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Etilefrine vs. phenylephrine for hypotension during spinal anesthesia for cesarean section: Multicenter, randomized, double blind controlled clinical trial☆

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ABSTRACT

Introduction: Hypotension after spinal anesthesia in cesarean section should be minimized. The use of vasopressors is an effective measure to treat hypotension. The objective of this paper is to compare the safety and effectiveness of etilefrine vs. phenylephrine in the management of this condition.

Methods: This multicenter, double-blind trial between August 2009 and November 2010 included 196 patients with hypotension during spinal anesthesia for cesarean delivery; the patients were randomized to receive etilefrine or phenylephrine as vasopressor. The primary outcome was the fetal umbilical arterial pH. The secondary outcomes were: fetal acidosis (umbilical arterial pH < 7.20), Apgar score at 1 and 5 min, need for intubation and admission to the neonatal intensive care unit for newborns, and time of hypotension, total dose of vasopressor, atropine requirement, intravenous fluids volume and incidence of nausea and vomiting in mothers.

Results: 98 patients received etilefrine and 98 phenylephrine. There were no differences in umbilical arterial pH (7.27 vs. 7.28, respectively, $P = 0.493$). The total dose of vasopressor (5.66 vs. 6.51 ml, respectively, $P = 0.024$) and total time of hypotension (2.78 vs. 3.25 min, respectively, $P = 0.021$) were lower in the etilefrine group. Other outcomes studied showed no statistically significant differences.

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Conclusion: Etilefrine and phenylephrine are equally effective for the treatment of hypotension during spinal anesthesia for cesarean delivery. This study found no difference in the maternal or fetal outcomes.

Etilefrina vs fenilefrina en hipotensión por anestesia espinal para cesárea: ensayo clínico multicéntrico, controlado, aleatorizado y doble ciego

Palabras clave:
Fenilefrina
Anestesia raquídea
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RESUMEN

Introducción: La hipotensión que ocurre luego de anestesia espinal para cesárea debe minimizarse. El uso de vasopresores es una medida eficaz para su tratamiento. El objetivo de este trabajo es comparar la seguridad y efectividad de etilefrina vs fenilefrina para manejo de esta condición.

Métodos: En este estudio multicéntrico y doble ciego, entre agosto de 2009 y noviembre de 2010, 196 pacientes con hipotensión durante anestesia espinal para cesárea, fueron asignadas aleatoriamente para recibir etilefrina o fenilefrina como vasopresor. El resultado primario fue el pH arterial umbilical fetal. Los resultados secundarios fueron: acidosis fetal (pH arterial umbilical < 7,20), puntaje Apgar al 1 y 5 minutos, necesidad de intubación e ingreso a la unidad de cuidados intensivos neonatal para los recién nacidos; y tiempo de hipotensión, dosis total de vasopresor, necesidad de uso de atropina, líquidos endovenosos totales e incidencia de nausea y vómito para las madres.

Resultados: 98 pacientes recibieron etilefrina y 98 fenilefrina. No se encontraron diferencias en el pH arterial umbilical (7,27 vs 7,28 respectivamente; p = 0,493). La dosis total de vasopresor (5,66 vs. 6,6 ml, respectivamente; P = 0,024) y el tiempo total de hipotensión (2,78 vs. 3,25 min, respectivamente; p = 0,021), fueron menores en el grupo de etilefrina. Los demás desenlaces estudiados no presentaron diferencia estadísticamente significativa.

Conclusión: La etilefrina y la fenilefrina son igualmente efectivas para el tratamiento de la hipotensión por anestesia espinal para cesárea. Este estudio no encontró diferencia en los resultados fetales ni maternos.

Introduction

In the last few years there has been an increasing incidence of cesarean sections worldwide, with rates ranging from 25 to 30%.[1] Regional anesthesia is considered superior to general anesthesia for cesarean delivery because it reduces maternal morbidity, although mortality and neonatal outcomes are similar as compared to general anesthesia.[2,3] Spinal anesthesia has become the technique of choice for this procedure because it is safer and simpler to use, is administer in a shorter time, has a quick onset of action, and is more comfortable for the patient.

Maternal hypotension is an unwanted consequence of spinal block. Its incidence ranges from 55 to 90%,[4–6] and is more frequent in patients scheduled for elective cesarean section and no labor.[7]

Hypotension during spinal anesthesia – regardless of how mild or short duration – results in deleterious effects for both the mother and the fetus. There is decreased uteroplacental blood flow (UBF) causing hypoxia and fetal acidosis, as well as neonatal depression.[1,8] The mother experiences low cardiac output symptoms, including nausea, vomiting, dizziness, and decreased consciousness. Several interventions have been studied and implemented to reduce the incidence of hypotension; i.e., uterine displacement, intravascular volume expansion with intravenous fluids, and the use of vasopressors.[9,4]

Despite the use of pre-load or co-load of intravenous fluids, there is still a high frequency of hypotension and vasopressors are required in a high proportion of patients.[10]

Though most studies have shown that the incidence of fetal acidosis following spinal anesthesia is secondary to hypotension, others feel that acidosis may be associated to the transfer of the vasopressor across the placenta.[8,11–14]

Phenylephrine is one of the most studied vasopressors and is the drug of choice in obstetrics because of its high transfer rate across the placental barrier, increased fetal metabolism due to direct stimulation of the α and β receptors, and because it increases catecholamines and $PaCO_2$. Phenylephrine has shown less transfer across the placenta with enhanced uteroplacental blood flow and improved acid–base fetal status.[12–15]

Etilefrine is the most frequently used vasopressor in Colombia for the treatment of hypotension from spinal anesthesia during cesarean section.[16] Etilefrine is a direct action sympathomimetic agent that stimulates the α-1 and β-2