

# Comparison of a “rule of threes” algorithm versus continuous infusion of oxytocin during elective caesarean delivery: A randomized clinical study

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## Abstract

**Background:** Uterine atony is a leading cause for post-partum haemorrhage, and the most commonly used agent for the prevention and treatment of uterine atony is oxytocin. **Aim and objectives:** To compare “rule of threes” algorithm with continuous infusion of oxytocin during elective caesarean delivery. **Materials and Methods:** Eighty parturients undergoing elective caesarean delivery were randomized into “RULE” and “STANDARD CARE” groups. In Rule group, patients received intravenous oxytocin (3 IU/3ml) and a “wide-open” infusion of 0.9% normal saline (500ml); The Standard care group received intravenous 0.9% normal saline (3ml) and a “wide-open” infusion of oxytocin (30 IU in 0.9% normal saline/500ml). Uterine tone was assessed at 3, 6, 9, and 12min, and if inadequate, additional uterotonic agents were administered at pre-determined intervals. Uterine tone, total dose of oxytocin required, timing of uterotonic agents used, maternal haemodynamics, and side effects were recorded. **Results:** Adequate uterine tone was achieved with lower oxytocin doses in the Rule versus Standard care group (mean, 4.43 vs 7.75 IU; P < 0.001). At 3 minutes, higher VAS scores were achieved in the Standard care group as compared to the Rule group (P=0.005). No differences in the uterine tone, maternal haemodynamics (or) side effects were observed. **Conclusion:** A “Rule of threes” algorithm using oxytocin 3 IU results in lower oxytocin doses for achieving adequate uterine contraction.

**Keywords:** PPH; uterine atony; uterotonic agents; oxytocin; VAS score.

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Received Date: 21/02/2021 Revised Date: 13/03/2021 Accepted Date: 29/04/2021

DOI: <https://doi.org/10.26611/10151831>

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	Accessed Date: 02 June 2021

## INTRODUCTION

Uterine atony is the leading cause for post-partum haemorrhage, resulting in increased maternal mortality rate.<sup>1</sup> The most commonly used uterotonic agent for the

prevention and treatment of uterine atony during caesarean delivery is oxytocin.<sup>2</sup> However, rapid administration and increasing doses of oxytocin can result in haemodynamic instability, cardiovascular collapse, and death.<sup>2</sup> To date there is no consensus about the ideal regime of its administration.<sup>4</sup> Despite the demonstration of adequate uterine tone after caesarean delivery with low doses (<3 IU) of oxytocin<sup>3,5</sup> the current practice is the continuous infusion of doses greater than 20 to 40 IU.<sup>6,7</sup> Based on these observations, a clinical “rule of threes”<sup>2</sup> oxytocin algorithm was originated, which incorporated oxytocin and alternative uterotonic agents, for use during caesarean delivery.<sup>2,12</sup> In cases where oxytocin-induced uterine tone proved inadequate, this algorithm also provides for the systematic timed inclusion of alternative uterotonic agents (i.e., methylergonovine, carboprost tromethamine and

misoprostol) and this systematic approach may diminish their inadvertent use and thereby limiting the side effects associated with their use.

We used the same algorithm to recheck its validity and feasibility among Asian population.

**Aim and objectives:** To determine the dose of oxytocin administered with a “rule” versus standard care protocols to obtain adequate uterine tone in women undergoing elective caesarean delivery under spinal anaesthesia.

**MATERIALS AND METHODS**

**Place of study:** M.S.Ramaiah teaching hospital, Bangalore.

**Study type:** Prospective Randomized Study.

**Period of study:** 18 months : October 2016 to March 2018.

**Study population:** ASA physical status II patients aged between 18-40 years undergoing elective lower segment caesarean section were included in the study.

**Sample size:** 80 patients,divided into two groups, rule group (R) and standard care group (S).

**Inclusion criteria**

1. ASA – Physical status II
2. Patients in age group of 18-40 yrs
3. Elective caesarean surgeries.

**Exclusion criteria**

1. Parturients with the presence of labour
2. Ruptured membranes
3. Maternal or foetal risk factors for uterine atony
4. Previous uterine surgery (except for one previous caesarean delivery with a low-transverse uterine incision)
5. Maternal risks for haemorrhage
6. Contraindications to spinal anaesthesia or any of the uterotonic agents
7. Maternal or obstetrician refusal.

**Methodology:**

After obtaining Institutional ethical committee clearance (Ref.No. SS-1/EC/44/2016), a total of 80 patients were included in the study and randomized into two groups.

A standardized protocol for anaesthesia was followed for all patients. A T4 sensory level was achieved before the start of surgery. Upon foetal delivery (time 0 min), all subjects received an intravenous study drug infusion at a wide-open flow rate using a I.V drip set. The rule group R received an infusion of 0.9% saline 500 ml and a syringe with oxytocin 3 IU in 0.9% saline to a total of 3 ml. The standard care group S received an infusion of oxytocin 30 IU in 0.9% saline 500 ml and a syringe with 0.9% saline 3 ml. Using manual palpation, the attending obstetrician provided a subjective uterine tone assessment (adequate/inadequate) and verbal assessment score (VAS; 0 to 10 linear analog scale, with 0 complete atony and 10 excellent uterine tone) every 3 min for total of 12 min. In R group, at 3 and 6 min, an “inadequate” uterine tone assessment resulted in continued saline infusion and an additional oxytocin 3 IU in 3ml saline as boluses. Whereas in S group, in case of inadequate uterine tone at 3 and 6 min, the oxytocin infusion was continued and 3ml of 0.9% saline was given as boluses. At 9 and 12 min, an “inadequate” uterine tone assessment resulted in the administration of intramuscular methylergonovine 0.2 mg and intramuscular carboprost tromethamine 0.25 mg, respectively in both the groups. An obstetrician’s request for methylergonovine and carboprost tromethamine before 9 and 12 min, respectively, resulted in administration of intramuscular 0.9% saline 1 ml. At 15 min, an “inadequate” uterine tone assessment resulted in the administration of misoprostol 600 µg buccally. An “adequate” uterine tone rating for either group at any time point resulted in the continuous infusion being stopped and converted to a maintenance infusion by pump of oxytocin (30IU in 0.9% 500 ml saline) at 3 IU/h for total of 6 h. Postpartum, the patients were followed hourly for 6 h for any signs of uterine atony or bleeding, and if diagnosed, the choice of additional uterotonic agents was at the discretion of the obstetrician.

**RESULTS**

**Table 1: TOTAL DOSE OF OXYTOCIN REQUIRED FOR ACHIEVING ADEQUATE UTERINE CONTRACTION:**

Totaldoseof Oxytocin (IU)	Rule	Standard
1-6	36(90%)	18(45%)
7-12	4(10%)	19(47.5%)
>12	0(0%)	3(7.5%)
Mean ± SD	4.43±1.86	7.75±2.30

P<0.001\*\*, Significant, Student t Test

**Table 2 : TIME TAKEN TO ACHIEVE ADEQUATE UTERINE TONE**

Time taken to achieve adequate uterine tone	Rule	Standard	P value
3min	26(65%)	37(92.5%)	0.003**
6min	37(92.5%)	40(100%)	0.241
9min	38(95%)	40(100%)	0.494
12min	38(95%)	40(100%)	0.494
15min	40(100%)	40(100%)	1.000

Significant, Fisher Exact Test

**Table 3: VAS-SCORE COMPARISON IN TWO GROUPS OF PATIENTS**

VAS Score	0 min	3 min	6 min	9 min	12 min	15 min
Rule (n=40)						
• 0	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
• 1-3	28(70%)	4(10%)	1(2.5%)	0(0%)	0(0%)	0(0%)
• 4-6	12(30%)	10(25%)	3(7.5%)	2(5%)	2(5%)	0(0%)
• 7-10	0(0%)	26(65%)	36(90%)	38(95%)	38(95%)	40(100%)
Standard (n=40)						
• 0	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)	0(0%)
• 1-3	27(67.5%)	2(5%)	0(0%)	0(0%)	0(0%)	0(0%)
• 4-6	11(27.5%)	1(2.5%)	0(0%)	0(0%)	0(0%)	0(0%)
• 7-10	2(5%)	37(92.5%)	40(100%)	40(100%)	40(100%)	40(100%)
P value	0.656	0.005**	0.116	0.494	0.494	1.000

Chi-Square/Fisher Exact Test

**Table 4: USE OF ANY ALTERNATIVE UTEROTONIC AGENTS**

Use of any alternative uterotonic agents	Rule (n=40)	Standard (n=40)
Nil	38(95%)	40(100%)
Inj.methergin @9 min	2(5%)	0(0%)
Inj carboprost @12 min	2(5%)	0(0%)

P=0.494, Not Significant, Fisher Exact Test

**Table 5: ADVERSE EVENTS**

Adverse Events	Rule (n=40)	Standard (n=40)	Total (n=80)
Nil	40(100%)	36(90%)	76(95%)
Yes	0(0%)	4(10%)	4(5%)
• Nausea	0(0%)	3(7.5%)	3(3.8%)
• VPCs IN ECG	0(0%)	1(2.5%)	1(1.3%)

P=0.116, Not Significant, Fisher Exact Test

## DISCUSSION

A common practice during CD followed by many obstetricians and anaesthesiologists is a slow IV bolus of oxytocin 5 IU. According to a survey conducted by Wedsinghe *et al.*,<sup>14</sup> efficacy of such routine use of 5 IU bolus of oxytocin is not yet proven. Oxytocin infusion in the dose range of 5-20 IU have been used during caesarean delivery by Sarna *et al.*,<sup>16</sup> and they found no differences in the incidence of uterine atony between the high and low dose oxytocin infusion. However the investigators did not assess the effect of low dose oxytocin (< 5 IU). In our study, adequate uterine tone was achieved with small bolus doses of oxytocin in accordance with the "rule of threes"<sup>2</sup> algorithm compared with a continuous oxytocin infusion

protocol (mean±SD = 4.43±1.86 vs 7.75±2.30). Our results were in concurrence with a similar study conducted by Vesela P. Kovacheva *et al.*,<sup>2</sup> who concluded that rule of threes algorithm results in a lower total dose of oxytocin as compared to a continuous infusion protocol (4.0 ± 0.9 vs 8.4 ± 4.8 IU). Our study found no significant differences in side effects between the two groups. In our study, no differences were observed in the incidence of facial or chest flushing, nausea, or headache. In contrast Sartain *et al.*,<sup>18</sup> observed more nausea and antiemetic use with oxytocin 5 IU (32.5%) versus 2 IU (5%; P = 0.003) administered over 5 to 10 s. The lower incidence of these side effects observed in our study and others is likely related to the smaller dose and rate of oxytocin delivery. In

our study, we utilised a “timed inquiry<sup>2</sup>” method for administering the additional doses of oxytocin and other uterotonic agents and it has been used prior by Vesela. P. Kovacheva *et al.*,<sup>2</sup> in a similar study. The timed inquiry was done every 3 min: this allows oxytocin to exert its uterotonic effects, thus limiting the requirement of additional and alternative uterotonic agents. Rule of threes<sup>2</sup> algorithm used in this study also provides for the systematic inclusion of alternative uterotonic agents. The advantage of this particular element is that one can avoid the unwanted effects associated with the use of additional doses of oxytocin and other alternative agents (methyl ergonovine, carboprost, misoprostol). We recommend that adherence to fixed drug protocols will also help to mitigate the adverse effects associated with the inadvertent use of oxytocin and other uterotonic agents.

## CONCLUSION

By using oxytocin 3 IU (iv) as a controlled bolus dose over a period of 15 seconds as mentioned in the “rule of threes” algorithm results in a less total dose of oxytocin being delivered as compared to continuous oxytocin infusion practice in parturients undergoing elective caesarean delivery under spinal anaesthesia

We also recommend that the utilization of “timed inquiry” practice included in our study algorithm, to evaluate the adequacy of uterine contraction can fill in as a strategy to restrain extra dosages of uterotonic agents and thus the unwanted effects associated with their utilization.

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Source of Support: None Declared  
Conflict of Interest: None Declared