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Effect of Intravenous Calcium Gluconate on Prevention of Post Spinal Hypotension during Spinal Anaesthesia for Caesarean Section: A Randomized Double-Blind Controlled Study

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ABSTRACT

Background: Calcium, a physiological ion, causes vasoconstriction and has a positive ionotropic action on heart. Its use to prevent post-spinal hypotension has been suggested but never formally evaluated for patients undergoing caesarean section. This study investigated the hemodynamic effects of calcium administration in parturients with the primary aim of comparing the incidence of post-spinal hypotension.

Methods: Sixty healthy full-term pregnant patients scheduled for caesarean section were randomly allocated to two equal groups to receive either calcium gluconate or normal Saline bolus over 20min by syringe infusion pump under electrocardiography monitoring immediately after the patient was turned supine following spinal anaesthesia. Blood pressure and heart rate were recorded at baseline, and at regular intervals following spinal. Maternal calcium levels were estimated before and after infusion. Neonatal blood gas analysis and calcium level were analyzed. Total mephentermine requirement was recorded in both groups.

Results: The heart rate values remained comparable to baseline value in group calcium gluconate while in group normal Saline, it decreased significantly at 8,12 and 16min. Blood pressure decreased significantly as compared to the baseline value from 4min onwards in both the groups. However, it was comparable in the two groups at all time points(0.622). Nineteen patients(63.33%) required mephentermine infusion in group calcium gluconate as compared to 23 patients(76.6%) in group normal Saline for maintenance of systolic blood pressure.(p=0.791) Umbilical venous pH (p=0.038) and partial pressure of carbon dioxide(p=0.038) were significantly better in group calcium gluconate.

Conclusions: Calcium used for prophylaxis of hypotension in healthy parturients undergoing caesarean section reduced the vasopressor requirements and total mephenteramine dose, but the difference did not attain statistical significance.

Keywords: Cesarean section, fetal acidosis, hypotension, vasopressors.

INTRODUCTION

Hypotension is a common adverse event under spinal anaesthesia in parturients which may have adverse effects on the mother and foetus.[1-5] Many techniques have been investigated for prevention/management of post-spinal hypotension(PSH) during spinal anaesthesia including preloading/co-loading, physical methods and vasopressors.[2-6] None of them is ideal in eliminating hypotension when used alone and the majority are associated with adverse effects like foetal acidosis and maternal tachycardia/bradycardia at effective doses.[7,8]

Calcium is a physiological ion that causes vasoconstriction, positive chronotropic and ionotropic action on the heart.[2,9] In a study, intravenous calcium was found safe and effective in the management of PSH during the first 10minutes in abdominal surgeries.[10,11] This initial post-spinal period is crucial to maintain fetal blood supply before delivery.[12] Till date no study has evaluated its role in preventing PSH in the caesarean section.

This study investigated the hemodynamic effects of calcium administration in preventing PSH in parturients undergoing caesarean section.

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METHODS

The study was conducted in a tertiary care centre after getting approval from the Institutional Ethics Committee-Human Research of a tertiary care teaching institution. The patients were enrolled for the study after they fulfilled the eligibility criteria and gave written informed consent. Full-term parturients with a singleton pregnancy who had no associated systemic illness and who were planned for caesarean section under spinal anaesthesia were included in the study. They were randomly allocated to the two groups by using a computer-generated randomisation sequence maintained in sequentially numbered sealed opaque envelopes. Patients with a history of cardiovascular, endocrine, neurological, respiratory diseases, compromised renal or hepatic functions, history of eclampsia and preeclampsia, antepartum haemorrhage, severe anaemia, multiple pregnancies, polyhydramnios, patients on digitalis, calcium channel blocker and anticoagulant therapy, history of hypersensitivity to local anaesthetics and foetal distress were excluded from the study.

Patients in group CG received 10% 10 ml calcium gluconate infusion.

Patients in group NS received 10 ml of 0.9% of normal saline infusion.

The infusion was prepared by an independent anaesthesiologist in an isolated area and was handed over to the person conducting anaesthesia. Hence, the nature of the solution infused was unknown to the patients and to the anesthesiologist observing the patient during surgery. The infusion was given over 20min by syringe infusion pump under continuous electrocardiography (ECG) monitoring after the patient was turned supine following spinal anaesthesia.

On arrival to the operating room, monitoring for continuous ECG, heart rate (HR), non-invasive blood pressure (NIBP-systolic(SBP), diastolic (DBP) and mean arterial pressure(MAP)), pulse oximetry(SpO_2) of all patients was started and their baseline values were recorded. Two intravenous (IV)cannulas, one in each forearm, were secured to be used for Ringer lactate (RL) infusion and the other one for calcium gluconate or normal saline (NS) infusion as per the group allocated and for the mephentermine infusion as rescue, vasopressor to manage hypotension if it occurred. The maternal venous blood sample was taken for estimation of preoperative calcium level. All the patients were premedicated with injection ranitidine 50mg IV and injection metoclopramide 10mg IV stat. In all the patients, co-loading was started with RL at 20ml/kg for 20min and after that fluid therapy was given according to the requirement. Oxygen was delivered by a face mask at the flow rate of 4 l/min. Spinal anaesthesia was given with 25G Quincke's needle(Medispine™) in the left lateral position at L_3-L_4 or L_4-L_5 intervertebral space. 0.5% bupivacaine heavy 2.2ml (Bupitroy, Troika Pharmaceuticals) and fentanyl 25µg were injected under all aseptic precautions by the conventional method. The patient was turned to supine and horizontal position and a 15° wedge was placed under the right hip for uterine displacement. 10 ml Injection10% calcium gluconate (Rathi laboratories [Hindustan] Pvt. Ltd.) or 10ml 0.9% normal saline solution was infused intravenously as per the group allocation. Baseline Hemodynamic parameters (SBP, DBP, MAP and HR) were recorded before the procedure and every 2min for 30min following spinal anaesthesia and every 5min thereafter till the end of surgery. Episodes of hypotension (SBP<100mm of Hg or reduction in SBP >20% from the baseline value) were treated with injection mephentermine infusion by another syringe pump in opposite arm at the rate of 0.5 ml/min in the concentration of 1 mg/ml, infusion rate was titrated to achieve systolic blood pressure ≥100mm of Hg or near baseline value. Mephentermine infusion was stopped gradually after achieving sustained systolic blood pressure near the baseline value. After spinal anaesthesia, dermatomal sensory block level was evaluated by pin prick method every 1min using a blunted hypodermic needle. Surgery could start once T_8 level was achieved, and maximum level of sensory block and time taken to achieve it were recorded.

Any incidence of nausea or vomiting was documented and was managed with ondansetron 4 mg IV stat and bradycardia (HR<50 beats/min) was treated with atropine 0.005mg/kg IV (maximum 0.3mg). After delivery, 5U IV oxytocin was given slowly and other 5U was given along with IV fluids infusion. The maternal venous blood sample was taken for the estimation of calcium level after completion of calcium gluconate infusion. Apgar score of the neonate was assessed at 1min and 5min after delivery of the baby. Neonatal arterial and venous blood samples from a double clamped segment of the umbilical cord was used for blood gas analysis(Combisys II, Eschweiler BGA plus E) and calcium level estimation.

The number of patients requiring mephentermine infusion and the total dose of mephentermine required to maintain the desired level of systolic blood pressure during the procedure was recorded in patients of both groups.

At the end of surgery approximate total blood loss was assessed and recorded. Adverse effects like

nausea, vomiting, bradycardia, arrhythmias, pruritus, respiratory depression, or any other effect reported by the patient were recorded and treated.

Sample size calculation: The incidence of hypotension was our primary outcome measure of interest. In a previous study, in a similar patient population, the incidence of PSH was 75%.[13]Considering a clinically significant reduction in the incidence of PSH to 50% with calcium infusion, a sample size of 27 patients in each group was required using a one-sided, two-proportion Z-test method with a pooled variance and the study power of 80%, with the permitted alpha error of 0.05 and beta error of 0.02. We decided to recruit a total of 60 patients to account for any attrition.

The research data collected was tabulated using MS Excel package while Statistical Package for the Social Sciences software (ver. 20; IBM Inc. Chicago, USA) was used for data analysis. Descriptive statistics of mean and standard deviation were used to report continuous data while the categorical data were expressed as numbers and percentages. Statistical analysis was done by using repeated measures of ANOVA to compare the haemodynamic parameters between the groups, Dunnett's test to compare the haemodynamic parameters at various time intervals with preoperative baseline values of the respective group and unpaired Student's t-test for other maternal and foetal parameters. Mann-Whitney test was used for analysis of total mephentermine requirement. P value <0.05 was considered statistically significant.

RESULTS

The present randomised controlled double-blind trial was conducted to assess the effect of intravenous calcium gluconate on haemodynamic parameters during caesarean section under spinal anaesthesia. A total of 70 patients were screened for eligibility and of these 60 patients were included as per inclusion criteria. The flow of participants in the study has been depicted in the consort diagram.(Figure 1) The demography parameters, approximate blood loss and mean total intravenous fluid infused were comparable in the two groups (Table 1).

The mean HR between two groups at any given point of time was comparable. (*p=0.966*) The mean HR values were decreased significantly at 8, 12 and 16 min as compared to its preoperative value in group NS while there no significant difference in group CG.(Figure 2) Statistical analysis depicted no difference in mean SBP values between the two groups at any given point of time. (*p=0.622*) The SBP, DBP and MAP values were significantly lower than their preoperative baseline values following spinal anaesthesia from 4-min onwards in both the groups (Figure 3).

The maximum height of spinal anaesthesia achieved was T6 or above in 96.66% of patients while it was T4 or above in 50% of patients in both groups. The total amount of mephentermine required to maintain SBP above 100 mm Hg was comparable in both groups(5.44±7.42 vs 6.19±6.83; *p=0.352*; Table 2) Nineteen patients (63.33%) in group CG while in group NS, 23 patients (76.66%) required mephentermine infusion for maintenance of SBP.(*p=0.791*; table 2)

The time to the highest level of sensory block group CG: 306.00±96.29 sec; group NS 314.00±95.43 sec). (*p= 0.748*; Table 1) was comparable in both the groups.

Maternal serum calcium levels at the preoperative and post-infusion time were comparable in both the groups on statistical analysis.(*p=0.576 and 0.774;* Table 2*)* There was no significant rise in maternal serum Ca^{+2} level in group CG after calcium gluconate infusion. The umbilical arterial blood gas parameters were similar in the groups. (Table 2) Mean umbilical arterial and venous calcium level were also comparable in the two groups (*p=0.655 and 0.834*) However, the umbilical venous pH (*p=0.038*) and PCO_2 (*p=0.038*)(Table 2) was significantly different in the two groups. The mean of Apgar scores at 1-min (8.63±0.80 vs 8.77±0.50; *p=0.477*) and 5-min (8.90±0.54 vs 8.96±0.18; *p=0.530*)were comparable in groups CG and NS respectively.(Figure-4) However, Apgar score at 5-min showed a statistically significant improvement over Apgar score at 1-min in group CG (*p= 0.000*) while it was comparable in group NS (*p=0.155*). Only one patient in group CG and two patients in group NS had nausea and vomiting.

Table1. Patients characteristics, total intravenous fluid infused, blood loss, time to achieve sensory block, surgical times.

	Group CG (n=30)	Group NS (n=30)	p-value
Age (yrs.)	25.66±03.46	26.83±07.89	0.461
Body Weight (Kg)	61.00±08.08	68.60±23.65	0.101
Height (cm)	153.00±02.51	153.30±03.61	0.711
Total IV fluid (ml)	1590.00±180.71	1626.67±224.27	0.488
Blood Loss (ml)	825.67±59.63	864.00±68.61	0.024#

Table1. Patients characteristics, total intravenous fluid infused, blood loss, time to achieve sensory block, surgical times.

	Group CG (n=30)	Group NS (n=30)	p-value
TSB (sec)	306.00±96.30	314.00±95.43	0.748
SI- UI (sec)	255.60±171.01	396.00±251.04	0.014#$
SI-Delivery (sec)	354.83±164.03	574.33±276.96	0.001#$
UI-Delivery (sec)	109.90±43.37	176.33±127.58	0.011#$

p>0.05 - N.S. (Not significant), TSB= time to achieve highest level of sensory block, SI=skin incision, UI= uterine incision. #: statistically significant, $ Welch test (variances violates the homogeneity condition)

Table2. Maternal serum calcium levels (mmol/l), mephentermine (mg) required, and APGAR scores in both groups.

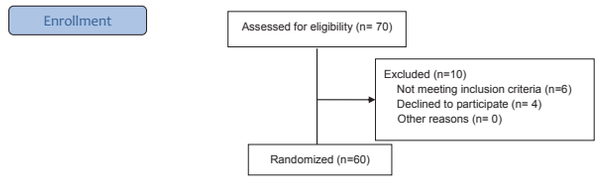
Variable	Group CG (n=30)	Group NS (n=30)	p value
Preoperative Ca^{+2} level (mmol/l)	1.05±0.36	1.01±0.19	0.576$
Post infusion Ca^{+2} level (mmol/l)	1.06±0.32	1.04±0.20	0.774
Mephentermine required (mg)	5.44±7.42	6.20±6.83	0.683
No. of patients (%)	19 (63.33%)	23 (76.66%)	0.791
APGAR score			
1 min	8.63±0.80	8.77±0.50	0.477
5 min	8.90±0.54*#	8.96±0.18	0.530

**p value =0.000 from the 1 min Apgar score of CG group. #: statistically significant $ Welch test*

Table 3. Umbilical arterial blood gas parameters and umbilical venous blood gas parameters.

Umbilical arterial blood gas parameters			
Variable	**Group CG (n=30)**	**Group NS (n=30)**	**p value**
pH	7.33±00.04	7.31±00.05	0.072
PO_2 (mmHg)	13.08±03.48	15.07±04.62	0.053
PCO_2 (mmHg)	47.05±06.76	49.07±10.20	0.370$
Oxygen Saturation (%)	14.24±08.21	19.42±11.89	0.054
Ca^{+2} (mmol/l)	1.18±00.26	1.15±00.22	0.655
Standard bicarbonate(m-mol/l)	22.51±02.11	22.26±03.55	0.749
Base deficit (mmol/l)	-2.32±03.22	-3.01±02.57	0.361
Umbilical venous blood gas parameters			
pH	7.35±00.03	7.34±0.04	0.038#
PO_2 (mmHg)	20.92±05.27	21.64±05.55	0.609
PCO_2 (mmHg)	39.78±07.02	44.17±08.86	0.038#
Oxygen Saturation (%)	33.89±13.31	34.30±13.68	0.906
Ca^{+2} (mmol/l)	1.17±00.30	1.18±00.24	0.834
Standard bicarbonate(m-mol/l)	22.18±01.80	22.21±02.37	0.946
Base deficit(mmol/l)	-2.98±02.71	-2.95±03.31	0.969

#: statistically significant $: Welch test



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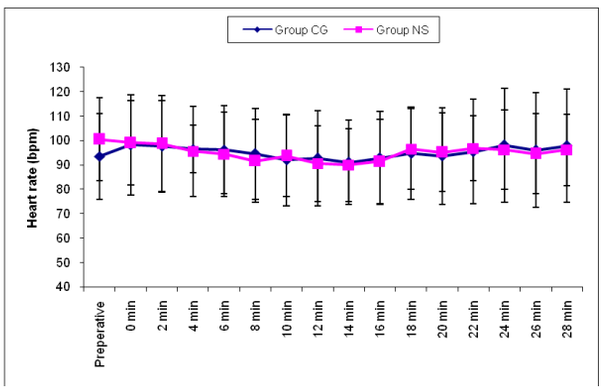

Figure2. Heart rate at corresponding time intervals in the two groups.

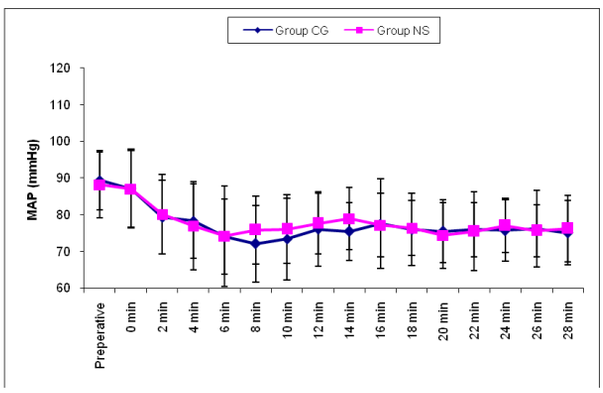

Figure 3. Mean arterial pressure at corresponding time intervals in the two groups.

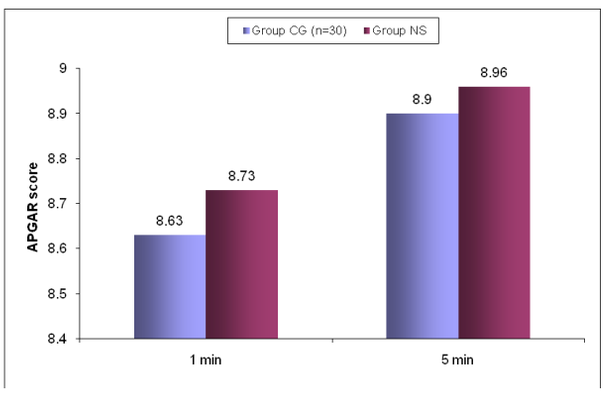

Figure 4. APGAR score at 1 and 5 minute in the two groups.

DISCUSSION

This is the first study investigating the effect of IV administration of calcium on the prevention of PSH in healthy parturients undergoing caesarean section under spinal anaesthesia.

In this study, the administration of calcium gluconate following spinal anaesthesia resulted in a reduction in the incidence of PSH and requirement of mephentermine though the difference was statistically insignificant. The fetal umbilical venous pH and pCO_2 were significantly better than the control group, though the APGAR score was comparable.

Spinal anaesthesia is a commonly used anaesthetic modality for caesarean delivery because of its rapid onset, reliable, dense sensory and motor blockade, excellent patient comfort, and reduced risk of complications. Nonetheless, PSH has a remarkably high incidence in pregnant patients (up to 80%) and can jeopardize the foetal and its maternal outcomes.[13,14]

Vasopressors have been found to be effective for prophylaxis, but do not eliminate hypotension and are associated with various undesirable side effects like supraventricular tachycardia and fetal acidosis. Phenylephrine is the currently considered standard vasopressor agent for prophylaxis, but its use has been related to a dose-dependent deceleration in heart rate, and even a fall in cardiac output.[15] A recent Cochrane review by Chooi et al., none of the techniques which have been tested for preventing PSH were shown to fully abolish the incidence of maternal hypotension and the consequent need to treat it.[7]

Calcium is a physiological ion, that regulates blood pressure by increasing calcium in vascular smooth muscle cells that leads to vasoconstriction, and increases intravascular volume through the renin-angiotensin-aldosterone system(RAAS).[16] Animal experiments have suggested that effects of calcium due to stimulation of alpha-adrenergic vascular receptors and catecholamine release from the adrenal medulla.[17] Calcium also has an inotropic action which is purported to be due to the increased availability of intracellular calcium for the process of contraction of myofibrils.[2,10] In patients undergoing anaesthesia and those recuperating from cardiopulmonary bypass, the administration of calcium chloride elevates MAP, cardiac contractility and systemic vascular resistance(SVR).[18,19] However, the changes in vascular smooth muscle tone following its infusion are unpredictable as they are affected by baseline calcium levels, underlying cardiac function and contractility, autonomic function, and mode of anaesthesia.[9]

Boztug N.[11] had also administered 10ml 10% calcium gluconate as an infusion(duration not specified) after administration of spinal anaesthesia and found that the MAP was significantly higher after administration of IV calcium during the first 10 min. This prevention of the initial PSH would be particularly useful in preventing the potential negative consequences of hypotension on the fetus.[20] The MAP in our study did not show a similar rise probably because of physiological differences in the surgical population involved. His study was conducted on the patients undergoing lower abdominal surgeries while the present study enrolled pregnant patients undergoing caesarean section. In his published data (an abstract), Boztug N.[11] had not mentioned the dermatomal level of block and serum calcium levels after calcium infusion while in the present study, most patients had the highest block-level above T6 and serum calcium levels in both groups were comparable pre- and post-infusion of calcium.(table 2)

Calcium should prevent bradycardia due to its inotropic properties. In our study, though the HR remained comparable between the groups, the HR showed a downward trend in the control group while it remained stable in the group CG. In a study by Faber et al.[21] calcium was co-administered with oxytocin following the caesarean delivery and they had demonstrated a rise in HR in the patients administered calcium as compared to placebo. In their study, the effect of the rise in HR may have become evident due to the physiological effects of delivery and oxytocin as effects of calcium are dependent on the baseline cardiac contractility. The variation may also be due to the different preparation, timing, method, and dose of calcium administration. Furthermore, they found that plasma ionized calcium concentration was significantly higher in their study group while in the present study, it was found comparable in both the groups.

The newborn baby's umbilical cord blood pH is the best indicator of the status of placental perfusion immediately before delivery.[22] In the present study, the umbilical venous blood gas pH was significantly better in the CG group. This may be because of the relatively higher incidence of hypotension in the NS group. However, the pH was well above 7.3 in both groups. Other parameters were comparable in the 2 groups except for pCO2 where it was higher in group NS, but it was also within an acceptable range (table 2). There was no sign of foetal acidosis. APGAR scores at 5-min showed a statistically significant improvement over APGAR score at 1-min in group CG. (p= 0.000) The reason for this difference could not be identified. It might be because of calcium ions reaching the foetus through the placenta increased cardiac contractility and improved the condition of the newborn (table 2).

The calcium gluconate administration was not associated with any significant side effects.

This is the first study investigating the effectiveness of calcium in the prevention of post-spinal hypotension during caesarean section. Further large-scale studies in varying patient profiles and doses or infusion timings are required to explore the exact role of calcium in the prevention of PSH in parturients undergoing caesarean section under spinal section and could be the future directions for research in this area.

Our study has certain limitations. Only a single dose of calcium was tested against a placebo. The effective dose may be higher, and a dose-ranging study might have yielded the optimum dose of calcium to prevent hypotension. Calcium was infused slowly over 20 min just after the spinal block. Faster or slower infusion or infusion of calcium or at some time prior to the institution of spinal block or use of another preparation (calcium chloride) might have resulted in a more effective preventive effect against spinal induced hypotension, but the literature at present remains insufficient to answer these questions. Only healthy parturients with singleton uncomplicated pregnancy were recruited in the study. The preventive effects of calcium may be more evident in certain specific obstetric populations as its effects are dependent on baseline cardiac contractility and autonomic system. The study showed a decreased trend to hypotension in the calcium administration group, but the difference did not attain statistical significance. It is possible that the assumption of a 50% decrease in hypotension was an optimistic one and if we had explored a smaller difference, the higher sample size might have made the action of calcium more evident, and a statistical significance could have been attained.

CONCLUSIONS

Calcium gluconate infusion could not significantly reduce the incidence of hypotension or mephenteramine consumption during caesarean section in healthy parturients though there was a trend towards reduced incidence of hypotension in the group which received calcium gluconate. Further large-scale studies with infusion of calcium in various patient population, doses, rates, and timing in relation to spinal anaesthesia are required to conclusively prove the same.

CONFLICT OF INTEREST

None.

REFERENCES

1. Ratcliffe FM, Evans JM. Neonatal wellbeing after elective caesarean delivery with general, spinal, and epidural anaesthesia. Eur J Anaesth 1993; 10: 175-81.[Article]

2. Biricik E, Ünlügenç H. Vasopressors for the Treatment and Prophylaxis of Spinal Induced Hypotension during Caesarean Section. Turk J Anaesthesiol Reanim 2021; 49: 3–10.[Article]

3. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of Spinal Anesthesia-Induced Hypotension in Adults. Local Reg Anesth 2020;13:39-46.[Article]

4. Emmett RS, Cyna AM, Andrew M, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev 2002; 3:CD002251.[Article]

5. Roberts SW, Leveno KJ, Sidawi JE, Lucas MJ, Kelly MA. Fetal acidemia associated with regional anesthesia for elective cesarean delivery. Obstet Gynecol 1995; 85:79–83.[Article]

6. Mercier FJ. Fluid loading for cesarean delivery under spinal anaesthesia: have we studied all the options? Anesth Analg 2011; 113: 677-80.[Article]

7. Chooi C, Cox JJ, Lumb RS, Middleton P, Chemali M, Emmett RS, et al. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev 2020;7:CD002251.[Article]

8. Reynolds F, Seed PT. Anaesthesia for caesarean section and neonatal acid-base status: a meta-analysis. Anaesthesia 2005;60:636–53.[Article]

9. Drop LJ. Ionized calcium, the heart, and hemodynamic function. Anesth Analg 1985;64:432–51.[Article]

10. Denlinger JP, Kaplan JA, Lecky JH, Wollman H. Cardiovascular responses to calcium administered intravenously to man during halothane anesthesia. Anesthesiology 1975; 42: 390-7.[Article]

11. Boztug N. Use of intravenous calcium in prevention of spinal anaesthesia induced hypotension:202. Reg Anesth Pain Med 2003; 28: 34.[Article]

12. KangYC, Abouleish E, Carirtis S. Prophylactic intravenous ephedrine infusion during spinal anesthesia for caesarean section. Anesth Analg 1982; 61: 839-42.[Article]

13. Ueyama H, He YL, Tanigami H, Mashimo T, Yoshiya I. Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective cesarean section. Anesthesiology 1999; 91: 1571–6. [Article]

14. Habib AS. A review of the impact of phenylephrine administration on maternal hemodynamics and maternal and neonatal outcomes in women undergoing cesarean delivery under spinal anesthesia. Anesth Analg 2012;114:377–90.[Article]

15. Magder S. Phenylephrine and tangible bias. Anesth Analg 2011; 113:211-3.[Article]

16. Villa-Etchegoyen C, Lombarte M, Matamoros N, Belizán JM, Cormick G. Mechanisms Involved in the Relationship between Low Calcium Intake and High Blood Pressure. Nutrients 2019;11:1112.[Article]

17. Horwitz LD, Lifschitz MD. Role of the autonomic nervous system in pressor response to calcium in conscious dogs. Cardiovasc Res 1980;14:522–9.[Article]

18. Erdmann E, Reuschel-Janetschek E. Calcium for resuscitation? Br J Anaesth 1991;67:178–84.[Article]

19. Butterworth 4th JF, Strickland RA, Mark LJ, Kon ND, Zaloga GP. Calcium does not augment phenylephrine's hypertensive effects. Crit Care Med 1990;18:603–6. [Article]

20. Dyer RA, Reed AR, Van Dyk D, Arcache MJ, Hodges O, Lombard CJ, et al. Hemodynamic effects of ephedrine, phenylephrine, and the coadministration of phenylephrine with oxytocin during spinal anesthesia for elective cesarean delivery. Anesthesiology 2009;111:753–65. [Article]

21. Farber MK, Schultz R, Lugo L, Liu X, Huang C, Tsen LC. The effect of co-administration of intravenous calcium chloride and oxytocin on maternal hemodynamics and uterine tone following cesarean delivery: a double-blinded, randomized, placebo-controlled trial. Int J Obstet Anesth2015;24: 217-24.[Article]

22. Thorp JA, Sampson JE, Parisi VM, Creasy RK. Routine umbilical cord blood gas determinations? Am J Obstet Gynecol 1989; 161: 600-5.[Article]