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RESEARCH ARTICLE
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MANAGEMENT OF POST-SPINAL HYPOTENSION IN C SECTION - A RETROSPECTIVE COMPARISON BETWEEN EPHEDRINE AND MEPHENTERMINE

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ABSTRACT

INTRODUCTION

Obstetric anesthesia practice has adapted to a better understanding of maternal-fetal conditions, risks, and benefits. Caesarean deliveries have become one of the most commonly performed surgical procedures. Most often, neuraxial techniques are the anesthetic of choice.[1] Spinal, Epidural, Combined Spinal Epidural (CSE), Epidural volume extension, and sequential are all neuraxial blockades described. Spinal anesthesia provides rapid onset, dense blockade with a definite endpoint. Hence spinal anesthesia is the most preferred technique. Due to the profound sympathetic down, hypotension is the most common side effect; this may be exaggerated by the aortocaval compression by the gravid uterus. Hypotension is clinically significant as it may lead to fetal acidosis due to diminished uteroplacental flow. Strategies to manage hypotension include positioning, fluids, and vasopressors. In this study, we intend to compare two vasopressors in identical dosage which may overcome the unpleasant pharmacological effects of one over the other. The vasopressors which are commonly used are being retrospectively analyzed for their pharmacological and clinical effects.

AIMS AND OBJECTIVES

- To compare the efficacy of ephedrine and mephentermine in post-spinal hypotension in C sections.
- To evaluate the recommendation of the right vasopressor in mothers with comorbidities.

MATERIALS AND METHODS

Study Type: Retrospective / as recommended by obstetricians
Study Population: All C sections under ASA 2 & 1
Study Period: October 24 - December 2024
Sample Size 50

Exclusion Criteria: ASA II & IV

- All patients were shifted in the left lateral position to the operation theatre and coloaded with one liter of Ringer's lactate solution.
- Lumbar subarachnoid block with 2 ml of 0.5% bupivacaine heavy was administered at L3-L4 by 25 G Quincke's needle.

- Pulse rate, systolic, diastolic, and mean arterial blood pressure were noted every 3 minutes until 15 minutes after spinal anesthesia along with preoperative values.
- The first group of 25 patients received 6 mg of inj. ephedrine and the second group of 25 patients received 6 mg of inj. Mephentermine when systolic blood pressure drops below 90 mmHg. The drug was given intravenously and response was noted every 3 minutes. The need for incremental doses, the presence of tachycardia, sustenance of uterine contraction, and any hypotensive response were noted. The results were tabulated and analyzed.

RESULTS

In general, the systolic blood pressure drops at the 3rd minute and may fall again at the 9th or 12th minute depending on obstetric reasons (Big baby / difficult extraction). There is also a concomitant mild fall in pulse rate. In **Ephedrine group**, the first fall in SBP at the 3rd minute to 90 mm Hg had the first increment. Mean heart rate increased to 107 and maintained above a mean of 96 per minute. 16 out of 25 patients needed a repeat dose of ephedrine (6 mg), and 3 patients needed 2 repeat doses. In **Mephenteramine group**, the first fall in SBP at the 3rd minute had the first increment of 6 mg intravenously. The mean heart rate was 86 per minute, which maintained at a mean of 90 per minute. There was no need for an incremental dose, and no abnormal rise in diastolic blood pressure was noted. The indications for C-sections and distribution were nearly identical in both groups.

CONCLUSION

Post-spinal hypotension is a side effect of the lumbar subarachnoid blockade, which could occur in spite of adequate fluids and left lateral tilt. Appropriate vasopressors are needed and must be judiciously used by individual patient parameter trends. Ephedrine is an alpha, beta one, and beta two agonist and enjoys privilege though tachyphylaxis and tachycardia are well documented. Alternative vasopressors are needed where these effects are undesirable. Though an alpha agonist, the property of potentiating endogenous noradrenaline by mephentermine is beneficial. In comparable doses of 6 mg could be considered. Being molecularly associated with methamphetamine, mephentermine is not widely available and offers limitations to its usage.

KEYWORDS

Ephedrine, Mephentermine, Post-Spinal Hypotension.

INTRODUCTION

Physiological changes in the cardiovascular system during pregnancy ensure adequate uteroplacental flow. However, the mechanical effects of a gravid uterus, the flexibility of the spine causing an exaggerated lumbar lordosis, and pressure changes in the epidural vascular system tend to cause hypotension, especially in the supine position.[2]

In most parturients, the resting sympathetic tone is elevated which compensates for the effects of venacaval compression. When sympathetic tone is abolished as in neuroaxial blockade, hypotension sets in. Positioning to avoid venacaval compression, and maintaining extracellular volume by preloading or co-loading with intravenous crystalloids serve to deal with the hypotension.

In addition, the use of vasopressors at least until fetal delivery has been advocated as hypotension occurs despite the other two measures.

Vasopressors including ephedrine, phenylephrine, methoxamine, mephentermine, and even noradrenaline have all been tried and studies have desired clear indications and contraindications.

In this study, we have taken up ephedrine, the common and popular drug to be compared with mephentermine in equal doses of 6 mg each. Alternatives to ephedrine are needed in specific clinical situations and to avoid unpleasant complications.

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In **Ephedrine group**, the first fall in SBP at the 3rd minute to 90 mm Hg had the first increment. Mean heart rate increased to 107 and maintained above a mean of 96 per minute. 16 out of 25 patients needed a repeat dose of ephedrine (6 mg), and 3 patients needed 2 repeat doses.

In **Mephentermine group**, the first fall in SBP at the 3rd minute had the first increment of 6 mg intravenously. The mean heart rate was 86 per minute, which maintained at a mean of 90 per minute. There was no need for an incremental dose, and no abnormal rise in diastolic blood pressure was noted.

The indications for C-sections and distribution were nearly identical in both groups.

Ephedrine

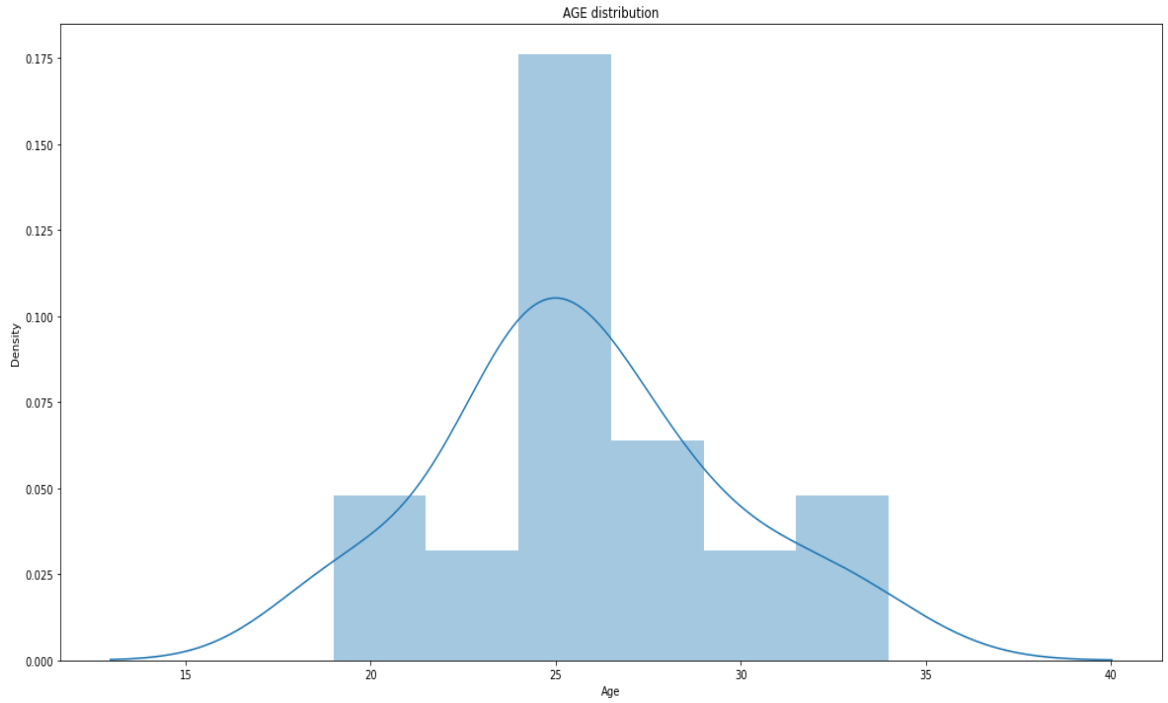

Figure 1: Ephedrine Distribution Age

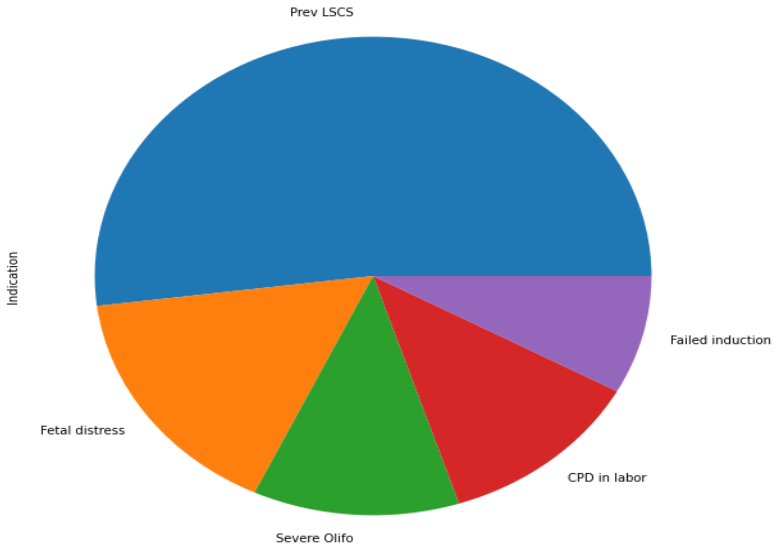

Figure 2: **Ephedrine Indication**

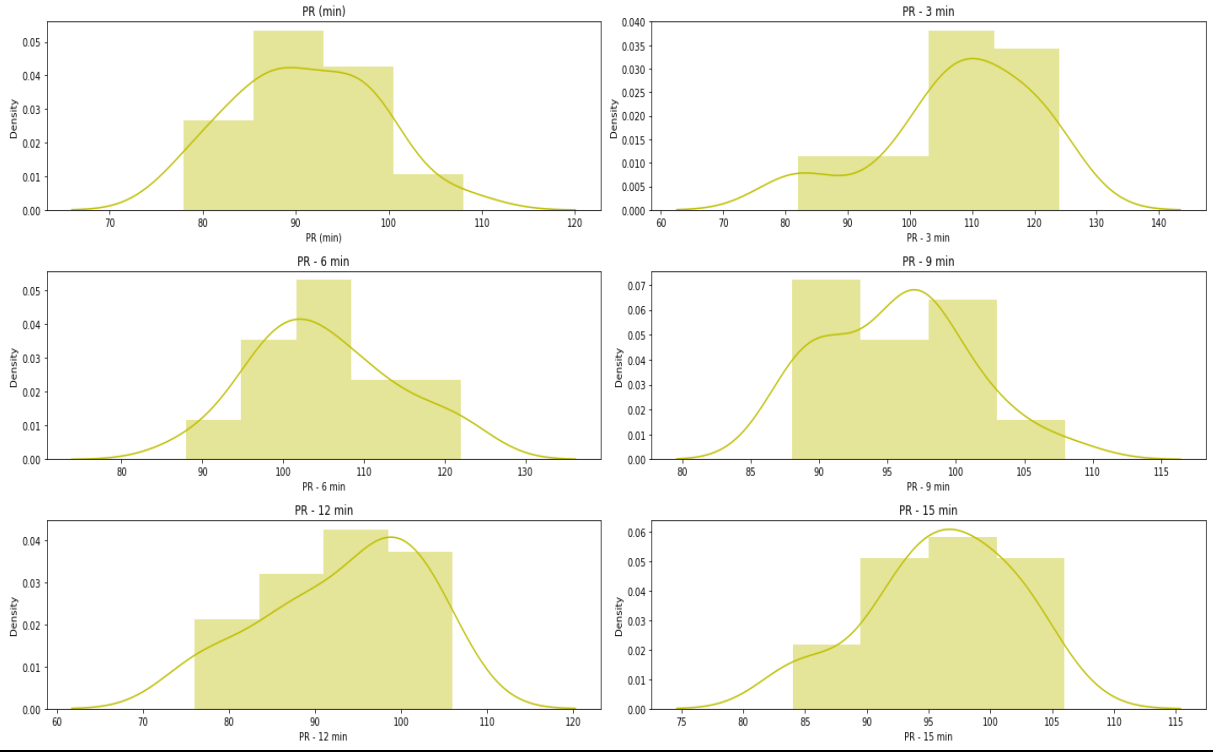

Figure 3: Ephedrine Distribution Plots PR

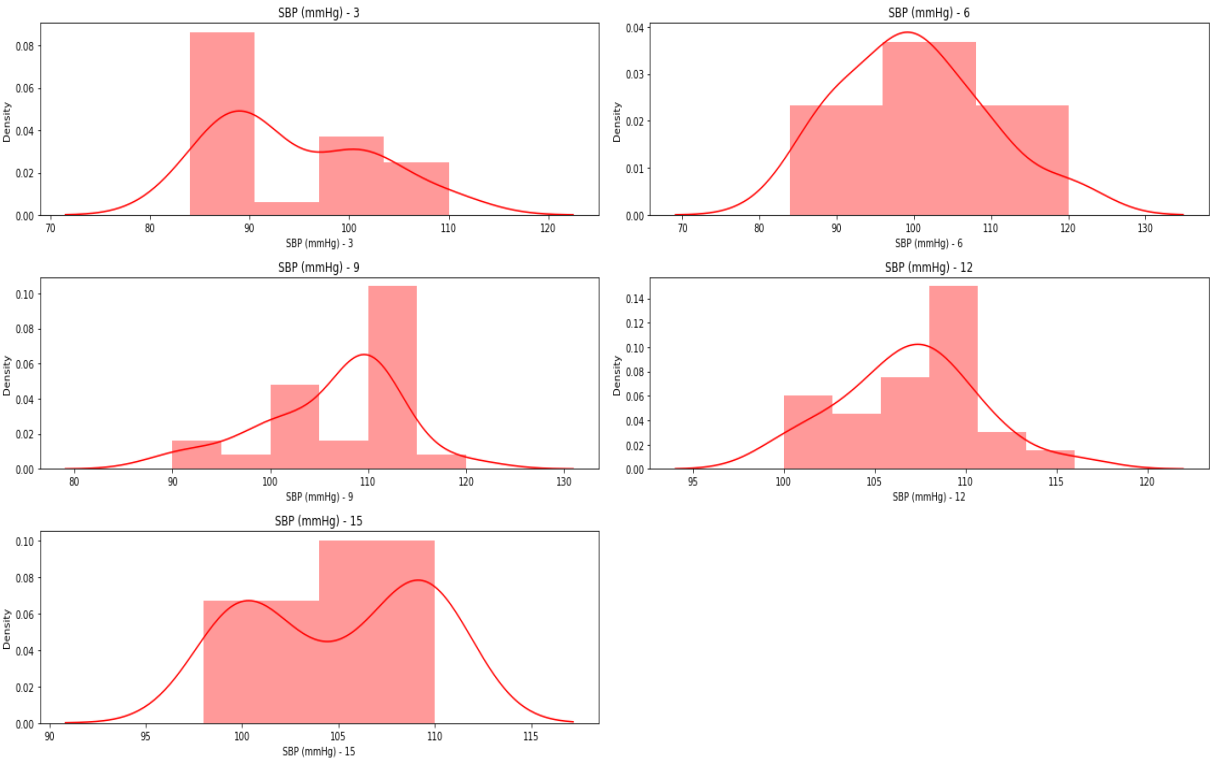

Figure 4: Ephedrine - Distribution plot SBP

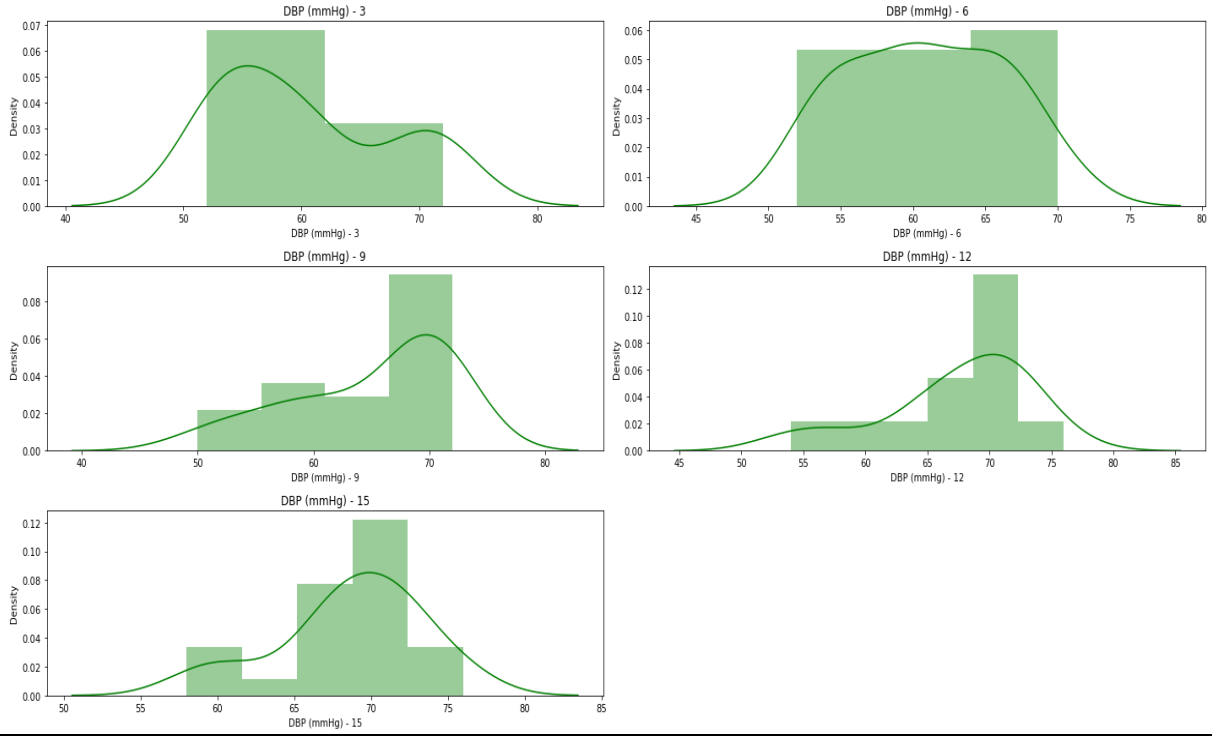

Figure 5: Ephedrine - Distribution plot DBP

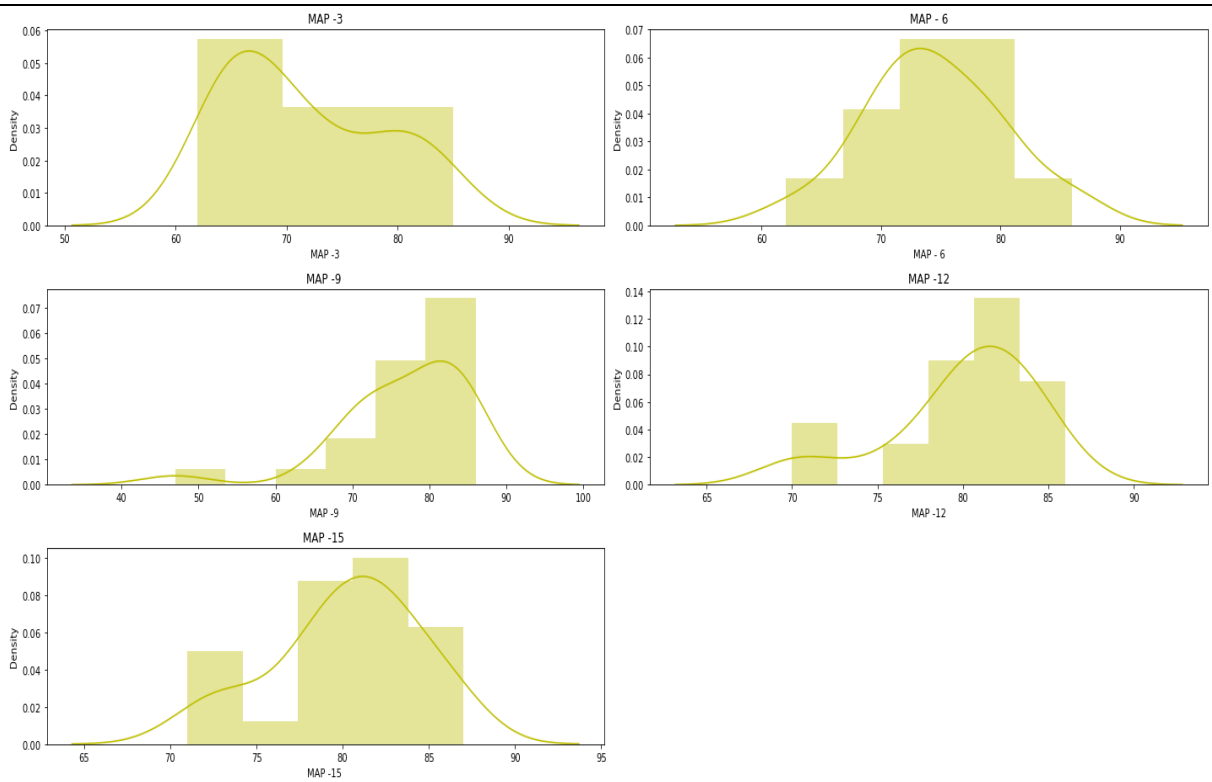

Figure 6: Ephedrine - MAP

	Column	Mean	std_deviation
0	Age	25.68	3.83
1	PR (min)	90.96	7.64
2	PR - 3 min	107.84	12.34
3	PR - 6 min	105.20	8.98
4	PR - 9 min	95.60	5.32
5	PR - 12 min	93.36	9.07
6	PR - 15 min	96.00	5.94
7	SBP (mmHg) - 3	94.32	7.93
8	SBP (mmHg) - 6	100.00	9.43
9	SBP (mmHg) - 9	106.24	6.94
10	SBP (mmHg) - 12	106.88	3.79
11	SBP (mmHg) - 15	105.04	4.55
12	DBP (mmHg) - 3	60.40	7.26
13	DBP (mmHg) - 6	60.88	5.39
14	DBP (mmHg) - 9	65.04	6.88
15	DBP (mmHg) - 12	67.36	5.96
16	DBP (mmHg) - 15	68.64	4.74
17	MAP -3	71.60	7.18
18	MAP - 6	74.48	5.85
19	MAP -9	76.76	8.52
20	MAP -12	80.00	4.33
21	MAP -15	80.20	4.25
22	Dose	25.00	0.00

Figure 7: Ephedrine - Mean & Std Deviation

Mephentermine

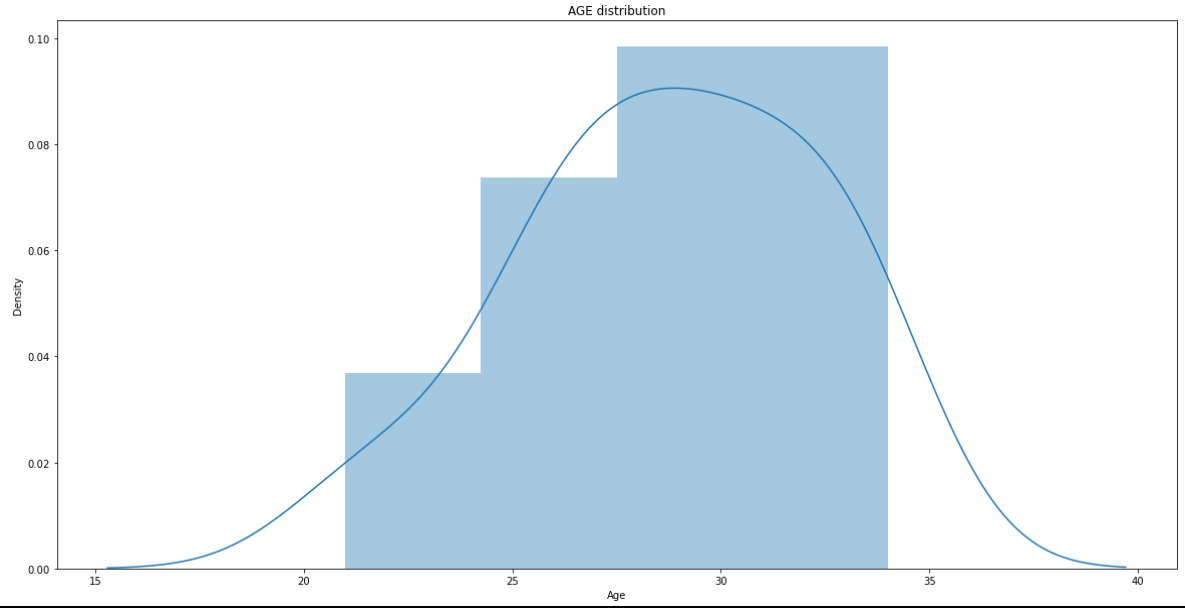

Figure 8: Mephentermine - Age Distribution

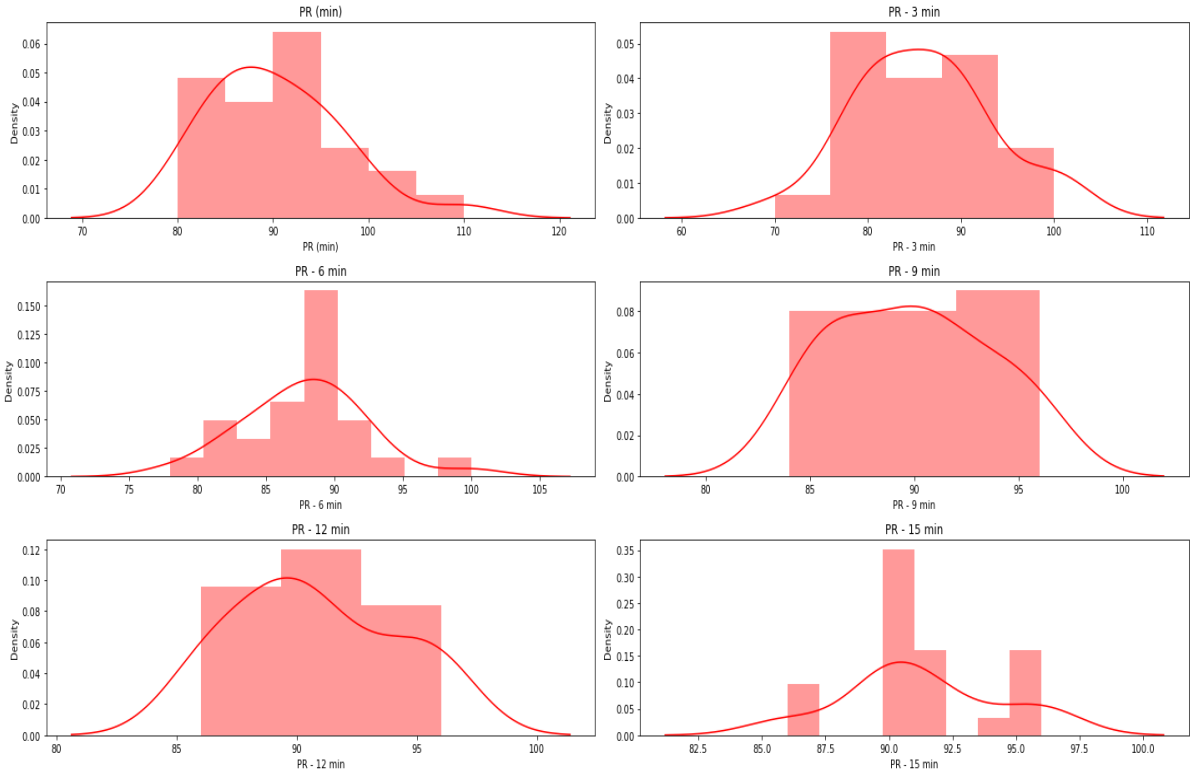

Figure 9: Mephentermine - PR Distribution

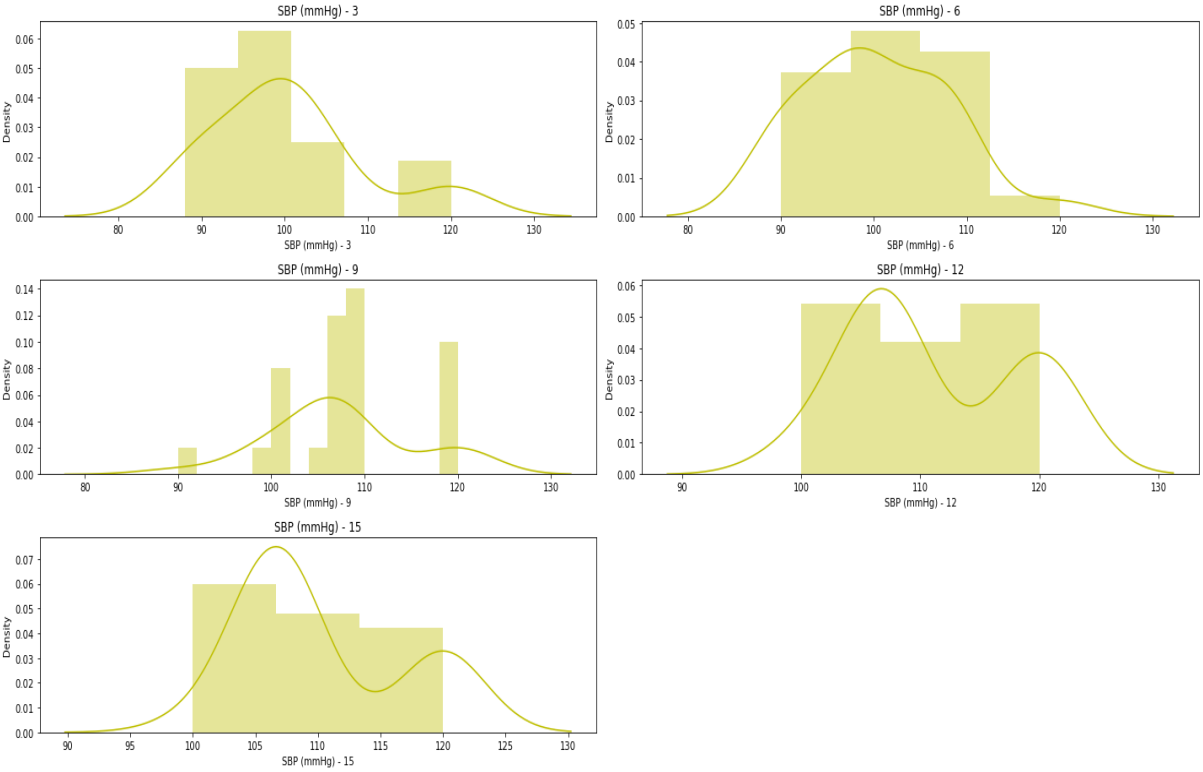

Figure 10: Mephentermine - SBP Distribution

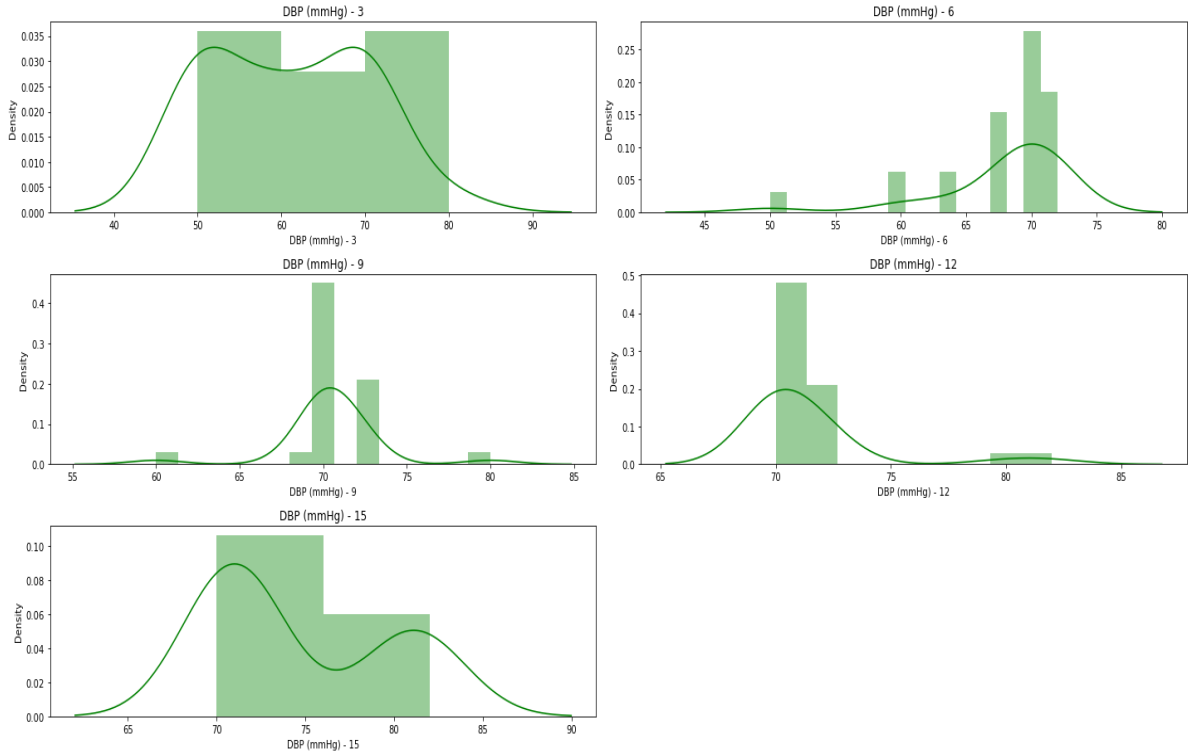

Figure 11: Mephentermine - DBP Distribution

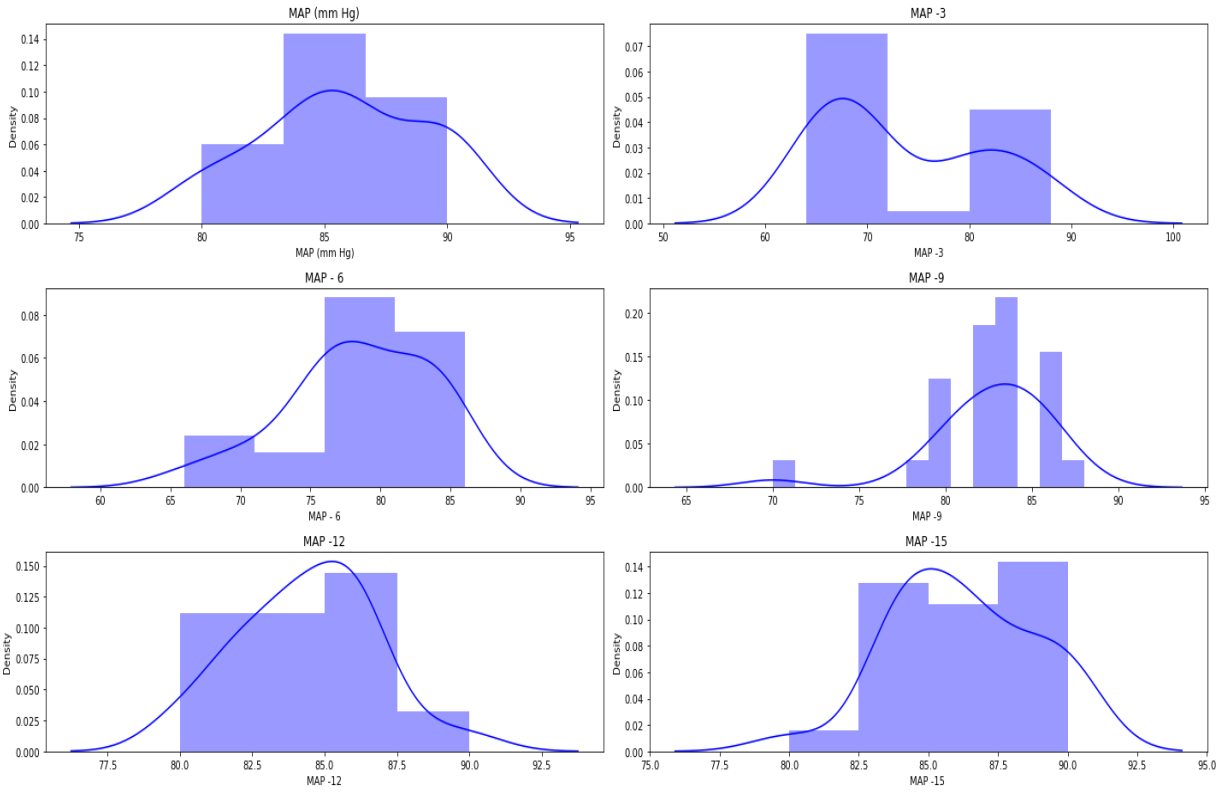

Figure 12: Mephentermine - MAP Distribution

	Column	Mean	std_deviation
0	Age	28.76	3.62
1	PR (min)	90.24	7.06
2	MAP (mm Hg)	85.76	3.38
3	PR - 3 min	86.00	7.46
4	PR - 6 min	87.84	4.58
5	PR - 9 min	89.84	3.78
6	PR - 12 min	90.76	3.41
7	PR - 15 min	91.28	3.05
8	SBP (mmHg) - 3	100.28	9.15
9	SBP (mmHg) - 6	100.32	7.76
10	SBP (mmHg) - 9	107.40	7.70
11	SBP (mmHg) - 12	111.08	7.13
12	SBP (mmHg) - 15	110.16	6.49
13	DBP (mmHg) - 3	60.88	9.29
14	DBP (mmHg) - 6	68.00	5.07
15	DBP (mmHg) - 9	70.48	3.07
16	DBP (mmHg) - 12	71.44	3.03
17	DBP (mmHg) - 15	74.64	5.06
18	MAP -3	73.60	8.14
19	MAP - 6	78.48	5.14
20	MAP -9	82.64	3.59
21	MAP -12	84.40	2.38
22	MAP -15	86.24	2.60

Figure 13: Mephentermine - Mean and Std Deviation

Time (minutes)	Mean Pulse/minute		Mean SBP mmHg	
	E	M	E	M
3	107	86	94	100.2
6	105	87	100	100.3
9	95	89	106.2	107.4
12	93	90	106.8	111.08
15	96	91	105.04	110.16

Table 1: Mean Pulse and SBP Chart

E = Ephedrine
M = Mephentermine

DISCUSSION

Lumbar subarachnoid block involves blockade of preganglionic B fibers leading to profound sympathectomy. Hypotension is the commonest side effect of spinal anaesthesia, whereas neurological deficits, lignocaine toxicity, and total spinal are examples of complications of spinal anesthesia. Several factors in pregnancy have been attributed to post-spinal hypotension. Uteroplacental blood flow increases progressively from about 100 ml per minute in the nonpregnant state to 700-900 ml per minute (approximately 10% of cardiac output at term). Uterine blood flow has minimum autoregulation. The uterine vasculature remains essentially fully dilated in pregnancy. Uterine and placental blood flow depends on maternal cardiac output, directly related to uterine perfusion pressure, and inversely related to uterine vascular resistance. Decreased perfusion pressure can result from maternal hypotension secondary to multiple causes, including hypovolemia from blood loss or dehydration, decreased systemic resistance from general and neuraxial anaesthesia, or aortocaval compression. Increased venous pressure from aortocaval compression, frequent or prolonged uterine contractions, or prolonged uterine contractions or prolonged Valsalva during second stage pushing can all lead to decrease in uterine perfusion. Neuraxial blockade does not alter

uterine blood flow as long as maternal hypotension is avoided, but decreases in maternal blood pressure during neuraxial or general anaesthesia should be immediately corrected.[3]
Endogenous maternal catecholamines and exogenous vasopressors may cause increasing uterine arterial resistance and decreasing uterine blood flow depending on the class and amount given. In pregnant ewe model, use of α-adrenergic vasopressors-methoxamine and metaraminol-increased uterine vascular resistance and decreased uterine blood flow, whereas administration of ephedrine did not reduce uterine blood flow despite dose-induced increases in maternal arterial blood pressure.[4]
As a result, ephedrine was the vasopressor of choice in treatment of hypotension caused by neuraxial anaesthesia in pregnant women. In complete contrast Recent human trials demonstrate the use of phenylephrine which is an α adrenergic agonist for prophylaxis or treatment of neuroaxial induced hypotension, but also is associated with less fetal acidosis and base deficit than use of ephedrine.[5] Phenylephrine is now considered the vasopressor of choice with accumulating evidence of prophylactic infusion.[6] But phenylephrine an alpha agonist results in slowing of maternal heart rate and decrease in cardiac output. Compared to phenylephrine, norepinephrine has similar efficacy on maintaining arterial blood pressure but there was greater heart rate and cardiac output in treatment of post spinal hypotension of section Studies by Dewan et al showed that the use of Adrenergic agents such as phenylephrine, norepinephrine, and methoxamine will increase uterine blood flow in spite of a normalised maternal MAP. In contrast, ephedrine is a mixed α and β agonist which will restore maternal MAP while increasing UBF.

Ephedrine

Ephedrine is a phenethylamine derivative with a pKa of 9.5. It can exist in both ionised and non-ionised forms, depending on the pH of the environment. It has two enantiomers: d-ephedrine and l-ephedrine, with d-form more pharmacologically active. Ephedrine hydrochloride is a mixed-acting sympathomimetic agent. With α agonism, it causes vasoconstriction and increases blood pressure. With β1 agonism, it increases heart rate and contractility. With β2 agonism, it causes bronchodilation and relaxes smooth muscles of bronchi. The drug increases the release of norepinephrine from sympathetic nerve endings, which also contributes to its sympathomimetic effects. Ephedrine inhibits the reuptake of catecholamines and prolongs their actions. Ephedrine crosses the blood-brain barrier and the uteroplacental barrier.[7] Another uudesirable property of ephedrine is tachyphyiaxis where redosing requires increasing doses due to depletion of catecholamine.[8]
It may cause anxiety, insomnia, dizziness, hypertension, and tachycardia. Ephedrine may cause fetal tachycardia in pregnant patients.

OH
|
(Hexagonal benzene ring) - CH - NH
|
CH3

Ephedrine is primarily metabolised in the liver, with some contribution from the kidneys. The elimination half-life is 6 hours, and the duration of action is 60 minutes. The advantages of ephedrine as a vasopressor in post-spinal hypotension (e.g., in C-section) include the maintenance of uterine and uteroplacental blood flow. Counters the bradycardia of spinal anesthesia due to sympathetic blockade. Ephedrine reduces afterload in valvular or functional regurgitation and also in peripartal cardiomyopathy. The undesirable effects of ephedrine are hallucinations, delayed gastric emptying, and urinary retention.

Mephentermine

Mephentermine is an alpha-adrenergic agonist indirectly releasing endogenous norepinephrine to act as a vasopressor and sympathomimetic in the treatment of hypotension.[9] Duration of action is 4 hours and T max is 5-15 min.

It increases cardiac output, but the change in heart rate is variable depending on the degree of vagal tone. High doses of mephentermine (more than 30 mg) can produce hypotension and CNS stimulant symptoms. Mephentermine is rapidly demethylated and hydroxylated. It is excreted unchanged and as metabolites in the urine. Studies comparing the potency of ephedrine and mephentermine in the prevention of postspinal hypotension in C-section were studied by Mohta, Aggarwal, and Gupta et al.[10] Doses less than 15 mg are desirable, whereas large doses may depress the myocardium or produce CNS effects such as anxiety, insomnia, and psychostimulation.

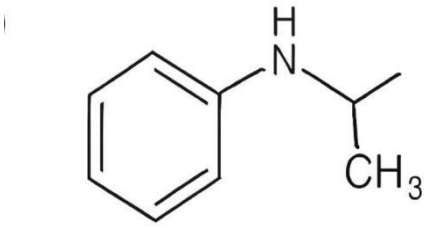

Figure 14

Mephentermine is a substituted phenethylamine and amphetamine and is closely related to phentermine and methamphetamine.[11] Due to recreational abuse, it was made widely unavailable. For hypotension secondary to spinal anesthesia in obstetric patients, 15 mg has been tried as a single dose. In the event of other measures to prevent hypotension, such as co-loading with crystalloids and left uterine displacement, smaller doses such as 6 mg have been used effectively via the intravenous route. Drug-induced hypotension due to phenothiazines, in pheochromocytoma, and patients receiving MAOI drugs, mephentermine is contraindicated. Additive vasoconstricting effects occur with ergot alkaloids and oxytocin. Thus, mephentermine is thought to act as a releasing agent of norepinephrine and dopamine. Indirect stimulation of β receptors through the release of noradrenaline from storage sites leads to a positive inotropic effect on the myocardium, AV conduction, and refractory period.

The refractory period of the AV node is shortened with an increase in ventricular conduction velocity. Mephentermine tends to dilate arteries and arterioles in skeletal muscle and the mesenteric vascular bed, increasing venous return.

CONCLUSION

Post-spinal hypotension is of particular significance in obstetrics in view of reduced uteroplacental blood flow and eventual fetal hypoxia. Increasing C-section deliveries also involves high-risk pregnancies and comorbidities. Post-spinal hypotension in C-section has been a concern.

Traditionally treated with Ephedrine, a mixed sympathomimetic, for its maintenance of uteroplacental blood flow. The frequency of need for repeated doses, tachyphylaxis, and tachycardia demanded a search for either a supplement or an alternative. Mephentermine, which was in considerable usage in the last decade, has been taken up in low doses such as 6 mg intravenously, and appears to satisfy the requirements of a stable heart rate, a sustained response with a single dose, and the absence of overshoot hypotension, along with normal umbilical venous pH levels. In the absence of organic hypotension and mood disorders, mephentermine promises a suitable alternative to ephedrine. However, limitations pertain to the availability of the drug, as it is branded to be a drug of recreational abuse.

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