Impact of an Educational Intervention on Current Guidelines to Attenuate Spinal Induced Hypotension with Ondansetron

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Dedication & Acknowledgments

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Lastly, I am dedicating this project to my beloved Aunt, Sarah Rock, whose life on earth was cut too short. She was my childhood idol - I dedicate this three-year doctoral project to her free spirit and sweet soul.

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Abstract

Background: Spinal anesthesia (subarachnoid block; SAB) is the preferred anesthetic technique used for elective cesarean sections (CS). While this technique is safe, hypotension and bradycardia are commonly occurring complications, putting both mother and baby at risk. Recent studies have examined the practice of administering prophylactic ondansetron, co-loading of crystalloids, and using sequential compressive devices as effective methods to reduce the incidence of spinal induced maternal hypotension and bradycardia.

Purpose: This Doctor of Nursing Practice (DNP) project aimed to examine the impact of an educational intervention provided to Certified Registered Nurse Anesthetists (CRNAs) on evidence-based guidelines to attenuate spinal induced maternal hypotension and bradycardia. Outcomes assessed included identifying knowledge gaps, knowledge gained post educational intervention, and perceptions of ondansetron's efficacy on reducing spinal induced hypotension (SIH).

Methods: The project utilized a post-intervention follow-up study design consisting of a pre-intervention survey, an online educational voice-over PowerPoint, and a post-intervention survey.

Results: Although results were not statistically significant, they revealed improvement of CRNA knowledge on best-practice guidelines to reduce SIH. CRNA's who implemented preprocedural ondansetron in their practice reported an apparent reduction in SIH. In addition, two knowledge gaps were identified providing insight for future practice change opportunities.

Conclusion: The findings of this project identified SIH as an adverse effect of spinal anesthesia and a noted reduction with the administration of preprocedural ondansetron. Educational interventions containing EBR, and best practice guidelines could enhance provider knowledge encouraging clinical practice change.

Keywords: ondansetron, spinal anesthesia, hypotension, cesarean section

Background & Significance

Neuraxial anesthesia is the preferred anesthetic of choice for mothers undergoing cesarean section. Neuraxial anesthesia, also known as a "spinal or SAB" avoids risks associated with general anesthesia and provides better postoperative pain relief. Hypotension is a common side effect of neuraxial anesthesia that requires close monitoring, prevention, and quick intervention by anesthetists. Hypotension can be hazardous to the mother and child as uteroplacental blood flow is not autoregulated and depends solely on maternal systolic blood pressure for adequate perfusion and oxygenation. Hypotension is generally defined as a greater than 20% decrease in the patient's systolic blood pressure (Morgan et al., 2018). Hypotension experienced during neuraxial anesthesia is due to decreased sympathetic tone and is greatly accentuated by aortocaval compression seen in parturient women (Morgan et al., 2018). In addition, neuraxial anesthesia results in sympathetic nerve blockade, causing vasodilation, decreased venous return, and decreased systemic vascular resistance. Evidence based research (EBR) has found sympathetic inhibition caused by spinal anesthesia can decreases the hearts effectiveness as a pump up to 80% of normal (Hall, 2016). Hypotension of this degree can be challenging to treat and reverse rapidly.

The triad of vasodilation, decreased venous return, and decreased systemic vascular resistance seen after spinal anesthesia results in a paradoxical increase in vagal tone and can lead to a reflex known as the Bezold Jarish Reflex (BJR). The BJR is a cardio-inhibitory reflex in which mechanoreceptors located in the left ventricle sense severe hypovolemia reflexively increasing vagal tone in pursuit of increasing fill-time to increase cardiac output (Nagelhout & Plaus., 2014). However, in the case of spinal anesthesia venous pooling in combination with a paradoxical increase in vagal tone results in sudden, profound bradycardia and further

hypotension (Nagelhout & Plaus., 2014). Mechanoreceptors responsible for sensing hypovolemia transmit their signals via the afferent limb of the BJR through activation of 5-hydroxytryptamine 3 (5-HT3, serotonin) receptors located on the sensory vagal nerve endings in the heart (Hall, 2016).

Ondansetron is a pharmaceutical 5-HT3 serotonin receptor antagonist. It is commonly known in anesthesia providers for its antiemetic effects at the chemoreceptor trigger zone due to the antagonism of serotonin receptors. However, research has demonstrated ondansetron's antagonism of serotonin receptors is also beneficial in reducing spinal induced hypotension (SIH). Centrally mediated serotonin antagonism from ondansetron administration prior to spinal anesthesia suppresses the vagus nerve peripherally, reducing bradycardia mediated by the BJR. Proactive administration of ondansetron prior to spinal anesthesia antagonizes the 5-HT3 serotonin receptors on the vagus nerve directly impeding the BJR subsequently decreasing episodes of bradycardia and hypotension seen after spinal anesthesia.

Current practice guidelines recommend co-loading fluids before neuraxial anesthesia at 20cc/kg, intravenous boluses of phenylephrine, supplemental oxygen, and positional changes (Nagelhout & Plaus., 2014). However, hypotension is still an ongoing concern for patients undergoing a cesarean section. Recent studies have found that ondansetron, a 5-HT3 antagonist given before spinal anesthesia, can significantly reduce maternal hypotension, vasopressor use, and nausea & vomiting

Purpose

The purpose of this project is to provide CRNAs with recommendations from EBR to reduce the adverse effects of maternal hypotension triggered by spinal anesthesia in obstetric

patients. This project utilized a post-intervention design consisting of a pre-intervention survey, an educational video presentation for CRNAs, and a post-intervention survey. This project established and sought after three goals. The first goal was to identify if a knowledge gap existed between CRNAs clinical practice and recommendations of EBR. The second goal examined barriers encountered with employing new practice change. Lastly, the third goal evaluated CRNAs perceived perception of patient outcomes with practice change. Utilization of current EBR ensures anesthesia providers deliver the safest anesthetic while simultaneously ensuring a positive childbirth experience.

Review of Current Evidence

A literature search was conducted to assess the existing evidence-based knowledge on the use of ondansetron prior to spinal anesthesia and its influence on the BJR, maternal hemodynamic effects, neonatal outcomes, vasopressor requirements, and nausea and vomiting. A comprehensive review of the literature was performed. Research article inclusion criteria were as follows: 1) articles related to spinal anesthesia, 2) limited to peer-reviewed articles, 3) written in English, 4) literature synthesis focused primarily on meta-analysis, systematic reviews, and randomized controlled trials. Databases accessed were through The University of North Carolina Greensboro's (UNCG) online library consisting of CINAHL, Medline, Cochrane, PubMed, and The National Guideline Clearinghouse. Search terms used were ondansetron, spinal anesthesia, cesarean section, Bezold-Jarish Reflex, neonatal outcomes, and hypotension.

Spinal Anesthesia for Cesarean Section

Maternal deaths are not common in the United States. However, the maternal mortality due to general anesthesia is 32 deaths per 1,000,000 live births, whereas spinal anesthesia-related

deaths is 1.9 per 1,000,000 live births (Neggers, 2016). Pulmonary aspiration of gastric contents and failed endotracheal intubation are the major causes of maternal mortality associated with general anesthesia (Nagelhout & Plaus., 2014). The utilization of spinal anesthesia effectively avoids the risks associated with general anesthesia. Additional advantages of spinal anesthesia include (1) rapid onset, (2) reliable pain relief, (3) less neonatal exposure to medication, (4) decreased risk of maternal pulmonary aspiration, (5) awake parturient that can experience the birth, and (6) the ability to administer spinal opioids for post-operative pain relief.

Spinal anesthesia is commonly achieved with bupivacaine due to its fast onset, moderate duration, and ability to hyperpolarize the cell. Spinal anesthesia leads to inhibition of somatic, visceral sensation blockade of afferent and efferent motor outflow (The New York School of Regional Anesthesia [NYSORA], 2021). Inhibition of autonomic outflow subsequently causes parasympathetic overactivity resulting in bradycardia due to the BJR, vasodilation, hypotension, and shivering (Nagelhout & Plaus., 2014). Hypotension in pregnant women can cause vomiting, loss of consciousness, aspiration, decreased uteroplacental blood flow, and cardiac collapse if not swiftly treated (Mercier et al., 2013). Mercier et al. (2013) noted that hypotension occurs in 70-80% of all cesarean deliveries when pharmacological prophylaxis is omitted. Current evidence-based practice guidelines to reduce hypotension after spinal anesthesia include co-loading of crystalloid fluids, left uterine displacement, sequential devices on lower extremities, and the use of vasopressors (Šklebar et al., 2019). Recent studies suggest adding ondansetron, a 5-HT3 antagonist, to inhibit the BJR before initiation of SAB reduces hypotension and bradycardia (Gao et al., 2015). Rashad and Farmawy (2013) and Wang et al. (2014) found that 4mg of ondansetron given prior to spinal anesthesia significantly reduced hypotension and decreased vasopressor use.

Coloading Fluids

Intravenous fluid administration is a mainstay therapy utilized to attenuate SIH during the perioperative and operative period during cesarean section. However, the type and specific timing of fluid administration remains controversial in the anesthesia community. Multiple studies have shown SIH was reduced when colloids were administered (Mercier et al., 2014; Mercier et al., 2013; Ni et al., 2017). However, costs, allergic reactions, and coagulation disturbances reduce colloid solutions' mainstream use (Ferre et al., 2020; Lee et al., 2017; Ni et al., 2017). Crystalloids are less expensive alternatives; therefore, their use and timing of administration to prevent SIH have been investigated (Ferre et al., 2020; Tan et al., 2020). Coloading fluids is defined as administering intravenous solution at the initiation of spinal anesthesia (Nagelhout & Plaus., 2014). Preloading fluids is defined as administration of intravenous solution prior to initiation of spinal anesthesia (Nagelhout & Plaus., 2014). A meta-analysis of 824 parturient patients (10 RCTs) receiving spinal anesthesia for cesarean delivery concluded co-loading of crystalloids reduced hypotension incidence compared to preloading (Ni et al., 2017). However, research has shown the administration of crystalloids alone does not reliably attenuate SIH. Therefore, EBR recommends a multimodal approach for treatment of SIH with use coloading intravenous fluids and vasopressors (Sklebar et al., 2019; Lee et al., 2017; Ni et al., 2017).

Sequential Compression Devices

During pregnancy, hormonal changes and vena cava compression by the gravid uterus increase blood pooling in the lower extremities (Sujata et al., 2012). Blood pooling decreases cardiac preload, further promoting hemodynamic instability observed after spinal anesthesia. Sujata et al. (2012) analyzed the efficacy of sequential compression devices on lower extremities in reducing maternal hypotension during elective cesarean section (Sujata et al., 2012). The

findings demonstrated a reduction of hypotensive episodes when compression devices were used. However, the providers concurrently used vasopressors and co-loading of fluids (Sujata et al., 2012).

A random control trial of 75 patients compared the use of leg elevation with pillows to regular supine positions and found a reduction of hypotension and intraoperative vasopressor use by 40.9% (Hasanin et al., 2017). Hasanin et al. (2017) concluded that leg elevation would help prevent and manage SIH when combined with other measures. The use of compression devices may synergistically work with other modalities to attenuate SIH by increasing venous return and decreasing hypotensive episodes.

The Role of the Bezold-Jarish Reflex

The exact mechanism responsible for bradycardia and the BJR during spinal anesthesia is unknown; however, several proposed theories are investigated in the research. Stoelting's Anesthesia by Katherine Marschall (2017) describes the BJR as unopposed parasympathetic nervous activity that results from spinal induced sympathectomy. Carpenter et al. (1992) illustrated the most important cause for the BJR after spinal anesthesia is the reduction in venous return activating the mechanical and chemosensitive receptors in the left ventricle rather than an interruption of sympathetic flow to the heart. Decreased venous return seen after spinal anesthesia activates serotonin (5-HT3) receptors located in the autonomic nervous system, specifically the vagus nerve, resulting in bradycardia and activation of the BJR in-pursuit of increasing cardiac output (Yamano et al., 1995).

Various studies have shown that chemoreceptors on the ventricular wall are serotonin sensitive (Campagna & Carter, 2003; Watts & Davis, 2011; Kinsella, 2001). Additionally, studies have shown that bolus injections of 5-HT3 agonist generated temporary bradycardia and

the BJR in rats, cats, dogs, and rabbits (Yamano et al., 1995). Conversely, Miyata et al. (1991) found that selective 5-HT3 receptor antagonists can inhibit the BJR in anesthetized rats. Gao et al. (2015) conducted a meta-analysis investigating ondansetron's prophylactic use on hemodynamic changes following spinal anesthesia to create best practice guidelines. They found ondansetron attenuated the BJR with a decreased incidence of hypotension, bradycardia, and vasopressor use with spinal anesthesia (Gao et al., 2015).

Ondansetron Use Prior to Spinal Anesthesia

Hypotension

Decreased perfusion and oxygenation from hypotension negatively affects both fetus and mother. Reduced uteroplacental perfusion can cause fetal acidosis decreasing APGAR scores, and if left untreated can lead to fetal demise. Untreated hypotension in the parturient can lead to nausea, vomiting, decreased cerebral perfusion, aspiration, and eventually cardiac collapse (Xu et al., 2018). Ondansetron has been studied to mitigate the BJR, hypotension and bradycardia to decrease the incidence of SIH and improve outcomes.

Six randomized controlled trials (RCT) assessing the effectiveness of ondansetron in patients undergoing elective cesarean section on SIH and the BJR were published between 2013 and 2014. Hypotension was defined as a 20% decrease in mean arterial pressure (MAP) from baseline and/or an 80% decrease in systolic blood pressure (SBP) (Marashi et al., 2014; Rashad & Farmawy, 2013; Trabelsi et al., 2014; Wang et al., 2013; Wang et al., 2014). One study by Ortiz-Gomez et al. (2014) defined hypotension as less than 75% baseline of SBP.

All six studies' participants were randomized and placed into either a control or intervention group (Marashi et al., 2014; Rashad & Farmawy, 2013; Trabelsi et al., 2014; Wang

et al., 2013; Wang et al., 2014; Ortiz-Gomez et al., 2014). The control groups received normal saline as a placebo, whereas the interventional groups received anywhere between 2-12mg (dependent on the study) of pre-procedural ondansetron. Hypotension after spinal anesthesia was significantly decreased in the intervention groups receiving pre-procedural ondansetron in five studies (Marashi et al., 2014; Rashad & Farmawy, 2013; Trabelsi et al., 2014; Wang et al., 2013; Wang et al., 2014).

Trabelsi et al. (2014) conducted a randomized controlled, double-blind study in which patients were divided into one of two groups. One group received 4mg of ondansetron five minutes prior to spinal anesthesia, whereas the second group received normal saline (placebo) five minutes before anesthesia. They found that patients in the ondansetron group had statistically significant fewer episodes of hypotension ($p < 0.001$) and bradycardia ($p < 0.022$) (Trabelsi et al., 2014). Marashi et al. (2014) conducted a similar study to Trabelsi and colleagues, except Marashi et al. had one control group (receiving normal saline) and two experimental groups receiving six and 12 milligrams of ondansetron five minutes prior to spinal anesthesia. The mean arterial pressure (MAP) was statistically lower in the control groups compared to both experimental groups ($p=.04$) (Marashi et al., 2014). Wang et al. (2014) conducted a dose-dependent study in which there were 150 participants with five groups total (n=30). The control group received normal saline, and the other four groups received 2, 4, 6, or 8mg of ondansetron before spinal anesthesia. Compared to the saline group, the incidence of maternal hypotension was significantly lower in the groups that received four and six milligrams of Ondansetron ($P < 0.05$) (Wang et al., 2014). Wang et al., 2014 concluded that two milligrams was not sufficient to prevent maternal hypotension and that eight milligrams had minor effects on the hemodynamic parameters. Like Wang et al. (2014), Rashad and Farmawy (2013) found that four milligrams of

ondansetron produced statistically significant decreases in hypotension ($p < 0.05$) and thus the BJR. EBR demonstrates antagonism of the vagus nerve with administration of ondansetron prior to spinal anesthesia leads to a reduction of bradycardia and hypotension.

Bradycardia

Of the six articles mentioned earlier, three defined bradycardias as less than 50 beats per minute (BPM) (Wang et al., 2013; Rashad & Farmawy, 2013; Marashi et al., 2014). Two articles defined bradycardia as less than 45 BPM (Ortiz-Gomez et al., 2014; Trabelsi et al., 2014). Wang et al. 2014 conducted a dose dependent study with 2, 4, 6 & 8mg of preprocedural ondansetron. They found a reduction in bradycardia in all groups who received preprocedural ondansetron. However, no statistical significance was observed between groups and was attributed to the small sample size (n=66). However, Wang et al. (2014) observed more episodes of bradycardia in the 2mg group of preprocedural ondansetron. While the 4,6, and 8mg groups revealed no episodes of bradycardia.

In addition to testing ondansetron against the saline placebo in SIH and bradycardia, Rashad and Farmawy (2013) added granisetron, another 5-HT3 antagonist, for comparison. There was no significant difference in HR between groups. However, no bradycardia was experienced in the ondasetron group, whereas bradycardia mutually occurred in the saline and granisetron groups. Furthermore, there was a significant increase in ephedrine use, an alpha and beta-agonist used to increase HR.

Heart rate is a key physiological factor in maintaining hemodynamic stability during spinal anesthesia for cesarean section. In addition, decreased oxygenation and perfusion can occur from maternal bradycardia and can be detrimental to both the mother and the fetus.

Administration of ondansetron prior to spinal anesthesia is effective in preventing spinal-induced bradycardia promoting hemodynamic stability during childbirth.

Vasopressor Use

Maternal SIH can compromise uterine blood flow, potentially resulting in adverse effects of neonates' acid-base status and hypoxia (Sklebar et al., 2019). Fortunately, maternal hypotension can rapidly be corrected by vasopressor use. Current EBR recommends prophylactic administration of phenylephrine or ephedrine to prevent hypotension (Xu et al., 2018). However, research on vasopressors and their effects on the neonate has remained controversial.

Xu et al. (2018) conducted a meta-analysis comparing treatment with phenylephrine or ephedrine, determining which results in lower fetal acidosis rates. They found that phenylephrine had a lower incidence in fetal acidosis (RR 0.18, 95% CI 0.06 to 0.048) in addition to higher umbilical artery pH (WMD 0.04, 95% CI 0.03 to 0.06) (XU et al., 2018). A meta-analysis was recently conducted by Fitzgerald et al. (2020). They observed that the umbilical artery pH was significantly lower with ephedrine, and maternal bradycardia was increased with phenylephrine. In conclusion, they suggested further studies are needed to find alternatives that provide a safer and more effective means of treating SIH. Out of the five studies stated above, four of those studies had statistically significant decreases in vasopressor use in the groups who received ondansetron before spinal anesthesia (Marashi et al., 2014; Rashad & Farmawy, 2013; Trabelsi et al., 2014; Wang et al., 2013). Ituk et al. (2016) demonstrated that less vasopressor use is associated with better fetal acid-base status which may improve fetal outcomes.

In the dose-dependent study conducted by Wang et al. (2014), consumption of phenylephrine in the 4mg Ondansetron group was significantly less ($p < 0.05$) than the saline

group. Furthermore, they found statistically significant results that the 4mg dose increased the pH and decreased the PC02 in the fetal umbilical vein. Thus, they concluded that four milligrams of ondansetron is the optimal dose before spinal anesthesia (Wang et al., 2014).

Neonatal Outcomes

Intrauterine fetal growth retardation can result from uteroplacental insufficiency. Severe maternal hypotension can result in fetal demise. (Nagelhout & Plaus., 2014). At term, the placenta receives 10% (600 to 700ml/min) of the maternal cardiac output (Nagelhout & Plaus., 2014). Therefore to preserve placental flow, treating hypotension should be of the utmost importance to the anesthesia provider. Current guidelines for prevention of hypotension for cesarean section are fluid co-loading, sequential compression devices, and left uterine tilt. Recent literature on ondansetron's attenuating effects on hypotension, and inhibition of the BJR has gained popularity within the anesthesia community. Ondansetron is safe for pregnant women and is used frequently to treat nausea experienced throughout pregnancy. However, there remains existing hesitancy with ondansetron's use prior to spinal anesthesia within the anesthesia community. This reluctance is likely from the lack of familiarity of ondansetron pharmacodynamics in relation to the BJR.

A study conducted in 2013 investigated adverse neonatal outcomes of ondansetron administered during pregnancy on 603,385 parturients. They found that recipients who received ondansetron during pregnancy did not have an increased risk of spontaneous abortion, no significant risk of stillbirth, or any major birth defects (Pasternak et al., 2013). Corke et al. (1982) found that neonates born to hypotensive mothers were significantly more acidotic than normotensive mothers. APGAR scores are the mainstay assessment tool used to assess newborns' health post-delivery. Trabelsi et al. (2015) analyzed blood gases from the umbilical artery and

recorded APGAR scores at 1, 3, 5, and 10 minutes after birth. APGAR scores were found to be higher in the mothers who received ondansetron before spinal anesthesia ($p < 0.001$), and the umbilical pH was found to be less acidotic ($p < 0.01$). These findings suggest that ondansetron can be safely administered to the mother before spinal anesthesia and may improve neonatal outcomes.

Nausea & Vomiting

Nausea and vomiting in the parturient undergoing cesarean section via spinal anesthesia often occurs as a secondary symptom of hypotension. Ondansetron is well known in the anesthesia community for its' antiemetic effects and is often given as a rescue antiemetic. However, it can also prevent hypotension and subsequentially block nausea from the source if given before spinal anesthesia. A meta-analysis conducted by Tubog et al. (2017) concluded that ondansetron should be considered a prophylactic measure to prevent spinal-induced hypotension, nausea, and vomiting. In addition, several studies demonstrated that the use of ondansetron before spinal anesthesia significantly reduced the incidence of nausea and vomiting in expecting mothers (Zhou et al. (2018); Wang et al. (2013). Vomiting during cesarean section is an unpleasant experience for the parturient, and it carries an increased risk for aspiration leading to respiratory complications. Administration of prophylactic ondansetron concurrently increases the paturients experience during childbirth while mitigating the risks associated with vomiting. Prophylactic ondansetron should be considered a mainstay of anesthetic practice for cesarean section under SAB in preventing hypotension, nausea, and vomiting.

Theoretical Framework

The theoretical framework used in this project was Lewin's Change Theory. This model represents a simple yet practical model for understanding and implementing the change process in three steps: unfreezing, changing, and refreezing. This model emphasizes identifying the driving forces that facilitate change while simultaneously inhibiting barriers that hamper change. Thus, step one is the process of altering behavior to "unfreeze" or agitate the status quo. Phase two, "change, " involves CRNAs forming new perspectives. Lastly, step three is "refreezing" or maintain the new equilibrium so that new behaviors and desired outcomes can be integrated into an organization (Lewin, 1951).

In this project, the pre-survey assesses knowledge and driving forces of current practice. The initial survey serves as step one of "unfreezing." Here, current practice's status quo is examined, and new evidence-based practice research is provided through an educational intervention, ultimately challenging the status quo. Step two in this project, "changing," incorporates the adjustment of practice in response to the educational intervention evaluated by the post survey. Step three, "refreezing," analyzes barriers identified in the post survey and guides the organization's action plan to encourage long-term practice change. Lewin's Change Theory is a valuable tool for this study as it helps manage and influence the change process.

Translational Framework

The IOWA Model of Evidence-Based Practice (EBP) was utilized to guide this project in identifying an opportunity for improvement in current practice. The IOWA model provides a step-by-step guide for the EBP process. The steps of this model are as follows:

Step. 1: Identification of a "trigger" where EBP is warranted.

Step 2: Gathering and evaluating the research related to the desired practice change.

Step 3: Critiquing and synthesizing research found during the literature search.

Step 4: Determining how change can be implemented into practice.

Step 5: Creating a study and design to promote practice change.

Step 6: Evaluation on the efficacy of the variable implemented and dissemination of the results to key personnel.

Following the steps of The IOWA Model, a topic was identified to improve current practice. The PI of this study noted hypotension after spinal anesthesia as a frequent side effect. After identification of an area of improvement, an in-depth evaluation of the current research was conducted. Once the research was consolidated, pertinent studies were synthesized, revealing an opportunity to decrease SIH. Thus, a practice change was warranted. The PI evaluated existing clinical practice and created a post-intervention study design to promote a practice change. This project included a team of key personnel pertinent in creating practice change. A voice-over PowerPoint educational intervention was disseminated to pertinent personnel. The educational intervention presented current EBR, its significance on patient experience, and potential outcomes. Following the educational intervention, the PI evaluated the practice change and disseminated the results, and recommendations with key personnel.

Methodology

Project Design

The project utilized a post-intervention follow-up study design, consisting of a pre-intervention survey, an educational voice-over PowerPoint presentation, and a post-intervention survey. The pre-intervention survey assessed baseline knowledge on: 1) definitions of hypotension and bradycardia, 2) side effects from neuraxial anesthesia, 3) perceptions of tactics to minimize spinal induced hypotension and bradycardia such as co-loading fluids, SCD's and

vasopressors, 4) perceptions of nausea and vomiting after spinal anesthesia, 5) familiarity with the Bezold-Jarisch Reflex, 6) pre-procedural ondansetron benefits and mechanism of action, 7) effects of vasopressors on fetal pH, 8) familiarity with current EBP for managing SIH. In addition, the presurvey was utilized to evaluate knowledge gaps, where the post-survey analyzed the efficacy of the educational intervention.

The educational intervention was presented by the principal investigators (PIs) of this study, Student Registered Nurse Anesthetists (SRNAs). The presentation included EBR to attenuate SIH including coloading of crystalloids, mechanical compression devices and administration of pre-procedural ondansetron. Negative physiological effects of spinal-induced hypotension were described including decreased uteroplacental perfusion, increased vasopressor use affecting acid-base balances for both the mother and fetus, reduction in neonatal APGAR scores and increased incidence of nausea and vomiting. Education concerning preprocedural ondansetron focused on the physiological effects such as reduction in bradycardia, nausea, vasopressor requirements and improvement of fetal acid-base status. In addition, education was included on ondansetron's mechanism of action, role on inhibiting the BJR and fetal safety with in-utero administration. The presentation's conclusion encouraged CRNAs to utilize multimodal EBR methods to manage SIH enhancing patient safety and creating a positive childbirth experience.

The post-intervention survey evaluated knowledge in the eight identified topics presented in the pre-survey. In addition, the post-intervention survey assessed participants perceptions of pre-procedural ondansetron effectivness. These perceptions included the occurrences of nausea, vomiting, bradycardia, and vasopressor requirements. Lastly, the post-intervention survey evaluated incidence of practice change including barriers encountered.

The primary outcome of this study assessed if the educational intervention created practice change. The secondary outcome evaluated perceptions of clinical practice change with the use of ondansetron before spinal anesthesia. The third and final outcome assessed barriers in the utilization of ondansetron before spinal anesthesia.

Project Setting and Sample

The entirety of this project was conducted online where participants could access all parts of the project anywhere they had internet access. Participants were recruited through convenience sampling of CRNAs currently practicing obstetric anesthesia at a private 660- bed urban tertiary care center. A recruitment email was sent to the chief CRNA, who then forwarded the recruitment message to all actively employed CRNAs. Inclusion criteria for participation included CRNAs actively practicing and administering spinal anesthesia. Exclusion criteria included SRNAs, anesthesiologists, and CRNAs not practicing obstetric anesthesia. A target of 30 participants was desired, with a maximum of 50 participants.

Instruments

The PIs of this study developed a pre-intervention and post-intervention survey (Appendix A & B). The pre-intervention survey included multiple-choice, Likert-scale, and binary responses. The post-interventioned mirrored the pre-intervention survey, however a open-ended response was included for assessment of barriers to practice change. Two faculty members reviewed the surveys for reliability and validity before use. Qualtrics platform was utilized by the PIs of this study to transcribe, distribute and store data from surveys. The educational intervention was recorded on PowerPoint and converted to a YouTube video.

Data Collection

Prior to implementation site approval was obtained from the medical facility. After site approval was obtained the project was approved by the Institutional Review Board (IRB) at The University of North Carolina, Greensboro.

The chief CRNA was the liaison between the PIs of this study and CRNAs at the medical facility. Following Institutional Review Board (IRB) approval, a recruitment email was sent by the PIs and described the purpose of the study. The chief CRNA forwarded this recruitment email to all CRNA staff at the facility. At the end of the recruitment email a link was provided to complete the pre-intervention survey. The survey link first directed participants to an information sheet. The information sheet explained the project's purpose, voluntary participation, completion time requirements, risks, and benefits associated with participation. After reading the information sheet CRNAs were promoted to select "Next". After proceeding to the next page participants were requested to submit an email address and their mothers date of birth. Participants were notified that their email was strictly for distribution of the post-intervention survey and their mothers' date of birth functioned as identification to compare pre- and post- data. Recruitment began in September 2021 and lasted for a month.

Inclusion criteria was screened at the beginning of the pre-intervention survey. Survey results were not included in the final data analysis if the subject did not meet inclusion requirements. Once the pre-intervention survey was completed participants were provided a link to watch the 8 minute educational PowerPoint intervention presented by the PIs. The post-intervention surveys were emailed one month after completion of the pre-intervention survey and educational intervention. Each email sent to participants followed the same format and invited participants to complete the 1-month follow up survey (Appendix C).

Data Analysis

Data was analyzed by the PIs of this project with Microsoft Excel 365. Data analysis was guided by a DNP faculty advisor and statistician at The University of North Carolina of Greensboro. Prior to analysis, data was inspected and cleaned appropriately for quality control. Two sample and paired t-test were used to analyze pre-and post-intervention data on knowledge gap and knowledge gain. Descriptive statistics were used to describe percentages and express reoccurring themes of responses on pre- and post-intervention surveys. Themes analyzed through descriptive statistics included: identification of a clinical problem, practice change, knowledge gap & gain, perceived efficacy, and barriers to practice change.

Results

A total of 40 anesthesia providers participated in the study. Of the 40 initial participants, 7 did not complete the survey, and 3 reported never practicing obstetric anesthesia (n=10). Therefore, the pre-intervention sample consisted of 30 participants. A total of 10 participants completed the post-intervention survey. Unfortunately, 6 surveys were unable to be linked to the pre-survey due to inconsistent values on their mothers' date of birth. Thus, 4 surveys were used to link the pre- and post-intervention data.

Participant demographic data was collected and reported in appendix F, including age, sex, degree, years practicing anesthesia, and frequency of delivering obstetric anesthesia.

Identifying a Clinical Problem

After requesting demographic data, the pre-intervention survey assessed participants' experiences on spinal anesthesia side effects. A 5-point Likert scale ranging from never, rarely, occasionally, frequently, and very frequently was utilized for analysis. For discussion, responses

of occasionally to very frequently (60-100% in agreement) were grouped as frequent and deemed to be a meaningful response.

93% of participants reported hypotension defined by a 20% or greater decrease in MAP occurs following spinal anesthesia. The occurrence of nausea following spinal anesthesia was reported at 86%, with vomiting at 56%. Bradycardia (60BPM or less) following spinal anesthesia was noted by 53% of anesthesia providers. However, zero participants reported experiencing severe bradycardia (less than 40BPM). Lastly, all participants reported using vasopressors to treat hypotension after spinal anesthesia.

Knowledge

Baseline knowledge levels were assessed during the pre-intervention survey through a 5-point Likert scale (Appendix A). The scale ranged from strongly disagree, disagree, neither disagree nor agree, agree, and strongly agree. These same questions were placed in the post-intervention survey to compare knowledge achieved after the educational intervention (Appendix B). All data was first checked for normality with a result of less than 0.8. Therefore, a 2-sample t-test was performed on each pre-intervention survey question. Unfortunately, all questions were found to have p-values greater than .05. Paired t-tests were utilized to compare linked pre- and post-survey data; all results contained p-values greater than .05. Subsequently, descriptive statistics were utilized to compare pre- and post-survey knowledge levels.

Seventy percent of participants were familiar with the BJR prior to the educational intervention, whereas after the educational intervention, 100% reported familiarity. Interestingly, 70% initially agreed they were familiar with the current EBP to reduce SIH. However, there was only a slight increase in familiarity in EBP at 75% post educational intervention. Only 60% of

participants recognized that ondansetron antagonizes cardiac receptors during the pre-survey. However, the knowledge level on ondansetron's mechanism of action increased to 75% on the post-survey. When participants were asked about preprocedural ondansetron and its effect on decreasing the incidence of SIH, 64% disagreed that it diminishes SIH on both the pre- and post-survey. In addition, 84-88% of respondents in both pre-and post-survey disagreed that the fetal pH is adversely affected using multiple vasopressors. Lastly, almost all participants agreed that vomiting occurs due to hypotension in both surveys (87-93%).

Practice Change & Barriers Encountered

Practice change was analyzed by comparing participants' responses on their reported administration of ondansetron before initiation of spinal anesthesia, both pre- and post-survey. In the pre-educational survey, 70% of participants reported utilization of ondansetron prior to spinal anesthesia. On the post-educational survey, 75% reported using ondansetron. Additionally, 80% agreed to continue to administer pre-procedural ondansetron to alleviate hypotension seen after a spinal. Finally, barriers were evaluated on the post-educational survey. The prominent barriers discovered included the facility's exclusion of ondansetron from their protocol to prevent SIH (50%) and the discomfort of employing foreign interventions (50%).

Perceived Efficacy of Patient Outcomes

Perceived efficacy was analyzed in the post-educational survey with a 5-point Likert scale. The rating scale included no effect, minor effect, moderate effect, strong effect, and very strong effect. Here participants rated ondansetron's efficacy on SIH, bradycardia, nausea, vomiting, and intraoperative vasopressor requirement. In addition, results were included if they scored from moderate to very strong effect. Preprocedural ondansetron was reported to alleviate:

nausea by (90%), vomiting (80%), SIH (80%), intraoperative vasopressor use (60%), and bradycardia (33%). In the pre-educational survey, 93% of participants reported observing hypotension after spinal anesthesia. After the educational intervention, 80% of respondents who administered preprocedural ondansetron saw a moderate to very strong effect on reducing hypotensive episodes after spinal anesthesia.

Discussion

This project aimed to educate CRNAs on EBR for treating SIH and encourage practice change. The project results offer insight on CRNA familiarity with EBR to reduce SIH, practice trends, barriers, and knowledge gained through the educational intervention. In addition, the project identified two knowledge gaps. The first knowledge gap identified was the impact of pre-procedural ondansetron on reducing SIH. The second knowledge gap included adverse effects of vasopressor use on fetal acid-base balance. Mutually, these knowledge gaps were consistent with findings in the literature (Corke et al., 1982; Trabelsi et al., 2014; Marashi et al., 2014).

Overall, CRNAs demonstrated some familiarity with older EBR to reduce SIH, such as co-loading with crystalloids (93% agreed in pre-survey, 100% agreed post-survey). However, only 36% of CRNAs agreed that preprocedural ondansetron reduces SIH. Therefore, a knowledge gap was revealed, establishing a learning opportunity. Although no statistical significance was reported, it is clinically significant to recognize that the beneficial effects of reducing SIH were not fully understood. Similarly, only 16% of CRNAs agreed that vasopressors adversely affect fetal ph. The knowledge gaps identified give insight to practice change opportunity and improved patient outcomes.

Creating successful practice change can be challenging; however, change becomes permanent when the stakeholders see the benefits of change. Improved patient outcomes are desired by health providers and typically drive practice change. For example, at this urban tertiary care center, the current practice norm includes the administration of high-dose vasopressors to treat SIH, where 100% of respondents reported using vasopressors after spinal anesthesia. In addition, 84% of respondents disagreed that vasopressors negatively affect the fetal pH. Practice change can be motivated by the new evidence that vasopressors may compromise patient outcomes. As new evidence is presented current practice will change to improve patient outcomes.

This predicament in creating practice change is examined in Lewin's Change Theory. The first phase involves "unfreezing" and agitating the status quo. Secondly, the "change phase" allows a new perspective to be formed in response to analyzing the status quo. This project aimed to agitate the status quo with the educational intervention and create practice change by integrating newly obtained knowledge. CRNAs lack of familiarity with EBR on preprocedural ondansetron could be the culprit for hampered practice change (Lewin's Change Phase). However, the CRNA respondents in this project who reported practice change with preprocedural ondansetron (n=10) demonstrated positive results, with 80% reporting an apparent reduction in SIH. Multiple research studies, including Marashi et al., 2014, Rashad & Farmawy, 2013, Trabelsi et al., 2014, Wang et al., 2014 & Ortiz-Gomez et al., 2014 reflect similar results demonstrating a statistically significant decrease in hypotension following spinal anesthesia. Both Rashad and Farmaway (2013) and Wang et al. (2014) found that 4mg of preprocedural ondansetron significantly reduced vasopressor use. Similarly, 60% of CRNAs who utilized preprocedural ondansetron saw a reduction in intraoperative vasopressor requirement. These

results emulate current EBP on preprocedural ondansetron revealing the attenuating potential on SIH, and vasopressor requirement.

The findings of this project mirrored results of current literature, both identifying a clinical problem. Mercier et al. (2013) conducted a literature synthesis, and depicted hypotension occurs in 70-80% of all cesarean deliveries. Comparably, 93% of CRNAs in this project reported observing hypotension following spinal anesthesia. Hall. (2016) charged bradycardic episodes experienced following spinal anesthesia to the BJR. In addition, Hall (2016) speculated that the BJR stems from the increased vagal tone and venous pooling resulting in sudden and profound bradycardia. The results of this project support Hall's theory in two ways. First, over half of participating CRNAs reported observing bradycardia following spinal anesthesia. In addition, 100% of the CRNAs reported using vasopressors after spinal anesthesia to combat hypotension caused by significant venous pooling. In addition, 86% of CRNAs reported observing nausea, and 56% witnessed vomiting after spinal anesthesia in this project. These undesirable side effects following spinal anesthesia echo current EBR findings, indicating a clinical problem and an opportunity to improve anesthetic practice exists.

In this project, knowledge did not improve on using pre-procedural ondansetron to reduce SIH. However, knowledge did improve in several other topics between the pre-and post-interventional surveys. For example, after the educational intervention, CRNAs scores improved on the familiarity of the BJR (70% pre to 100% post), mechanism of action of ondansetron on cardiac serotonin receptors (60% pre to 75% post), and perceived knowledge on EBR regarding SIH (70% pre and 75% post). This data reveals that educational interventions can successfully enhance CRNA knowledge and create practice change.

Barriers to practice change were analyzed using the "refreezing phase" of Lewin's Change Theory. During analysis of the pre- and post-educational survey several themes prevailed. Interestingly, 100% of CRNAs agreed that ondansetron carries no adverse effects to the fetus. Yet, 50% of CRNAs still reported being uncomfortable with utilization of an unfamiliar intervention to manage SIH. In addition, 50% agreed that preprocedural ondansetron was not part of their facilities protocol. "Refreezing" and synthesizing barriers encountered revealed CRNAs would be more inclined to utilize preprocedural ondansetron if it was included in their facilities protocol and further learning opportunities were provided

Strengths and Limitations

Several limitations of this project were identified. First, a significant limitation of this project was the uncertainty of whether each CRNA viewed the entire educational intervention. Providing an educational intervention requiring participants to view the entirety of the presentation before proceeding to the survey could have enhanced knowledge on the use of preprocedural ondansetron. Secondly, the inability to link the majority of pre- and post-surveys restricted data analysis. The third limitation was the small sample size in both pre-and post-survey data. A larger sample size and a better participant response rate on surveys could have yielded more meaningful results. The last limitation identified was the absence of reliability or validity scores for surveys created by the DNP student. Despite the surveys being content reviewed by anesthesia faculty, it was unclear whether the surveys measured intended outcomes.

A strength of this project included the evaluation of EBR and its importance for anesthetic practice. In addition, results illustrated by this project mirror EBR suggesting a clinical problem and the opportunity for change exists. Finally, the project also demonstrated that

online educational interventions could effectively enhance knowledge and impact anesthesia practice.

Future Implications and Recommendations

While existing EBR supports the utilization of pre-procedural ondansetron, several studies reviewed had limitations of limited sample size and time constraints. Further research with larger-scale randomized control trials and diverse sample sizes is warranted to confirm the true efficacy of pre-procedural ondansetron prior to spinal anesthesia during cesarean section. This project's literature synthesis excluded research studies whose population was not obstetrical. Evaluation of pre-procedural ondansetron prior to spinal anesthesia in diverse patient populations could allow a more comprehensive analysis of ondansetron's efficacy in reducing SIH.

Replication of this project with minor additions and modifications could enhance the data's statistical quality and validity. First, this study's results were the subjective experience of individual CRNAs. Future studies could assess both CRNAs perceived efficacy of ondansetron and evaluation of patient vitals via individual chart reviews. Adding chart reviews would provide objective numerical evidence on pre-procedural ondansetron's efficacy. Secondly, providing an educational in-service in person rather than online could increase engagement, participation, and overall knowledge. Lastly, we recommend choosing a facility that does not include a phenylephrine drip in their existing protocol. Preprocedural intravenous phenylephrine drips can decrease the hemodynamic changes seen after spinal anesthesia but may result in fetal acidosis and reduced APGAR scores (Trabelsi et al., 2015). The administration of vasopressors such as phenylephrine could alter the occurrence of hypotension and bradycardia observed skewing data.

Overall, anesthesia providers have a duty to remain educated on best practice methods in providing anesthesia. Hence, periodic educational in-services are recommended to keep anesthesia providers up to date with current evidence-based practice. In addition, facilities should integrate EBR into their facilities protocols to promote best practice guidelines and improve patient care.

Conclusion

In summary, this DNP project sought to examine the impact of an educational intervention provided to CRNAs on evidence-based guidelines to attenuate spinal-induced maternal hypotension and bradycardia. Two knowledge gaps were identified demonstrating an area for clinical improvement. Familiarity with pre-procedural ondansetron improved after the educational intervention, and barriers were examined and reported back to the facility. Despite the lack of statistical significance found in the data, the goals of this project were met.

Research demonstrates the utilization of pre-procedural ondansetron before spinal anesthesia improves patient outcomes and enhances the perioperative and childbirth experience. Protocols should be established for best practice and quality outcomes. In addition, anesthesia providers should employ educational interventions to ensure understanding of best practice guidelines. Anesthesia providers who utilize EBR will deliver the safest anesthetic while simultaneously ensuring a positive childbirth experience.

References

Campagna, J. A., & Carter, C. (2003). Clinical relevance of the bezold-jarisch reflex. *Anesthesiology*, 98(5), 1250–60.

Carpenter, R. L., Caplan, R. A., Brown, D. L., Stephenson, C., & Wu, R. (1992). Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology*, *76*(6), 906–916.

Corke, B. C., Datta, S., Ostheimer, G. W., Weiss, J. B., & Alper, M. H. (1982). Spinal anaesthesia for Caesarean section. The influence of hypotension on neonatal outcome. *Anaesthesia*, *37*(6), 658–662. https://doi.org/10.1111/j.1365-2044.1982.tb01278.x

El Khouly, N. I., & Meligy, A. M. (2016). Randomized controlled trial comparing ondansetron and placebo for the reduction of spinal anesthesia-induced hypotension during elective cesarean delivery in Egypt. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *135*(2), 205–209. https://doi.org/10.1016/j.ijgo.2016.06.012

Ferré, F., Martin, C., Bosch, L., Kurrek, M., Lairez, O., & Minville, V. (2020). Control of spinal anesthesia-induced hypotension in adults. Local and Regional Anesthesia, 13, 39–46. http://dx.doi.org/10.2147/LRA.S240753

Fitzgerald, J. P., Fedoruk, K. A., Jadin, S. M., Carvalho, B., & Halpern, S. H. (2020). Prevention of hypotension after spinal anaesthesia for caesarean section: a systematic review and network meta-analysis of randomised controlled trials. *Anaesthesia*, 75(1), 109–121. https://doi.org/10.1111/anae.14841

Gao, L., Zheng, G., Han, J., Wang, Y., & Zheng, J. (2015). Effects of prophylactic Ondansetron on spinal anesthesia-induced hypotension: A meta-analysis. *International Journal of Obstetric Anesthesia*, *24*(4), 335–343. https://doi.org/10.1016/j.ijoa.2015.08.012

Hall, J. E. (2016). Guyton and Hall Textbook of Medical Physiology (13th ed.). W B Saunders.

Hasanin, A., Aiyad, A., Elsakka, A., Kamel, A., Fouad, R., Osman, M., Mokhtar, A., Refaat, S., & Hassabelnaby, Y. (2017). Leg elevation decreases the incidence of post-spinal hypotension in cesarean section: A randomized controlled trial. *BMC Anesthesiology*, *17*. http://dx.doi.org/10.1186/s12871-017-0349-8

Ituk, U. S., Cooter, M., & Habib, A. S. (2016). Retrospective comparison of ephedrine and phenylephrine for the treatment of spinal anesthesia induced hypotension in pre-eclamptic patients. Current Medical Research and Opinion, 32(6), 1083–1086. https://doi.org/10.1185/03007995.2016.1159953

Kinsella, S. M., & Tuckey, J. P. (2001). Perioperative bradycardia and asystole: relationship to vasovagal syncope and the bezold-jarisch reflex. British Journal of Anaesthesia, 86(6), 859–68.

Lee, J. E., George, R. B., & Habib, A. S. (2017). Spinal-induced hypotension: Incidence, mechanisms, prophylaxis, and management: Summarizing 20 years of research. Best Practice & Research Clinical Anaesthesiology, 31(1), 57–68. https://doi.org/10.1016/j.bpa.2017.01.001

Lewin, K. (1951). Field theory in social science. New York: Harper & Row

The New York School of Regional Anesthesia (NYSORA). (2021, February). Spinal Anesthesia. NYSORA. https://www.nysora.com/techniques/neuraxial-and-perineuraxial-techniques/spinal-anesthesia/

Marashi, S. M., Soltani-Omid, S., Soltani Mohammadi, S., Aghajani, Y., & Movafegh, A. (2014). Comparing two different doses of intravenous ondansetron with placebo on attenuation of spinal-induced hypotension and shivering. *Anesthesiology and pain medicine*, *4*(2), e12055. https://doi.org/10.5812/aapm.12055

Mercier, F. J., Augè, M., Hoffmann, C., Fischer, C., & Le Gouez, A. (2013). Maternal hypotension during spinal anesthesia for caesarean delivery. *Minerva anestesiologica*, *79*(1), 62–73.

Morgan, G. E., Mikhail, M. S., & Murray, M. J. (2018). Obstetric Anesthesia. New York: Lange Medical Books, Clinical Anesthesiology 6th ed., pp.870-871. McGraw Hill Medical Publisher Division.

Nagelhout, J. J., & Plaus, K. L. (2014). Nurse Anesthesia. (5th ed.). St. Louis, MO: Elsevier.

Neggers, Y. H. (2016). Trends in maternal mortality in the United States. *Reproductive Toxicology*, *64*, 72–76. https://doi.org/10.1016/j.reprotox.2016.04.001

Ni, H.-F., Liu, H., Zhang, J., Peng, K., & Ji, F.-H. (2017). Crystalloid Coload Reduced the Incidence of Hypotension in Spinal Anesthesia for Cesarean Delivery, When Compared to Crystalloid Preload: A Meta-Analysis. BioMed Research International, 2017, 3462529. https://doi.org/10.1155/2017/3462529

Pasternak, B., Svanström, H., & Hviid, A. (2013). Ondansetron in pregnancy and risk of adverse fetal outcomes. *The New England journal of medicine*, *368*(9), 814–823. https://doi.org/10.1056/NEJMoa1211035

Rashad, M. M., & Farmawy, M. S. (2013). Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia

in parturients undergoing cesarean section. Egyptian Journal of Anaesthesia, 29(4), 369–374. https://doi.org/10.1016/j.egja.2013.04.004

Šklebar I, Bujas, T., & Habek, D. (2019). Spinal anaesthesia-induced hypotension in obstetrics: prevention and therapy. *Acta Clinica Croatica*, *58*, 90–95. https://doi.org/10.20471/acc.2019.58.s1.13

Sujata, N., Arora, D., Panigrahi, B. P., & Hanjoora, V. M. (2012). A sequential compression mechanical pump to prevent hypotension during elective cesarean section under spinal anesthesia. International Journal of Obstetric Anesthesia, 21(2), 140–145. https://doi.org/10.1016/j.ijoa.2012.01.003

Tubog, T. D., Kane, T. D., & Pugh, M. A. (2017). Effects of Ondansetron on Attenuating Spinal Anesthesia–Induced Hypotension and Bradycardia in Obstetric and Nonobstetric Subjects: A Systematic Review and Meta-Analysis. *AANA journal*, *85*(2), 113–122.

Wang, M., Zhuo, L., Wang, Q., Shen, M. K., Yu, Y. Y., Yu, J. J., & Wang, Z. P. (2014). Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during cesarean delivery: a dose-dependent study. International Journal of Clinical and Experimental Medicine, 7(12), 5210-5216.

Watts, S. W., & Davis, R. P. (2011). 5-hydroxtryptamine receptors in systemic hypertension: an arterial focus. Cardiovascular Therapeutics, 29(1), 54–67. https://doi.org/10.1111/j.1755-5922.2010.00173.x

Xu, C., Liu, S., Huang, Y., Guo, X., Xiao, H., & Qi, D. (2018). Phenylephrine vs ephedrine in cesarean delivery under spinal anesthesia: A systematic literature review and meta-

analysis. *International journal of surgery (London, England)*, *60*, 48–59. https://doi.org/10.1016/j.ijsu.2018.10.039

Yamano, M., Ito, H., Kamato, T., & Miyata, K. (1995). Characteristics of inhibitory effects of serotonin (5-HT)3-receptor antagonists, YM060 and YM114 (KAE-393), on the von Bezold-Jarisch reflex induced by 2-Methyl-5-HT, veratridine and electrical stimulation of vagus nerves in anesthetized rats. *Japanese journal of pharmacology*, *69*(4), 351–356. https://doi.org/10.1254/jjp.69.351

Zhou, C., Zhu, Y., Bao, Z., Wang, X., & Liu, Q. (2018). Efficacy of Ondansetron for spinal anesthesia during cesarean section: a meta-analysis of randomized trials. *The Journal of international medical research*, *46*(2), 654–662. https://doi.org/10.1177/0300060517716502

Appendix A

Pre -Intervention Survey

Please enter the month and year (xx/xx) of your mother's birthday. (This is used to link pre & post surveys)					
Please submit your email address (This will be used to send the post-intervention survey)					
Sex	Male☐ Female☐ Other☐				
Age	<25☐ 26-35☐ 36-45☐ 46-55☐ 55-65☐ >65☐				
Degree	Certificate☐ Masters☐ Doctorate☐				
Number of years practicing anesthesia	< 1☐ 1-5☐ 6-10☐ 11-15☐ 16-20☐ >20☐				
How often do you practice obstetric anesthesia?	Daily☐ 2-3x Weekly☐ 2-3x Monthly☐ Never☐				
Please select what is most applicable to your experience/practice following spinal anesthesia in obstetrics.	**Never**	**Rarely**	**Occasionally**	**Frequently**	**Very Frequently**
Hypotension (a 20% or greater decrease in MAP) occurs following spinal anesthesia.					
Bradycardia (60BPM or less) occurs following spinal anesthesia.					
Severe bradycardia (less than 40BPM) occurs following spinal anesthesia.					
In your practice, how often do you see parturient patients become nauseous after receiving spinal anesthesia?					
In your practice, how often do your parturient patients vomit after receiving spinal anesthesia?					
In your practice, how often do you have to administer vasopressors following spinal anesthesia?					
I administer ondansetron before spinal anesthesia.					

Please select what is most applicable to your knowledge and experience.	**Strongly Disagree**	**Disagree**	**Neither Disagree nor Agree**	**Agree**	**Strongly Agree**
I am familiar with the Bezold-Jarisch Reflex.					
Ondansetron antagonizes cardiac serotonin receptors.					
Pre-procedural Ondansetron reduces the incidence of spinal-induced hypotension.					
Co-loading with crystalloids reduces the incidence of spinal-induced hypotension.					
Sequential Compression Devices reduce the incidence of spinal-induced hypotension.					
Administration of multiple doses of vasopressors adversely affects fetal pH.					
Nausea is a result of post-spinal hypotension.					
Vomiting is a result of post-spinal hypotension.					
I am familiar with the current evidence-based practices for managing spinal-induced hypotension.					

Appendix B

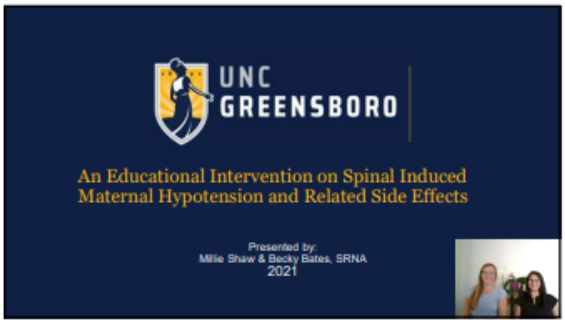
Post-Intervention Survey

Please enter the month and year (xx/xx) of your mother's birthday. (This is used to link pre-and post-surveys)					
In the **LAST MONTH**, how often did you practice obstetric anesthesia?	Daily☐ 2-3x Weekly☐ 2-3x Monthly☐ Never☐				
In the last month, please indicate your perception of the effectiveness of preprocedural ondansetron, co-loading of crystalloids, and sequential compression devices on the following:	**No effect**	**Minor Effect**	**Moderate Effect**	**Strong Effect**	**Very strong Effect**
Spinal-induced hypotension					
Bradycardia					
Nausea					
Vomiting					
Intraoperative vasopressor requirement					
Please select what is most applicable to your knowledge and experience	**Strongly Disagree**	**Disagree**	**Neither Disagree nor Agree**	**Agree**	**Strongly Agree**
I am familiar with the Bezold-Jarisch Reflex.					
Ondansetron antagonizes cardiac serotonin receptors.					
Pre-procedural Ondansetron reduces the incidence of spinal-induced hypotension.					
Co-loading with crystalloids reduces the incidence of spinal-induced hypotension.					
Sequential Compression Devices reduce the incidence of spinal-induced hypotension.					
Administration of multiple doses of vasopressors adversely affects fetal pH.					
Nausea is a result of post-spinal hypotension.					

Vomiting is a result of post-spinal hypotension.					
I am familiar with the current evidence-based practices for managing spinal-induced hypotension.					

Please select what is most applicable to your experience/practice following spinal anesthesia in obstetrics.	**Never**	**Rarely**	**Occasionally**	**Frequently**	**Very Frequently**
I administer ondansetron before spinal anesthesia					
Please select the answer most applicable to your practice	**Strongly Disagree**	**Disagree**	**Neither Disagree**	**Agree**	**Strongly Agree**
I believe ondansetron ***has adverse*** effects on the fetus at term.					
My colleagues ***do not*** support the use of pre-procedural ondansetron.					
I need to see more evidence-based support in the literature to integrate the presented interventions into my practice.					
I have time constraints that prevent me from administering ondansetron before spinal anesthesia.					
Ondansetron is currently not part of my facility's protocol on managing spinal-induced hypotension.					
I am ***not*** comfortable using unfamiliar interventions to manage spinal-induced hypotension.					
I will continue to utilize pre-procedural ondansetron for reducing spinal-induced hypotension.					
Please indicate any barrier(s) you have encountered when implementing the presented interventions to manage spinal-induced hypotension in your clinical practice.					

Appendix C



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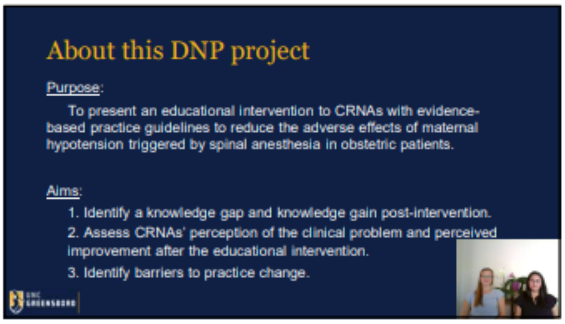

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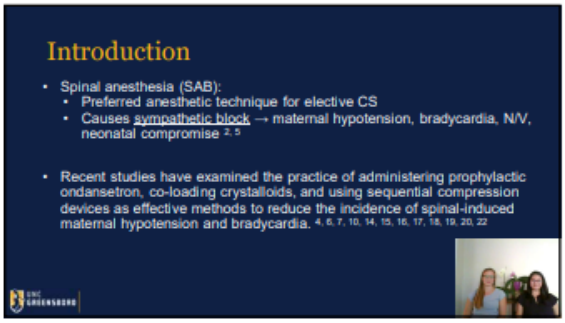

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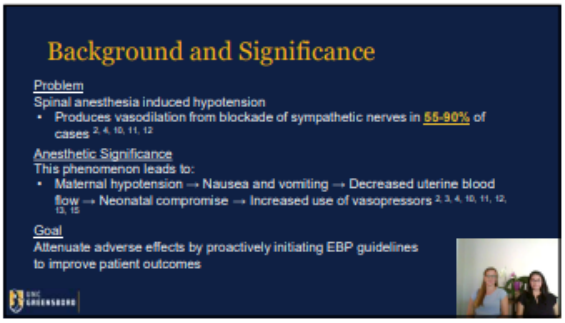

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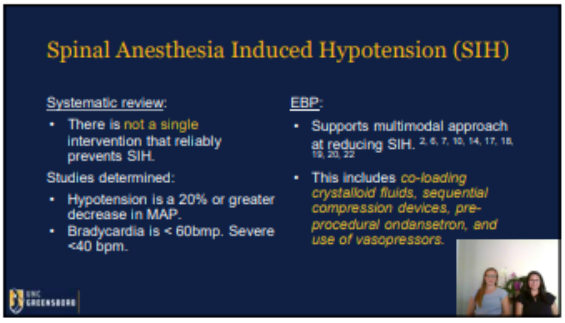


6

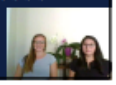
Ondansetron

Literature review

- A 5-HT3 antagonist.
- SIH stimulates the 5-HT3 receptors located in the intracardiac vagal nerve endings and chemoreceptor trigger zone. [11, 12, 16, 21]
- SIH activates the Bezold-Jarisch reflex via the 5-HT3 receptors. As a result, the *Bezold-Jarisch reflex causes bradycardia*. [1, 9, 11, 12, 21]

EBP

- Groups that received ondansetron prior to spinal anesthesia had: [13, 14, 15, 16]
  - fewer episodes of hypotension
  - fewer episodes of bradycardia
  - fewer episodes of nausea and vomiting
  - decreased use of vasopressor use
  - better neonatal outcomes
- Ondansetron antagonizes cardiac serotonin receptors, therefore reducing the incidence of SIH. [4, 6, 7, 16, 18, 19, 20, 22]



7

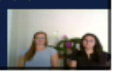
Neonatal Outcomes

Literature review

- Neonates born to mothers with prolonged SIH were significantly more acidotic, hypoxic, and had an increased risk of neurological deficits. [3, 10, 11, 12, 13]
- Exposure to ondansetron during pregnancy does not cause any major birth defects, spontaneous abortion, or preterm delivery. [7, 15, 18, 22]

EBP:

- With administration of pre-procedural ondansetron, neonates experienced higher Apgar scores and less acidosis. [3, 4, 15, 18, 19, 22]
- *Evidence supports the use of ondansetron 5 minutes prior to spinal anesthesia to improve the metabolic and vital parameters in the newborn.* [4, 6, 7, 16, 18, 19, 20, 22]



8

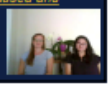
Nausea & Vomiting

Literature review

- Parturient patients are always considered a full stomach with a high risk of aspiration. [11, 12]
- SIH leads to nausea/vomiting from decreased cerebral blood flow. [2, 10,11, 12, 16, 19, 20, 22]

EBP

- Found significantly lower incidences of nausea & vomiting caused by SIH during CS in ondansetron groups when compared to control groups. [4, 6, 7, 16, 18, 20, 22]
- *Administering ondansetron five minutes prior to spinal anesthesia prevents nausea and vomiting at its origin.*



9

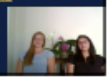
Co-loading Crystalloids

Literature review

- Crystalloids are less expensive and have little to no risk of allergic reactions or coagulation disturbances. [14]
- Crystalloids are retained in the intravascular space for a *maximum of 30 mins.* [11, 12]

EBP

- Coloading crystalloids is defined as administering solution at the initiation of spinal anesthesia. This practice reduces SIH when compared to preloading. [11, 12, 14]
- *Coloading 15-20 ml/kg of crystalloids increases intravascular volume and reduces maternal SIH.*



10

Sequential Compression Devices

Literature review

- Blood pooling in the lower extremities occurs due to hormonal changes and vena caval compression from pregnancy. [11, 12]
- Due to the sympathetic block, SIH will further increase blood pooling. Resulting in decreased preload leading to maternal hypotension. [2, 3, 10, 11, 12, 13]

EBP

- Sequential compression devices reduce SIH by increasing venous return.
- *The use of compression devices can reduce SIH when used in combination with coloading of fluids.* [17]

11

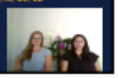
Vasopressor requirements

Literature review

- Vasoactive medications decrease uteroplacental perfusion, which can contribute to fetal acidosis. [3, 6, 10, 11]
- Ephedrine was associated with higher incidence of fetal acidosis when compared to neosynephrine. [8]

EBP

- Further studies are needed to find safer alternatives to treat SIH while minimizing fetal adverse effects.
- Pre-procedural ondansetron is effective at decreasing vasopressor requirements, therefore minimizing fetal acid-base disturbances. [4, 6, 18, 20, 22]

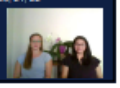


12

Conclusion

Studies have shown that a multimodal approach is safe and effective at reducing the incidence of SIH by:

- Sequential compression devices
  - Increases venous return [17]
- Coloading crystalloids
  - Increases vascular volume [11, 12, 14]
- Administering ondansetron five minutes before spinal anesthesia
  - Reduces the Bezold-Jarisch reflex [18, 19, 20]
  - Antagonizes cardiac serotonin receptors [7, 11, 12, 16, 18, 19, 20, 21, 22]
  - Decreases nausea and vomiting [4, 6, 7, 16, 18, 19, 20, 21, 22]
  - Decreases vasopressor requirements [4, 6, 7, 18, 19, 20, 22]



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Thank You

In 1 month, you will receive a link (via email) to complete a follow-up survey to assess for your utilization of pre-procedural IV ondansetron, perceived barriers to its utilization, and to evaluate self-reported efficacy in patient outcomes.

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References

1. Campagna, J. A., & Carter, C. (2003). Clinical relevance of the bezold-jarisch reflex. Anesthesiology, 98(5),1250–60.
2. Carpenter, R. L., Caplan, R. A., Brown, D. L., Stephenson, C., & Wu, R. (1992). Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology*, *76*(6), 906–916.
3. Corke, B. C., Datta, S., Ostheimer, G. W., Weiss, J. B., & Alper, M. H. (1982). Spinal anaesthesia for Caesarean section. The influence of hypotension on neonatal outcome. *Anaesthesia*, *37*(6), 658662. https://doi.org/10.1111/j.1365-2044.1982.tb01278.x
4. El Kheuly, N. L., & Meligy, A. M. (2016). Randomized controlled trial comparing ondansetron and placebo for the reduction of spinal anesthesia-induced hypotension during elective cesarean delivery in Egypt. *International journal of gynaecology and obstetrics: the official organ of the International Federation of Gynaecology and Obstetrics*, *133*(2), 205–209. https://doi.org/10.1016/j.ijgo.2016.06.012
5. Fenaroli, V., Molgora, S., Dodaro, S., Svelato, A., Gesi, L., Molidoro, G., Saita, E., & Ragusa, A. (2019). The childbirth experience: Obstetric and psychological predictors in Italian primiparous women. BMC Pregnancy and Childbirth, 19(1), 419. https://doi.org/10.1186/s12884-019-2561-7

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References

6. Fitzgerald, J.P., Fedorak, K.A., Jadin, S.M., Carvalho, B. and Halpern, S.H. (2020), prevention of hypotension after spinal anesthesia for caesarean section: a systematic review and network meta-analysis of randomized controlled trials. Anaesthesia, 75,109 https://doi.org/10.1111/anae.14841
7. Gao, L., Zheng, G., Han, J., Wang, Y., & Zheng, J. (2015). Effects of prophylactic Ondansetron on spinal anesthesia-induced hypotension: A meta-analysis. *International Journal of Obstetric Anesthesia*, *24*(4), 335–343. https://doi.org/10.1016/j.ijoa.2015.08.012
8. Irak, U. S., Cooter, M., & Habib, A. S. (2016). Retrospective comparison of ephedrine and phenylephrine for the treatment of spinal anesthesia induced hypotension in pre- eclamptic patients. Current Medical Research and Opinion, 32(6), 1083–1086. https://doi.org/10.1185/03007995.2016.1159953
9. Kinsella, S. M., & Tuckey, J. P. (2001). Perioperative bradycardia and asystole: relationship to vasovagal
10. Mercier, F. J., Augé, M., Hoffmann, C., Fischer, C., & Le Gouez, A. (2013). Maternal hypotension during spinal anesthesia for caesarean delivery. *Minerva anestesiologica*, *79*(1), 62–73.
11. Morgan, G. E., Mikhail, M. S., & Murray, M. J. (2018). Obstetric Anesthesia. New York: Lange Medical Books, Clinical Anesthesiology 6th ed., pp.870-871. McGraw Hill Medical Publisher Division.
12. Nagelhout, J. J., & Plaus, K. L. (2014). Nurse Anesthesia. (5th ed.). St. Louis, MO: Elsevier.

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References

13. Neggers, Y. H. (2016). Trends in maternal mortality in the United States. *Reproductive Toxicology*, *64*, 72–76. https://doi.org/10.1016/j.reprotox.2016.04.001
14. Ni, Hai Fang., Liu, H., Zhang, J., Peng, K., & Ji, F.-H. (2017). Crystalloid Coload Reduced the Incidence of Hypotension in Spinal Anesthesia for Cesarean Delivery, When Compared to Crystalloid Preload: A Meta-Analysis. BioMed Research International, 2017, 3462529. https://doi.org/10.1155/2017/3462529
15. Pasternak, B., Svanström, H., & Hviid, A. (2013). Ondansetron in pregnancy and risk of adverse fetal outcomes. *The New England journal of medicine*, *368*(9), 814–823.https://doi.org/10.1056/NEJMoa1211035
16. Rashad, M. M., & Farmawy, M. S. (2013). Effects of intravenous ondansetron and granisetron on hemodynamic changes and motor and sensory blockade induced by spinal anesthesia in parturients undergoing cesarean section. Egyptian Journal of Anaesthesia, 29(4), 369–374. https://doi.org/10.1016/j.egja.2013.04.004
17. Sujata, N., Arora, D., Panigrahi, B. P., & Hanjoora, V. M. (2012). A sequential compression mechanical pump to prevent hypotension during elective cesarean section under spinal anesthesia. International Journal of Obstetric Anesthesia, 21(2), 140–145. https://doi.org/10.1016/j.ijoa.2012.01.003

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References

18. Trabelsi, W., Roudhani, C., Elsakri, H., Sammoud, W., Benzaïah, M., Labbene, L. & Ferjani, M. (2015). Effect of Ondansetron on the occurrence of hypotension and on neonatal parameters during spinal anesthesia for elective caesarean section: A prospective, randomized, controlled, double-blind study. Anesthesiology Research & Practice, 2015, 1–7. https://doi.org/10.1155/2015/158061
19. Tubog, T. D., Kane, T. D., & Pugh, M. A. (2017). Effects of Ondansetron on Attenuating Spinal Anesthesia –Induced Hypotension and Bradycardia in Obstetric and Nonobstetric Subjects: A Systematic Review and Meta-Analysis. AANA journal, 85(2), 113–122.
20. Wang, M., Zhao, L., Wang, Q., Shen, M. K., Yu, Y. Y., Yu, J. J., & Wang, Z. P. (2014). Efficacy of prophylactic intravenous ondansetron on the prevention of hypotension during cesarean delivery: a dose-dependent study. International Journal of Clinical and Experimental Medicine, 7(12), 5210-5216
21. Yamano, M., Ito, H., Kamato, T., & Miyata, K. (1995). Characteristics of inhibitory effects of serotonin (5-HT)3-receptor antagonists, YM060 and YM114 (KAE-393), on the von Bezold-Jarisch reflex induced by 2-Methyl-5-HT, veratridine and electrical stimulation of vagus nerves in anesthetized rats. Japanese journal of pharmacology, 69(4), 351–356. https://doi.org/10.1254/jjp.69.351
22. Zhou, C., Zhu, Y., Bao, Z., Wang, X., & Liu, Q. (2018). Efficacy of Ondansetron for spinal anesthesia during cesarean section: a meta-analysis of randomized trials. The Journal of international medical research, 46(2), 654–662. https://doi.org/10.1177/0300060517716502

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