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Prophylactic Phenylephrine Infusion Versus Bolus Regimens During Spinal Anesthesia For Cesarean Section

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Abstract

Hypotension is a well-recognized phenomenon associated with any spinal anesthesia. It is most particularly evident in the parturients as a higher block is required for cesarean section (C-section) (Nagelhout, 2014). These populations are also more prone to the effect of sympathectomy because of decreased sensitivity to endogenous vasoconstrictors in addition to increased synthesis of endothelium vasodilators (Miller, 2009). Sympathectomy results in hypotension and other adverse effects such as nausea and vomiting. Many studies over the decades have examined the best management option for the hypotension. This review seeks to determine the best management regimen for the use of the vasopressor phenylephrine. Eleven studies are used to examine the use of prophylactic intravenous (IV) phenylephrine infusion versus IV bolus regimen to manage the sympathectomy-induced hypotension associated with spinal anesthesia in parturients undergoing C-section. Nine out of the eleven had better hemodynamic outcomes with the use of infusion over bolus regimes. When the use of a weight-based prophylactic IV phenylephrine infusion was compared to a non-weight based infusion, the intervention group was hemodynamically more stable compared to the control group whose weights were omitted in the dose. While there were incidences of reactive hypertension with the control group, there was no statistically significant adverse effect on the parturients and the fetus. These findings suggest that it is best for anesthesia providers to use a weight-based prophylactic IV phenylephrine infusion for the management of spinal-induced hypotension.

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Introduction

Although the definition of hypotension may vary from one study to the other, according to Klohr, Roth, Hofmann, Rossaint, and Heesen (2010) approximately 80% of parturients undergoing cesarean section (C-section) under spinal anesthesia develop hypotension without adequate prophylaxis. For this paper, hypotension is defined as systolic blood pressure (SBP) less than 80% of baseline value. Severe hypotension can result in adverse effects that include nausea and vomiting, unpleasant feeling of impending doom and fetal acidosis (Kee, Khaw, Ng & Lee, 2004). Hypotension must be managed in a timely manner before cardiovascular collapse occurs. Treating the hypotension is not the only concern for the anesthesia provider, but choosing the right vasopressor regimen is essential to prevent unwanted adverse effects. Providers must be enlightened on this as studies have shown that significant variations exist in the regimen used in managing the hypotension associated with spinal anesthesia (Allen, Muir, George, & Habib, 2009).

Over the years, the use of vasopressors in spinal associated hypotension has evolved. It took more than four decades to arrive at a conclusion that phenylephrine is the ideal vasopressor for the management of spinal-induced hypotension (Cooper, 2012). Whether to give a prophylactic intravenous (IV) phenylephrine infusion or an IV bolus immediately after intrathecal administration or to wait and initiate an infusion or give a bolus with the onset of hypotension remains uncertain. The paper presented here will give an overview of the physiological changes with pregnancy, spinal anesthesia with C-sections and its hemodynamic outcome as well as vasopressors available for management. Also, relevant studies on IV

phenylephrine infusion and IV phenylephrine bolus administration for managing the hypotension with spinal anesthesia will be analyzed. Based on the analysis of the literature, a policy recommendation will be developed to help improve patient outcome in anesthesia practice.

Background

Obstetrics anesthesia is a high-risk area of anesthetic practice. The physiological changes during pregnancy and the addition of a fetus or fetuses pose unique challenges to the care provider administering the anesthesia (Nagelhout, 2014). Currently, evidence-based guidelines and technologies are in place to guide consistent and safe anesthesia management of this population. However, anesthesia providers still have to face problems such as advanced maternal age, maternal obesity, and an increased complexity of medical problems, which may affect women during this period of time (Jadon, 2010). Another concern is the physiological changes that occur as a result of pregnancy.

Physiological Changes with Pregnancy

Pregnancy affects different body systems. The physiological changes associated with it are due to the effect of changes in the maternal hormone balance, biochemical shifts related to larger metabolic demands of the fetus and the placenta, as well as mechanical forces from the gravid uterus (Rollins & Lucero, 2012). However, the changes to the cardiovascular system have important anesthetic implications, particularly if spinal anesthesia is administered (Nagelhout, 2014). With cardiac changes, systemic vascular resistance decreases owing to increased progesterone, nitric oxide, and prostacyclin with a decreased response to norepinephrine and angiotensin causing renal artery and aortic dilatation. Cardiac output is increased, due to an increase in heart rate as well as the role of the renin-angiotensin system. Renin-angiotensin increases blood volume by stimulating angiotensin I to be converted to angiotensin II by

angiotensin-converting enzymes (ACE). Angiotensin II constricts blood vessels, increases antidiuretic hormone (ADH) and aldosterone causing an increase in blood pressure. With placental delivery, relief of aortocaval compression and contraction of the uterus causes a greater increase in blood volume as well (Hines & Marschall, 2008).

The position the parturients is in also affects hemodynamic status. Irrespective of the high blood volume, hypotension usually occurs in a supine position as the gravid uterus can compress the aorta and vena cava, decreasing cardiac preload and output. The aortoiliac artery compression by the gravid uterus further decreases uterine perfusion regardless of the maternal blood pressure (Rollins & Lucero, 2012). The addition of these natural physiological changes to the physiological effect of decreased sympathetic tone in spinal anesthesia can have a major impact on the cardiovascular system (Nagelhout, 2014).

Spinal Anesthesia for C- Section

In most cases of C-section, spinal anesthesia is used unless there are contraindications. Some of the contraindications from the literature of why regional may not be used in the parturients include coagulopathy, maternal refusal, medical history such as spinal abnormality, the experience of the anesthesia provider, indication and urgency of the C-section, and maternal status (Schmidt & Auler, 2012; Yeoh & Li, 2013). Rollins and Lucero (2012) also identify infection at the needle insertion site, hypovolemic shock and increased intracranial pressure as other contraindications for neuraxial anesthesia.

One advantage of neuraxial anesthesia is that it allows for the birthing process to be more meaningful. Single dose spinal (commonly used for C-section) has a faster onset and is reliable in providing surgical anesthesia from the mid-thoracic level to the sacrum (Rollins & Lucero, 2012). There is the advantage of a faster procedure and for the mother to be awake during

delivery to experience and participate in the birthing process as well as to interact and bond with the baby.

Another advantage to neuraxial anesthesia is low anesthetic exposure to the fetus, resulting in a higher Apgar score (Schmidt & Auler, 2012). As supported by the study done by Abdallah, Elzayyat, Abdelhaq, and Gado (2014) the Apgar score in one and five minutes were higher in newborns of parturients who received regional instead of general anesthesia. The authors attributed this to the effect of sedation that accompanies general anesthesia. Also, in the study done by Mancuso et al. (2010) to compare the effect of general and spinal anesthesia for elective C-section, umbilical cord artery pH, Apgar score, the need for assisted ventilation and fetal outcome was more favorable with spinal anesthesia compared to general anesthesia.

While there are benefits to spinal anesthesia, there are also some drawbacks. One of the most common complications in the parturients is post dural puncture headache (PDPH). The rate is as high as 30% (Jadon, 2010). PDPH usually occurs with the use of cutting needle tip designs although it can also occur with the use of thinner quincke-type spinal needles and pencil point needles. Not managing this complication can lead to subdural hematoma which may be of high morbidity and mortality. PDPH can be self-limiting; if not, the most common effective management is the use of an epidural blood patch, which is the definitive treatment with a success rate of 96-98% (Jadon, 2010).

In addition to the above, a common complication of spinal anesthesia is the hypotension it produces. The adverse effect of sympathetic blockage that usually accompanies spinal anesthesia does not only affect the mother but also the fetus due to uteroplacental hypoperfusion, which could lead to an acute fall in intervillous blood flow with the potential for fetal acidemia (Abdallah, et al., 2014). In fact, in the studies by Abdallah et al. (2014) regional anesthesia was

associated with a lower systolic and diastolic blood pressure in the parturients compared with general anesthesia as a result of the sympathetic block that it causes.

Physiology of Spinal Anesthesia

Spinal block involves administration of a local anesthetic. It's usually an intrathecal injection of 10mg to 15mg of hyperbaric bupivacaine at lumbar four to five (L4 to L5) spinal segment for a block at the level of thoracic four (T4) vertebra (Nagelhout, 2014). This dose is the 95% effective dose (ED95) of parturients undergoing C-section and provides approximately 90 to 120 minutes of surgical anesthesia. Adjuncts such as fentanyl, sufentanil, and epinephrine may be added to improve the density of the block and preservative free morphine 0.10mg to 0.25mg can also be added to reduce postoperative (postop) pain up to 18 to 24 hours (Miller, 2009). Dermatomal block at T4 is often associated with extensive spread of anesthesia resulting in hypotension in the parturients, which if untreated can cause fetal compromise (Nagelhout, 2014).

Different body systems are affected by spinal anesthesia. The central nervous system, the cardiovascular system, the respiratory system, and the gastrointestinal system are all physiologically affected. The effect of anesthesia is produced through the inhibition of nerve impulse conduction in the central nervous system. This occurs when the local anesthetic concentration exceeds the minimum blocking concentration of a nerve exposed to a drug. As the local anesthetic spreads from its site of injection, the concentration gradient decreases, and the most susceptible nerves get blocked, leaving some nerves unblocked. This explains why differential blocks occur with neuraxial anesthesia. With differential block, sympathetic fibers may be blocked by six to seven segments higher than somatic sensory fibers (Nagelhout, 2014). The unmyelinated sympathetic fibers are affected before the myelinated sensory and motor fibers. Overall, the effect of spinal anesthesia on the cardiovascular system primarily depends on

the overall degree of sympathetic blockage as well as the spread of the anesthetic and the level of central sympathetic inhibition (Miller, 2009).

Sympathectomy has a major effect on cardiovascular collapse. As sympathetic nervous system blockage results in arterial vasodilation, decreased systemic vascular resistance, venous pooling, and a reduction in venous return (Miller, 2009). These physiological changes often lead to a redistribution of blood resulting in hypotension. At the level of T4 blockage, which is usually the requirement for C-section, cardiac accelerators (nerves of the sympathetic innervation of the heart) are anesthetized. An imbalance between the vagus fibers, resulting in decrease heart rate, baroreceptor reflexes, volume receptor reflexes, and decreases in central sympathetic outflow all contribute to the complex cardiovascular response to neuraxial anesthesia (Miller, 2009; Nagelhout, 2014). The outcome is the loss of normal cardiovascular homeostatic reflexes and the ability to compensate for cardiovascular changes.

The effects of hypotension affect both the mother and the fetus. Fetal adverse effects are decreased uteroplacental blood flow impairing fetal oxygenation with the risk of asphyxial stress and fetal acidosis. Decrease in maternal cardiac output, nausea and vomiting, dizziness and decreased consciousness are some of the parturient's adverse effects. Maintaining the blood pressure within 80% of baseline is significant to prevent the unpleasant effects of nausea and vomiting as well as prevent fetal oxygen deprivation (Lee, Kee, & Gin, 2002). Prophylactic IV phenylephrine administration prevents these unwanted adverse effects.

The Ideal Vasopressor

Phenylephrine was used to manage the hypotension associated with spinal anesthesia beginning in the 1960's. However, there were concerns about placental perfusion due to increased uterine vascular resistance with subsequently decreased uterine blood flow due to the

alpha effects of phenylephrine (Cooper, 2012). The use of ephedrine then became prevalent and the gold standard vasopressor of choice for the management of spinal-induced hypotension. This was based on observation in pregnant sheep, which revealed better preservation of uteroplacental blood flow with ephedrine. However, there was a change with the use of ephedrine back to phenylephrine due to newer studies revealing fetal acidosis with ephedrine (Copper, 2012). This transition started in 2002 when Lee et al. (2002) published a quantitative systematic review changing the traditional idea that ephedrine was superior to phenylephrine in the management of the hypotension associated with spinal anesthesia in term parturients undergoing elective C-section. In their study, they found the groups that received phenylephrine delivered babies with a higher umbilical arterial pH compared to the group that received ephedrine.

In addition, newer studies are indicating that ephedrine has a five-fold higher risk of fetal acidosis and is also more likely to cross the placenta. Crossing the placenta raises the level of lactate, glucose, and catecholamines in the fetal circulation (Butwick, Columb, & Carvalho, 2014). Its slow onset of action due to its indirect mechanism of action also makes phenylephrine a better option. Moreover, physiologically, response to spinal anesthesia involves decreased systematic vascular resistance, increased heart rate, and cardiac output (Nagelhout, 2014). With these physiological changes, the use of ephedrine does not make sense because ephedrine affects both alpha and beta receptors. The pharmacodynamic response will be an increase in heart rate and cardiac output from the beta one effects with vasoconstriction from the alpha one effect (Miller, 2009; Nagelhout, 2014). However, the use of ephedrine should not be totally ruled out in this population, though its use needs to be judicious.

Phenylephrine, on the other hand, is a synthetic sympathomimetic amine with direct activity for the alpha one adrenergic receptor. Alpha one receptors mediate smooth muscle

contraction and vasoconstriction, and it also has a non-hemodynamic function of salivation, gastrointestinal relaxation, sweating, gluconeogenesis, and glycogenolysis (Miller, 2009). Phenylephrine, with an alpha one receptor activity increases blood pressure by vasoconstriction as well as increasing peripheral vascular resistance (Miller, 2009; Nagelhout, 2014). Reflex bradycardia usually occurs secondary to baroreceptor stimulation. It has an immediate onset of action and lasts between five to twenty minutes. Given that, the hemodynamic changes of spinal anesthesia are caused by preganglionic sympathetic blockage, using a vasopressor that will maintain adrenergic activity seems appropriate (Cooper, 2012). The use of phenylephrine to manage the spinal-induced hypotension in the parturients is not the only important factor, but how it is used can have a significant effect, as it will be seen in the literature review.

Literature Review

To determine which vasopressor regime is more effective in managing the hemodynamics of this population, a literature search on the topic was conducted from 2000 to present using CINAHL and ProQuest databases. The reference lists of the retrieved studies were also examined. Eleven blinded randomized control trials (RCTs) and one analysis study were used for this review. The sample population was physical status (PS) one and two parturients with term pregnancy of a single fetus undergoing elective C-section under spinal anesthesia. The hypothesis was IV phenylephrine infusion would cause less hypotension in the parturients as compared to IV phenylephrine bolus regimen under spinal anesthesia with elective C-section. The primary outcome was hypotension. The secondary outcomes were nausea and vomiting, umbilical blood gas and Apgar score. Research that used these outcomes was used so comparisons and conclusions can easily be made.

Phenylephrine can be administered as a weight-based or a non-weight based prophylactic IV infusion or in intermittent, IV single boluses. The treatment can either be started immediately after the administration of the intrathecal, anticipating a decrease in blood pressure, or it can be administered once the parturient becomes symptomatic (Cooper, 2012). To understand the optimal management of hypotension in this population, different authors have conducted many studies. One of these studies was by Doherty, Ohashi, Downey, and Carvalho (2012). In this double blind RCT, 30 parturients received IV phenylephrine at a fixed infusion rate of 120mcg/min immediately after intrathecal injection of local anesthetic. An additional bolus of 120mcg of IV phenylephrine was given when SBP decreased 20% from baseline. The other 30 patients in the control group received IV phenylephrine bolus of 120mcg each time the SBP dropped 20% from baseline. From the conclusion of this study, there were no clinical benefits to administering IV phenylephrine infusion versus IV bolus regimens for managing hypotension in the parturients with spinal anesthesia during C-section.

Although there were no clinical benefits to IV phenylephrine infusion in this study, the group that received the IV boluses had blood pressures closer to the baseline initially after the spinal (Doherty et al. 2012). The intervention groups showed a statistically significant decrease (p=0.007) in blood pressure in the first six minutes after intrathecal administration and as such, required a higher total dose of phenylephrine to maintain maternal blood pressure close to the baseline. There was no difference in the rate of nausea and vomiting, Apgar score and umbilical blood gases between the two groups. The question about this study is whether the results can be generalized, as the dose of phenylephrine used (120mcg) is higher than the dose commonly used in other centers. Also, on examining the sample characteristics, the average weight of the parturients in the bolus group was 74kg compared to the 78kg in the infusion group. Perhaps

parturients with the larger average weight used more phenylephrine compared to the group with the lower average weight.

Kee et al. (2004) have done various studies on hypotension associated with spinal anesthesia in the parturients. One of those studies is a double blind RCT with 50 subjects to investigate prophylactic IV phenylephrine infusion versus therapeutic IV bolus regimens. In this study, the intervention group (the group that received phenylephrine infusion) showed a statistically significant decrease in the incidence of hypotension compared to the control group. Similar to the study by Doherty et al. (2012), larger doses of IV phenylephrine were used in the intervention group compared to the control group, and there was no statistically significant difference in Apgar scores and umbilical cord blood gases between the two groups. However, nausea and vomiting were not measured in this study, and the dose of IV phenylephrine used was 100mcg/min. Kee et al. (2004) concluded by indicating that using 100mcg/min of IV phenylephrine infusion is a safe and effective method of preventing the hypotension associated with spinal anesthesia in this population. The study was conducted in 2004 and is not as current as the study by Doherty et al. (2012); however, it is highly relevant to this systematic review and has minimal limitations although the sample size could be questionable. They used 26 parturients in the intervention group and 24 in the control group.

Doherty et al. (2012) and Kee et al. (2004) both use an estimated IV phenylephrine dose without considering specific characteristics of the parturients. From a different perspective, Siddik-Sayyid, Taha, Kanazi, and Aouad (2014) as well as Neves et al. (2010) took account of the weights of the parturients in dosing the IV phenylephrine in their studies. In the double blind RCT involving a total of 80 parturients conducted by Siddik-Sayyid et al. (2014) weight-based IV phenylephrine infusion rate and rescue boluses were assessed. The intervention group was

given prophylactic IV phenylephrine infusion at a starting rate of 0.75mcg/kg/min, and the control group received IV normal saline infusion at the same rate. Rescue IV boluses were administered in both groups when SBP fell 20% from the baseline. Hypotension was 20% in the intervention group compared to 90% in the control group. Nausea and vomiting were 10% in the intervention group compared to 44% in the control group. However, the difference between the neonatal outcomes between the two groups was not different. A limitation of this study was there was bias in maintaining SBP very close to the baseline in the intervention group and below the baseline in the control group. The authors did not specify the reason for the bias. Blinding physicians effectively were also questionable as indicated by the study (Siddik-Sayyid et al., 2014).

Similarly, Neves et al. (2010) conducted a double blind RCT involving 160 parturients divided into three equal groups. A weight-based IV phenylephrine infusion for the intervention group (group one) at a rate of 0.15mcg/kg/min was used after the injection of the spinal anesthetic. Group two received a bolus of 50mcg IV phenylephrine immediately after spinal administration, and group three received 50mcg of IV phenylephrine bolus whenever SBP or diastolic blood pressure (DBP) dropped by 20% from the baseline. Similarly, to the study by Siddik-Sayyid et al. (2014), hypotension was significantly seen in the group that did not receive any prophylactic IV phenylephrine, which was group three, affecting 85%, compared to 33% and 17% in group two and group one respectively. Nausea and vomiting were statistically significant affecting 40% in group three, 15% in group two and 10% in group one. The differences in the Apgar score among the groups were not statistically significant (Neves et al., 2010).

Using a parallel approach, Lee et al. (2016) compared three different weight-based IV phenylephrine boluses in a RCT involving 184 subjects. Group 1 (PHE 1) received 1mcg/kg,

group 1.5 (PHE 1.5) received 1.5mcg/kg and group 2 (PHE 2) received 2mcg/kg of IV phenylephrine immediately after the spinal block. The control group received two ml of 0.9% normal saline. Hypotension was significant in the control group, accounting for 72%. In the intervention group, hypotension was 69% in the PHE1 group, 37% in the PHE1.5 group and 46% in the PHE2 group. There were no significant differences in nausea and vomiting, umbilical cord blood gas, and Apgar scores among the group. The authors recommended phenylephrine bolus of 1.5mcg/kg for controlling the hemodynamics changes associated with spinal anesthesia in this population. One limitation of this study is that it cannot be generalized because they used a low dose local anesthetic (7mg of bupivacaine with 15mcg of fentanyl) for the spinal block. The usual dose as indicated by Nagelhout (2014) is 10 to 15mg of bupivacaine.

Equally, to Lee et al. (2016), Tanaka, Balki, Parkes, and Carvalho (2009) carried out a double blind RCT with 50 parturients to determine the ED95 of phenylephrine for the management of spinal-induced hypotension and nausea with C-section. The first parturient was administered 40mcg of IV phenylephrine, and the dose to subsequent parturients differed by 10mcg increments or decrements. The recommendations of Tanaka et al. (2009) for the ED95 of IV phenylephrine were 122mcg to 159mcg to manage spinal induced-hypotension in parturient. There is, however, a question with the tool they used to measure the ED95. The tool may be inaccurate as there is a wide gap for the ED95, making it difficult to determine a precise, effective dose. This is a limitation of this study; therefore, the study cannot be generalized.

Kee et al. (2004) took a different approach to conducting another RCT with 75 parturients divided into three groups to determine the optimal hemodynamic support during spinal anesthesia with C-section. In this study, IV phenylephrine 100mcg/min was infused for two minutes after intrathecal block. After the two minutes mark, depending on the parturients

randomly assigned group (maintain SBP at 100% baseline, at 90% baseline, or at 80% baseline), the phenylephrine infusion was either continued or stopped. The group with the 100% baseline presented with a low incidence of hypotension compared to the group with the 90% and 80% baseline. Umbilical pH was higher in the group with 100% baseline than in the group with 80%. Also, the group with 80% baseline had a higher incidence of nausea and vomiting, followed by the group with 90% baseline. These authors concluded by indicating that, for optimal management, phenylephrine needs to be titrated to maintain SBP near baseline in these populations.

While Kee et al. (2004) used different percentages of baseline SBP to determine the optimal hemodynamic support, Allen, George, White, Muir, and Habib (2010) used four fixed rates of IV phenylephrine infusion regimens (25mcg/min, 50mcg/min, 75mcg/min and 100mcg/min) in a double blind RCT with 100 parturients. The various groups received the applicable IV phenylephrine infusions rates and the control group received a placebo. The authors concluded by indicating that IV prophylactic phenylephrine infusion was effective in reducing the hypotensive episodes with spinal during C-section. Also, 25mcg/min and 50mcg/min infusions provided greater maternal hemodynamic stability as there was a high incidence of hypertension in the 75mcg/min and 100mcg/min group. However, the difference in the incidence of nausea and vomiting, umbilical cord blood gas and Apgar score among the groups was not statistically significant. Two liters of crystalloids were co-administered with the IV phenylephrine infusion in this study. This makes the generalizability of the study questionable because different anesthesia providers may use various types of fluids (crystalloids versus colloids) at different times (before or after intrathecal injection). At such, the findings of the

study may be different if another type of fluid was administered and/or the time of administration was different.

Stewart et al. (2010) as well as Ansari, Hashem, Hassan, Gamassy, and Saleh (2011) conducted RCTs studies involving 75 and 117 parturients respectively. Both studies initiated IV phenylephrine infusion immediately after spinal block at rates of 50mcg/min and 100mcg/min with the addition of boluses to maintain SBP at 80% of baseline. Both studies did not find significant difference in the incidence of hypotension, nausea, and vomiting as well as umbilical blood gas among the groups (Stewart et al., 2010; Ansari et al., 2011). The limitation of Stewart et al. (2010) study was that there was no control group to compare to the intervention group.

In Cooper et al. (2006) prospective evaluation of phenylephrine for SBP control during spinal anesthesia, 100 parturient were used. One dose of IV phenylephrine infusion at 67mcg/min was started after spinal administration and was titrated to keep SBP at 80% to the baseline. It was not indicated in the study as to why this dose was chosen. There were still episodes of hypotension and nausea in the study; they reported 15% and 13% respectively. There are, however, concerns with regards to the ethical review of the research. The authors indicated ethical review board was not needed since recording arterial blood pressure was a standard procedure, and there were to be no other interventions.

In the Mwaura, Mung'ayi, Kabugi, and Mir (2016) RCT, 108 parturient were recruited. This study did something different by giving the intervention group a weight-based IV phenylephrine infusion at 0.5mcg/kg/min immediately after spinal block while the control group received IV phenylephrine at a fixed infusion rate of 37.5mcg/min. The incidence of hypotension was statistically significantly low on the weight-adjusted dose group compared to the fixed dose

group (p=0.05). These authors recommended weight-based infusion regimen for management of spinal-induced hypotension.

Discussion

The studies presented in this paper used different approaches to determine which method of phenylephrine administration provided the best hemodynamic outcomes. From the review, prophylactic IV phenylephrine infusion had a better outcome in controlling the hemodynamics of parturients scheduled for C-section under spinal anesthesia. To prevent periodic hypertension with the IV prophylactic infusion, it is recommended for anesthesia providers to use a weight-based phenylephrine infusion. Although there are slight differences in the study designs used, a major similarity is that they were all level one RCTs except for the study by Cooper et al. (2012), which was an analysis. Being a level one study makes it easier for comparison of the outcomes since they have control groups.

Another similarity in the study designs was all the studies had very similar inclusion and exclusion criteria. The parturients in all of the studies were a PS one or two, carrying a term single fetus and where undergoing an elective C-section under spinal anesthesia. Patient refusal, contraindications to spinal anesthesia, allergy to phenylephrine, hypertension, cardiac or cerebrovascular disease, fetal abnormalities, and diabetes excluding gestational diabetes were the exclusion criteria used in the studies. However, some of the studies failed to indicate how old the parturients were. Older parturients may respond hemodynamically different under spinal anesthesia, compared to younger parturients. Bajwa, Kulshrestha, and Jindal (2013) identified the age 35 years and older as a risk factor for developing severe hypotension with spinal anesthesia in C-section. Future studies on this topic should include the age of the population used as it can have an impact on the results of the study.

One significant difference in the study designs that may have influenced the results was the use of fluid boluses. The majority of the studies indicated fluid boluses were administered; however, the authors do not specify whether the fluid was administered before the spinal or after the spinal. Also, some of the studies did not administer fluid boluses. They only used fluids to keep the vein open. Moreover, different studies used different type of fluids; some used crystalloids and others used colloids. Colloids are more effective in optimizing blood volume during spinal anesthesia due to their longer half-life (Bajwa et al., 2013). The different effects of the fluids in the intravascular compartment may have had an impact on the results of the studies. This makes the study hard to be generalized in this population since the timing and the type of fluid administered is unclear in some of the studies. Future studies need to be specific on the time and type of fluid administered as this is an important piece of hemodynamic stability and may have an impact on the outcome if the study was to be generalized.

The outcomes of the studies used were the same. However, different studies used different factors as primary outcome. For example, the study by Kee et al. (2004) used fetal umbilical blood gas as their primary outcome while the study by Stewart et al. (2010) used hypotension as their primary outcome. This is a limitation of this review, as a more definite conclusion would have been drawn if the studies used all had the same primary outcome. Future analysis on this subject can try to review studies with exactly the same primary outcomes. However, it may not be a large review as there are a limited number of studies using the same primary outcome in this topic.

Another limitation of the review is the studies used different doses of bupivacaine and some studies added adjuncts such as fentanyl and morphine to the spinal anesthetic. Most of the studies used 0.5% hyperbaric bupivacaine with doses ranging from 10mg to 13.5mg. There were

few studies that used 0.75% hyperbaric bupivacaine, 12mg to 12.75mg. Preservative free fentanyl 10mcg to 15mcg and preservative free morphine 100mcg to 150mcg were the adjuncts added. The different dose of spinal anesthetic will result in different hemodynamic outcomes with high spinal resulting in a more profound hypotension (Nagelhout, 2014). It would have been preferred to use studies with the same doses of spinal anesthetic so that the generalizability of the outcome can be certain. However, the probability of getting an adequate number of studies that are using the same dose of bupivacaine is very small. In fact, there were a limited number of primary studies on the topic. Being selective of the dose of spinal anesthetic would have made this review impossible.

The policy recommendation derived from the analysis of the literature presented here is that anesthesia providers should use a weight-based prophylactic IV phenylephrine infusion to manage the hypotension associated with spinal anesthesia in the parturients undergoing C-section. Prophylactic IV phenylephrine infusion prevents the profound hypotension and its associated unfavorable outcomes such as nausea and vomiting, feeling of impending doom, decreased umbilical pH and decreased Apgar score (Lee, Kee, & Gin, 2002). Adopting this practice will reduce these unwanted adverse effects and may improve patient satisfaction and outcome. As anesthesia providers aim to provide vigilant, safe, and competent care with minimum complications, they also ensure patients have a good experience in the process.

Conclusion

The research presented here supports the use of prophylactic IV phenylephrine infusion to manage the sympathectomy-induced hypotension associated with spinal anesthesia in parturients undergoing C-section. Using a weight-based prophylactic IV phenylephrine infusion was superior in stabilizing hemodynamics in the parturients compared to a non-weight based IV

phenylephrine infusion. This is because there were incidences of reactive hypertension with the non-weight based prophylactic IV phenylephrine infusion, although there was no statistically significant adverse effect on the parturients and the newborns. Thus, it would be recommended to anesthesia providers to use a weight-based prophylactic IV phenylephrine infusion to manage the hypotension associated with spinal anesthesia in the parturients undergoing C-section. Providing optimal hemodynamic support in this population is important to prevent the unpleasant effects of nausea and vomiting as well as the adverse effects of cardiovascular instability, and most importantly, a decrease in fetal oxygenation. Adopting the recommendation from this literature analysis into practice may contribute to better patient outcome and satisfaction.

This review's findings can be generalized to the parturients population scheduled for C-section under spinal anesthesia. However, factors such as dose of local anesthetic, adjuncts added to the local anesthetic, age, type and kind of fluid administration were not well defined in the studies, and may have an impact on the outcome if the studies were to be generalized. Future studies on the subject should be more specific and clear on those factors. There is a question of whether the hemodynamic outcome of the parturients would have been different if it were an emergency C-section. Future studies can explore more on phenylephrine regimes in emergency C-section under spinal anesthesia.

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