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Brain damage after general anesthesia☆

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ABSTRACT

Background and objective: S100B protein is a serum marker of cerebral damage. The objective was to evaluate the brain damage caused by general anesthesia, by determining the concentration of serum S100B protein before and after of general anesthesia.
Patients and method: Patients with chronic adenotonsillar hypertrophy and indications for tonsillectomy were included. A venous blood sample was taken from the patients before general anesthesia (basal sample). The patients were anaesthetized using the following intravenous anesthetic drugs: midazolam, fentanyl and propofol; and inhaled sevoflurane. A second venous blood sample (postoperative sample) was taken from patients after the surgery, in the operating room. The concentration of serum S100B protein was determined in the basal sample (S100Bb) and postoperative sample (S100Bp) by immunoassay electro-chemiluminescence in MODULAR E-170 (Roche Diagnostics).
Results: Seventy-six patients were included, 46 males and 30 females, aged between 3 and 14 (median 5 years). In all the patients, serum S100B protein levels increased after general anesthesia. The values of S100Bp (median 164.0 ng/l) were significantly higher than the values of S100Bb (median 94.5 ng/l). The median of the difference between S100Bp and S100Bb was 58.0 ng/l. There were statistically significant differences between S100Bb and S100Bp using the Wilcoxon test ($p < 0.0001$).
Conclusions: The concentration of serum S100B protein increased significantly after general anesthesia. This indicates that general anesthesia may cause brain damage.

Daño cerebral postanestesia general

Palabras clave:
Proteína S100B
Anestesia general
Daño cerebral
Midazolam
Fentanilo
Propofol
Sevoflurano

RESUMEN

Fundamento y objetivo: La proteína S100B es un marcador sérico de daño cerebral. El objetivo fue evaluar el daño cerebral producido por la anestesia general mediante la determinación de la concentración de proteína S100B sérica antes y después de la anestesia general.
Pacientes y método: Se incluyeron pacientes con intervención quirúrgica programada de amigdalectomía por hipertrofia amigdalar. En la consulta de preanestesia se extrajo una muestra de sangre venosa (muestra basal). Los pacientes fueron sometidos a anestesia general utilizando los siguientes fármacos anestésicos intravenosos: midazolam, fentanilo y propofol; y sevoflurano inhalado. Al finalizar la intervención quirúrgica y con el paciente aún en quirófano, se extrajo una segunda muestra de

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sangre venosa (muestra postexposición). Se determinó en suero la concentración de la proteína S100B en la muestra basal (S100Bb) y en la muestra postexposición (S100Bp), mediante inmunoanálisis de electroquimioluminiscencia en el MODULAR E-170 (Roche Diagnostics).
Resultados: Se incluyeron 76 pacientes, 46 varones y 30 hembras, con edades entre 3 y 14 años (mediana 5 años). En todos los pacientes, los niveles de proteína S100B sérica aumentaron tras la anestesia general. Los valores obtenidos de S100Bp (mediana 164,0 ng/l) fueron significativamente mayores que los obtenidos de S100Bb (mediana 94,5 ng/l). La mediana de la diferencia entre S100Bp y S100Bb fue de 58,0 ng/l. Mediante el test de Wilcoxon se encontraron diferencias estadísticamente significativas entre S100Bb y S100Bp ($p < 0{,}0001$).
Conclusiones: La concentración de proteína S100B sérica aumentó significativamente tras la anestesia general. Esto indica que la anestesia general puede producir daño cerebral.

Introduction

Exposure to anesthetic drugs can trigger apoptosis of the glial and neuronal cells of the central nervous system (CNS), that might cause brain damage.[1] There are studies available linking exposure to general anesthesia at an early age with a deficient cognitive development, including language delay and delay in acquiring some mathematics skills.[2–4]

Some of the anesthetic drugs frequently used include propofol, midazolam, fentanyl and sevoflurane. Propofol is the intravenous (iv) hypnotic agent universally used as an induction agent in general anesthesia. It involves the CNS lowering cerebral blood flow (CBF) and metabolism. It depresses respiratory function and decreases myocardial contractility and peripheral vascular resistance, at a cardiorespiratory level. Midazolam is one of the iv benzodiazepine most used in premedication due to its ability to cause anterograde amnesia, and it also decreases the CBF and depresses respiratory function. However, its cardiac depressant effects are minimal. Fentanyl is an opioid widely used in anesthesia to provide analgesia to the patient. These drugs do not depress myocardial contractility, but they do cause mild hypotension. Sevoflurane is a fluorinated halogenated liquid which subjected to high pressures becomes a gas and can be supplied for inhalation. It is often used as a hypnotic anesthetic agent for maintenance of anesthesia. It causes unconsciousness and amnesia, increasing the CBF due to its vasodilator effect, and decreasing the cerebral metabolic rate. Like propofol, it depresses respiratory function and decreases myocardial contractility and peripheral vascular resistance.[5]

S100B protein is a calcium binding protein located in the CNS cells, as part of the structure of astrocytes and Schwann cells.[6–9] It is also located in other tissues such as skin, adipose tissue and skeletal muscle as well as in melanoma tumor cells.[6] S100B protein is one of the most accurate serum markers of brain damage.[6,10] In a healthy patient, the serum S100B protein levels are low and it acts as a neurotrophic factor. However, in patients with brain damage it increases and acts as a neuro apoptotic factor.[6,11,12]

The aim of this study was to evaluate brain damage from general anesthesia by determining the concentration of serum S100B protein before and after exposure to anesthetic agents in children with tonsillar hypertrophy undergoing general anesthesia with propofol, midazolam, fentanyl and sevoflurane for tonsillectomy surgery.

Patients and methodology

Descriptive cross-sectional clinical trial of patients after exposure to anesthetic pharmacology. This clinical trial has been approved by the Research and Ethics Committee of the Puerto Real University Hospital and all participants have signed informed consent.

Patients

Pediatric patients were included consecutively for 6 months, from 1 February to 31 July 2015. They received assistance at the pre-anesthesia consultation and were referred from the Department of Otolaryngology to undergo tonsillectomy due to tonsillar hypertrophy. The children included had no personal history of neurological disease and without clinical manifestations indicative of neurological dysfunction in their medical history. Patients with neurological disorders, history of prematurity, emergency surgery, blood dyscrasias or impaired liver or kidney functions, soft tissue and cartilage tumors or large injuries were excluded within 3 months before the intervention.

Method

In the pre-anesthesia department a sample of peripheral venous blood was drawn from every patient included in this study into a serum gel tube (Vacuette®) (baseline sample). Every patient underwent tonsillectomy under general anesthesia using the following anesthetic drugs: iv midazolam as an ananxiolytic agent, iv fentanyl as an analgesic agent, iv propofol is used to induce anesthesia and sevoflurane is used as an inhalational anesthetic for induction and maintenance of general anesthesia. Inhalational induction was conducted by administering 8% sevoflurane fraction through an external Mapleson type D circuit. The resulting mixture of fresh gas is air, oxygen and sevoflurane. After losing consciousness the inhaled infraction decreases up to 2% in order to maintain a minimum alveolar concentration (MAC) of about 1. At that moment, the venous route for administration of iv anesthetic drugs is canalized. The level of hypnosis is established using the patient's MAC and in no case MAC is over 1. Tonsillectomy was performed in all cases through a 3–5 mm resection of the anterior tonsillar pillars, with electrocautery at 15 W. After surgery, while awakening from anesthesia and the patient still in the operating room, one more peripheral venous blood sample (postexposure sample) was drawn. Baseline and post-exposure blood samples of each patient were centrifuged for 4 min at 4000 rpm to obtain serum. Serum S100B protein levels were determined in both samples through electrochemiluminescence immunoassay in the MODULAR E-170 autoanalyzer (Roche Diagnostics) with reference values for normality ranging from 5 to 105 ng/l.

Statistical analysis

The obtained data were processed using SPSS® and MedCalc® statistical programs, statistical significance being defined as $p < 0.05$. To determine the type of variable distribution, the D'Agostino–Pearson test for normal distribution was used. Descriptive statistics is shown with the frequency of qualitative variables; with minimum, maximum value, the arithmetic mean