

Reduced Hypotension After Subarachnoid Anaesthesia With Ondansetron Most Colloids In Parturients Undergoing Caesarean Section. A Retrospective Study.

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Citation

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Abstract

The purpose of this retrospective study was to estimate the frequency of hypotension and bradycardia in parturients undergoing caesarean section, after the introduction of a protocol providing for the administration of colloids (HydroxyEthylStarch, HES 6%) 500 ml for hypotension prevention after spinal anaesthesia and the administration of Ondansetron (8 mg) for nausea and vomiting prevention. We reviewed the anaesthesiology records of the patients who underwent to caesarean section in spinal anaesthesia, in Nocera Inferiore Hospital (Salerno), between January 2012 and May 2012. 54 patients were examined. Retrospective examination of the records showed a 16,6% incidence of systolic hypotension, and 25,9% of diastolic hypotension. The average consumption of Ephedrine was 5.91 mg. Only 4 (7,4%) patients had an episode of bradycardia, HR < 60, no < 58. The association HES 6% plus Ondansetron seems to reduce the incidence of arterial hypotension in parturients undergoing caesarean section, compared to the incidence of hypotension reported in literature.

INTRODUCTION

Spinal anaesthesia is the preferred anaesthetic technique for elective Caesarean deliveries. Hypotension and bradycardia are the most common side effect [1, 2] and have both maternal and neonatal consequences. The incidence of hypotension and bradycardia has been reported to be 33% and 13%, in non obstetric patients, in obstetric, non labouring patients, the incidence of hypotension has been estimated to be as high as 50-60%. Both of them may be induced by sympathetic nerve blockade. Hypotension occurs from decreases in systemic vascular resistance and central venous pressure from sympathetic block with vasodilation [3-6]. Bradycardia can occur from shift in cardiac autonomic balance toward the parasympathetic system, from activation of left ventricular mechanoreceptors from a sudden decrease in left ventricular volume (Bezold Jarisch reflex) (BJR), or from increases in baroreflex activity [7]. The Bezold Jarisch reflex may be mediated by peripheral serotonin receptors (5-HT₃) [8].

Different strategies have been attempted to prevent spinal-induced hypotension. Prophylactic measures include prehydration with crystalloid or colloid or administration of vasoactive agents.

Sahoo et al. observed that Ondansetron 4 mg, given intravenously 5 min before subarachnoid block reduced hypotension and vasopressor use in parturients undergoing elective caesarean section [9].

From 6 months in our Anaesthesia Care Unit it is used as premedication in the obstetric patient to undergo elective Caesarean section, a protocol that provides for the administration of Colloid 500 ml and Ondansetron 8 mg for nausea and vomiting prevention.

The aim of this retrospective study was to verify that the blockade of serotonin receptors type 5 HT₃ by intravenous ondansetron administration plus the colloid premedication might reduce hypotension and bradycardia induced by spinal anaesthesia in parturients undergoing caesarean section.

MATERIAL AND METHOD

This Retrospective cohort study, has been designed to testify that spinal induced hypotension and bradycardia could be minimized with the use of intravenous Ondansetron[®] (Fresenius Kabi) associated to preanaesthesia administration of colloid HydroxyEthylStarch (HES) 6% (Voluven[®] Fresenius Kabi), in parturients undergoing caesarean section.

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We reviewed the anaesthesiology records of the patients who underwent to caesarean section in spinal anaesthesia, in Nocera Inferiore Hospital (Salerno), between January 2012 and May 2012.

Because patients were not submitted to investigational actions, but treated with usual care and the routinely gathered patient data are collected in the anaesthesiology records, there was no need for written informed consent and it was not sought the opinion of ethics committee.

The decision to proceed with operative delivery was made by obstetric team independent of the investigators.

Since 6 months in our Anaesthesia Care Unit a new protocol in preanaesthesia is used in parturients undergoing caesarean section that expected for the administration of colloids, HES 6% (Voluven®) 500 ml to prevent arterial hypotension after spinal anaesthesia and ondansetron 8 mg for the prevention of nausea and vomiting.

Obstetric patients who were ASA physical status I, II, between 20 and 45 years of age and undergoing an elective caesarean section were included.

Exclusion criteria were as follows: patients with contraindications to subarachnoid block (patient refusal, unstable haemodynamic, coagulation abnormality), history of hypersensitivity to Ondansetron or local anaesthetic agents, cardiovascular insufficiency, gestational hypertension, chronic hypertension, receiving selective serotonin reuptake inhibitors, diabetes, weight > 100 kg, twin pregnancy, anaemia, known issues fetal.

The antepartum management was according to the established protocol of our institution. In the preanaesthesia room, a peripheral 18-gauge i.e. cannula was inserted. All patients received prehydration with colloid solutions, HES 6% given 30 min before subarachnoid anaesthesia and ranitidine 1 mg/Kg. In the operating room non invasive blood pressure (BP), pulse rate, and pulse oximetry (SPO₂) were recorded.

Patients received intravenous Ondansetron 8 mg diluted in 10 ml of normal saline solution over 1-5 min before spinal anaesthesia.

The spinal technique was performed with the patient in sitting position at L3-L4, L2-L3 interspace using a 27-gauge Whitacre spinal needle.

When free flow of cerebrospinal fluid was observed, 0,5% hyperbaric bupivacaine 2 ml (10 mg) was injected without barbotage. Subsequently, the patients were placed in the lithotomy position and bladder catheter was inserted.

Usually, data regarding age, height and weight, haemodynamic parameters, the presences of nausea, vomiting, discomfort or inadequate analgesia is collected in the anaesthesiology records.

Motor block was assessed after the subarachnoid anaesthesia using the modified Bromage scale, and scored as 0 = no motor block, 1 = being unable to move the hip, 2 = being unable to move the knee, and 3 = being unable to move the ankle. Fifteen minutes after intrathecal injection, the level of sensory block was assessed.

Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), Mean blood pressure (MBP) and oxygen saturation (SPO₂) were recorded at time of spinal anaesthesia and at 5-min intervals until the end of surgery. The intraoperative IV sedative medications, fluid volume administered, and estimated blood loss were also recorded.

Side effects of spinal anaesthesia were recorded.

Hypotension defined as SBP < 90 mmHg or MBP < 70 mmHg were treated with I.V. Ephedrine boluses of 5 mg, if any patient required more than 50 mg Ephedrine, this was interpreted as tachyphylaxis and Phenylephrine 50 ug was administered. HR < 60 beats/min was treated with Atropine 0,5 mg. Pain was treated with Tramadol and Fentanyl. If pain persisted after a single dose of Fentanyl was considered a failed spinal anaesthetic, converted to general anaesthesia.

STATISTICAL ANALYSIS

Statistical analysis was performed by using SPSS 20.

Data were expressed as mean ± standard deviation and frequencies. Multiple comparisons of SBP and MBP were performed using an analysis of variance (ANOVA) test for repeated measurements, followed by Bonferroni test for post hoc testing.

Paired Student's test was used for comparing measures of SBP and MBP with baseline value as the control. All analysis was 2-tailed. P < 0,05 was considered statistically significant.

RESULTS

A total of 54 patients were identified. The demographic data

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of patients are shown in table 1. 10 patients were excluded from the analysis, 2 > 100 kg, 1 gestational diabetes, 7 coagulation abnormalities.

9 patients had an episode of systolic blood hypotension, 16,6%, 14 had a diastolic blood hypotension, 25,9% (Table 1, Figure 1).

As can be seen from Table 1, the average consumption of Ephedrine was 5.91 mg. No other vasoconstrictor medication was used.

1 patient had discomfort such as to require the administration of Tramadol 100 mg (table 1). 2 patients had motor block of Bromage score 1; all the rest had a Bromage scale score 0. Only 4 (7,4%) patients had an episode of bradycardia, HR < 60, no < 58 (Table1, Figure 1).

It was performed analysis of variance for repeated measures to test whether there were differences in systolic and mean arterial pressure in the patient population studied in 5 different times of the Caesarean delivery, baseline, after 5 minutes, 10 minutes, 15 minutes and 20 minutes after subarachnoid anaesthesia. The test proved significant, $F = 23.051$, $p < 0,01$ (SBP), $F = 11.918$, $P < 0,01$ (MBP). Subsequent post-hoc tests, performed with Bonferroni correction of significance level, showed that there were significant differences between the values of 5, 10, 15 and 20 minutes, while blood pressure was significantly higher only in the baseline (Figure 2, 3).

Subsequently, paired sample t-tests, using as a reference value of systolic and mean arterial pressure, beyond which we considered low blood pressure, 90 mmHg for SBP, 70 mmHg for the MBP, to see if the baseline systolic and mean arterial pressure, were significantly different from values detected after subarachnoid anaesthesia. The result was that after 5, 10, 15, 20 minutes after subarachnoid anaesthesia, the values of the SBP and MBP were significantly higher compared to 90 and 70 mmHg (Figure 2, 3).

Figure 1

Table 1. Maternal Data and results

| | Min | Max | Mean | |
|---------------------|-----------|----------|----------------|----------|
| Age (yr.) | 19 | 40 | 31,34 ± 5,344 | Mean |
| Weight (Kg) | 55 | 100 | 77,39 ± 11,624 | Mean |
| Height (cm) | 148 | 170 | 159,25 ± 5,653 | Mean |
| Ephedrine (mg) | 0 | 50 | 5,91 ± 15,069 | Mean |
| Block of Bromage | 0 = 52 Pz | 1 = 2 Pz | 2 = 0 Pz | 3 = 0 Pz |
| Results | | | | |
| Discomfort (n. Pz.) | 1/54 | | 1,85% | |
| SBP | < 90 mmHg | 9/54 | 16,6% | |
| | > 90 mmHg | 45/54 | 83,3% | |
| DBP | < 60 mmHg | 14/54 | 25,9% | |
| | > 60 mmHg | 40/54 | 74% | |
| Bradycardia | < 60 HR | 4/54 | 7,4% | |
| Bradycardia | < 58 HR | 0/54 | 0% | |

Abbreviations: SBP: systolic blood pressure. DBP: diastolic blood pressure. Pz: patients

Figure 2

Figure 1: results. SBD: Systolic Blood Pressure. DBP: diastolic Blood Pressure

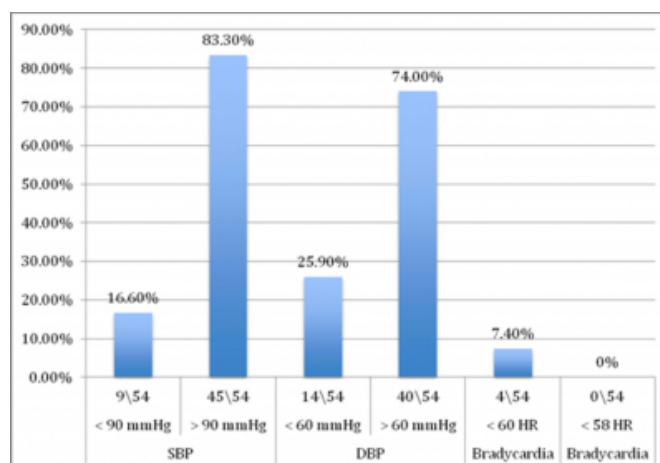


Figure 3

Figure 2: The result was that after 5, 10, 15, 20 minutes after subarachnoid anaesthesia, the values of the SBP (Systolic Blood Pressure) were significantly higher compared to 90 mmHg

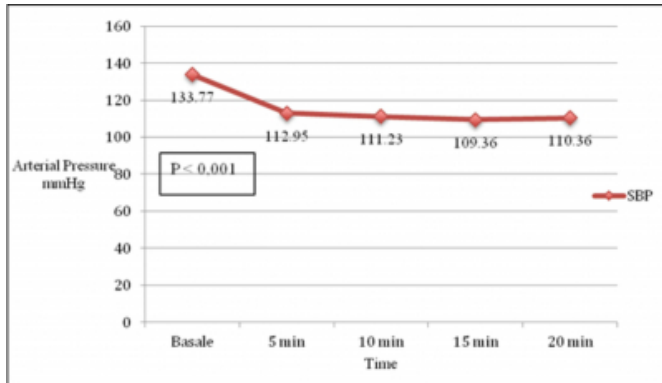
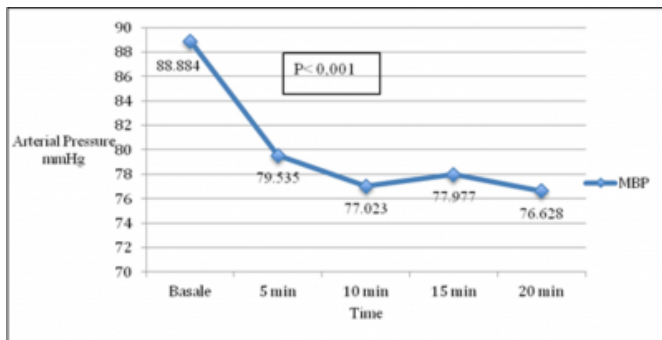


Figure 4

Figure 3: The result was that after 5, 10, 15, 20 minutes after subarachnoid anaesthesia, the values of the MBP (Mean Blood Pressure) were significantly higher compared to 70 mmHg



DISCUSSION

Different strategies have been attempted to prevent spinal-induced hypotension. Prophylactic measures include prehydration with crystalloid or colloid or administration of vasoactive agents. Prehydration of crystalloid (250 – 2,000 ml) [2, 6, 10-13] does not appear to confer additional benefit over small volumes (250 ml) and may be detrimental to patients with limited cardiopulmonary reserve.

Although current evidence has shown crystalloid prehydration (preload) not to be effective for preventing hypotension, a survey of practice shows that fluid therapy remains popular [14].

Prehydration with colloid (≥ 500 ml) appears to be more effective than crystalloid at maintaining arterial blood pressure and perhaps decreasing incidence of hypotension

[12]. The greater effectiveness of colloid is a result of effect for increasing central venous pressure and cardiac output caused by slower redistribution out of the intravascular space.

Recent studies have reconfirmed that colloids are more effective than crystalloids. Madi-Jebara et al. [15] compared prehydration with 1000 ml lactated Ringer's solution versus 500 ml hydroxyethyl starch (HES) 130/0.4 solution. In the colloid group, the incidence of hypotension was smaller (63.9 versus 81.4%, $P = 0.033$), the minimal recorded SBP was higher and the maximum recorded HR was lower.

Tamilselvan et al. [16] used suprasternal Doppler ultrasound to measure CO changes after prehydration with either 1500 ml lactated Ringer's solution, or either 500 ml or 1000 ml 6% HES solution. They showed that prehydration increased CO in all groups but the effect was greater with colloid and more sustained in the larger volume colloid group. There was no difference in the incidence of hypotension among groups, although the study was not powered for this outcome.

Colloid solutions, such as 5% albumin, 6% hydroxyethylstarch (HES), and gelatin, are also used for preventing the hypotension associated with spinal anaesthesia [17, 18]. Preloading the circulation with crystalloids or colloids is aimed at the volume expansion that alleviates the vasodilation induced by spinal anaesthesia.

Different studies [19, 20] indicate that colloid is superior to crystalloid in preventing post spinal hypotension for elective caesarean delivery.

A physiologic explanation of the differences between crystalloid and colloid can be found in Ueyama study [12], which elegantly showed that, at 30 minutes, only 28% of the administered lactated Ringer's solution remained in the intravascular space compared with 100% of the HES solution.

With increasing volumes of HES, there was an increase in blood volume and cardiac output and a decrease in the incidence of hypotension. Colloid is a more effective volume expander because it remains longer in the intravascular compartment.

Nevertheless, even aggressive expansion of the intravascular space cannot completely abolish the risk of hypotension.

Rout and Rocke [3, 13] suggest that colloids may contribute

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to decreased afterload via atrial natriuretic peptide release from a stretched atrium or by peripheral vasodilation caused by reduced arterial blood oxygen content. Reducing before central sympathetic block may play an important role in the prevention of post spinal hypotension.

Various colloids were used and Vercauteren et al. [21] showed that HES was superior to modified gelatin but failed to offer an explanation.

Prophylactic administration of pharmacologic agents may be more effective than prehydration for prevention of hypotension [22]. α -Adrenergic agonists (phenylephrine) reliably increase arterial blood pressure by increasing systemic vascular resistance; however, heart rate and cardiac output may decrease because of increased afterload [2, 6, 23].

Data from elective cases have shown that phenylephrine does not appear to be harmful to the fetus when given in the dose range required to prevent hypotension. Evidence for this comes from the observation that phenylephrine has fewer propensities to depress fetal pH [24] and base excess than ephedrine. However, a number of controversies remain.

Mixed α - and β -adrenergic agents (ephedrine) are also effective for increasing arterial blood pressure and preventing hypotension but act by primarily increasing heart rate and cardiac output with a smaller increase in systemic vascular resistance [4].

Historically, ephedrine was recommended as the vasopressor of choice in obstetrics but there is now increasing evidence that ephedrine has the propensity to decrease fetal pH and base excess, especially in comparison with other vasopressors.

The reason why ephedrine depresses fetal acid–base status more than phenylephrine is controversial. Older studies focused on differential effects of vasopressors on uteroplacental circulation. However, Ngan Kee et al. [25] showed that ephedrine crosses the placenta more readily than phenylephrine. This was associated with greater fetal concentrations of lactate, glucose and catecholamines, and thus supports the hypothesis that depression of fetal pH and metabolic effects secondary to stimulation of fetal beta-adrenergic receptors cause base excess with ephedrine.

Anaesthesia textbooks recommend bupivacaine in a dose of between 12 and 15 mg [26, 27]. However this dose range has

been associated with an incidence of maternal arterial hypotension of 69% to > 80% [28].

The use of a lower dose aims to decrease maternal side effects (hypotension, nausea, vomiting). However, such a strategy could compromise the adequacy of anaesthesia, and require supplementary analgesia, with possible neonatal consequences and may require conversion to general anaesthesia [29, 30].

In our anaesthesia care unit since in use an aesthetic protocol that provides for the administration 500 ml of colloid (Voluven[®]) and ondansetron[®] 8 mg before subarachnoid anaesthesia in elective Caesarean section, with a standard dose of hyperbaric bupivacaine 10 mg.

This protocol is the result of a growing awareness of both patients and anaesthesiologists in minimizing the side effects of subarachnoid without reducing analgesia or increasing discomfort for patients.

The most important finding of our retrospective study is the observation of a low percentage of hypotension in patients who received Ondansetron[®] and Voluven[®] as premedication before subarachnoid anaesthesia.

In fact, the percentage of systolic hypotension was 16,6% and diastolic hypotension of 25,9%.

Large surveillance studies observed incidences of hypotension around 33% and bradycardia around 13% in non obstetric populations [1, 2]. Risk factors for hypotension in non obstetric populations include block height T5 or greater, age 40 yr. or greater, baseline systolic blood pressure less than 120 mmHg, and spinal puncture above L3–L4.

Cardiovascular effects of spinal anaesthesia typically include a decrease in arterial blood pressure and central venous pressure with minor decreases in heart rate, stroke volume [3, 4]. Our data clearly show that the incidence of systolic hypotension, around 16%, is lower than the average in the non obstetric population.

A Cochrane Collaboration's review [31] has clarified this issue.

Although some interventions, such as colloids, ephedrine can reduce the incidence of hypotension, none have been shown to eliminate the need to treat maternal hypotension during spinal anaesthesia for caesarean section. In control

(untreated) groups in this review, the incidence of hypotension was about 70%. This was reduced to about 50% in women treated with colloids or lower limb compression, and to about 40% in women treated with ephedrine (average over several doses) [31].

While hypotension results primarily from decreased vascular resistance, bradycardia is secondary to a relative parasympathetic dominance, increased baroreceptor activity, or induction of the Bezold Jarisch Reflex (BJR).

Owczuk et al. [8] observed that intravenous ondansetron attenuated spinal-induced hypotension.

Mechanoreceptors in the heart wall that trigger the BJR, participate in systemic responses to hyper- and hypovolaemia [32, 33]. In response to hypovolaemia, stimulation of cardiac sensory receptors in the left ventricle induces the BJR and results in reflex bradycardia, vasodilation and hypotension [34].

Chemoreceptors are activated in response to decreased blood volume by serotonin [33], which is released from activated thrombocytes. Activation of 5-HT₃ receptors, which are G protein coupled, ligand-gated fast-ion channels, results in increased efferent vagal nerve activity, frequently producing bradycardia [35].

Sahoo et al. [9] hypothesized that ondansetron prevented the serotonin-induced BJR, suppressed venodilatation, augmented venous return to the heart and resulted in lesser reductions in SBP and MBP.

In our retrospective study, the percentage of bradycardia was 7.4% (heart rate < 60); no patient had a heart rate < 58.

We can observe in the present study a larger reduction of SBP than DBP. These data are similar with those observed by Owczuk et al. [8].

Moreover the drop of systolic and mean pressure is significant only after 5 minutes after subarachnoid anaesthesia, while after 10, 15 and 20 minutes the values remain constant.

Analysing in particular the drop in blood pressure after the first five minutes after subarachnoid anaesthesia, we noted that compared to 90 mmHg for the SBP and 70 mmHg for the MBP, values under which we define hypotension, SBP and MBP remain significantly higher than the corresponding values for us to hypotension.

This study revealed that a fall systolic and mean blood pressure might be reduced by premedication with Ondansetron and colloid HES 6% before spinal anaesthesia in the caesarean section.

Limitations in this study are the retrospective character, large prospective randomized are needed to evaluate that ondansetron plus colloid premedication can attenuate decreases in blood pressure following spinal anaesthesia in parturients undergoing elective caesarean section.

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