Utilization of Ondansetron Prior to Spinal Block to Attenuate Spinal-Induced Adverse Effects During Cesarean Section

Amanda Thornton DNP, CRNA, APRN
Hallie Evans DNP, CRNA, APRN
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Author
Amanda Thornton DNP, CRNA, APRN
Hallie Evans DNP, CRNA, APRN

Editor-in-Chief
Trey Early, MSN, CRNA

Copy Editor
Jennifer Holmes, ELS and Amber Parsell

Journal Designer
Sheri Harvey, Shar Graphics

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Nicholas G. Crofut CRNA

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INTRODUCTION

Cesarean section (C-section) has become the most common major surgery in America.1 Spinal anesthesia (SA) is the anesthetic technique of choice for non-emergent C-sections since it decreases maternal mortality, reduces aspiration risk, allows mother participation, and better pain control.2,3 Despite SA being the most common technique for a C-section, still over 50% of parturients suffer from spinal-induced bradycardia and hypotension.4 Currently, no treatment has been shown to treat these well-known side effects (SE) entirely and there are many variations in practice.4 Current techniques include fluid preloading, fluid coloading, vasopressor pushes or vasopressor drips, lateral uterine displacement (LUD), and leg compression.4 Many of the current methods have only been somewhat efficacious and some have their risks.5

Preventative management of hypotension includes preloading with crystalloid or colloid solutions before the start of the C-section, but excessive fluid therapy can lead to fluid overload and urinary retention.6 Vasopressor use (VU) is a standard treatment but some controversy exists over which is the vasopressor of choice.7 Traditionally, ephedrine has been a mainstay in obstetric (OB) anesthesia because it was believed to affect uterine artery blood flow less than others.8 However, recent research shows ephedrine crosses the placenta and causes fetal beta-adrenergic stimulation, which results in fetal acidosis.9 Due to the possibility of fetal acidosis, many anesthetists now prefer their first-line vasopressor to be phenylephrine.5 Although, phenylephrine directly stimulates alpha 1 receptors that increase peripheral vascular resistance (PVR), which triggers the baroreceptor reflex to cause bradycardia with a subsequent decrease in maternal cardiac output (CO).2 Both medications can lead to adverse outcomes.

Uterine blood flow is not autoregulated and relies on maternal mean arterial blood pressure (MAP), CO, and uterine vascular resistance.5,6 The most common SE of SA is hypotension and the associated chance of decreased uteroplacental perfusion, which can lead to late decelerations and increase the risk of fetal hypoxemia.8 There are around one million C-sections performed annually; there must be further effort put into the anesthetic management of SA's SEs to better the birthing experience.7 It is imperative to find an evidence-based approach to subside SA's SEs to improve parturient outcomes physiologically and psychologically.

Background

SA is performed by placing a needle in the subarachnoid space in the lumbar region at Tuffier’s line (i.e., L4-L5 interspace).5 During a C-section a sufficient spinal block must cover up to T4 dermatome level.5 Three main modifiable factors determine the local anesthetics (LA) distribution including the LA solution's baricity, the dose, and the patient positioning.5 The main benefit is the LA provides pain relief by acting on the myelinated preganglionic fibers of the spinal nerve roots.5 There are also risks of developing SA complications though. SA's SEs of concern include nausea, vomiting, hypotension, and bradycardia.8 The primary mechanism of action for the SA hypotension is the rapid onset of the sympatheticomty that occurs with giving LAs in the subarachnoid space.9 The LA given during SA primarily causes a preganglionic sympathetic blockade within the B fibers, which causes both systemic venous and arterial vasodilation rapidly. The sudden sympathectomy gives minimal time for the body to compensate.5 The sympathetic block causes cardiovascular effects by affecting preload, afterload, heart rate (HR), contractility, and SVR.8 Preload is significantly affected since the venous system is fully dilated causing a decrease in venous return.3 In addition to hypotension, the risk of bradycardia increases with higher levels of blockade.

The spinal-induced bradycardia effect is complicated and stems from a variety of mechanisms including the sympathetic blockade of cardiac accelerator fibers and via the Bezold-Jarisch reflex (BJR).8 The cardiac accelerators are between T1 to T4, and during SA up to T4 for C-section these nerve fibers become anesthetized.3 As a result, bradycardia can occur due to the sympathetic blockade of the cardiac accelerators.8,9 A reasonably new postulated mechanism for spinal-induced bradycardia is due to decreased venous return, which triggers the BJR.8,11
BJR is a cardiac inhibitor reflex that produces bradycardia and hypotension. The BJR essentially slows the heart down when there is profound hypovolemia and a low preload to give the heart more time to fill. The BJR's afferent pathway involves 5-hydroxytryptamine 3 (i.e., 5-HT3, serotonin) receptors located on the sensory vagal nerve endings in the heart that are triggered when the heart is empty. The afferent pathway of the BJR sends its signal to the vasomotor center in the medulla and stimulates the vagus nerve. Ondansetron, a 5-HT3 antagonist, is a promising agent that has been postulated through 5-HT3 antagonism to attenuate spinal-induced bradycardia and hypotension via inhibition of the BJR. Ondansetron is used to prevent and treat nausea and vomiting. Serotonin is an endogenous neurotransmitter and approximately 1% to 2% is located in the central nervous system and afferent vagal nerve endings. Reflexes including the BJR mediate serotonin's hemodynamic effects including vasoconstriction or dilation. Recently, numerous studies have shown prophylactic administration of intravenous (IV) ondansetron before SA to attenuate spinal-induced SEs. With ondansetron, a 5-HT3 antagonist, there is no transmission of the afferent vagal nerve endings to the brain via the BJR, which results in less parasympathetic outflow with a decreased chance of bradycardia, vasodilation, nausea, and vomiting. Ondansetron has the potential to offer a better surgical experience for the OB patient while also lessening the need for excess vasopressor and fluid use.

METHODOLOGY

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was used to guide the search and format of the systematic review. The search utilized MedLine (ProQuest), Excerpta Medica Database (EMBASE), and Cumulative Index of Nursing and Allied Health Literature (CINAHL) electronic databases. Table 1 below shows the search strategy. The PICO (i.e., population, intervention, comparison, outcome) question format was used to create the original question: “In ASA I and II obstetric Cesarean section patients, does the use of ondansetron five minutes prior to spinal block compared to no ondansetron prior to spinal block reduce spinal-induced hypotension, bradycardia, and vasopressor use?” The question helped develop the concepts and keywords in the table. A total of 341 articles resulted from all 3 searches. Duplicates were removed, leaving 319 to be appraised.
### Table 1. Database Search Table

<table>
<thead>
<tr>
<th>Concepts/Topics</th>
<th>Zofran or Ondansetron</th>
<th>Spinal/subarachnoid</th>
<th>Anesthesia</th>
<th>Obstetric</th>
<th>Filters Applied</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CINAHL</strong></td>
<td>(MH “Ondansetron”) OR (MH “Serotonin Antagonists”) OR (MH “Antiemetics”) OR Zofran OR Ondansetron OR “5-HT3*” OR “5-hydroxytryptamine receptor” OR antiemet* OR anti-emet* OR serotonin*</td>
<td>(MH “Anesthesia, Spinal”) OR (MH “Nerve Block”) OR Spinal OR subarachnoid OR CSE OR neuraxial OR nerve block</td>
<td>(MH “Anesthesia”) OR (MH “Anesthesia, Spinal”) OR Block OR regional OR anesthet* OR anaesth*</td>
<td>(MH “Anesthesia, Obstetrical”) OR (MH “Surgery, Gynecologic”) OR (MH “Gynecology”) OR Obstetric* OR parturient* OR labor OR gynecologic* OR pregnant</td>
<td>• Peer reviewed filter applied and 129 results found</td>
</tr>
<tr>
<td><strong>MEDLINE</strong></td>
<td>MESH.EXACT(“Serotonin Antagonists”) OR MESH.EXACT(“Ondansetron”) OR MESH.exact(“Ondansetron – therapeutic use”) OR MESH.EXACT(“Serotonin 5-HT3 Receptor Antagonists”) OR Zofran OR odansetron OR “5-HT3*” OR “5-hydroxytryptamine receptor” OR antiemet* OR anti-emet* OR serotonin*</td>
<td>MESH.exact(“Injections, Spinal”) OR MESH.exact (“Anesthesia, Spinal -- adverse effects”) OR MESH.exact(“Subarachnoid Space”) OR Spinal OR subarachnoid OR CSE OR neuraxial OR nerve block</td>
<td>MESH.exact(“Injections, Spinal”) OR MESH. exact (“Anesthesia, Spinal -- adverse effects”) OR MESH.exact(“Subarachnoid Space”) OR MESH.exact(“Subarachnoid Space”) OR MESH.exact (“Nerve Block -- methods”) OR Block OR regional OR anesthet* OR anaesth*</td>
<td>MESH. EXACT(“Obstetrics and Gynecology Department, Hospital”) OR MESH. EXACT(“Obstetrics”) OR Obstetric* OR parturient* OR labor OR gynecologic* OR pregnant</td>
<td>• 1477 results • applied peer reviewed, female filter, English Filter, 2007-2017, Human Filter, and Journal Article type to get 188 results</td>
</tr>
<tr>
<td><strong>EMBASE</strong></td>
<td>‘serotonin 3 antagonist’/exp OR ‘ondansetron’/exp OR ‘antiemetic agent’/exp OR Zofran OR Ondansetron OR “5-HT3*” OR “5-hydroxytryptamine receptor” OR antiemet* OR anti-emet* OR serotonin*</td>
<td>‘spinal anesthesia’/exp OR ‘intraspinal drug administration’/exp OR ‘neuraxial anesthesia’/exp OR Spinal OR subarachnoid OR CSE OR neuraxial OR nerve block</td>
<td>‘spinal anesthesia’/exp OR ‘intraspinal drug administration’/exp OR ‘neuraxial anesthesia’/exp OR Block OR regional OR anesthet* OR anaesth*</td>
<td>‘obstetric delivery’/exp OR ‘gynecologic surgery’/exp OR Obstetric* OR parturient* OR labor OR gynecologic* OR pregnant</td>
<td>232 results found Filters applied: Female, Article publication type, drugs ondansetron, and dates 2007-2017. 41 results then found • EMBASE ONLY (removed Medline duplicates) and came out to 24 results</td>
</tr>
</tbody>
</table>

### Study Selection and Screening Method with Inclusion/Exclusion Criteria

Two investigators screened titles and abstracts found in relation to the PICO question. The investigators organized the selected articles via RefWorks into a “Background” folder, “Irrelevant” folder, and “Relevant” folder. Thirteen articles were placed into the “Relevant” folder. The two investigators then completed a full-text screening process on the thirteen relevant RCTs based on strict criteria shown below in Table 2. All other results were excluded. Seven studies met the eligibility requirements and were included in this systematic review. Below is a PRISMA flow diagram in Figure 1 that provides a visual representation of the systematic review screening process phases.16
Table 2. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion</th>
<th>Exclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population:</td>
<td>Population:</td>
</tr>
<tr>
<td>• Female</td>
<td>• Male</td>
</tr>
<tr>
<td>• Obstetric (OB)</td>
<td>• Non-OB</td>
</tr>
<tr>
<td>Type of procedure:</td>
<td>• Children (&lt;18 years old)</td>
</tr>
<tr>
<td>• Spinal anesthesia for Cesarean delivery</td>
<td>Type of procedure:</td>
</tr>
<tr>
<td></td>
<td>• Anything other than spinal anesthesia for Cesarean delivery (e.g., epidural, cystoscopy procedure with spinal)</td>
</tr>
<tr>
<td></td>
<td>Type of study:</td>
</tr>
<tr>
<td></td>
<td>• English language</td>
</tr>
<tr>
<td></td>
<td>• Randomized controlled trials</td>
</tr>
<tr>
<td></td>
<td>• Publication date 2007-Present</td>
</tr>
<tr>
<td></td>
<td>Interventions:</td>
</tr>
<tr>
<td></td>
<td>• Ondansetron given to TREAT hypotension (not prevent)</td>
</tr>
<tr>
<td></td>
<td>• Other 5-HT3 antagonist (not ondansetron)</td>
</tr>
<tr>
<td></td>
<td>Outcomes:</td>
</tr>
<tr>
<td></td>
<td>• Anything other than hypotension, bradycardia, vasopressor use (e.g., pruritus)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Non-English</td>
</tr>
<tr>
<td></td>
<td>• Publication date pre-2007</td>
</tr>
<tr>
<td></td>
<td>• Systematic reviews</td>
</tr>
<tr>
<td></td>
<td>• Meta-analysis</td>
</tr>
<tr>
<td></td>
<td>• Questionnaire</td>
</tr>
<tr>
<td></td>
<td>• Dissertations/theses</td>
</tr>
</tbody>
</table>

Figure 1. PRISMA Flow Diagram
Collection, Analysis, and Data Items

The selected studies were then extracted in a systematic method. Studies were vigilantly evaluated using the Johns Hopkins research evidence appraisal tool. One reviewer collected and analyzed the data while the second reviewer checked the data obtained. Meetings and discussions between the two investigators resolved disagreements. Subsequently, an evaluation table was made to summarize and critique findings from each study and to categorize the individual study characteristics. After the evaluation, each study had an evidence rating based on Johns Hopkins’ tool, and strengths/weaknesses are displayed in Table 3.17

RESULTS

Study Selection

- **Demographic Characteristics.** The selected peer-reviewed RCTs had a total of 642 patients. The parturients in the studies were identified as female, healthy or classified as either ASA I or II. Terkawi et al. was the only study that did not explicitly state their inclusion criteria; they only discussed their exclusion criteria. The other six studies’ patient ages ranged from 18 to 40 years old. The RCTs had smaller to moderate sample sizes ranging from 50 to 150 participants. The hospitals involved were located around the world and most came to the same conclusions.

- **Methodology.** Personnel varied and included: anesthesiologists or residents, anesthesia or registered nurses, and pharmacists. Four RCTs preloaded with crystalloids or colloids while two studies only coloaded with crystalloids. One RCT did not mention fluid management. All studies compared ondansetron versus placebo 5 minutes before SA, while one study compared ondansetron, granisetron, versus placebo 5 minutes before SA. Hyperbaric 0.5% bupivacaine was given for all the studies except Terkawi et al., which injected 0.75%. SA was given between L3-L5 in all studies, and SA was done sitting and patient was quickly positioned after in LUD. Two RCTs did not mention positioning. Two studies added opioids to the SA, but this must be considered since this is a different technique and could potentially affect ondansetron’s efficacy. Data collection varied among all RCTs regarding dependent variables and recording times; although, many variables were similar in all studies, which made it possible to appraise them.

Definitions and Findings of Outcomes

There were three main outcomes evaluated for this review: hypotension, bradycardia, and VU. Table 3 below summarizes the data collected in highlighted studies. Of the seven level 1-evidence articles, five were rated as high quality (A) and two were rated as medium quality (B) based on Johns Hopkins’ scale.17

- **Attenuation of hypotension.** Five of the seven RCTs ultimately found giving IV ondansetron prophylactically five minutes before SA to parturients undergoing elective C-sections significantly attenuated spinal-induced hypotension. Wang et al. found in December 2014 that prophylactic ondansetron 4 mg or 6 mg were the optimal doses. Terkawi et al. found that 8 mg ondansetron showed blood pressure (BP) differences between the two groups, but the results were not significant.18

- **Attenuation of bradycardia.** Spinal-induced bradycardia was reported in all seven RCTs. Two of the seven RCTs found prophylactic ondansetron to have a significant difference in HR. The remaining studies also found fewer decreases in HR in the ondansetron group, but it was not statistically significant.

- **Lessening the need for vasopressor use.** All studies reported how many patients needed to be treated with vaspressors. Five out of the seven studies observed a significant decrease in VU in the ondansetron group than in the placebo group. Five studies showed the use of ondansetron did not decrease the number of patients needing vasopressors; however, the use of ondansetron did significantly decrease the dose of vasopressor given.

Risk of Bias

There are several sources of bias in the RCTs and Cochrane Handbook Collaboration’s Risk of Bias tool was used to assess these. Six RCTs had an overall low risk of selection bias. Rashad and Farmawy did not state their method of randomly grouping patients, so it was difficult to assess the risk of selection bias. All other studies used a random sequence generation. Six of the RCTs discussed their concealment method including sequence-generated codes or utilizing sealed envelopes. Again, Rashad and Farmawy did not specifically mention their allocation concealment. Performance bias was another concern. All studies included were double-blinded. Only the authors of Terkawi et al.’s study and El Khouly and Meligy’s study discussed exclusion reasons including failed spinal block. This can make these RCTs at high risk of attrition bias because of the possibility of incomplete data collection.
<table>
<thead>
<tr>
<th>Author (Year) &amp; Level of Evidence</th>
<th>Study, Participants, Interventions, &amp; Setting</th>
<th>Findings in Ondansetron Treated Group (O Group)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rashad and Farwmawy (2013) Level 1 Quality B</td>
<td>60 ASA I-II pts 20-40 years old undergoing Cesarean section under SA Randomly divided into 3 groups- 20 pts per group Preloaded with LR and coloading with LR 2mls of 0.5% Hyperbaric Bupivacaine= 10 mg Given 5 minutes before SA: IV ondansetron 4 mg (O Group), Granisetron 1 mg (G Group), Placebo with 10 ml NS (S Group)</td>
<td>Higher MAP at 5, 10, 15, 20, and 25 minutes (p &lt; 0.05) No incidences of bradycardia (p=0.21) Lower vasopressor administration (p &lt; 0.05) Decreased incidence of nausea (p=0.008)</td>
</tr>
<tr>
<td>Sahoo et al. (2012) Level 1 Quality A</td>
<td>52 ASA I pts 20-40 years old undergoing Cesarean section under SA Randomly divided into 2 groups- 26 pts per group Preloaded with LR 2mls of 0.5% Hyperbaric Bupivacaine= 10 mg All given 5 minutes before SA: IV ondansetron 4 mg (O Group), Placebo with 10 ml NS (S Group)</td>
<td>Higher MAP from 14 min until 35 min (p &lt; 0.05) Higher HR statistically significant at 24 min (p=0.031) and 43 min (p=0.02) Lower vasopressor use (p=0.009) Decreased incidence of nausea and vomiting (p=0.049)</td>
</tr>
<tr>
<td>Wang et al. (Feb. 2014) Level 1 Quality A</td>
<td>65 ASA I-II pts 18-35 years old undergoing Cesarean section under SA Randomly divided into 2 groups- 33 pts in ondansetron group (O group) and 32 in placebo (S group) Coloaded with LR 2mls of 0.5% Hyperbaric Bupivacaine= 10 mg All given 5 minutes before SA: IV ondansetron 4 mg (O Group), Placebo with 5 ml NS (S Group)</td>
<td>Higher SBP (p=0.008) Higher MAP (p=0.025) Less phenylephrine use (p=0.029) Decreased incidence of nausea and vomiting (p=0.004) Umbilical venous pH higher (p=0.006) No incidences of bradycardia (p=0.238)</td>
</tr>
<tr>
<td>El Khouly and Meligy (2016) Level 1 Quality A</td>
<td>100 ASA I-II pts 20-40 years old undergoing Cesarean section under SA Randomly divided into 2 groups- total of 50 pts each No mention of preloading or coloading 2mls of 0.5% Hyperbaric Bupivacaine= 10 mg All given 5 minutes before SA: IV ondansetron 4 mg (O Group), and placebo with 10 ml NS (S Group)</td>
<td>Higher SBP among pts at all time points (p &lt; 0.05) Higher heart rates at 20 and 50 minutes (p &lt; 0.05) Decreased incidence of nausea (p=0.02) and vomiting (p=0.031) Only 30% of pts in O Group received vasopressors compared to 38% of pts in Group S (p= 0.005) Lower vasopressor use (p=0.010)</td>
</tr>
<tr>
<td>Terkawi et al. (2015) Level 1 Quality B</td>
<td>86 ASA I-II pts 28 to 35 years old undergoing Cesarean section under SA Randomly divided into 2 groups- 44 pts in ondansetron group (O group) and 42 in placebo (S group) Preloaded with Hetastarch 15 mg of 0.75% bupivacaine with 20 mcg of fentanyl and 100 mcg of preservative-free morphine All given 5 minutes before SA: IV ondansetron 8 mg (O Group), and placebo with 10 ml NS (S Group)</td>
<td>No significant difference in SBP (p=0.78), MAP (p=0.89), DBP (p=0.82), or HR (p=0.18) No significant difference in vasopressor requirements (p=0.30) No difference in nausea or vomiting incidence Methodology differed from other studies due to higher bupivacaine dose and intrathecal opioids given Mechanism of action of ondansetron may be central and affected by intrathecal opioids</td>
</tr>
<tr>
<td>Wang et al. (Dec. 2014) Level 1 Quality A</td>
<td>150 ASA I-II pts 18-35 years old undergoing Cesarean section under SA Randomly divided into 5 groups- 30 pts in each group Coloaded with crystalloids 2mls of 0.5% Hyperbaric Bupivacaine= 10 mg All given 5 minutes before SA: IV ondansetron 2 mg (O2 Group), ondansetron 4 mg (O4 group), ondansetron 6 mg (O6 group), ondansetron 8 mg (O8 group), and Placebo with 5 ml NS (S Group)</td>
<td>Higher MAP in Groups O4 and O6 (p &lt; 0.05). Minimal changes in SBP, DBP, and MAP observed in Group O4 (p &lt; 0.05) Umbilical venous pH was significantly higher in Group O4 (p &lt; 0.05) No occurrence of bradycardia seen in O4, O6, or O8 groups (p &gt; 0.05) Lower phenylephrine use in Group O4 (p &lt; 0.05) Decreased incidence of nausea in O4 and O6 (p &lt; 0.01) and O8 (p &lt; 0.05)</td>
</tr>
</tbody>
</table>
DISCUSSION

Summary of Evidence
The results of this systematic review are summarized below:

• Five studies found 4 mg of ondansetron administration 5 minutes prior to 2 millimeters (ml) of 0.5% bupivacaine SA for elective C-section significantly attenuated hypotension.19,21,22,23,24
• Two studies found prophylactic 4 mg of ondansetron 5 minutes prior to SA had a significant decrease in bradycardia over time.19,21
• Five RCTs reported the ondansetron group to have a significant decrease in the dose of vasopressor requirements.19,21,22,23,24
  A single study reported only 5% of patients in the ondansetron group required VU while 35% of patients in the placebo group required ephedrine.24
  Two studies that showed no reduction in bradycardia and hypotension used intrathecal opioids and varying bupivacaine doses.18,20

Limitations of the Systematic Review
The investigators must acknowledge the limitations to this review. Part of the inclusion criteria was solely English articles. Another limitation was unpreventable high heterogeneity among the RCTs. One fundamental difference was various definitions and differences in data collection. The heterogeneity in types of fluid must be considered since colloids solutions have proven to be more effective at treating spinal-induced SEs than crystalloids. Terkawi et al. and Ortiz-Gomez et al. found ondansetron not to make a significant difference, but both studies only used preloading.18,20 Research has shown coloading is better than preloading at managing spinal-induced SEs. There were also various anesthetic techniques with six studies using bupivacaine 0.5% intrathecal, while Terkawi et al. used 0.75%; using a lower spinal dose has been associated with better maternal hemodynamics. By Terkawi et al. using a more concentrated dose, this may have produced a flawed conclusion. Another limitation was the sample sizes included in the RCTs were of small-to-medium effect size. Another limiting factor was some RCTs conducted their research at a single center. In addition, the participants were considered healthy ASA I and II patients and the ondansetron effects cannot be generalized to the whole OB population.

Recommendations for Future Research
To further reduce the significant SEs of SA, additional research must focus on being homogenous by making measurement outcomes similar to other published studies. In addition, larger scale RCTs should be done in multi-centers to make the results more generalizable. Future RCTs should include a high-risk pregnancy group and unplanned C-sections to confirm ondansetron’s effects are consistent with the entire OB population. A point to consider is IV ondansetron’s onset is rapid, but the peak is 15 to 30 minutes and this may influence ondansetron’s optimal effect. Another suggestion is to compare different dosing times. Lastly, no RCTs discussed cost-effectiveness. Ondansetron is cost effective by reducing the excessive amount of crystalloid solutions, colloid solutions, and vasopressors used during SA SE management. Ondansetron 4 milligram (mg) vials cost $1.96 and are already used during C-sections to prevent nausea and vomiting.27 There is no additional cost since the timing of administration is the only practice change. Additionally, phenylephrine pre-filled syringes cost $4.81 while ephedrine ones cost $12.78. Two Plasma-Lyte bags are used per C-section and each cost roughly $25. Some providers use colloids instead; Albumin 5% 250 ml bags cost $38.40.

Recommendations for Practice Presented in an Algorithm
No single intervention reduces the incidence of SA’s SEs, but the combination of techniques with ondansetron has shown through the external evidence to decrease reductions in BP responsible for negative SEs. Recommended methods include the use of 4 mg ondansetron prior to SA, LUD, limit intrathecal opioids, fluid preloading and coloading, and VU when needed. Anesthetists need to have an evidence-based guideline via the algorithm shown below in Figure 2 on how to deal with this common phenomenon to reduce variations in practice. Figure 2 is based on this systematic review, other current literature, and guidelines suggested for anesthesia providers’ clinical practice.
CONCLUSIONS

After thorough appraisal of each study, the empirical evidence showed that administration of 4 mg IV ondansetron prophylactically 5 minutes before 0.5% bupivacaine SA in ASA I and II C-section parturients is recommended to attenuate spinal-induced hypotension and excessive VU responsible for negative maternal and fetal SEs. Ondansetron 4 mg administration 5 minutes prior to SA serves as a safe adjunct to decrease morbidity in the elective C-section parturient. This systematic review results show that the administration of ondansetron before SA has a favorable effect on the parturient and improves clinical outcomes to provide a more stable birthing experience via C-section both physiologically and potentially psychologically. The implementation of an evidence-based algorithm utilizing 4 mg ondansetron has the potential to lead to improved patient outcomes, decreased cost, and increased patient satisfaction. Spinal-induced hypotension during C-section is an ongoing concern for the OB population, and the capability to administer ondansetron to reduce both hypotension and VU is of the utmost importance to ensure safety to both the mother and fetus. This systematic review has shown ondansetron to be effective, and a change in current practice is indicated.
References


Post Test

1. Which medication has been shown to increase the risk of fetal acidosis?
   A. Ephedrine
   B. Phenylephrine
   C. Ondansetron
   D. 5% Albumin

2. At least how much percentage of obstetric patients suffer from spinal-induced hypotension and bradycardia?
   A. 30%
   B. 40%
   C. 50%
   D. 60%

3. When this nerve fiber is blocked it causes a sympathectomy:
   A. A-alpha
   B. A-beta
   C. B
   D. C

4. Tuffier’s line is an anatomical landmark used for neuraxial anesthesia and it intersects the spine at the _____ interspace.
   A. L1-L2
   B. L3-L4
   C. L4-L5
   D. L5-S1

5. A patient has received a spinal block and develops bradycardia. What could have caused this?
   A. High spinal
   B. Decrease in cardiac accelerator function and decrease in preload
   C. Oculocardiac reflex
   D. Bainbridge reflex

6. What level of spinal anesthesia is necessary for a Cesarean section?
   A. T4
   B. T8
   C. T10
   D. L1

7. A decrease in which of the following is the most responsible for spinal-induced hypotension following a T4 spinal block?
   A. Preload
   B. Afterload
   C. Systemic vascular resistance
   D. Stroke Volume

8. IV ondansetron is believed to attenuate spinal-induced hypotension and bradycardia via inhibition of the _____ reflex.
   A. Bainbridge
   B. Oculocardiac
   C. Bezold-Jarisch
   D. Baroreceptor

9. The Bezold-Jarisch reflex’s afferent pathway involves _______ receptors located on the sensory vagal nerve endings in the heart.
   A. Alpha
   B. Beta
   C. Gamma-aminobutyric acid
   D. 5-hydroxytryptamine 3

10. What manifestation may be seen when the Bezold-Jarisch reflex is activated?
    A. Hypertension
    B. Tachycardia
    C. Hypotension
    D. Coronary artery vasoconstriction
11. Which of the following stimulates the Bezold-Jarisch reflex?
   A. Venous return is too high
   B. Venous return is too low
   C. Ocular compression
   D. High flow rate of CO2 insufflation

12. According to the systematic review, what is the recommended prophylactic IV ondansetron dose to attenuate spinal-induced hypotension and excessive vasopressor use in elective Cesarean section?
   A. 2 mg
   B. 4 mg
   C. 6 mg
   D. 8 mg

13. According to the systematic review, IV ondansetron should be given at least how many minutes before spinal anesthesia for elective Cesarean section?
   A. 1 minute
   B. 5 minutes
   C. 10 minutes
   D. 30 minutes

14. The systematic review only included randomized control trials (RCTs). What level of evidence are RCTs considered?
   A. Level 1
   B. Level 2
   C. Level 3
   D. Level 4

15. Which bupivacaine concentration is recommended to attenuate spinal-induced hypotension and excessive vasopressor use based on the presented algorithm?
   A. 0.125%
   B. 0.25%
   C. 0.5%
   D. 0.75%

16. According to the provided algorithm, if a parturient’s blood pressure drops 20% or more below baseline and their heart rate is above 60, which vasopressor should be given to reduce variations in practice?
   A. 20 mcg of phenylephrine
   B. 40 mcg of phenylephrine
   C. 5 mg of ephedrine
   D. 10 mg of ephedrine

17. Traditional techniques for managing spinal-induced side effects include:
   A. Fluid preloading
   B. Fluid coloading
   C. Incremental doses of vasopressors
   D. All of the above

18. T or F: Ondansetron has the potential to be cost effective by reducing the excessive amount of crystalloid solutions, colloid solutions, and vasopressors used during spinal-induced management. Unfortunately, no RCTs currently discuss cost-effectiveness.
   A. TRUE
   B. FALSE

19. T or F: Two studies included in the review that showed there was no reduction in bradycardia and hypotension used intrathecal opioids and varying intrathecal bupivacaine doses.
   A. TRUE
   B. FALSE

20. T or F: The systematic review recommends the administration of 4 mg IV ondansetron prophylactically 5 minutes before 0.5% bupivacaine spinal anesthesia in ASA I-IV parturients to attenuate spinal-induced side effects.
   A. TRUE
   B. FALSE

21. T or F: The systematic review found that 4 mg of IV ondansetron 5 minutes before spinal anesthesia for Cesarean section attenuates only spinal-induced hypotension and excessive vasopressor use, not spinal-induced bradycardia.
   A. TRUE
   B. FALSE