Preliminary Report

Re-evaluation of *im* ephedrine as prophylaxis against hypotension associated with spinal anaesthesia for Caesarean section

A.A. Webb MMED (anaesth),
E.A. Shipton DMED FFA (SA)

Purpose: To assess the safety and efficacy of 37.5 mg ephedrine *im* in preventing hypotension associated with spinal anaesthesia for Caesarean section.

Methods: In a double-blind randomised controlled study, 40 patients (20 in each group) were given either 37.5 mg ephedrine or placebo *im*. The following parameters were recorded: (i) blood pressure; (ii) heart rate; (iii) ephedrine *iv* supplementation; (iv) umbilical venous blood gases and neonatal Apgar scores.

Results: The incidence of hypertension in the study group was 30% compared with 20% for the control group (P :NS). There was no difference in mean highest blood pressure or mean highest heart rate between the groups. The incidence of hypotension was lower but not significantly lower in the study group (50%) than in the control group (80%) (P :NS). However, the incidence of delayed hypotension was only 10% in the study group patients compared with 50% in the control group patients ($P < 0.05$).

Conclusion: Giving 37.5 mg ephedrine *im* prior to spinal anaesthesia was not associated with reactive hypertension or tachycardia. Intramuscular ephedrine provided more sustained cardiovascular support than intravenous ephedrine.

Objectif : Évaluer la sécurité et l'efficacité de 37,5 mg d'éphédrine par voie intramusculaire pour prévenir l'hypotension associée à l'anesthésie rachidienne pour la césarienne.

Méthodes : Dans une étude aléatoire à double insu, 40 parturientes, 20 dans chaque groupe, ont reçu par voie intramusculaire 37,5 mg d'éphédrine ou un placebo. Les paramètres suivants ont été enregistrés: 1) la tension artérielle 2) la fréquence cardiaque 3) les besoins supplémentaires d'éphédrine *iv* 4) les gaz veineux ombilicaux et le score d'Apgar.

Résultats : L'incidence d'hypertension dans le groupe éphédrine a été de 30% comparativement à 20% pour le groupe témoin ($P=n.s.$). Il n'y a pas eu de différence en ce qui concerne la tension artérielle maximale moyenne et la fréquence cardiaque maximale moyenne dans les deux groupes. L'incidence d'hypotension a été plus faible dans le groupe éphédrine (50%) que dans le groupe témoin (80%), mais ce de façon non significative ($P=n.s.$). Cependant, l'incidence d'hypotension tardive n'a été que de 10% dans le groupe éphédrine comparativement à 50% dans le groupe témoin ($P<0,05$).

Conclusion : L'administration de 37,5 mg d'éphédrine par voie intramusculaire avant l'anesthésie rachidienne n'a pas été associée à une hypertension ou à une tachycardie. L'éphédrine par voie intramusculaire apporte un support cardiovasculaire plus soutenu que l'éphédrine par voie intraveineuse.

From the Department of Anaesthesiology, Chris Hani Baragwanath Hospital and University of The Witwatersrand, P.O. Bertsham, Johannesburg, 2013, South Africa.

Address correspondence to: Prof. E.A. Shipton, 14 Montreuil Street, Montroux 2195, South Africa. Telefax: 2711-888-5286.

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THE incidence of hypotension after intrathecal anaesthesia for Caesarean section remains unacceptably high despite fluid preloading and lateral uterine displacement.^{1,2} Intramuscular ephedrine given prior to induction of anaesthesia has been shown to reduce the incidence substantially³ but has been associated with excessive hypertension.⁴⁻⁶ A controlled prospective study is described which re-evaluated the safety and efficacy of intramuscular ephedrine in spinal anaesthesia for Caesarean section.

Ephedrine doses of 25 or 50 mg are suggested for intramuscular use by contemporary text books.⁷ Our pilot studies indicated that a dose of 37.5 mg would be safer than 50 mg with regard to reactive hypertension and more effective than 25 mg with regard to preventing hypotension.

Methods

With ethics committee approval and informed consent, 40 patients receiving spinal anaesthesia for elective Caesarean section were randomly allocated to one of two treatment regimens: 37.5 mg ephedrine *im* or 1.5 ml normal saline *im* (control group). The following exclusion criteria were applied: (i) obesity resulting in impalpable lumbar spines; (ii) hypertension (blood pressure > 150/90 mmHg); (iii) conventional contraindications to spinal anaesthesia (coagulopathy, sepsis, hypovolaemia).

Baseline blood pressure and heart rate were measured using a study-dedicated automated non-invasive blood pressure monitor (Criticon-Dinamap). Baseline values were taken as the average of three successive readings. Intravenous fluid preloading of 500 ml Ringers' Lactate was then administered over 15 to 20 min.

At this time, patients received an *im* injection into the left deltoid of either ephedrine or normal saline. Following this injection, blood pressure and heart rate were recorded at: one minute intervals for 30 min; five minute intervals for the next 40 min; 10 minute intervals for the next 20 min. Spinal anaesthesia was instituted with the patient in the sitting position on the operating table -2.5 ml hyperbaric bupivacaine 0.45% were injected through a 25 G needle inserted at the L₃₋₄ spinal interspace.

Hypotension was defined as a decrease in systolic pressure to < 100 mmHg, or < 70% of the baseline values. Hypotension was treated immediately by increasing the rate of *iv* fluid administration and by 5 mg ephedrine *iv* bolus every minute until systolic pressure increased to the above values. The total *iv* ephedrine dose required was recorded. Times of ephedrine injection, spinal injection, skin incision, uterine incision, umbilical cord cross clamp and conclusion of surgery

were recorded. The foetus was assessed by Apgar scoring and by analysis of umbilical venous blood.

The following statistical tests were performed as appropriate using the GraphPad InStat programme, version 2.05 A (GraphPad Software Inc. San Diego, California, USA), Fisher's Exact Probability Test, and Student's *t* test for unpaired samples. Results are expressed as mean $\pm$ SD. Any *P* < 0.05 was considered to be statistically significant.

Results

All patients in the study experienced satisfactory analgesia throughout the operation. No differences could be demonstrated between the two groups with respect to maternal height, weight, age or baseline blood pressure and heart rate.

Six patients (30%) in the ephedrine group became hypertensive (increase in systolic pressure > 30% from baseline after ephedrine was administered) compared with four patients (20%) in the control group (*P*:NS). The mean highest systolic pressure was not greater in the ephedrine group (153 $\pm$ 11 mmHg) than in the control group (150 $\pm$ 12 mmHg) (*P*:NS). Persistent hypertension (increase in systolic pressure > 30% from baseline in the post operative period) occurred in only one patient (5%) in the ephedrine group and did not occur in the control group (*P*:NS). The mean systolic pressures immediately before intrathecal injection and immediately following delivery were 140 $\pm$ 9.8 mmHg and 127 $\pm$ 11.6 mmHg for the ephedrine group compared with 133 $\pm$ 14.9 mmHg and 122 $\pm$ 14.6 mmHg for the control group respectively (*P*:NS).

Fourteen patients (70%) in the ephedrine group developed severe tachycardia (heart rate > 120 beats-min), compared with 13 (65%) in the control group (*P*:NS). The mean highest pulse rate in the ephedrine group was 130 beats-min $\pm$ 21.4 compared with 123.4 beats-min $\pm$ 20.5 for the control group (*P*:NS).

The mean lowest systolic blood pressure after induction of spinal anaesthesia was higher in the ephedrine group (99 $\pm$ 12.8 mmHg) than that in the control group (89 $\pm$ 15.8 mmHg) (*P* < 0.05). The overall incidence of hypotension in the ephedrine group was not different from that of the control group. Ten patients (50%) in the ephedrine group became hypotensive compared with 16 (80%) in the control group (*P*:NS). However, only two patients (10%) in the ephedrine group suffered delayed hypotension (hypotension occurring > 30 min after intrathecal injection) compared with 10 patients (50%) in the control group (*P* < 0.05).

No Apgar score < 8 was found at 1 or 5 minutes in any of the babies. The mean umbilical vein pH of the

ephedrine group was 7.31 ± 0.06 compared with 7.35 ± 0.05 in the control group ($P < 0.05$). There were no differences between the groups in respect of the other blood gas variables (PCO_2 , PO_2 , and HCO_3).

Discussion

Intramuscular prophylactic vasopressors have been advocated for preventing hypotension associated with spinal anaesthesia for Caesarean section.³ Opposition to their use has been based on concerns about reactive hypertension. Two controlled studies have demonstrated reactive hypertension when *im* ephedrine was used in epidural and general anaesthesia.^{5,6}

This study found no increase in either the incidence or the severity of hypertension in patients given 37.5 mg ephedrine *im* prior to spinal anaesthesia for Caesarean section. No persistent postoperative hypertension was detected. There was also no evidence of increased heart rates in the ephedrine group.

With regard to efficiency in preventing hypotension, a previous study using 50 mg ephedrine *im* noted an incidence of 25%.³ The higher incidence of hypotension (50%) in the current study may be related to the lower dose of ephedrine, and to the modest fluid preload used (500 ml Ringer's lactate). It may also relate to an inadequate interval between ephedrine injection and spinal induction. In this regard, two subgroups evolved within the ephedrine group – 10 subjects had their spinal induction approximately five minutes after ephedrine injection (5–8 min) and 10, their induction approximately 10 min (9–14 min) after ephedrine injection. Considerable cardiovascular instability was evident in the “5 min subgroup,” hypotension in 70% and decrease in systolic blood pressure of 24%. Compared with 30% and 13% in the “10 minute subgroup.”

Possibly the most important finding was that of a substantially lower incidence of postoperative or delayed hypotension in the ephedrine group. It is evident that *im* ephedrine provides more sustained cardiovascular support than *iv*. This may be particularly advantageous as postoperative hypotension is often undetected.

As the primary focus of this study was on maternal haemodynamics, only umbilical venous blood was collected so that gross biochemical derangement in the foetus could be excluded. Although there were differences between the groups, all the pH values were within normal reference ranges.⁸ There were no clinically detectable consequences of the lower venous pH values in the ephedrine group (Apgar scores > 8).

In conclusion, the findings of this study indicate that ephedrine administered in the above manner is safe with regard to maternal haemodynamics. The findings sug-

gest that the timing of the ephedrine injection may be important, and that a 10 min delay before spinal induction would improve the efficacy of the technique.

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