue doses of oxytocin into the study design. Consequently, data analysis by intention to treat was used.

We agree that the initial period after placental delivery during CS is important in terms of bleeding risk. Early assessment and confirmation of adequate uterine tone is vital in potentially reducing the risk of post-partum hemorrhage. As a result, we set our primary time point for assessment at 2 min after oxytocin injection. The use of low doses of oxytocin as an infusion may result in a significant time-delay in achieving the initial uterotoncic effect, as the half-life of oxytocin is 5–12 min and metabolic clearance rates are high.8 Sarna and colleagues showed that oxytocin infused at 1 unit min−1 produces high uterine scores, however the first assessment was made at 5 min after the start of infusion.9 A recent study reported the ED50 of oxytocin as an infusion to be 0.29 units min−1,10 but 17.5% of patients in this study required additional uterotonics due to inadequate uterine tone. On the basis of current evidence, we believe that low-dose oxytocin bolus administration followed by carefully titrated oxytocin infusion for maintaining adequate uterine tone is justified.

We found no differences in parity or number of previous CS between study groups which were reported in our paper. More stringent inclusion criteria would have reduced the external validity of our results. Careful distinction is also required for risk factors associated with post-partum haemorrhage from those specifically associated with uterine atony. A large, observational study of uterine atony after primary CS11 reported that the association of specific clinical risk factors and uterine atony was too imprecise for practical clinical use.

No rescue dosing was given before assessment at 2 min, therefore rescue dosing did not affect the calculation of ED50/ED95 of oxytocin at 2 min. As stated in our paper, all patients received uterine massage. Our previous response6 provided supplemental data and commentary on uterine exteriorization. We acknowledged that uterine massage techniques were not standardized in our paper. An oxytocin infusion was commenced for patients who achieved adequate uterine tone during the study period. We apologize if this was incompletely described in the methods. It is likely that our oxytocin infusion (0.08 units min−1) may have been subtherapeutic for the maintenance of adequate uterine tone after initial oxytocin dosing (in patients achieving initial adequate uterine tone).10 Therefore, we speculate that the oxytocin infusion during the study period is unlikely to have significantly affected uterine tone assessments during the study period. We understand that further work is planned to assess different oxytocin regimens (bolus vs bolus + infusion) in the postpartum period.12 13 As reported in the paper, we found no differences in estimated blood loss, postoperative haematocrit values, or i.v. crystalloid volumes between the groups. Previous studies investigating oxytocin effect during CS have used uterine tone as their primary outcome measure,5 7 and manual assessment of uterine tone after oxytocin administration is in keeping with obstetric clinical practice.

Conflict of interest
None declared.

A. J. Butwick*
B. Carvalho
Stanford, USA
*E-mail: ajbut@stanford.edu
The authors should be congratulated for their study and point out some of its limitations; the phrase ‘sniffing the morning air’ is not the traditional sniffing position analogy. The authors use a manikin for their study and point out some of its limitations; the phrase ‘sniffing the morning air’ is not the traditional sniffing position analogy. Furthermore, the justification for continued use of the sniffing analogy cannot just be because it ‘fulfilled a purpose’. It needs to be shown objectively to fulfil that purpose well. That analogy was conceived over 70 yr ago, without supporting evidence, and in this case, we must teach it right. This means promoting not only to evidence-based clinical practice, but also evidence-based education. Objective data, albeit imperfect, are what we have provided. With respect, the best way to contradict our findings would be with contrary objective data. Furthermore, the justification for continued use of the sniffing analogy cannot just be because it ‘fulfilled a purpose’. It needs to be shown objectively to fulfil that purpose well. That analogy was conceived over 70 yr ago, without supporting data, and several studies have questioned its efficacy. Overall, our data showed that the sniffing position was statistically no better than no instructions. Furthermore, the likelihood of atlanto-occipital extension was lower than if no instructions were given. This means, at best it may be a waste of limited educational time, and, at worst, may actually be detrimental. Our data also showed statistically superior positioning with the win with the chin analogy. Therefore, it seems reasonable to conclude that this alternate analogy could replace the sniffing analogy. Dr Bone is an airway expert. Nobody is arguing that he should change his personal practice. We state in our manuscript: ‘even if airway experts believe that the sniffing position analogy conveys the recommended airway position our objective data show that novices disagree’. We continue ‘this is