URINE PROTEIN SEPARATION BY GEOMETRICAL ELECTROPHORESIS AFTER ANAESTHESIA WITH SEVOFLURANE

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Abstract: Protein determination in urine above the normal values after low-flow anaesthesia with Sevoflurane has led us to study its nature and significance. Proteinuria after anaesthesia is caused by Sevoflurane degradation by carbon dioxide absorbers and the increased amount of fluorine ions in kidneys. Compound A resulting from Sevoflurane degradation by carbon dioxide absorbers causes renal toxicity in animals with tubular necrosis, clinically evidenced by proteinuria and glycosuria. Materials and method: We observed 62 patients in the Intensive Care Unit who were anesthetised with Sevoflurane for different surgical interventions on medium and long term. Thus, we analyzed 186 urine samples from the anesthetized patients by spectrophotometry at 600 nm and by electrophoresis. Urine samples were taken from patients, preoperatively and at 24 and 72 hours postoperatively and were analyzed without having been previously preserved in order to remove any possible errors. The patients who were accepted in the study had an anaesthetic risk ASA I-III, according to the classification of the American Society of Anesthesiology, without a known renal pathology, with normal blood urea nitrogen and serum creatinine level in the preoperative period. The proteinuria was analyzed in a specialized laboratory of Mureș County Hospital with a Konelab 30i autoanalyzer by spectrophotometry at 600 nm. Protein electrophoresis was performed in the laboratory of the Department of Pathophysiology within the University of Medicine and Pharmacy of Târgu Mureș. Urinary protein levels were statistically analyzed, by applying the ANOVA test. The obtained data were statistically analyzed by calculating the "p" value which was considered statistically significant at a value less than 0.05. Results: A number of 61 patients were included in the study, with an average age of 59 years old, a mean BMI=23 and a sex ratio F/M=29/32 with an anaesthetic risk, ASA I-III=1/22/8, according to the classification of the American Society of Anesthesiology. The anaesthetic characteristics were the following: an average duration of anaesthesia of 200 minutes (between 80 and 300 minutes) and a minimal alveolar concentration (MAC) of 1.8 (1.4 to 2.2). Discussion: This study is a prospective, observational one, in which we demonstrate the presence of proteinuria with statistical significance (p<0.0001) after anaesthesia with Sevoflurane, data that we partially found in literature. Compound A, incriminated as triggering glomerular toxicity after anaesthesia with Sevoflurane has to reach a level of 800 ppm (parts per million) in order to be toxic to the kidneys. The literature also mentions the appearance of albuminuria after Desfluran anaesthesia although the degradation of this anaesthetic agent by carbon dioxide absorbers does not produce the compound A.


Keywords: Sevoflurane, electrophoresis, anestezia, proteinurie

Cuvinte cheie: Sevoflurane, electroforeză, anestezie, proteinurie
CLINICAL ASPECTS

INTRODUCTION

Protein determination in urine above the normal values after low-flow anesthesia with Sevoflurane has led us to study its nature and significance. Proteinuria after anesthesia is caused by Sevoflurane degradation by carbon dioxide absorbers and the increased amount of fluor ions in the kidneys.(1,2,3,4) Compound A resulting from Sevoflurane degradation by carbon dioxide absorbers causes renal toxicity in animals with tubular necrosis, clinically evidenced by proteinuria and glycosuria.(5,6,7,8,9,10) Monitoring the blood urea nitrogen and serum creatinine level after general anesthesia with Sevoflurane does not evidence the occurrence of renal toxicity attributable to anesthesia.(11,12,13,14) The monitoring of urine protein level reveals the existence of post anesthetic kidney changes.(15) Protein determination in urine using the electrophoresis method, patented by Professor Schiopu Alexandru in 1997, brings us extra information about the type of protein that crosses the glomerular barrier.(16)

PURPOSE

In the present study we aimed at demonstrating the presence of proteinuria with statistical significance (p<0.0001) after anesthesia with Sevoflurane.

METHODS

We observed 62 patients in the Intensive Care Unit who were anesthetised with Sevoflurane for different medium and long term surgical interventions. Thus, we analyzed 186 urine samples from anesthetized patients by spectrophotometry at 600 nm and by electrophoresis. Urine samples were taken from the patients, preoperatively and at 24 and 72 hours postoperatively and were analyzed without having been previously preserved in order to remove any possible errors. The patients accepted in the study had an anesthetic risk ASA I-III, according to the classification of the American Society of Anaesthesiology, without a known renal pathology, with normal blood urea nitrogen and serum creatinine level in the preoperative period. The anesthetic protocol included anesthetic induction with Thiopental sodium, Esmeron, Fentanyl and maintenance of anesthesia with Sevoflurane, Fentanyl and Esmeron. We used for induction a fresh gas flow of 5 litres/minute which we decreased at 2 litres/minute when we opened Sevoflurane at a MAC of 1,5-2 Sevoflurane. The duration of anesthesia was over 150 minutes. The proteinuria was analyzed in a specialized laboratory of Mureș County Hospital with a Konelab 30i autoanalyzer by spectrophotometry at 600 nm. Blood urea nitrogen and serum creatinine level were determined in the same laboratory. Protein electrophoresis was performed in the laboratory of the Department of Pathophysiology within the University of Medicine and Pharmacy of Târgu Mureș. The obtained data were statistically analyzed by calculating the “p” value which was considered statistically significant at a value less than 0.05. We also analyzed and evaluated the demographic data and anesthetic characteristics.

RESULTS

A number of 61 patients were included in the study, with an average age of 59 years, a mean BMI=23 and a sex ratio F/M=29/32 with an anesthetic risk, ASA I/II/III=1/22/38, according to the classification of the American Society of Anaesthesiology. The anesthetic characteristics were the following: an average duration of anesthesia of 200 minutes (between 80 and 300 minutes) and a MAC of 1,8 (1,4 to 2,2). Patients with stage I-II of blood pressure, without preoperative renal impairment, were also accepted. Urinary protein levels were statistically analyzed, by applying the ANOVA test (Figure no. 1). Preoperative blood urea nitrogen (at 24 and 72 hours) and serum creatinine level were statistically analyzed as shown in figures no. 2 and 3. In figure no. 4, we exhibit a graphical representation of electrophoresis to detect an appropriate mathematical difference between preoperative proteinuria and proteinuria at 24 and 72 hours.

Figure no. 1. Preoperative blood urea nitrogen at 24 and 72 hours

![Urine proteins at 24, 72 hours preoperatively](image)

Figure no. 2. Preoperative blood urea nitrogen at 24 and 72 hours. Case study

![Blood urea](image)

Figure no. 3. Preoperative serum creatinine level at 24 and 72 hours. Case study

\[ p = 0.307 \]

Patient ME 61197

Figure no. 4. Preoperative urinary electrophoresis

Figure no. 5. Preoperative protein fractions

Figure no. 6. Urinary electrophoresis at 24 hours postoperatively

Figure no. 7. Protein fractions at 24 hours postoperatively

Figure no. 8. Urinary electrophoresis at 72 hours postoperatively

Figure no. 9. Protein fractions at 72 hours postoperatively

DISCUSSIONS

This study is a prospective, observational one, in which we demonstrate the presence of proteinuria with statistical significance \((p < 0.0001)\) after anaesthesia with Sevoflurane. Partially, we found similar data in literature.\(^{17,18,19}\) The compound A, incriminated as triggering glomular toxicity after anaesthesia with Sevoflurane has to reach a level of 800 ppm (parts per million).\(^{20}\) The literature also mentions the appearance of albuminuria after Desflurana anaesthesia although the degradation of this anaesthetic by carbon dioxide absorbers does not produce the compound A. Statistically insignificant changes in blood urea nitrogen and serum creatinine level is demonstrated by other studies but they do not exclude the glomerular damage.
Monitoring the postoperative proteinuria is more accurate and should be taken into account since for 1 mg creatinine level increase, there should be 25% glomeruli destruction. It is important to know about transient proteinuria, as shown in this study, to avoid prolonged anaesthesia and repeat the same type of anaesthesia in a patient with iatrogenic affected glomeruli.

CONCLUSIONS

Data presented in graphics demonstrate significant proteinuria after anaesthesia with Sevoflurane. It is important for us to know that, beside albumins, alpha and beta proteins were also observed, highlighted by a special method of electrophoresis patented in 1997 by Professor Schiopu Alexandru that helped us demonstrate the appearance in urine of proteins other than albumins.

There are no data in literature demonstrating the presence of alpha and beta proteins after anaesthesia. Blood urea nitrogen and serum creatinine level did not change significantly after anesthesia with Sevoflurane, but this does not exclude the glomerular damage. The routine use of low gas flow under 2 litres/minute is dangerous and not recommended.

REFERENCES