Hypotension after spinal anaesthesia is not always the rule in parturients undergoing caesarean section

Mona Refaat Hosny[1*], Mohamed Saleh Ahmed[2], Wail Ahmed Abdelaal[1], Dalia M Elfawy[1]
Assistant Professor of Anaesthesiology[1], Lecturer[2], Faculty of Medicine, Ain -Shams University, Cairo, Egypt
Corresponding author: monamourmar@hotmail.com
ORCID ID: https://orcid.org/7027120=8066
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Background
General anaesthesia is a real challenge for the anaesthetist when anaesthetizing obstetric patients due its well-known complications of difficult intubation and thereby increasing morbidity and mortality of pregnant women. These risks can be easily avoided by regional anaesthesia.

Spinal anaesthesia is frequently associated with hypotension which can have detrimental effects both on the mother and the neonate. Prophylactic phenylephrine administration had been widely practiced to prevent post-spinal hypotension during caesarean section. The goal of this study is to prove and determine that it is not always necessary to use a vasoconstrictor to avoid hypotension after spinal anesthesia for parturients undergoing caesarean section.

Methods
We enrolled 100 patients in this randomized controlled study who were having elective caesarean delivery.

Spinal anaesthesia was performed under aseptic conditions. Immediately following spinal blockade, patients were randomly allocated to receive either a single bolus of phenylephrine 100µg in a volume of 10 ml, or equivalent volume of normal saline 0.9%.

Incidence of post-spinal hypotension was used as the primary outcome. Maternal haemodynamic parameters, intraoperative nausea and vomiting, the need for phenylephrine or glycopyrrolate administration, neonatal Apgar score at 1, 5 minutes, and base excess (BE) value of the neonatal umbilical venous blood were all recorded and reflected the secondary outcome

Results
There was no significant difference regarding the incidence of post-spinal hypotension in phenylephrine and placebo group. There was no difference in neonatal Apgar score at 1, 5 minutes, and base excess in both groups.

Conclusion
The present study had demonstrated that it is not always necessary to provide a vasoconstrictor to avoid hypotension that results from spinal anaesthesia in caesarean sections.

Keywords: Caesarean delivery; vasoconstrictors; regional blockade

Introduction

It is well known that performing spinal anaesthesia for caesarean delivery decreases the risk of morbidity and mortality of general anaesthesia which could expose the obstetric patient to incidence of difficult intubation or Mendelson's syndrome.

It is as well-known that hypotension is a very common complication after spinal anaesthesia particularly in obstetric patients undergoing caesarean delivery and it's probable and possible sequalae on both the mother and the foetus in deceasing the utero-placental blood flow resulting in fetal acidosis.[1]

Over the last two decades, studies compared ephedrine versus alpha adrenergic agonists in avoiding foetal acidosis after caesarean sections.

Phenylephrine is a synthetic non-catecholamine α_1 adrenergic agonist that has

a short duration of action being metabolized by catechol O-methyltransferase and monoamine oxidase. Phenylephrine was considered not suitable for obstetric anaesthesia because of the concerns regarding vasoconstriction induced diminished placental blood flow.[2]

The goal of this study is to prove and demonstrate that it is not always necessary to use a vasoconstrictor to avoid hypotension after spinal anaesthesia for parturients subject to caesarean delivery.

Patients and Method

This study was performed at Ain Shams University Maternity Hospital after obtaining consent from all patients and getting the ethical committee approval. The study was registered on Pan African Clinical Trials Registry.

100 patients were enrolled into this prospective double blinded randomized controlled study. Inclusion criteria were ASA I or II patients, full term, single pregnancy, elective caesarean section, aged 20-35 years old, and height 160-170 cm. Exclusion criteria were emergency caesarean section, any maternal or fetal comorbidity, or a BMI >35kg/m^2.

Patients were randomly divided into two equal groups using computer-generated sequence. Allocation concealment was done using sequentially numbered, opaque sealed envelopes. The envelope was opened, and subsequent injectant was prepared by clinical pharmacist. Data collection and data analysis were done by anaesthetist who was blinded to the patient's allocation group.

Anaesthetic technique was standardized for all patients. After careful history taking, a thorough physical examination was conducted which included assessment of the mother's general condition, cardiac, chest and airway examination and a review of the results of laboratory investigations.

Patients were premedicated with ranitidine 150mg given two hours before arriving to the operative theatre. Metoclopramide 10mg and Na citrate syrup 30ml were also given 30 minutes before arriving to the operative theatre. Midazolam 2mg was given upon admission to the operative theatre.

In both groups and just before being admitted to theatre, patients were preloaded with 500ml of ringer lactate solution and another 500ml was given whilst performing the spinal anaesthetic.

In the operating theatre, all patients were put on ASA standard monitoring, including 5 lead ECG, non-invasive blood pressure monitoring and pulse oximetry for oxygen saturation. Baseline values were recorded for all patients. Any deviation from normal values subjected the parturient involved to be excluded from the study.

Spinal anaesthesia was performed in the left lateral decubitus position under aseptic conditions, using 25-gaugeWhitacre needle at lumbar level 3-4. Hyperbaric levobupivacaine 0.5% (7.5 mg), and fentanyl 25µg, were slowly injected over a period of 30 seconds after observing CSF flow.

Immediately following spinal blockade, patients were turned into supine position with 15^0 left lateral tilt to avoid aortocaval compression. Face oxygen mask 5 liters was applied. Patients were randomly allocated into one of the following groups:

- Group 1: received a single bolus of phenylephrine 100µg in 10ml normal saline (phenylephrine hydrochloride solution, Claris Lifesciences, Inc., India).
- Group 2: received equivalent volume of normal saline 0.9%

The injectant was anonymous to the anaesthetist who was performing the spinal anaesthesia. After performing the block, the patient was immediately turned to the supine position with 15 degrees left lateral tilting. Sensory blockade was assessed bilaterally using cold ice. T5 block was considered satisfactory. and this level was achieved to all of our patients included in this study.

Surgeon was allowed to start surgery 5 minutes after the spinal anaesthesia. Any deviation from the above criteria rendered the patient to be excluded from the study.

Blood pressure was measured every 2 minutes till skin incision and every 5 minutes thereafter. Hypotension was considered if systolic pressure decreased below 30% from the patient baseline value or if she experienced any kind of dizziness, nausea, vomiting or respiratory depression. A bolus dose of open label phenylephrine 0.1µg/ kg was injected on this occasion as a rescue and was recorded.

Any drop of the heart rate below 50 beats / minute, glycopyrrolate 0.1mg was given.

Another 500ml of ringer lactate solution was started slowly after delivery of the baby to which 20 IU of oxytocin was added and was continued till the patient was discharged to the recovery room.

Parameters of the study

Incidence of post-spinal hypotension was used as the primary outcome. Post-spinal hypotension was defined as a decrease in the systolic arterial pressure below 30% from the baseline value, or the patient became symptomatic in the form of dizziness, nausea, vomiting or respiratory depression.[3]

Maternal haemodynamic parameters, intraoperative nausea and vomiting, the need for phenylephrine or glycopyrrolate, neonatal Apgar score at 1, 5 minutes, and base excess (BE) value of the neonatal umbilical venous blood were measures of the secondary outcome.

Statistical analysis

Data were analyzed using Statistical Package for Social Science (SPSS) version 21.0. Chicago, Illinois, USA. Quantitative data were expressed as mean ± standard deviation. Qualitative data were expressed as count and percentage. The independent-samples t-test was used to compare between means in the two groups, and independent samples-median test was used to compare between medians in both groups. Chi square test was used to compare proportions between two qualitative parameters. $P < 0.05$ was considered significant and $P < 0.01$ was considered highly significant.

Sample size calculation

Sample size was calculated using PASS program, setting alpha error at 5%, and power at 80%, assuming 20% difference between the 2 study groups, produced a minimal sample size of 42 per group, rounded to 50 cases per each group.

Results

The study enrolled pregnant ladies between 20 and 35 years of age and their gestational age was between 39 and 40 weeks**.**

Equal amount of fluids was administered to both groups until the baby's delivery. Nausea and vomiting were higher in the control group, but without clinical significance (6 in phenylephrine group while 8 in control group). There was difference regarding rescue dose administration and of extra phenylephrine and glycopyrrolate given in both groups (Table 1). Findings which were evaluated among pregnant women enrolled showed no significant difference regarding the incidence of hypotension (need for phenylephrine) (Table 1) between the two groups, however there was decrease in mean systolic blood pressure in both groups at T1, T2 as well as incidence of tachycardia, reactive hypertension and need for infusion discontinuation. There was no statistical difference between the two groups as reflected in (Figure 1, 2). Clinical evaluation of newborns showed no difference in Apgar scores at the 1st minute; was 8 in both groups and then became 10 in 5th minute between the two groups, the acid base of umbilical blood sample (Base excess was 1.714 at phenylephrine group, 1.738 in control group without significant difference) (Table 2)

Table 1: Descriptive analysis of the parturients, side effects and rescue doses needed

	Group phenylephrine (50)	Control group (50)	P value
Age (years)	29.10±3.683	28.58±2.612	0.417°
Gestational age (weeks)	39.876±.3761	39.810±.3559	0.370°
Nausea & vomiting no. of patients (%)	6(12%)	8(16%)	0.564*
Need for phenylephrine no. of patients (%)	4(8%)	10(20%)	0.084*
Need for glycopyrrolate no. of patients (%)	3(6%)	8(16%)	0.110*

Data are presented as mean± SD or count (%)
Measured by independent t-test
*Measured by chi-square test

Table 2: Neonatal parameters in both groups

	Group Phenylephrine (50)	Control group (50)	P value
Apgar score 1 minute	8(7-9)	8(7-9)	0.758°
Apgar score 5 minutes	10(9-10)	10(9-10)	0.538°
Base excess BE (meq/l)	1.714±0.247	1.738±0.219	0.609*

Data are presented as mean± SD or median(range)
°Measured by independent samples median test
*Measured by independent t-test

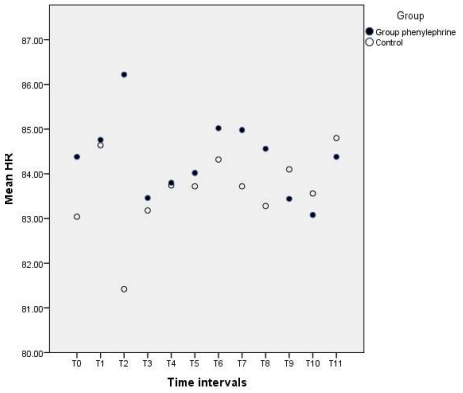

Figure 1: Scatter plot showing mean heart rate in both groups at different time intervals

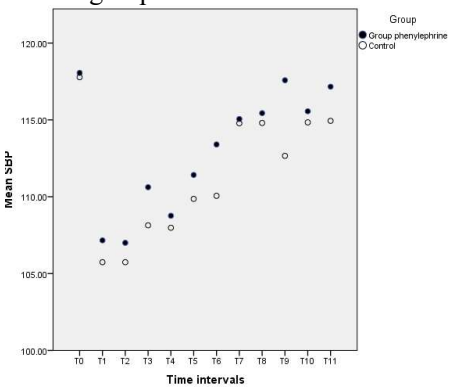

Figure 2: Scatter plot showing mean systolic blood pressure in both groups at different time intervals

Discussion

Spinal anaesthesia had become the recommended anaesthetic technique for elective caesarean section, as it is associated with a relatively lower risk when compared to general anaesthesia.

However, spinal anaesthesia is still associated with complications of post-spinal hypotension which is not uncommon as per most research work worldwide. Post spinal hypotension may lead to lower placental perfusion, which is associated with neonatal acidosis and may lead to potentially unfavorable neonatal outcome. Early detection of post-spinal hypotension and proper management could effectively prevent maternal and neonatal complications.[1]

Post-spinal hypotension could be prevented and managed by intravenous fluid infusion, avoidance of aortocaval compression, and reasonable use of vasopressors. Yet, there is no single intervention that had demonstrated the avoidance of the use of vasoconstrictors in the management of post-spinal hypotension.[4]

No significant difference was found in the two study groups with regards to post spinal hypotension in both placebo and phenylephrine group. This could be explained by the adequate fluid preloading, as all our patients were hydrated with 500 ml of ringer's lactate, which was started before spinal anaesthesia. Although, Ueyama and colleagues have shown an inadequacy of fluid hydration due to rapid fluid redistribution[5], Xu and colleagues calculated the effective volume of fluid preload to prevent post-spinal hypotension to be approximately 13 mL.kg-1.[6]

Fear of aortocaval compression is routine in obstetric anaesthesia and that is supported by history and tradition. Patient positioning in supine with a 15-degree left lateral tilt after spinal anaesthesia had shown to be associated with less post-spinal hypotension, and improved cardiac output.[7]

Based on statistical analysis of computerized anaesthesia records, Brenck and colleagues identified maternal age, body mass index, and peak sensory block height as independent risk factors for post-spinal hypotension.[8]

In fact, advanced maternal age had been identified as a risk factor of post-spinal hypotension during caesarean section in a few number of studies which assessed multiple risk factors[8-9] with one study suggesting maternal age greater than 35 being the cut-off value.[12] Maternal age ranged between 20-35 years in our study. Moreover, incidence of hypotension is more common in patients with high body mass index (BMI) varying between 25 and 29 kg/m^2 which was the cutoff point.[10] In the present study, patients' BMI was less than 30.kg/m^2.

There are multiple factors that can affect intrathecal drug spread and thus the peak of the sensory block height including physical characteristics of injected solution, clinical technique during spinal anaesthesia, and the patient characteristics.[11]It had been demonstrated that intrathecal hyperbaric bupivacaine had a more rapid onset of sensory blockade when compared to isobaric bupivacaine.[12] Moreover, low-dose intrathecal levobupivacaine limits post-spinal hypotension.[13] In the present study, we used a low dose of hyperbaric levobupivacaine

supplemented with intrathecal fentanyl. which were injected at a very slow pace over 30 secs hence adopting optimal conditions to avoid hypotension. The local anaesthetic dose used was similar to that used by other authors in likewise studies.[14,15]

Selection of ideal vasopressor for management of post-spinal hypotension is a matter of debate. Systematic reviews and meta-analysis of clinical trials demonstrated that phenylephrine and ephedrine were both effective in preventing post-spinal hypotension. However, phenylephrine was associated with a lower risk of fetal acidosis when compared to ephedrine.[2.16,17] In this study, prophylactic bolus of phenylephrine used was close to the effective dose 95micgs proposed by Tanaka and colleagues, as they demonstrated that lower doses of phenylephrine bolus (60–80 ug) may not be as effective as larger doses (90–120 ug) in preventing post-spinal maternal hypotension.[18]

Interestingly, a recent meta-analysis by Singh and colleagues demonstrated that prophylactic use of phenylephrine, and ephedrine had the highest probability among other vasopressors used to adversely affect fetal acid-base status, and thus fetal outcome.[19]In another meta-analysis by Fitzgerald and colleagues showed that phenylephrine had caused maternal bradycardia more common than other vasopressors which were used.[20]

Our study demonstrated that, if the risk factors for post-spinal hypotension were avoided, prophylactic vasopressor administration might not be always necessary.

Conclusions

Based on the inclusion criteria, post-spinal hypotension was not significantly manifested in the patients enrolled in our study in both phenylephrine and placebo group, hence it is to be concluded that with careful considerations of certain precipitating factors which could predispose to hypotension, caesarean sections can be easily conducted without the need of vasopressors.

Further research work and metanalyses are still needed on a wider and broader scale of patients.

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