



# Effect of phenylephrine co-administration on prevention of oxytocin induced hemodynamic effects

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## ABSTRACT

**Objective:** Oxytocin is frequently used in obstetric patients for enhancing uterine contractions, and to control uterine bleeding; however, its use is associated with hemodynamic changes, especially tachycardia and hypotension. We aimed to determine the effectiveness of co-administration of phenylephrine in obtunding the hemodynamic effects of oxytocin administration in female patients undergoing elective cesarean section under spinal anesthesia.

**Methodology:** This randomized controlled trial was conducted from Sep 2017 to Oct 2018 in our hospital. We enrolled 60 pregnant females of ages 18 to 40 years, with singleton pregnancy who were planned for elective cesarean section under spinal anesthesia. Baseline heart rate (HR) and systolic blood pressure (SBP) were noted. In Group-P, 50 µg of phenylephrine diluted in 3 ml normal saline was given followed by oxytocin 3 units diluted in 5 ml normal saline over a period of 15 sec. In Group-N; only 3 ml normal saline was given before oxytocin administration. Mean HR and SBP were noted again after 3 min of oxytocin administration. Mean change in HR was also calculated.

**Results:** Mean age of patients included in this study was  $28.10 \pm 4.85$  y. There was reduction in heart rate in phenylephrine group while there was significant increase in Group-N patients. Mean change in HR was  $-09.13 \pm 5.80$  beats/min in Group-P versus  $11.32 \pm 13.81$  beats/min in Group-N ( $p < 0.001$ ). Mean change in SBP was  $-0.70 \pm 8.69$  mmHg in Group-P versus  $-6.46 \pm 16.29$  mmHg in Group-N ( $p = 0.09$ ).

**Conclusion:** Phenylephrine co-administration is very effective in reducing the risk of hypotension and tachycardia associated with oxytocin administration in female patients undergoing cesarean section in spinal anesthesia.

**Key words:** Oxytocin; Phenylephrine; C-section; Hemodynamics

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## INTRODUCTION

Incidence of obstetric hemorrhage (a major peripartum complication) is increasing worldwide.<sup>1,2</sup> Its occurrence can be prevented by the use of uterotonic agents, of which oxytocin is recommended as a first-line drug to prevent the incidence of post-

partum hemorrhage (PPH). Oxytocin can reduce the occurrence of PPH in about 40% cases.<sup>3</sup> Recent guidelines have recommended to give an initial bolus of 3 units of oxytocin to increase uterine contractions and to prevent PPH.<sup>4</sup> But oxytocin administration has some adverse side effects, e.g. hypotension and tachycardia or sudden collapse in hemodynamically compromised patients.<sup>5</sup>

## phenylephrine for oxytocin related hemodynamic effects

Alpha agonists are administered for management of hypotension in pregnant patients at the time of cesarean section (CS) under spinal anesthesia. Phenylephrine is a rapid acting alpha-agonist and has a quick control on blood pressure and heart rate.<sup>6</sup> Some studies have advocated that the co-administration of phenylephrine along with oxytocin can prevent the occurrence of hemodynamic instability associated with oxytocin administration.<sup>7,8</sup> On the contrary, other studies suggested no benefit of phenylephrine co-administration in similar situations.<sup>9</sup>

In present study we evaluated whether co-administration of phenylephrine with oxytocin is beneficial for obtaining the hemodynamic effects of oxytocin or not.

### METHODOLOGY

This randomized, controlled trial was conducted in Combined Military Hospital Multan, from Sep 2017 to Oct 2018. Approval from Institutional Review Board was taken before starting the study. We included 60 pregnant females of ages 18 to 40 years, who were planned for elective CS under spinal anesthesia. Patients having only singleton pregnancy were included. Patients having eclampsia, and those taking b-blockers or vasodilators during pregnancy were excluded. We followed the methodology cited in an earlier study conducted by Rumboll et al. At power of the test 90% and level of significance 5% the sample size of our study was calculated at least 19 individuals in each group.<sup>9</sup> But we included 30 patients in each group to cater for the drop outs and increase the reliability of the results.

We divided these 60 patients into two equal groups using draw randomization. In Group-P (phenylephrine group); patients received 50 µg bolus of phenylephrine diluted in 3 ml normal saline followed by oxytocin 3 units diluted in 5 ml normal saline over a period of 15 sec. In Group-N (normal saline group) patients, just 3 ml normal saline was given before oxytocin administration.

Spinal anesthesia was given using hyperbaric bupivacaine (0.75%) solution. Before anesthesia, venous access was secured using 18 or 16 G IV cannula, and lactated ringer solution was given @20 ml/kg before giving spinal anesthesia. No further fluid infused until blood loss was > 100 ml. Before administration of studied drugs, baseline heart rate (HR) and systolic blood pressure (SBP) were noted. Mean HR and SBP were noted again after 3 min of oxytocin administration. Mean change in HR

was also calculated. Repeated bolus of phenylephrine (50 to 100 µg) was given if SBP fell below 20% of the baseline value.

Data analysis was carried out using Statistical Package for the Social Sciences (SPSS) version 20.0. Independent sample t-test was used for comparison of differences in mean SBP and HR between the Group-P and N.  $p < 0.05$  was considered as significant difference.

### RESULTS

Mean age of patients included in this study was  $28.10 \pm 4.85$  y. Baseline HR and SBP of patients were similar in Group-P and Group-N patients. But mean HR and SBP after 3 min of oxytocin were significantly different between Group-P and N and this change was more in Group-N as compared to Group-P ( $p = 0.005$ ) (Table 1). Mean change in HR was  $-09.13 \pm 5.80$  beats/min in Group-P versus  $11.32 \pm 13.81$  beats/min in Group-N ( $p < 0.001$ ). Mean change in SBP was  $-0.70 \pm 8.69$  mmHg in Group-P versus  $-6.46 \pm 16.29$  mmHg in Group-N ( $p = 0.09$ ) (Table 1).

### DISCUSSION

Oxytocin a 9-amino acid polypeptide is secreted from posterior pituitary gland.<sup>10</sup> It has important role in preventing blood loss during placental detachment and PPH.<sup>11</sup> Therefore, it is recommended as a first line uterotonic agent. Oxytocin receptors are also found in heart and great vessels.<sup>12</sup> It has direct effects on systemic vascular resistance resulting in hypotension and tachycardia. Other adverse effects are headache, nausea, vomiting, cardiac arrhythmias and pulmonary edema.<sup>13</sup> So to prevent hemodynamic adverse effects vasoconstrictors are administered in these patients. Some studies have demonstrated that slow administration of oxytocin is more effective than IV bolus of oxytocin.<sup>14</sup>

In present study we used 50 µg bolus of oxytocin. Rumboll et al. compared different doses of oxytocin

**Table 1: Comparison of hemodynamic parameters in the groups**

Parameter	Group-P n = 30	Group-N n = 30	p-value
Baseline HR (Beats/min)	101.63 ±12.64	96.80 ± 15.53	0.19
HR after 3 min (Beats/min)	91.96 ± 12.79	102.60 ± 15.26	0.005
Mean change in HR (Beats/min)	-09.13 ± 5.80	11.32 ± 13.81	<0.001
Baseline SBP (mmHg)	123.60 ± 12.54	120.10 ± 13.60	0.30
SBP after 3 min (mmHg)	122.43 ± 12.24	112.50 ± 12.71	0.003
Mean change in SBP (mmHg)	-0.70 ± 8.69	-6.46 ± 16.29	0.09

Heart rate (HR), systolic blood pressure (SBP), phenylephrine group (P), normal saline group (N), Number of patients (n)

## sevoflurane versus TIVA with propofol

and concluded that 50  $\mu\text{g}$  bolus is equally effective to 75  $\mu\text{g}$  bolus of phenylephrine.<sup>9</sup> On the other hand Gangadharaiah et al. concluded that 75  $\mu\text{g}$  bolus of phenylephrine is more effective than 50  $\mu\text{g}$  bolus in obtunding the hypotension and tachycardia associated with oxytocin administration.<sup>8</sup> Mohta et al. compared three different doses; 100  $\mu\text{g}$ , 125  $\mu\text{g}$  and 150  $\mu\text{g}$  boluses of phenylephrine, and reported that there is no benefit of increasing the dose of phenylephrine on hemodynamic adverse effects of oxytocin.<sup>15</sup>

In current study, we found that co-administration of phenylephrine just before oxytocin administration is associated with significant reduction in hemodynamic instability caused by oxytocin. In our study mean change in HR was  $-09.13 \pm 5.80$  beats/min in Group-P versus  $11.32 \pm 13.81$  beats/min in Group-N. We even found decrease in HR in phenylephrine group. While mean change in SBP was  $-0.70 \pm 8.69$  mmHg in Group-P versus  $-6.46 \pm 16.29$  mmHg in Group-N.

Haider et al. also concluded that co-administration of phenylephrine is effective in obtunding the tachycardia and hypotension caused by oxytocin. In

their study mean change in HR was  $-14.06 \pm 11.29$  beat/min in phenylephrine alone versus  $5.80 \pm 13.81$  beats/min in control group. And mean change in SBP was  $-0.43 \pm 8.35$  mmHg in phenylephrine versus  $-8.13 \pm 18.02$  mmHg in control group.<sup>7</sup>

In contradiction to our study Rumboll et al. reported that there is no benefit of co-administration of phenylephrine to obtund the hemodynamic effects of oxytocin and it is not effective in preventing hypotension and tachycardia.<sup>9</sup>

## CONCLUSION

In summary we concluded that phenylephrine co-administration is very effective in reducing the risk of hypotension and tachycardia associated with oxytocin administration in female patients undergoing cesarean section under spinal anesthesia.

**Conflict of interest:** None declared by the authors

**Authors' contribution:**

MS & AAQ: Conceived study idea, manuscript writing, overall responsibility

SA & AS: Data analysis, manuscript writing, manuscript review

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