Ondansetron and Reduction of Spinal-Induced Hypotension

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INTRODUCTION

- Incidence of hypotension after spinal blockade can be up to 74%[2]
- Cause of hypotension induced by neuraxial anesthesia partly due to sympathectomy from the local anesthetic
- Bezold-Jarisch reflex is also activated upon initiation of spinal anesthesia
  - Afferent innervation via the unmyelinated, type C fibers of the vagus nerve[3]
  - Leads to inhibition of sympathetic outflow along with a triad of bradycardia, peripheral vasodilation, and hypotension[3]
  - Rapid decrease in end-diastolic volume due to drop in sympathetic tone and venous pooling
  - Activation of receptors from fast ventricular contractions around a chamber with very little volume[3]
- Chemoreceptors in the ventricles are identified as 5HT-3 receptors[4]
  - When these ligand-gated receptors are activated, increased efferent vagal nerve activity results[5]
  - Selective 5HT-3 antagonist (Ondansetron) can reduce the responses of the Bezold-Jarisch reflex

RESULTS

- 7 of 8 current studies demonstrate decreased occurrence of maternal hypotension with pre-spinal ondansetron[6-12]
  - 4 mg and 8 mg ondansetron effective at decreasing drop in blood pressure post spinal insertion[6-11]
  - 6 mg and 12 mg ondansetron also both proved successful, but no differences noted between the two doses[12]
- Single study showing no reduction in hypotension used intrathecal opioid and varying spinal doses of bupivacaine[13]
- No change in APGAR scores with ondansetron administration 5 minutes before spinal anesthetic[8]
- Consistently decreased vasopressor requirements when compared with placebo[6-12]

Evidence-Based Studies

Evidence Source	n	Intervention	Findings
Rashad et. al[6] (2013)	60	Participants were randomly divided in 3 groups (O, G, and S) Baseline BP was recorded and each group received LR 20 mg/kg 5 minutes prior to insertion of spinal (2 mL 0.5% hyperbaric bupivacaine) Group O received 4 mg ondansetron Group G received 1 mg granisetron Group S received a placebo MAP values were recorded at 5, 10, 15, 20, and 25 minutes post spinal 6 mg of ephedrine was administered for a decrease in MAP of more than 20% of the preoperative measurement	Significant difference in MAP between group O, G and S Patients receiving 4 mg ondansetron demonstrated a statistically significant stability in MAP 5% of group O required ephedrine use ,whereas 25% of Group G and 35% of Group S required ephedrine use
Sahoo et. al[7] (2012)	52	Participants randomly assigned into 2 groups 5 minutes prior to spinal anesthesia (2 mL 0.5% hyperbaric bupivacaine) Group O was given 4 mg ondansetron Group S was given a placebo of normal saline Each group was pre-hydrated with LR of 20 mg/kg, and had baseline vital signs MAP was recorded at 2-minute intervals up to 20 minutes and then 5-minute intervals until the end of surgery SBP less than 90 mmHg or DBP less than 60 mmHg treated with 50 mcg phenylephrine	Figure 1 *(see right)* demonstrates MAP difference between the 2 groups Use of phenylephrine to treat hypotension was significantly more common in Group S Phenylephrine was given to only 2 patients in Group O versus 11 patients in Group S
Wang et. al[8] (2014)	66	Participants randomly assigned into 2 equal groups 5 minutes before spinal anesthesia (2 mL of 0.5% hyperbaric bupivacaine) Group O was given 4 mg ondansetron Group S was injected with saline only Blood pressure measurements were obtained at 2-minute intervals for 30 minutes Each group was given LR 10 mL/kg 100 mcg of phenylephrine was given if maternal SBP decreased to less than 80% of baseline	The average maximal decrease in SBP was 18.9 mmHg in Group O and 30.7 in Group S Occurrence of hypotension in Group O was 25% compared to 56.3% in Group S Administration of phenylephrine notably lower in Group O 1,300 mcg was given in Group O 3,100 mcg in Group S No significant differences between groups in Apgar scores post-delivery
Goda et. al[9] (2012)	60	Participants randomly assigned into 2 equal groups 5 minutes before spinal anesthesia (2mL of 0.5% hyperbaric bupivacaine) Group O received 8 mg ondansetron Group S received a saline placebo Every patient was given LR 10 mL/kg Baseline vital signs were recorded at 5-minute intervals SBP less than 90 mmHg or DBP less than 60 mmHg treated with 5 to 10 mg of ephedrine	Figure 2 *(see right)* illustrates significantly different values for MAP between groups Dose of vasopressor used notably decreased in Group O when compared with Group S
Palmese et. al[10] (2012)	54	Retrospective chart review 500 mL of colloid and 8 mg of ondansetron prior to spinal anesthesia for C-section BP measurements recorded at the time of spinal anesthesia (2 mL 0.5% hyperbaric bupivacaine) and at 5-minute intervals Hypotension was defined as a SBP less than 90 mmHg or MAP of less than 70 mmHg	Systolic hypotension occurred in 16.6% of the cases At 5, 10, 15, and 20 minutes after spinal anesthesia, both SBP and MAP significantly higher Combination of 500 mL of colloid and 8 mg ondansetron helped attenuate hypotension from spinal anesthesia Data cannot be attributed to a single specific intervention
Owczuk et. al[11] (2008)	71	Participants randomly assigned into 2 groups 5 minutes before spinal anesthesia (4 mL of 0.5% hyperbaric bupivacaine) Ondansetron group, 36 patients received 8 mg Placebo group, 35 participants received an intravenous placebo None of patients were pre-hydrated Vital signs recorded at baseline and 5-minute intervals until 20 minutes after blockade	Systolic values at the 10, 15, and 20-minute intervals were significantly higher in the ondansetron group Lowest recorded MAP and SBP values significantly higher in ondansetron group A decrease in SBP below 90 mmHg occurred in 20% of the placebo group compared to 2.8% of the ondansetron group
Marashi et. al[12] (2014)	210	Participants randomized into 3 equal groups Before spinal anesthesia each patient received LR 5 mL/kg over 15 minutes 5 minutes prior to subarachnoid block (3ml of 0.5% hyperbaric bupivacaine) Patients given: ondansetron 6 mg, 12 mg, or saline (control group) Hemodynamic measurements recorded at baseline and 5-minute intervals to 25 minutes If MAP dropped below 80 mmHg or decreased more than 20%, 10 mg intravenous ephedrine was administered	12 patients (control group) with a MAP of <80 mmHg required IV ephedrine None of the patients in either ondansetron group experienced significant hypotension There were no significant differences in MAP between either ondansetron groups Both doses of intravenous ondansetron (6 and 12 mg) attenuate hypotension from spinal anesthesia
Marashi et. al[13] (2014)	128	Participants randomly allocated into 1 of 4 groups 3 received either 2, 4, or 8 mg of ondansetron 5 minutes prior to subarachnoid block A formula using the patient's height determined dose of 0.5% bupivacaine, along with 20 mcg of fentanyl included in the spinal anesthetic Hypotension defined as SBP less than 75% of baseline and treated with either 10 mg of ephedrine or 50 mcg of phenylephrine Vitals were recorded at baseline, at 2-minute intervals for 15 minutes after the spinal and then 5-minute intervals for a further 30 minutes	The total incidence of hypotension was 51.6% No significant differences between the 4 groups regarding total occurrence of hypotension No significant differences between groups in the requirement of vasopressor administration

DISCUSSION/CONCLUSION

- Current literature supports the reduction in hypotension by ondansetron administration prior to neuraxial blockade
- Definitive dose of ondansetron for maximal benefit has not been established
- More research and larger sample sizes are needed to gain greater validity
- Further research may lead to an increased margin of safety concerning hemodynamic stability after spinal anesthesia
- Additional studies are needed examining effects on the fetus to alleviate concerns

Figure 1 [7]

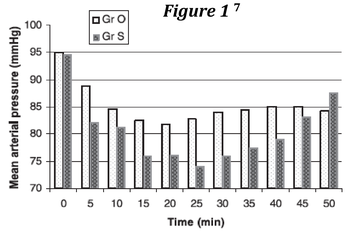
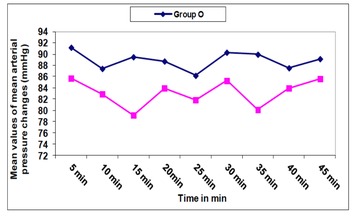


Figure 2 [9]



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