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Efedrina *versus* Fenilefrina: Prevenção de Hipotensão Arterial durante Anestesia Raquídea para Cesariana e Efeitos sobre o Feto*

Ephedrine versus Phenylephrine: Prevention of Hypotension during Spinal Block for Cesarean Section and Effects on the Fetus

Edno Magalhães, TSA[1], Catia Sousa Govêia, TSA[2], Luís Cláudio de Araújo Ladeira, TSA[2], Bruno Góis Nascimento[3], Sérgio Murilo Cavalcante Kluthcouski[3]

RESUMO

Magalhães E, Govêia CS, Ladeira LCA, Nascimento BG, Kluthcouski SMC — Efedrina *versus* Fenilefrina: Prevenção de Hipotensão Arterial durante Anestesia Raquídea para Cesariana e Efeitos sobre o Feto.

JUSTIFICATIVA E OBJETIVOS: *A hipotensão arterial durante a anestesia raquídea para cesariana deve-se ao bloqueio simpático e compressão aorto-cava pelo útero e pode ocasionar efeitos deletérios para o feto e a mãe. A efedrina e fenilefrina melhoram o retorno venoso após bloqueio simpático durante anestesia raquídea. O objetivo deste estudo foi comparar a eficácia da efedrina e da fenilefrina em prevenir e tratar a hipotensão arterial materna durante anestesia raquídea e avaliar seus efeitos colaterais e alterações fetais.*

MÉTODO: *Sessenta pacientes, submetidas à anestesia raquídea com bupivacaína e sufentanil para cesariana, foram divididas aleatoriamente em dois grupos para receber, profilaticamente, efedrina (Grupo E, n = 30, dose = 10 mg) ou fenilefrina (Grupo F, n = 30, dose = 80 µg). Hipotensão arterial (pressão arterial menor ou igual a 80% da medida basal) foi tratada com bolus de vasoconstritor com 50% da dose inicial. Foram avaliados: incidência de hipotensão arterial, hipertensão arterial reativa, bradicardia e vômitos, escore de Apgar no primeiro e quinto minutos e gasometria do cordão umbilical.*

RESULTADOS: *A dose média de efedrina foi 14,8 ± 3,8 mg e 186,7 ± 52,9 µg de fenilefrina. Os grupos foram semelhantes quanto aos parâmetros demográficos e incidência de vômitos, bradicardia e hipertensão arterial reativa. A incidência de hipotensão arterial foi de 70% no Grupo E e 93% no Grupo F ($p < 0,05$). O pH arterial médio do cordão umbilical e o escore de Apgar no primeiro minuto foram menores no grupo E ($p < 0,05$). Não houve diferença no escore do quito minuto.*

CONCLUSÕES: *A efedrina foi mais eficiente que fenilefrina na prevenção de hipotensão arterial. Ambos os fármacos apresentaram incidência semelhante de efeitos colaterais. As repercussões fetais foram menos freqüentes com o uso da fenilefrina e apenas transitórias com a utilização da efedrina.*

Unitermos: ANESTESIA, Obstétrica; CIRURGIA, Obstétrica: cesariana; COMPLICAÇÕES: hipotensão arterial; DROGAS: efedrina, fenilefrina.

SUMMARY

Magalhães E, Govêia CS, Ladeira LCA, Nascimento BG, Kluthcouski SMC — Ephedrine *versus* Phenylephrine: Prevention of Hypotension During Spinal Block for Cesarean Section and Effects on the Fetus**.**

BACKGROUND AND OBJECTIVES: *Hypotension during spinal block for cesarean section is secondary to the sympathetic blockade and aorto-caval compression by the uterus and it can be deleterious to both the fetus and the mother. Ephedrine and phenylephrine improve venous return after sympathetic blockade during the spinal block. The objective of this study was to compare the efficacy of ephedrine and phenylephrine in the prevention and treatment of maternal hypotension during spinal block and to evaluate their side effects and fetal changes.*

METHODS: *Sixty patients undergoing spinal block with bupivacaine and sufentanil for cesarean section were randomly divided in two groups to receive prophylactic ephedrine (Group E, n = 30, dose = 10 mg) or phenylephrine (Group P, n = 30, dose = 80 µg). Hypotension (blood pressure equal or lower than 80% of baseline values) was treated with bolus administration of the vasoconstrictor at 50% of the initial dose. The incidence of hypotension, reactive hypertension, bradycardia, and vomiting, and Apgar scores on the 1st and 5th minutes, and blood gases of the umbilical cord blood were evaluated.*

RESULTS: *The mean dose of ephedrine used was 14.8 ± 3.8 mg and of phenylephrine was 186.7 ± 52.9 µg. Demographic parameters and the incidence of vomiting, bradycardia, and reactive hypertension were similar in both groups. Hypotension had an incidence of 70% in Group E and 93% in Group P ($p < 0.05$). The mean arterial pH of the umbilical cord blood and the Apgar score in the 1st minute were lower in Group E ($p < 0.05$). Differences in the Apgar score in the 5th minute were not observed.*

CONCLUSIONS: *Ephedrine was more effective than phenylephrine in the prevention of hypotension. Both drugs had similar incidence of side effects. Fetal repercussions were less frequent with phenylephrine and were transitory with the use of ephedrine.*

Key Words: ANESTHESIA, Obstetrics; COMPLICATIONS: hypotension; DRUGS: ephedrine, phenylephrine; SURGERY, Obstetrics: cesarean section.

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diminuir a compressão aorto-cava e o bloqueio foi mantido no mesmo nível em todas as pacientes.

Apesar dos cuidados relacionados com o método empregado, alguns fatores podem limitar a interpretação do estudo. O número de pacientes envolvidas, embora maior que alguns estudos publicados, pode ser um fator de viés, uma vez que o tamanho da amostra não foi calculado. Outra limitação foi a diferença de tempo entre a coleta de sangue do cordão umbilical e a análise dos gases sanguíneos. Essa diferença pode ter alterado os valores dos gases sanguíneos e, possivelmente, interferido nos resultados.

Estudos prévios sugeriram que 30 mg de efedrina por via venosa em *bolus* seria a dose mais efetiva para prevenção de hipotensão arterial, mas à custa de incidência aumentada de hipertensão arterial reativa [22]. Em contraste, um estudo prospectivo observacional demonstrou que dose por via venosa, de 15 ou 20 mg de efedrina diminuiu a incidência de hipotensão arterial materna sem aumentar a ocorrência de hipertensão arterial reativa [20]. Em metanálise em 2004 [19], concluiu-se que doses maiores que 14 mg de efedrina não diminuíram a incidência de hipotensão arterial materna, mas causaram hipertensão arterial reativa e pequena redução no pH umbilical. No presente estudo, a dose considerada como eficaz e, ao mesmo tempo, com mínimos efeitos colaterais, foi de 10 mg de efedrina.

Em relação à fenilefrina, recente estudo demonstrou que mesmo com altas doses (acima de 2.000 µg) utilizadas para o controle da pressão arterial, não houve efeitos deletérios para o feto, medidos pelo escore de Apgar e gasometria do sangue do cordão umbilical [23]. No atual estudo, escolheu-se a dose de 80 µg de fenilefrina profilática, com base em estudo prévio, que mostrou ser essa uma dose eficaz quando administrada em *bolus* por via intravenosa, sem efeitos colaterais graves [12].

Para a avaliação do controle da hipotensão arterial, estudos demonstraram igual eficácia entre efedrina e fenilefrina na prevenção e no tratamento dessa complicação, tanto em *bolus* quanto em infusão contínua [23,24]. No presente trabalho, por praticidade, optou-se por utilizar administração das substâncias em *bolus*. A fenilefrina teve menor eficácia na prevenção de hipotensão arterial em relação à efedrina, como demonstrado pelo número de pacientes que apresentaram hipotensão arterial e número de episódios em cada grupo. Tal fato deve-se provavelmente à duração de ação mais fugaz desse vasopressor e a forma de administração empregada. Uma vez que foi administrada em *bolus* e de forma profilática, apenas repetindo-se a dose quando a pressão arterial fosse menor ou igual a 80% da medida basal, flutuações da concentração plasmática da substância também podem ter contribuído. Apesar de a fenilefrina apresentar controle menos eficaz da pressão arterial, não houve diferença na incidência de efeitos colaterais maternos, tais como náuseas, vômitos e alteração do nível de consciência, possivelmente porque a diminuição da pressão arterial não foi muito intensa.

Em revisão sistemática sobre os fatores associados a pH e excesso de bases após anestesia raquídea para cesariana, concluiu-se que o tempo entre a incisão uterina e a retirada do feto associou-se a valores baixos de pH e de excesso de bases [24]. Contudo, no presente estudo, não houve diferença entre os grupos em relação ao tempo cirúrgico decorrido entre a instalação do bloqueio e a retirada do recém-nascido. Não se acredita que idade gestacional ou peso do recém-nascido tenham causado algum grau de interferência na avaliação, uma vez que ambos os grupos apresentaram características semelhantes em relação a tais parâmetros. Estudos prévios relataram alterações na gasometria do cordão umbilical associadas ao uso de efedrina, mas sem repercussões deletérias para o feto, quando avaliadas pelo escore de Apgar no primeiro e no quinto minuto [18,19]. Alguns autores citaram possível interferência do fenômeno de taquifilaxia e alteração no metabolismo fetal por causa do efeito beta-adrenérgico da efedrina [18,19,24]. A fenilefrina, por ser uma substância alfa-agonista pura, não causaria tal alteração. No presente estudo, apesar da ausência de caracterização numérica de acidose fetal propriamente dita, a efedrina associou-se a pH arterial mais baixo que a fenilefrina. Tal fato pode sugerir interferência no metabolismo fetal, uma vez que o pH da veia não apresentou diferença significativa entre os grupos. Outra possível etiologia para alteração gasométrica poderia ser representada por alteração do fluxo uteroplacentário. Entretanto, os recém-nascidos no grupo E apresentaram valores de Apgar considerados baixos predominantemente no primeiro minuto, com melhoras no quinto minuto, indicando alterações de caráter transitório nos recém-nascidos, sem repercussão a médio e longo prazos.

Os resultados dão suporte apenas parcial à hipótese aventada, o que poderia ser justificado por deficiências técnicas no método e pelo tamanho da amostra. Contudo, as repercussões deletérias para o feto, analisadas pelo escore de Apgar e pela gasometria, foram menos freqüentes com o uso da fenilefrina e apenas transitórias com o uso da efedrina.

Ephedrine versus Phenylephrine: Prevention of Hypotension during Spinal Block for Cesarean Section and Effects on the Fetus

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INTRODUCTION

Hypotension during spinal block for cesarean section is secondary to the sympathetic blockade and it can be harmful to both the fetus and mother. Among the deleterious effects

one can mention a reduction in uterine and placental blood flow, disruption of fetal oxygenation and fetal acidosis, and maternal symptoms of reduced cardiac output, such as nausea, vomiting, and altered level of consciousness [1].

The incidence of hypotension after spinal block for cesarean section can be as high as 80% [2-4] if prophylactic measures, such as prior hydration, moving the uterus to the left side, and vasopressors, are not instituted [5,6].

Ephedrine is a non-catecholamine sympathomimetic agent that stimulates alpha and beta adrenergic receptors direct and predominantly indirectly, producing its effects by releasing norepinephrine from nerve endings in the autonomous nervous system. Traditionally it is the vasopressor of choice in obstetric anesthesia despite the lack of confirmation of its superiority over other vasopressors [7,8]. The intercurrences of epinephrine include maternal supraventricular tachycardia, tachyphylaxis, and fetal acidosis. Prior studies reported that the increase in blood pressure caused by ephedrine is related to preservation of uterine and placental blood flow, especially due to its beta-adrenergic action [9,10]. However, other authors have suggested that ephedrine can reduce umbilical cord pH without affecting Apgar scores [4,11].

Phenylephrine is considered a pure α_1-adrenergic agonist. It promotes dose-dependent vasoconstriction, which is more pronounced in the venous than in the arterial bed, improving venous return after the sympathetic blockade during spinal block. Studies have shown that phenylephrine maintain uterine and placental blood flow and higher umbilical cord blood pH than ephedrine, having similar efficacy in controlling hypotension but with a lower risk of fetal acidosis [5,12,13].

The present study hypothesized that the pharmacologic profile of phenylephrine regarding the vitality of the newborn is superior to that of ephedrine in the treatment of hypotension during cesarean section under spinal block. The objective of this study was to compare the efficacy of phenylephrine and ephedrine in the prevention and treatment of intraoperative maternal hypotension, evaluate the side effects of this therapy, and to study fetal changes using Apgar scores and arterial and venous umbilical cord blood gases.

METHODS

After approval by the Ethics on Research Committee (CEP, from the Portuguese) in humans of the University of Brasília and signing of the informed consent, 60 women were selected for this randomized, double blind, prospective study.

Inclusion criteria were as follows: physical status ASA I or II, term pregnancy of a single fetus, and indication for cesarean section. Exclusion criteria were refusal to participate in the study, patients younger than 18 years, preexisting or pregnancy-induced systemic hypertension, and presence of cardiovascular or cerebrovascular diseases, fetal abnormalities, history of allergy to the drugs used in the study, and contraindications to spinal block.

Monitoring included continuous electrocardiogram, non-invasive blood pressure, and pulse oximetry. Patients were placed in dorsal decubitus for a few minutes and blood pressure and heart rate were recorded every three minutes for three times to obtain mean baseline levels. With the patient in left lateral decubitus, spinal puncture was done with a 25 $\times$ 3.5 Quincke needle between L_2-L_3 or L_3-L_4 and a solution containing 10 mg of 0.5% hyperbaric bupivacaine and 3 µg of sufentanil was administered. Afterwards, with the patient in dorsal decubitus, a Crawford wedge was placed under her right hip to obtain left uterine displacement. Immediately after the subarachnoid injection and before the incision of the uterus, an infusion of two liters of Ringer's lactate was initiated, followed by a slow infusion.

Patients were randomly divided into two groups using sequential, sealed envelopes with random numbers generated previously by a computer. The result of the allocation was ignored by both the patients and the physicians responsible for collecting and analyzing the study parameters. The determination of sample size was based on prior studies [12,13]. Groups were composed of 30 patients each and denominated Group E (ephedrine) and Group P (phenylephrine). Patients in Group E received a prophylactic intravenous bolus of 10 mg of ephedrine immediately after the subarachnoid block and patients in Group P received a prophylactic intravenous bolus of 80 µg of phenylephrine. The syringes with the study drugs were prepared by a physician who was not involved in the collection of the data and analysis of the results.

Maternal hypotension was defined as a blood pressure equal or lower than 80% of baseline values and it was treated with a bolus of 50% of the initial dose of the vasopressor. Reactive hypertension was characterized as blood pressure 20% higher than baseline levels after the use of the vasopressor. Heart rate below 50 bpm characterized bradycardia, when accompanied by hypotension, and it was treated with 0.75 mg of atropine.

The level of sensitive blockade was evaluated every minute after the puncture, by painful stimuli with a needle, until the end of the procedure. Authorization for the surgical procedure was given only when the level of the blockade reached T_5. The time from the blockade to the incision of the skin, incision of the uterus, and removal of the fetus were recorded.

The incidence of maternal hypotension, reactive hypertension, bradycardia, nausea and vomiting, and the total dose of vasopressor were also analyzed.

Apgar scores on the first and fifth minutes of all newborns were determined and a score below eight was considered low. Venous and arterial blood were drawn from the umbilical cord immediately after delivery for blood gases determination, and a pH below 7.2 was considered fetal acidosis.

The Student *t* test for continuous data, Mann-Whitney test for ordinal data, and Chi-square test for nominal data were used to analyze the results. A $p < 0.05$ was considered significant.

RESULTS

The mean age of patients in Group E was 27.2 years, and 26.5 years in Group P. The mean body mass index (BMI) was similar in both groups, as well as the weight. Patients had a mean gestational age of 39 weeks. Other demographic parameters and physical status did not show statistically significant differences (Table I).

The mean time from the spinal puncture to skin incision in Group E was 7.4 minutes and 6.9 minutes in Group P. The mean time to uterine incision was 12.7 and 12.8 in Groups E and P, respectively, and the mean time for delivery of the fetus was 13.8 and 14.2 minutes. Those parameters did not show statistically significant differences. In Group E the mean dose of vasopressor used was 14 mg and in Group P 186 µg. As for the sensitive blockade in most patients it reached T_4 (Table II).

As for side effects, Group E had seven episodes of nausea and four of vomiting, while Group P had 10 episodes of nausea and six of vomiting. The incidence of reactive hypertension was similar: five episodes in Group E and four in Group P. Only one patient in Group P developed bradycardia, which was treated with atropine. Those differences were not statistically significant. In Group P, 28 patients (93%) developed hypotension and in Group E 21 (70%) patients developed this complication, and this difference was statistically significant ($p < 0.05$). The number of episodes of hypotension was significantly higher in Group P (80 episodes) than in Group E (29 episodes), $p < 0.05$ (Table III).

Group E had a higher proportion of newborns with Apgar scores in the first minute that were lower than 8 (27%) than group P (10%), and this difference was statistically significant ($p < 0.05$).

In Group E, eight newborns (27%) had Apgar scores in the first minute of seven, 17 (56%) had scores of eight, and five (17%) of nine. In Group P, three newborns (10%) had Apgar scores in the first minute of seven, fifteen (50%) of eight, eleven (37%) of nine, and one (3%) of 10.

Apgar scores in the fifth minute did not show differences between both groups. In Group E, two newborns (6%) had Apgar scores of eight, twenty (67%) had scores of nine, and eight (27%) of ten. In Group P, half of the newborns had Apgar scores in the fifth minute of nine and ten in the other half.

As for arterial and venous umbilical cord blood gases, mean pH showed statistically significant differences between both groups: 7.22 in Group E and 7.27 in Group P ($p < 0.05$). Table IV shows the mean blood gases levels.

Table I – Demographic Data

General Characteristics	Group E (n = 30)	Group P (n = 30)
Age (years)	27.2 ± 4.5	26.5 ± 5.1
Weight (kg)	83.5 ± 6.9	79.2 ± 9.7
Height (cm)	159,6 ± 5.3	158.5 ± 5.8
BMI ($kg.m^{-2}$)	32.8 ± 2.5	31.1 ± 3,.5
Gestational age (weeks)	39.5 ± 1.1	39.6 ± 1.3
Physical Status (ASA I / II)	20 / 10	20 / 10
Weight of the newborn (g)	3,641 ± 499.1	3,538 ± 535.4

Values expressed as Mean ± SD.
* $p < 0.05$.

Table II – Anesthetic-Surgical Parameters

Anesthetic-surgical parameters	Group E (n = 30)	Group P (n = 30)
Time from the blockade to skin incision (min)	7.4 ± 2.2	6.9 ± 2.4
Time from the blockade to uterine incision (min)	12.7 ± 2.2	12.8 ± 3.7
Time from the blockade to delivery (min)	13.8 ± 2.3	14.2 ± 3.5
Vasopressor dose	14 mg	186 µg
Sensitive level at T_4 (%)	22 (73.3%)	22 (73.3%)
Sensitive level at T_5 (%)	8 (26.7%)	8 (26.7%)

Values expressed as Mean ± SD.
* $p < 0.05$.

Table III – Side Effects, Number of Episodes, and Proportion

Side effects	Group E (n = 30)	Group P (n = 30)
Nausea (episodes)	7	10
Vomiting (episodes)	4	6
Hypotension (episodes)*	29	80
Hypotension (patients)*	21 (70%)	28 (93.3%)
Reactive hypertension (episodes)	5	4
Bradycardia (episodes)	0	1

* $p < 0.05$.

Table IV – Arterial and Venous Umbilical Cord Blood Gases

Blood gases	Group E (n=30)	Group P (n=30)
Arterial pH*	7.22 ± 0.03	7.27 ± 0.06
Arterial BE	-10.5 ± 2.6	-9.2 ± 4.2
Arterial pCO_2	40.0 ± 3.8	38.9 ± 8.9
Arterial pO_2	19.5 ± 3.6	18.0 ± 4.8
Arterial HCO^{-3}	16.2 ± 2.4	16.5 ± 4.0
Venous pH	7.27 ± 0.04	7.28 ± 0.06
Venous BE	-7.2 ± 3.5	-7. 9 ± 4.4
Venous pCO_2	34.7 ± 6.7	35.2 ± 11.1
Venous pO_2	25.6 ± 6.3	24.3 ± 7.1
Venous HCO^{-3}	18.4 ± 2.9	18.7 ± 3.5
Values expressed as Mean ± SD.		

* $p < 0.05$.

DISCUSSION

The indication of regional block in obstetrics has gained acceptance due to the reduction in maternal and fetal morbidity and mortality [14]. However, some studies have associated a greater incidence of fetal acidosis after spinal block, probably secondary to maternal hypotension or factors that modify uterine and placental blood flow [15,16].

Moving the uterus to the left and administering intravenous fluids have been used to reduce the severity of hypotension, but with limited efficacy. The administration of vasopressors is frequently necessary [17].

Historically, ephedrine has been the vasopressor of choice in obstetrics despite the uncertainty about its superiority [1,7,9]. It was believed that ephedrine increases maternal blood pressure, therefore preserving uterine and placental blood flow due to its beta-adrenergic action, while pure alpha-agonist vasopressors were associated with a reduction in this blood flow [8,10]. However, subsequent studies demonstrated that in the treatment of post-spinal block hypotension in cesarean sections ephedrine has similar efficacy, but it can occasionally promote fetal acidosis [18-20].

In the present study, parameters associated with post-spinal block hypotension were controlled to evaluate which drug would be more effective in the prevention of hypotension with fewer deleterious consequences to the fetus. Prior studies have presented different methodologies and questionable results regarding the ideal vasopressor, dose, and administration regimen, as well as the use of other techniques to control maternal blood pressure with minimal deleterious effects on the fetus [12,19,20].

To limit distortions, all patients were hydrated with 2,000 mL of Ringer's lactate, which was instituted after the spinal block since recent studies have demonstrated the inefficacious of prior hydration due to the fast redistribution [21]. The uterus was moved to the left to reduce aortocaval compression, and the blockade was maintained on the same level in all patients.

Despite the care with the method employed, some factors can limit the interpretation of the study. The number of patients involved although greater than in some studies reported can be a bias since sample size was not calculated. The difference of time between the time the umbilical cord blood was drawn and the analysis of blood gases is another limitation. This difference might have altered the results of blood gases and possibly interfered with the results.

Prior studies have suggested that a bolus of 30 mg of intravenous ephedrine would be more effective in the prevention of hypotension, but with an increased incidence of reactive hypertension [22]. In contrast, a prospective, observational study demonstrated that the intravenous administration of 15 to 20 mg of ephedrine reduced the incidence of maternal hypotension without increasing the incidence of reactive hypertension [20]. A 2004 metaanalysis [19] concluded that doses above 14 mg of ephedrine did not reduce the incidence of maternal hypotension, but they caused reactive hypertension in the mother and a small reduction in umbilical cord blood pH. In the present study, a dose of 10 mg of ephedrine was considered to be effective and, at the same time, had little side effects.

As for phenylephrine, a recent study demonstrated that even high doses (above 2,000 µg) were not associated with de-

leterious effects on the fetus, as determined by the Apgar scores and umbilical cord blood gases [23]. In the present study, the dose of 80 µg of phenylephrine was chosen based on a prior study that demonstrated that this was the effective dose when administered as an intravenous bolus, without severe side effects [12].

On evaluating the control of hypotension, several studies have demonstrated similar efficacy of ephedrine and phenylephrine on the prevention and treatment of this complication, both when used in bolus or continuous infusion [23,24]. In the present study, for practical purposes, it was decided to administer the medication as a bolus. Phenylephrine showed lower efficacy on the prevention of hypotension than ephedrine, demonstrated by the number of patients who developed hypotension and the number of episodes in each group. This probably was secondary to the shorter duration of action of this vasopressor and the way it was administered, since it was administered as a bolus and prophylactically, only repeating the dose when the blood pressure was equal or lower than 80% of baseline levels, and fluctuations in its plasma concentrations could also have contributed. Although phenylephrine is less effective in controlling blood pressure, differences in the incidence of maternal side effects, such as nausea, vomiting, and changes in the level of consciousness, were not detected probably because the reduction in blood pressure was not severe.

A systematic revision of the factors associated with pH and base excess after spinal block for cesarean section concluded that the time between uterine incision and removal of the fetus was associated with low pH and base excess [24]. However, in the present study, differences in the time between the installation of the blockade and removal of the fetus were not detected. We do not believe that gestational age and the weight of the newborn caused any interference with the evaluation, since those parameters were similar in both groups.

Prior studies reported changes in umbilical cord blood gases associated with the use of ephedrine, but without deleterious repercussions on the fetus, as demonstrated by the Apgar scores in the first and fifth minutes [18,19]. Some authors have mentioned possible interferences of tachyphylaxis and changes in fetal metabolism due to the beta-adrenergic actions of ephedrine [18,19,24]. Since it is a pure alpha-agonist, phenylephrine would not have the same effects. In the present study, despite the absence of numerical characterization of fetal acidosis, ephedrine was associated with a lower arterial pH than phenylephrine. This could suggest an influence in fetal metabolism, since venous pH did not show significant differences between both groups. Other possible etiology for this change in blood gases could be related to the change in uterine and placental blood flow. However, newborns in group E had low Apgar scores predominantly in the first minute, with a substantial improvement in the fifth minute, indicating transitory changes on the newborns, without medium- and long-term repercussions.

The results of the present study only give partial support to the hypothesis guiding this study, what could be justified by technical deficiencies of the method and the size of the study population. However, deleterious repercussions on the fetus, analyzed by the Apgar scores and blood gases, were less frequent with phenylephrine and only transitory with ephedrine.

REFERÊNCIAS – *REFERENCES*

01. Rout CC, Rocke DA — Prevention of hypotension following spinal anesthesia for cesarean section. Int Anesthesiol Clin, 1994;32:117-135.
02. Clark RB, Thompson DS, Thompson CH — Prevention of spinal hypotension associated with Cesarean section. Anesthesiology, 1976;45:670-674.
03. Hall PA, Bennett A, Wilkes MP et al. — Spinal anaesthesia for Caesarean section: comparison of infusions of phenylephrine and ephedrine. Br J Anaesth, 1994;73:471-474.
04. Kang YG, Abouleish E, Caritis S — Prophylactic intravenous ephedrine infusion during spinal anesthesia for cesarean section. Anesth Analg, 1982;61:839-842.
05. Morgan P — The role of vasopressors in the management of hypotension induced by spinal and epidural anaesthesia. Can J Anaesth, 1994;41:404-413.
06. Husaini SW, Russell IF — Volume preload: lack of effect in the prevention of spinal-induced hypotension at caesarean section. Int J Obstet Anesth, 1998;7:76-81.
07. Rout CC, Rocke DA, Levin J et al. — A reevaluation of the role of crystalloid preload in the prevention of hypotension associated with spinal anesthesia for elective cesarean section. Anesthesiology, 1993;79:262-269.
08. Ralston DH, Shnider SM, DeLorimier AA — Effects of equipotent ephedrine, metaraminol, mephentermine, and methoxamine on uterine blood flow in the pregnant ewe. Anesthesiology, 1974; 40:354-370.
09. Burns SM, Cowan CM, Wilkes RG — Prevention and management of hypotension during spinal anaesthesia for elective Caesarean section: a survey of practice. Anaesthesia, 2001;56: 794-798.
10. James FM 3rd, Greiss FC Jr, Kemp RA — An evaluation of vasopressor therapy for maternal hypotension during spinal anesthesia. Anesthesiology, 1970;33:25-34.
11. Ratcliffe FM, Evans JM — Neonatal well-being after elective caesarean delivery with general, spinal, and epidural anaesthesia. Eur J Anaesthesiol, 1993;10:175-181.
12. Lee A, Ngan Kee WD, Gin T — A quantitative systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg, 2002;94:920-926.
23. Ngan Kee WD, Khaw KS, Ng FF et al. — Prophylactic phenylephrine infusion for the prevention of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg, 2004; 98:815-821.
34. Hawkins JL, Koonin LM, Palmer SK et al. — Anesthesia-related deaths during obstetric delivery in the United States, 1979-1990. Anesthesiology, 1997;86:277-284.
45. Roberts SW, Leveno KJ, Sidawi JE et al. — Fetal acidemia associated with regional anesthesia for elective cesarean delivery. Obstet Gynecol, 1995;85:79-83.
56. Mueller MD, Brühwiler H, Schüpfer GK et al. — Higher rate of fetal acidemia after regional anesthesia for elective cesarean delivery. Obstet Gynecol, 1997;90:131-134.

67. Jackson R, Reid JA, Thorburn J — Volume preloading is not essential to prevent spinal-induced hypotension at Caesarean section. Br J Anaesth, 1995; 75:262-265.
78. Ngan Kee WD, Khaw KS, Ng FF — Prevention of hypotension during spinal anesthesia for cesarean delivery: an effective technique using combination phenylephrine infusion and crystalloid cohydration. Anesthesiology, 2005;103:744-750.
89. Lee A, Ngan Kee WD, Gin T — A dose-response meta-analysis of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anesthesia for elective cesarean delivery. Anesth Analg, 2004;98:483-490.
20. Simon L, Provenchère S, de Saint Blanquat L et al. — Dose of prophylactic intravenous ephedrine during spinal anesthesia for cesarean section. J Clin Anesth, 2001;13:366-369.
21. Ueyama H, He YL, Tanigami H et al. — Effects of crystalloid and colloid preload on blood volume in the parturient undergoing spinal anesthesia for elective cesarean section. Anesthesiology, 1999;91:1571-1576.
22. Ngan Kee WD, Khaw KS, Lee BB et al. — A dose-response study of prophylactic intravenous ephedrine for the prevention of hypotension during spinal anesthesia for cesarean delivery. Anesth Analg, 2000;90:1390-1395.
23. Emmett RS, Cyna AM, Andrew M et al. — Techniques for preventing hypotension during spinal anaesthesia for caesarean section. Cochrane Database Syst Rev, 2002;(3):CD002251.
24. Ngan Kee WD, Lee A — Multivariate analysis of factors associated with umbilical arterial pH and standard base excess after Caesarean section under spinal anaesthesia. Anaesthesia, 2003;58:125-130.

RESUMEN

Magalhães E, Govêia CS, Ladeira LCA, Nascimento BG, Kluthcouski SMC — Efedrina *versus* Fenilefrina: Prevención de Hipotensión Arterial durante Anestesia Raquidea para Cesárea y Efectos sobre el Feto.

JUSTIFICATIVA Y OBJETIVOS: *La hipotensión arterial durante la anestesia raquídea para cesárea se debe al bloqueo simpático y a la compresión aortocava por el útero y puede ocasionar efectos malignos para el feto y su madre. La efedrina y fenilefrina mejoran el retorno venoso después del bloqueo simpático durante la anestesia raquídea. El objetivo de este estudio fue comparar la eficacia de la efedrina y de la fenilefrina en prevenir y tratar la hipotensión arterial materna durante la anestesia raquídea y evaluar así sus efectos colaterales y las alteraciones fetales.*

MÉTODO: *Sesenta pacientes, sometidas a la anestesia raquídea con bupivacaína y sufentanil para cesárea, se dividieron aleatoriamente en dos grupos para recibir, profilácticamente, efedrina (Grupo E, n = 30, dosis = 10mg) o fenilefrina (Grupo F, n = 30, dosis = 80 µg). Hipotensión arterial (presión arterial menor o igual a un 80% de la medida basal) fue tratada con bolo de vasoconstrictor con un 50% de la dosis inicial. Se evaluaron: incidencia de hipotensión arterial, hipertensión arterial reactiva, bradicardia y vómitos, puntuación de Apgar en el 1° y 5° minutos y gasometría del cordón umbilical.*

RESULTADOS: *La dosis promedio de efedrina fue 14,8 mg (± 3,8) y 186,7 µg (± 52,9) de fenilefrina. Los grupos fueron similares en cuanto a los parámetros demográficos y a la incidencia de vómitos, bradicardia e hipertensión arterial reactiva. La incidencia de hipotensión arterial fue de un 70% en el Grupo E y un 93% en el Grupo F ($p < 0,05$). El pH arterial promedio del cordón umbilical y el puntaje de Apgar en el 1° minuto fueron menores en el grupo E ($p < 0,05$). No se registró diferencia en el puntaje del 5° minuto.*

CONCLUSIONES: *La efedrina fue más efectiva que la fenilefrina en la prevención de la hipotensión arterial. Los dos fármacos presentaron una incidencia similar de efectos colaterales. Las repercusiones fetales fueron menos frecuentes con el uso de la fenilefrina y apenas transitorias con el uso de la efedrina.*