PREVENTING HYPOTENSION CAUSED BY SPINAL ANESTHESIA IN NON PREECLAMPTIC PREGNANCIES WITH CAESAREAN SECTION

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ABSTRACT

Introduction. Caesarean method widely used and become popular among pregnant women. In general, this method mostly used regional anesthesia (spinal, epidural and CSE). However, many reports incidence of complication related to spinal anesthesia after the procedure. Maternal hypotension is the most common complication after spinal anesthesia procedure. Therefore, anesthesiologist need to prevent hypotension during spinal anesthesia in caesarean section. Method. The researcher examines several scientific journals from PubMed, BJA, Elsevier, Cochrane Library and BMC research until 10th August, 2023 for abstracts, conference proceedings, and full-text papers that evaluated prevention of hypotension in non-preeclampsia patients undergoing caesarean delivery under spinal anesthesia. In addition, the researchers examine the research conducted during 2016 to 2023. Result & Analysis. The researchers examine 28 scientific article (11,153 parturient) with 6 different methods to prevent hypotension. It was found that vasopressor is widely used in most research with incidence of hypotension varied from 4%-87,4%. IVCU studies reported the incidence of hypotension in 15,3%-43%. Leg Elevation a non-invasive technique studies reported the incidence of hypotension in 33,3-41,4%. Injection speed adjustment methods resulted incidence of hypotension in Fast injection 50 %-75% and Slow Injection in 36,7%-61%. In addition, granisetron methods diluted in normal saline reported the incidence of hypotension in 17,5%-42%. Low dose spinal anesthesia studies reported incidence of hypotension in 0% - 62,9%. Discussion. From all the research that has been reviewed, vasopressor (Phenylephrine), Leg Elevation and low dose spinal anesthesia could become primary options to prevent hypotension during spinal anesthesia in caesarean section since its effective to prevent hypotension, cost effective, and easy to applied in every medical facility.

Keywords: Caesarean Section, Hypotension, Vasopressors, Granisetron, IVCU

INTRODUCTION

Caesarean section is the surgical procedure by which baby is deliver through an abdominal and uterine wall incision (laparotomy). This method is widely used in the world and become popular among pregnant women since it more convenient than normal method. In general, this method mostly used regional anesthesia (spinal, epidural and CSE) because it is safer than general anesthesia. In addition, spinal anesthesia become primary choice because it’s easy to administer and has rapid onset (Rana et al., 2016). However, there are many reports incidence of complication related to
spinal anesthesia after the procedure such as hypotension, bradycardia, post operative nausea and vomiting (Karnina, Rahmadani and Faruk, 2022).

Maternal hypotension is the most common complication after spinal anesthesia procedure. The incidence of hypotension from 25%-75% in general population who are undergoing caesarean section due to physiological change of pregnancy that makes compression of inferior vena cava by hypertrophic uterus and growth of collateral venous plexus circulation in epidural space which result cephalad spread of spinal anesthetic (Shitemaw et al., 2020). Severe hypotension will reduce uteroplacental blood flow, leading to fetal acidosis, and further damages the central nervous system and puts the fetus in risk (Chen et al., 2020).

Therefore, anesthesiologist need to prevent hypotension during spinal anesthesia in caesarean section. This study performed a systematic review with the aim of summarizing the method to prevent hypotension during spinal anesthesia in caesarean section.

METHOD AND ANALYSIS

Identification Studies
The researchers searched PubMed, BJA, Elsevier, Cochrane Library and BMC study until August 10, 2023, for abstracts, conference proceedings, and full-text papers that evaluated prevention of hypotension in non-preeclampsia patients undergoing caesarean delivery under spinal anesthesia.

The researchers searched the research conducted from 2015 to 2023. The search term used were vasopressors, cesarean delivery, spinal anesthesia, obstetric anesthesia, spinal anesthesia, hypotension and prevention. The researchers included randomized controlled trials of preoperative interventions to prevent hypotension during elective caesarean.

C-section under spinal anesthesia in healthy pregnant women compared with active or inactive intervention. The researchers excluded quasi-randomized trials and up down- sequential dose-finding studies with following interventions: intravenous fluid infusion, categorized as colloid or crystalloid and categorized as before or after induction of anesthesia; leg compression; and the vasopressors phenylephrine, ephedrine, norepinephrine and metaraminol. The researchers defined inactive control for fluid infusion as less than or equal to 500 ml of crystalloid and no prophylactic drugs.

The researchers examine the research that fulfil above criteria and categorize based on author, number of patients, prevention, definition of hypotension and the result of each research. Then, categorized all of them into several category based on prevention that used during the research, along with analyze each prevention category.
## RESULT

**Table 1. Characteristics of 28 researchers**

<table>
<thead>
<tr>
<th>Research</th>
<th>Number of patients</th>
<th>Prevention</th>
<th>Hypotension definition</th>
<th>Incidence of hypotension</th>
</tr>
</thead>
<tbody>
<tr>
<td>McDonnell N.J 2017</td>
<td>188</td>
<td>Metaraminol and phenylephrine</td>
<td>SBP &lt;90 mmhg</td>
<td>Phenylephrine: 87.4% Metaraminol: 71.1%</td>
</tr>
<tr>
<td>Riffard C. 2018</td>
<td>200</td>
<td>Ephedrine</td>
<td>Decrease SBP &gt;20%</td>
<td>70%</td>
</tr>
<tr>
<td>Park J. 2019</td>
<td>120</td>
<td>Ephedrine</td>
<td>SBP &lt;90 mmhg</td>
<td>26.3%</td>
</tr>
<tr>
<td>Xiao f. 2020</td>
<td>117</td>
<td>Metaraminol</td>
<td>SBP &lt;90 mmhg</td>
<td>25%</td>
</tr>
<tr>
<td>Xue X. 2021</td>
<td>131</td>
<td>Metaraminol</td>
<td>SBP &lt;90 mmhg</td>
<td>22%</td>
</tr>
<tr>
<td>Gunda S. 2020</td>
<td>60</td>
<td>Ephedrine</td>
<td>SBP &lt;90 mmhg</td>
<td>20%</td>
</tr>
<tr>
<td>Zhou Y. 2021</td>
<td>75</td>
<td>Metaraminol Phenylephrine Norepinephrine</td>
<td>SBP &lt;90 mmhg</td>
<td>Metaraminol: 4% Phenylephrine: 20% Norepinephrine: 32%</td>
</tr>
<tr>
<td>Andrade P. 2018</td>
<td>126</td>
<td>Norepinephrine</td>
<td>SBP &lt;90 mmhg</td>
<td>32%</td>
</tr>
<tr>
<td>Mwaura L. 2016</td>
<td>104</td>
<td>Phenylephrine</td>
<td>SBP &lt;90 mmhg Decrease SBP &gt;20%</td>
<td>35.2%</td>
</tr>
<tr>
<td>Guo L. 2020</td>
<td>138</td>
<td>Phenylephrine Norepinephrine</td>
<td>SBP &lt;90 mmhg OR Decrease SBP &gt;20%</td>
<td>Phenylephrine: 14.5% Norepinephrine: 15.9%</td>
</tr>
<tr>
<td>Shah A. 2017</td>
<td>90</td>
<td>Phenylephrine</td>
<td>MAP &lt;60mmhg</td>
<td>11.12%</td>
</tr>
<tr>
<td>Samarah. 2018</td>
<td>152</td>
<td>Granisetron</td>
<td>SBP &lt;90mmhg</td>
<td>42%</td>
</tr>
<tr>
<td>Abhishek C. 2020</td>
<td>200</td>
<td>Granisetron</td>
<td>Fall in the systolic arterial blood pressure below 100 mmHg or a fall in mean arterial blood pressure of more than 20% from baseline</td>
<td>37%</td>
</tr>
<tr>
<td>Maheen W. 2021</td>
<td>120</td>
<td>Granisetron</td>
<td>Hypotension, defined as SBP fall more than 20% below the baseline</td>
<td>17.5%</td>
</tr>
<tr>
<td>Jaya S. 2020</td>
<td>34</td>
<td>Granisetron</td>
<td>Hypotension, defined as SBP fall more than 20% below the baseline</td>
<td>29.4%</td>
</tr>
<tr>
<td>Mehten A. 2021</td>
<td>120</td>
<td>Granisetron</td>
<td>30% decrease in systolic blood pressure compared to preoperative values</td>
<td>30%</td>
</tr>
<tr>
<td>Sofia A. 2019</td>
<td>48</td>
<td>Leg Elevation</td>
<td>Hypotension defined as systolic blood pressure (SBP) &lt;80% of baseline</td>
<td>33.3%</td>
</tr>
<tr>
<td>Sari M. 2020</td>
<td>140</td>
<td>Leg Elevation</td>
<td>The systolic arterial pressure under 90 mmHg or decrease &gt;20% above baseline</td>
<td>41.4%</td>
</tr>
<tr>
<td>Ahmed H. 2017</td>
<td>150</td>
<td>Leg Elevation</td>
<td>Systolic blood pressure (SBP) &lt;100 mmHg</td>
<td>34.7%</td>
</tr>
</tbody>
</table>
### Study Characteristics

1. **Drugs Used**
   
   Most of the research are using vasopressor such Metaraminol, phenylephrine, norepinephrine, and ephedrine. In addition, all research recommends different vasopressor drugs with its own advantages and side effect. Vasopressor become widely used because it directly counters the primary physiological derangement induced by the sympathetic block, arterial dilation and decrease vascular resistance. The incidence of hypotension from these studies varied between 20% - 87.4% (Mwaura et al., 2016; McDonnell et al., 2017; Andrade, Ortiz and Gamón, 2018; Riffard et al., 2018; Shah et al., 2018; Park et al., 2020; Gunda and Bekkam, 2021; Xiao et al., 2021; Zhou et al., 2022; Guo et al., 2022; Xue, Wang and Zhou, 2023).

2. **IVCU**
   
   Hypotension in spinal anesthesia during caesarean section is caused by decrease vascular resistance due to compression of Inferior Vena Cava (IVC) by gravid uterus that led to decrease venous return. Many methods were studied to prevent hypotension such IVCUS (Inferior Vena Cava Ultrasound) and IVCCI (Inferior Vena Cava Collapsibility Index). These methods aim to assessed fluid responsiveness to avoid hypotension during spinal anesthesia. The incidence of hypotension from these studies varied between 15.3% - 43% (Ceruti et al., 2018; Yao et al., 2021; Ni et al., 2022).
3. Leg Elevation
Leg elevation or leg raising method was done by elevate the legs of the patients at determined angle in horizontal plane using cushion or similar objects. This position will increase venous return from lower extremities. The incidence of hypotension with these methods are varied between 33.3%-41.4% (Hasanin et al., 2017; Assen, Jemal and Tesfaye, 2020; Sari and Ozyurt, 2022).

4. Injection Speed of Spinal Anesthesia
Injection speed of spinal anesthesia has a role in hypotension during caesarean section. It was caused by increase turbulence in subarachnoid space thereby increasing distribution of drugs towards cephalad. The incidence of hypotension in these anesthesia was varied and show fewer amount in slow injection than fast injection methods (Mwaura et al., 2016; Shah et al., 2018; Guo et al., 2022).

5. Granisetron
Granisetron is 5HT3 receptor antagonists that block serotonin uptake and reduce vasodilatation that led to prevent hypotension. The 5-HT3 receptors are present in the heart, lung, and spine. The result of this Granisetron anesthesia was varied, it was reported that the incidence of hypotension between 17.5% - 42% (Chatterjee et al., 2020; Samarah et al., 2020; Supriyanto, Suwarman and Rachman, 2020; Aksoy et al., 2021; Wahid et al., 2022).

6. Low Dose Spinal Anesthesia
The use of a lower dose aims to decrease maternal side-effects hypotension during spinal anesthesia. The most common drugs used in spinal anesthesia was bupivacaine. The usual dose is 10mg to 15mg. The most used dose in many centers conventionally is 12 mg for cesarean section. The result of hypotension in this anesthesia was varied between 0% - 62.9% (Regmi et al., 2019; Weiniger et al., 2021; Mahdytira et al., 2022).

DISCUSSION
Vasopressor become widely used to prevent hypotension induced by spinal hypotension because it directly counters the primary physiological derangement induced by the sympathetic block, arterial dilation and decrease vascular resistance (Karnina, Rahmadani and Faruk, 2022). Metaraminol is increasingly used in obstetric anesthesia. Metaraminol mainly stimulated α1-adrenergic receptor but had a weak effect on β-adrenergic receptor (Shitemaw et al., 2020). Metaraminol, as a mixed adrenergic receptor agonist activity, it rarely increases maternal myocardial oxygen consumption and fetal oxygen consumption, which may be a more ideal drug for the treatment of hypotension after spinal anesthesia (Gunda and Bekkam, 2021).

Phenylephrine is a synthetic, selective, sympathomimetic agent alpha 1 agonist (Mwaura et al., 2016). For the last decade, phenylephrine has been widely used as a vasopressor for maintaining blood pressure (BP) during spinal anesthesia for caesarean delivery. Phenylepherine has been shown to provide the best balance in achieving effective control of maternal blood pressure without reactive maternal hypertension (Andrade, Ortiz and Gamón, 2018).

The research conducted by Mcdonnell et al. metaraminol was associated with less hypotension and more effective than phenylephrine (McDonnell et al., 2017). This result is similar with 2 previous studies by Xue et al. and Xiao et al. that metaraminol less incidence of hypotension (Xiao et al., 2021; Xue, Wang and Zhou, 2023). Even though has less incidence of hypotension, metaraminol can increases in blood pressure above
baseline. Most of the patient experience increase of blood pressure above the baseline after given metaraminol rather than phenylepherine. Phenylephrine in high doses can cause a baroreceptor-mediated reflex bradycardia, a reduction in stroke volume due to increased afterload, and a shift of blood into the splanchnic venous circulation. In combination with decreased venous return, this can lead to a dose-dependent fall in cardiac output (McDonnell et al., 2017).

Ephedrine is a non-specific alpha and beta sympathetic agonist that has long been used in managing spinal anesthesia-induced hypotension. It has dominant effect on beta that increasing systolic blood pressure with increase of stroke volume and HR. Ephedrine is cost-effective and relatively safe to use in variety of patients receiving spinal anesthesia. Gunda et al. show finding about Ephedrine effectiveness with lower incidence of hypotension in spinal anesthesia in 20% (Gunda and Bekkam, 2021). Another study from Park et al. shows effectiveness of Ephedrine to reduce incidence of hypotension with 26.3% (Park et al., 2020). However, the pharmacokinetic of ephedrine will not allow continuous intravenous infusion, and it is mostly administered as intermittent intravenous bolus that results in peaks and troughs of plasma drug concentration. Moreover, considering that the potential ischemic harm conveyed by reduced MAP to major organs is dependent. On the other hand, IM injection is usually discouraged due to the unpredictable onset or offset. Ephedrine also has slow onset time of 15 to 20 minutes with its effects not lasting longer than 2 hours (Park et al., 2020).

Injection speed of spinal anesthesia has a role in hypotension during caesarean section. The research conducted Chiang et al. which examines if reducing the speed of injection would cause less hypotension to a parturient undergoing spinal anesthesia for Caesarean section. The speed of injection was timed by use of a Smartphone app: Pro Metronome, iOS. From the results, FAST injection speeds and SLOW injection speeds have similar incidence of hypotension. Thus, prolonging the injection time did not reduce this side effect (Chiang et al., 2017). Another research from Arif et al. shows the opposite which report the incidence of hypotension reported 87.5% in fast injection and 37.5% in slow injection, the incidence in fast injection is higher than in slow injection (Arif and Setiawan, 2015). Ersagun et al. show same result with incidence of hypotension in fast injection is 50% and in slow injection is 36.7%.

This happened because local anesthetic solution tends to move more cephalad or in the direction of the injection, in contrast to fast injection rates, which tend to cause a disturbed and turbulent flow (Tugcugil and Besir, 2022). The rapid injection effect increase turbulence in subarachnoid space increasing the distribution of drugs towards cephalad, moreover in pregnant women who experience influential physiological changes on the distribution of local anesthetics in subarachnoid space, such as increasing intraabdominal pressure, intrathecal space became narrower, and the nerves become more sensitive than before could increases the risk of occurring hypotension (Arif and Setiawan, 2015). However, the adjustment of injection speed of anesthesia is applied hardly in emergency caesarean that needs anything done as fast as the whole medical team could.

Hypotension in spinal anaesthesia during caesarean section is caused by decrease vascular resistance due to compression of Inferior Vena Cava (IVC) by gravid uterus that led to decrease venous return. IVCU (Inferior vena cava ultrasound) has been used in spontaneously breathing intensive care
patients and few data are available patients who are not critically ill. Moreover, stroke volume calculations using aortic velocity time integral have been shown to accurately correlate with fluid responsiveness. IVCUS is a non-invasive, quickly learned and performed, and well-validated examination that is often used in the emergency and critical care setting and is suitable for the induction area and the operating room as a perioperative screening and treatment monitoring-tool. Study of IVCU from Ceruti et al. reported the incidence of hypotension in 35% and conclude if IVCUS-guided protocols for patients undergoing surgery in spinal anesthesia should be encouraged.

Inferior vena cava (IVC) collapsibility index (IVCCI) as non-invasive, and easy technique for evaluating volume status. The IVCCI was calculated using the following formula: IVCCI = (dIVCmax – dIVCmin)/dIVCmax ×100%. The research from Ting Ni et al reported incidence of hypotension in 15.3%. They stated that IVCCI determined using ultrasound before spinal anesthesia is a reliable predictor of the incidence of hypotension following spinal anesthesia (Ni et al., 2022). However, disadvantages of this method are ultrasound is an operator dependent technique: even if all IVC Ultrasound examinations have been performed by a very small and homogeneous group of anesthesiologists, specifically trained for this trial and with a solid clinical experience in echography, a possible impact on the results for some interindividual differences in the performance of the technique cannot be excluded (Ceruti et al., 2018).

5-hydroxytryptamine 3 (5-HT3) receptors play an important role in the occurrence of the hypotension after spinal anesthesia. The 5-HT3 receptors are present in the heart, lung, and spine. The diminished venous return caused by spinal anesthesia stimulates the cardiac chemoreceptors, and parasympathetic activity increases, which results in bradycardia and hypotension. Granisetron is a potent and highly selective 5-HT3 receptor antagonist with little or no affinity for other serotonin receptors, including adrenergic, histaminic, dopaminergic, and opioid receptors. Aksoy et al. show that granisetron can reduce the incidence of hypotension in spinal anesthesia, 5-HT3 antagonists may attenuate spinal anesthesia-induced hypotension, thus inhibiting serotonin uptake and prevent BJR (Bezold Jarisch Reflex) in peripheral vasodilatation and increasing venous return to the heart (Aksoy et al., 2021).

This research has same result with Abhisek et al. which stated that granisetron can reduce the hypotension with incidence result 37% (Chatterjee et al., 2020). Another study of Granisetron by Maheen et al. reported same result with incidence of hypotension in 17.5% (Wahid et al., 2022). However, another research conducted by Samarah et al. has the different result that granisetron has no effect to counter hypotension in spinal anesthesia with total of hypotension incidence in 42% (Samarah et al., 2020). Granisetron is more expensive than Ondansetron that cause unavailability in small hospitals.

Leg elevation or leg raising method was conducted by elevate the legs of the patients at determined angle in horizontal plane using cushion or similar objects. Leg elevation (LE) creates an increase in venous return by translocation of blood from lower extremities to the thorax. Thus, LE leads to increased stroke volume (SV) and consequently cardiac output (CO). LE was previously used as a first aid maneuver in acute circulatory collapse, it has been also considered as a popular method for detection of fluid responsiveness. Hasanin et al. reported that incidence of hypotension in
spinal anesthesia with LE prevention was 34.7% (Hasanin et al., 2017). Another research by Sari et al. Reported similar result with Hasani that LE was effective in reducing the incidence of hypotension, although it could not fully prevent post-spinal hypotension. And still need to combine with vasopressors (Sari and Ozyurt, 2022). Sofia et al. reported in their research that leg elevation can reduce hypotension during spinal anesthesia with the incidence in 33.3% (Assen, Jemal and Tesfaye, 2020).

The use of a lower dose aims to decrease maternal side-effects hypotension during spinal anesthesia. The most common drugs used in spinal anesthesia was bupivacaine. The usual dose is 10mg to 15mg. The most used dose in most of centres, conventionally, is 12 mg for caesarean section (Mahdystira et al., 2022). In the research by Bharati et al., the patients are given 8 mg 0.5% heavy bupivacaine (1.6ml) plus 25μg fentanyl (0.5ml) resulted incidence of hypotension in 24.31% (Regmi et al., 2019). This result as same as research from Helmy et al. whose using low dose spinal anesthesia (Bupivacaine <7mg + Fentanyl 25mcg + morphine 50mcg) resulted incidence of hypotension in 0% compared to non-low dose spinal anesthesia (Bupivacaine >7mg) which result the incidence of hypotension in 14.3% (Mahdystira et al., 2022). In addition, another research from Carolyn et al. reported incidence of hypotension in 62.9% (Weiniger et al., 2021).

**CONCLUSION**

From all the reviewed research, the most effective way to prevent hypotension are vasopressor (Phenylephrine), Leg Elevation and Low dose spinal anesthesia. Despite of side effect of Phenylephrine, it was proved as an effective way to reduce the incidence of hypotension in spinal anesthesia in caesar section due its mechanism of action in human body and its can be found easily in every medical facility due it low cost.

Leg Elevation and low dose spinal anesthesia is a practical method that can applied easily by anesthesiologist during spinal anesthesia. Its proved could prevent hypotension, cost effective and has no side effect for the patients. It will be useful in the anesthesia management of caesarean section operations under spinal anesthesia. The limitation of this research was not doing any meta-analysis method. Then, further research are needed to observe the best way to prevent hypotension in spinal anesthesia undergoing caesarean section.

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