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Ondansetron Prior to Spinal Anesthesia to Prevent Hypotension during Cesarean Delivery

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Abstract

Subarachnoid blocks (SABs) are gold standard for elective cesarean sections, but this anesthetic technique commonly causes hypotension leading to undesirable effects for the mother (eg, nausea, vomiting) and baby (eg, decreased placental blood flow).[9] Vasoactive drugs are often administered, but this may also affect the placental blood flow.[6] The purpose of this case report is to explore effects of administering ondansetron, a $5HT_3$ receptor antagonist, on spinal anesthesia-induced hypotension when administered prior to the SAB and synthesize recent literature to make recommendations for future practice.

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Ondansetron Prior to Spinal Anesthesia to Prevent Hypotension During a Cesarean Delivery

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Introduction

- Spinal anesthesia (SA) is the standard of care for elective cesarean delivery, but consistently causes maternal hypotension from spinal-induced sympathectomy[1]
- Maternal hypotension can have numerous undesirable effects, which can potentially lead to a cascade of issues for the mother and fetus (figure 1)[1-7]

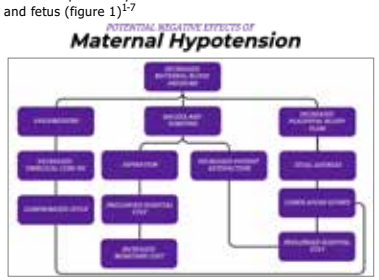

Figure 1. Potential Cascade of Events during Maternal Hypotension[1-7]

- Hypotension post-SA is due to sympathectomy, causing venous pooling and arterial dilation. Many receptors are involved in the activation of the Bezold-Jarisch reflex, including 5-Hydroxytryptamine receptors 3 ($5HT_3$), a serotonin-type of receptor[1,8,9]
- It has been theorized that utilizing a $5HT_3$ receptor antagonist prior to inducing SA may attenuate the Bezold-Jarisch reflex, decreasing the amount of hypotension[1-7]
- The purpose of this case study is to explore the effects of ondansetron administration prior to a subarachnoid block on spinal-induced hypotension

Case Report

- 34-year-old, G3P2, 39-weeks pregnant female, Ht 65 in, Wt 97 kg, BMI 35.6, ASA II, scheduled for elective repeat cesarean section

Preanesthetic evaluation

- PMH: preeclampsia with second pregnancy, but no other comorbidities; No issues this pregnancy
- Current medications: The patient was prophylactically on low-dose aspirin with her history of preeclampsia, but she was not preeclamptic for this pregnancy.
- PSH: Prior cesarean section x1
- Labs: CBC (WNL), urine drug screen, type and screen
- Medications: Aspirin
- Premedication: 500 mL LR
- Anesthetic Plan: Subarachnoid block with nasal cannula

Intraoperative course

- Standard monitors and 2L O2 via nasal cannula. Sitting for SAB
- Pre-procedure VS: BP: 150/80 (nervous), HR: 82
- 4 mg ondansetron administered 2 minutes before 0.75% bupivacaine (1.6mL) with 0.2 mg Duramorph + 15 mcg fentanyl for SAB. T6 sensory block confirmed, full motor block obtained
- BP 3 min post-SAB: **130/65 mmhg**, 6 min: **118/50 mmhg** (treated with 100 mcg phenylephrine to prevent nausea). 9 min after: **125/59 mmhg**. The lowest BP reading was **100/45 mmhg**, which was 35 min after the SAB.
- Total medication administration: 150 mcg phenylephrine, 800 mL LR
- EBL: 800 mL

Postoperative course

- VS: HR: BP: 122/67, HR: 75

Design	Population and Sample	Results	Conclusions
SR[1]	8 OB, 9 non-OB RCTs reviewed; N=1604 Undergoing: cesarean section and non-OB surgery Ages: >18 years	Combined: Ond effective in reducing hypotension (RR 0.54, 95% CI 0.36-0.8, I^2=79%) OB: Ond antagonist effective in reducing hypotension (RR 0.52, 95% CI 0.30-0.88) Non-OB: relevant reduction in hypotension (but not significant) (RR 0.50, 95% CI 0.22-1.16)	$5HT_3$ antagonist prior to spinal: Moderate effects only significant in OB patients, not significant in non-OB patients
RCT[2]	N=75 female patients undergoing cesarean section Ages: > 18 years Gestational age: >/=37 weeks Highest sensory block level: T3	ED_{95} phenylephrine Group A (ond 7 min prior): 0.33 mcg/kg/min Group B (ond 18 min prior): 0.36 mcg/kg/min Group C (ond 16 min prior): 0.41 mcg/kg/min	Ond given prior to the spinal decreased dose of prophylactic phenylephrine for hypotension, but no benefit for early administration
RCT[3]	N=140 patients Ages: 20-60 years ASA: I-II	Required Ephedrine: Group A: 19/70 (27%) Group B: 33/70 (47%)	4 mg prophylactic ond administration significantly reduces hypotension and shivering when administered prior to spinal anesthetic
RCT[4]	N=100 patients; Ages: 23-33 years Weight: 64-76 kg	Hypotension: Group A: 21/50 (42%) Group B: 34/50 (68%)	4 mg ond 5 minutes prior to SAB is effective in reducing hypotension
RCT[5]	N=53 elderly patients; Ages: >70 years	SBP: Ond Group: significantly higher at 5-minutes DBP: Ond Group: significantly higher at 10-, 15-, and 20 minutes MAP: Ond Group: significantly higher at 10-, 15-, and 20 minutes	Prophylactic administration of IV ond prior to SAB attenuates MAP and DBP drop in elderly patients
RCT[6]	N=71 patients Ages: 34-47 years Weight: 75-86 kg Height: 172-178 cm	MAP: Ond: significantly higher at 10-, 15-, and 20-minutes; SBP: Ond Group: significantly higher at 10-, 15-, and 20-minutes, 1/36 (2%) SBP dropped below 90 Placebo Group: 7/35 (20%) SBP dropped below 90; DBP: No significant difference	Prophylactic ond prior to SAB attenuates drop in SBP and MAP, but may not affect DBP or HR
MA[7]	N= 863 OB and non-OB from 10 RCTs	SA-induced hypotension after ond administration: RR: 0.53 (95% CI 0.32-0.86) in OB patients RR: 0.16 (95% CI 0.05-0.51) in non-OB patients Heterogeneity: OB patients: I^2=71% (significant)	Ond reduces SA-induced hypotension and vasopressor consumption

Background of the Bezold-Jarisch Reflex with Spinal Anesthesia

- After local anesthetic is injected into the subarachnoid space, a sympathetic blockade occurs 2-6 dermatomes above the sensory blockade[8]
- The sympathectomy causes arterial dilation and venous pooling, causing decrease blood return to the heart. Baroreceptors initially sense the decrease in blood pressure, decreasing their rate of fire to the vasomotor center of the medulla. A sympathetic response occurs[1,2,3,8,9]
- The contraction of a poorly filled ventricle activates mechanoreceptors and chemoreceptors
- The 5HT-3 receptors are among the chemoreceptors involved in transmission of signals to the vasomotor center. This receptor is not the typical g-protein coupled serotonin receptor. This receptor is a ligand-gated ion channel that produces effects much more rapidly[1,8]
- When activated, the $5HT_3$ receptor signals the vasomotor center to activate the Bezold-Jarisch reflex via unmyelinated C-fibers[8,9]
- The Bezold-Jarisch reflex is cardioinhibitory and causes an increase in parasympathetic activity, which leads to bradycardia, increased venous pooling, and hypotension (figure 2)[1,2,8,9]
- Studies have been conducted to evaluate the effects of ondansetron, a $5HT_3$ antagonist, on reducing the amount of hypotension seen with a spinal anesthetic[1-7]

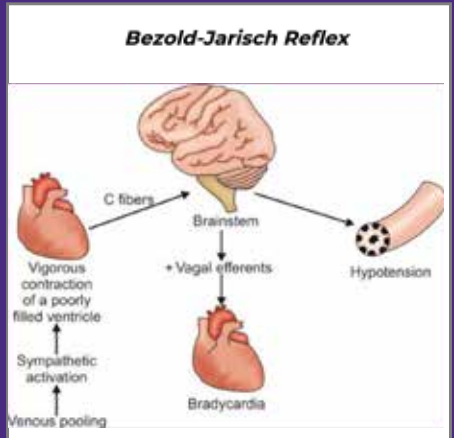

Figure 2. Depiction of Bezold-Jarisch Reflex[9]

Discussion

- All studies indicated that ondansetron prior to the administration of a spinal attenuate hypotension, but the degree of hypotension prevented is difficult to determine, as some studies measure hypotension alone[1,4-7] and some the amount measure vasopressor consumption[2,3]
- Ondansetron prevention of hypotension is not common knowledge, perhaps because many systematic reviews and meta-analyses have identified publication bias in the past, hindering its exposure. More recent studies have no indication of systematic bias [12]
- Many anesthesia providers posit ondansetron may be unsafe during pregnancy, however no adverse events reported in the literature.[1-7,11] No significant major congenital malformations or adverse events with the use of ondansetron during pregnancy[10,11]
- The most productive method of applying this information to practice would be to educate providers of the potential benefit of administering ondansetron prior to a SAB
- Ondansetron is not adequate to rely on as the only medication to use to prevent hypotension, just an additional medication to aid in minimizing hypotension

Case Critique

- For this case, the patient was given ondansetron 2 minutes prior to the spinal anesthetic. To follow the current literature, it would have been ideal to administer the ondansetron 5 minutes prior to the SAB
- The patient's blood pressure dropped minimally and only 1.5 mL of phenylephrine (100 mcg/ml) was administered
- Applying this clinically may be difficult as the timing of spinal anesthesia may be difficult to predict

Conclusions & Practice Recommendations

- Consider 4 mg ondansetron administration prior to spinal insertion to improve BP and decrease vasopressor use during elective cesarean section
- Ondansetron administration as a sole intervention may not be ideal, so use as an adjunct in a multimodal approach to decreasing overall maternal hypotension
- Protocol implementation may be excessive evidence utilization. However, dissemination of information and education regarding ondansetron prior to SAB may lead to increased use by anesthesia providers and leading to further research.

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