

## Original Research Article

**PREVENTING HYPOTENSION CAUSED BY SPINAL ANESTHESIA IN NON PREECLAPMTIC PREGNANCIES WITH CAESAREAN SECTION**I Gusti Agung Ngurah Radhitya<sup>1)\*</sup>, Razi Ageng Pratama<sup>2)</sup><sup>1)</sup>General Practitioner at Navy Base Clinic, Denpasar, Indonesia <sup>2)</sup> Specialist in Anesthesiology and Intensive Therapy at Soedibjo Sardadi Naval Hospital, Indonesia\*Corresponding Author, E-mail: [radhityawijaya8@gmail.com](mailto:radhityawijaya8@gmail.com)Co-Author: [ziianestesi@gmail.com](mailto:ziianestesi@gmail.com)**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 10<sup>th</sup> 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

Research	Number of patients	Prevention	Hypotension definition	Incidence of hypotension	of
McDonnell N.J 2017	188	Metaraminol and phenylephrine	SBP <90 mmhg	Phenylephrine: 87.4% Metaraminol: 71.1%	
Riffard C. 2018	200	Ephedrine	Decrease SBP >20%	70%	
Park J. 2019	120	Ephedrine	SBP <90 mmhg	26.3%	
Xiao f. 2020	117	Metaraminol	SBP <90 mmhg	25%	
Xue X. 2021	131	Metaraminol	SBP <90 mmhg	22%	
Gunda S. 2020	60	Ephedrine	SBP <90 mmhg	20%	
Zhou Y. 2021	75	Metaraminol Phenylephrine Norephinephrine	SBP <90 mmhg	Metaraminol : 4% Phenylephrine: 20% Norephinephrine: 32%	
Andrade P. 2018	126	Norephinephrine	SBP <90 mmhg	32%	
Mwaura L. 2016	104	Phenylephrine	SBP <90 mmhg Decrease SBP >20%	35.2%	
Guo L. 2020	138	Phenylephrine Norephinephrine	SBP <90 mmhg OR Decrease SBP >20%	Phenylephrine : 14.5% Norephinephrine : 15.9%	
Shah A. 2017	90	Phenylephrine	MAP <60mmhg	11.12%	
Samarah. 2018	152	Granisetron	SBP <90mmhg	42%	
Abhishek C. 2020	200	Granisetron	Fall in the systolic arterial blood pressure below 100 mmHg or a fall in mean arterial blood pressure of more than 20% from baseline	37%	
Maheen W. 2021	120	Granisetron	Hypotension, defined as SBP fall more than 20% below the baseline	17.5%	
Jaya S. 2020	34	Granisetron	Hypotension, defined as SBP fall more than 20% below the baseline	29.4%	
Mehnet A. 2021	120	Granisetron	30% decrease in systolic blood pressure compared to preoperative values	30%	
Sofia A. 2019	48	Leg Elevation	Hypotension defined as systolic blood pressure (SBP) <80% of baseline	33.3%	
Sari M. 2020	140	Leg Elevation	The systolic arterial pressure under 90 mmHg or decrease >20% above baseline	41.4%	
Ahmed H. 2017	150	Leg Elevation	Systolic blood pressure (SBP) <100 mmHg	34.7%	192

Chiang C.F 2017	94	Injection speed of spinal anesthesia	SBP <90 mmHg	Fast: 70% Slow: 61%
Ersagun. 2022	67	Injection speed of spinal anesthesia	Systolic blood pressure (SBP) below 90 mmHg and more than a 20% decline in baseline blood pressure	Fast: 50% Slow: 36.7%
Arif S. 2015	48	Injection speed of spinal anesthesia	Decrease >20% above baseline	Fast: 87.5% Slow: 37.5%
Ting Ni. 2021	31	IVCCI guided fluid	Systolic arterial pressure >90 mmHg or mean arterial pressure <60 mmHg	15.3%
Shi F. 2021	56	IVCUS	Hypotension was defined as a drop in systolic arterial pressure by >20% from the baseline	43%
Ceruti S. 2017	160	IVCUS guide Crystalloid Fluid	SBP <90 mmhg MAP <60 mmhg	35%
Helmy M. 2022	84	Low Dose Spinal Anesthesia	Hypotension, defined as SBP fall more than 20% below the baseline	LDSA: 0% NLDS: 14.3%
Bharati D. 2019	74	Low Dose Spinal Anesthesia	Hypotension, defined as SBP fall more than 20% below the baseline	24.31%
Carolyn W. 2021	8226	Low Dose Spinal Anesthesia	Hypotension, defined as SBP fall more than 20% below the baseline	62.9%

## 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 chepalad. 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; Mahdystira *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  $\alpha$ 1-adrenergic receptor but had a weak effect on  $\beta$ -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. Phenylephrine 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 phenylephrine. 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 increase 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:  $IVCCI = (dIVC_{max} - dIVC_{min})/dIVC_{max} \times 100\%$ . 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-HT<sub>3</sub>) receptors play an important role in the occurrence of the hypotension after spinal anesthesia. The 5-HT<sub>3</sub> 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-HT<sub>3</sub> 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-HT<sub>3</sub> 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 similiar 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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