Modification of Renal Permeability for Proteins after General Anesthesia with Sevoflurane and Desfluran

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Introduction: Sevoflurane degradation by carbon dioxide absorbents during low-flow anesthesia lead to the formation of a haloalkene called compound A, which causes nephrotoxicity.
Material and methods: We determined proteinuria by spectophotometry at 600 nm, preoperatively and postoperatively at 24 and 72 hours in 52 patients undergoing general anesthesia with sevoflurane and 25 patients undergoing general anesthesia with Desfluran. We selected patients without previous renal disease, with anesthetic risk ASA I–III who underwent major abdominal and thoracic surgery lasting more than 150 minutes and we used a 2 l/minute FGF-fresh gas flow, with a MAC-minimal alveolar concentration of 1.5 to 1.8 for Sevoflurane, and of 6–8 MAC for Desfluran.
Results: Renal permeability is impaired by general anesthesia with Sevoflurane ($p \chi 0.0001$) and Desfluran ($p > 0{,}001$). The amount of filtered protein has a maximum at 24 hours after surgery with gradual decrease within 72 hours, but without reaching the normal preoperative values.
Conclusions: There is proteinuria after exposure to volatile agents like Sevoflurane and Desfluran recording a maximum in the first 24 hours and there is also a tendency to normalization within 72 hours. We noticed a marked impairment of renal permeability in association with specific groups of pathology as septic patients, diabetics, hypertensives, especially after Sevoflurane anesthesia. There was no-one case of acute renal failure in which to criminalize Sevoflurane or Desfluran.

Keywords: proteinuria, anesthesia, sevoflurane, desfluran, low-flow

Introduction

Sevoflurane degradation by carbon dioxide absorbents during low-flow anesthesia leads to the formation of a haloalkene named compound A that causes nephrotoxicity [1–4]. Numerous studies show that the compound A formation after low-flow Sevoflurane anesthesia for a medium perioud does not affect renal function [5]. We followed the renal permeability for proteins and the changes for blood urea nitrogen and serum creatinine concentrations after exposure to moderate or long-term anesthesia with low-flow Sevoflurane or Desfluran in patients with normal renal function. Compound A (fluoromethyl 2,2-difluoro bromochlorodifluoroethylene and-a-trifluoromethyl) is formed after anesthesia with halothane and sevoflurane. Compound A causes nephrotoxicity in animals by causing proximal tubules necrosis which may be evidenced by proteinuria and glycosuria [6–11]. Numerous clinical studies have evaluated the formation of compund A and impairment of renal function after low-flow anesthesia with sevoflurane in closed circuit in which the maximum concentration of inspired compound varied from 8 to 24 ppm (parts per million) and 20–32 ppm with soda lime absorber respectively barium hydroxide lime [12–16]. Compound A causes toxicity at values over 800 ppm/hour [17]. The Food and Drug Administration recommends a lower limit of FGF of 1 l/min for an anesthesia shorter than an hour and FGF over 2 l/min for an anesthesia longer than an hour. Studies of long-term exposure to Sevoflurane, monitoring blood urea nitrogen and serum creatinine concentrations did not find any significant clinical renal effects [18].

Material and method

We determined proteinuria by spectophotometry at 600 nm, urea nitrogen and serum creatinine concentrations preoperatively and postoperatively at 24 and 72 hours in 77 patients undergoing general anesthesia with Sevoflurane and Desfluran.

We selected patients without previous renal disease, with anesthetic risk ASA I–III who underwent major abdominal and thoracic surgery with general anesthesia in Mureş County Hospital. Anesthetic protocol was similar for both groups of patients undergoing general anesthesia with Sevoflurane and Desfluran, without renal pathology, with major abdominal and thoracic surgery, prolonged intervention over 150 minutes, with CO_2 absorbent (Intersorb plus) – which contains NaOH, $Ca(OH)_2$, Ethyl violet, water. We performed anesthetic induction with Propofol or Thiopental, Fentanyl and muscle relaxant and the maintenance of anesthesia was achieved with Sevoflurane or Desfluran with FiO_2 >0.35, FGF 2 l/min, with MAC for Sevoflurane under 2% and between 6–8% for Desfluran. The maintenance of the hemodynamic stability was realized by adjusting the concentration of inspired anesthetic with intermittent administration of Fentanyl or Sufentanyl or intermittent administration of local neuraxial anesthetics through epidural catheter in combined anesthesia.

We monitored inspiratory and expiratory anesthetic concentration. We collected venous blood and urine for laboratory analysis in the morning of the operation, 24 hours and 72 hours after surgery. Urine was collected for 24 hours preoperatively, postoperatively between 0–24 hours and between 48–72 hours after surgery.

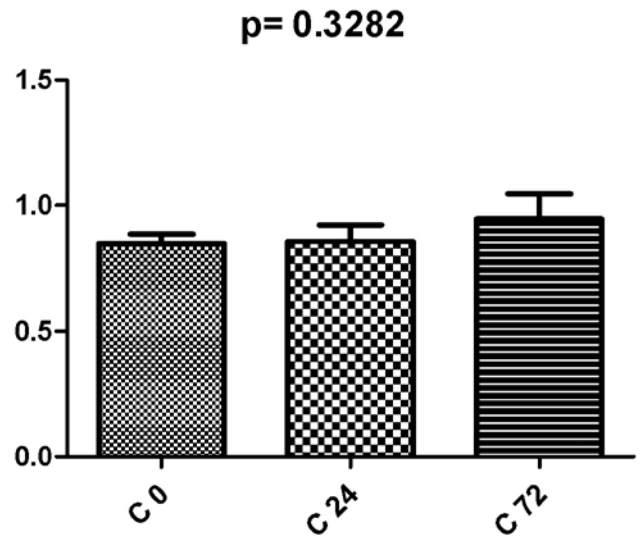

Fig. 1. Serum creatinine level before and after Desfluran anesthesia (C = serum creatinine (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery)

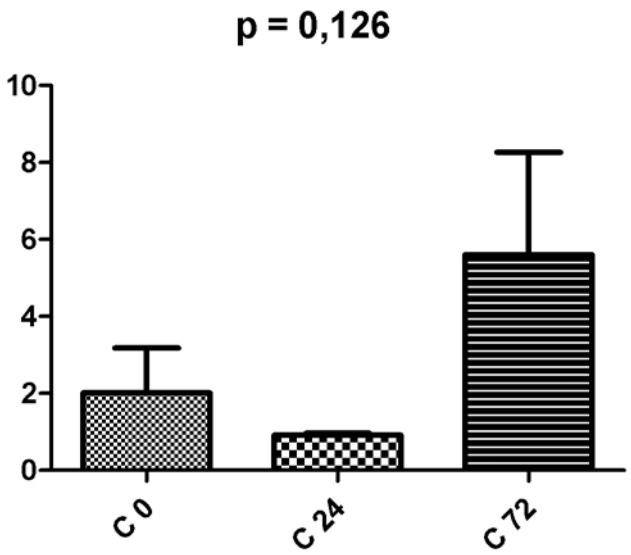

Fig. 2. Serum creatinine level before and after Sevoflurane anesthesia (C = serum creatinine (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery, 72 = 72 hours after surgery)

Proteinuria was analyzed in a specialized laboratory at Mures County Hospital with an autoanalyzer called Konelab 30i through spectophotometry at 600 nm. Blood urea nitrogen and serum creatinine level were determined in the same laboratory.

We analyzed the demographic data, the anesthetic status, the duration of anesthesia, the groups of surgical pathology, the comorbidities and laboratory data. For statistical analysis we used contincency tables and Fisher's exact test statistically significant $p < 0.05$.

Results

Patients undergoing anesthesia with Sevoflurane and Desfluran are similar in terms of age, weight, sex, ASA status, case mix, duration of anesthesia (Table I).

We found no significant differences between groups preoperatively and at 24 and 72 hours postoperatively, by measuring serum creatinine level in patients with low-flow Sevoflurane and Desfluran general anesthesia (Fig. 1, 2).

We found significant differences in the determination of blood urea nitrogen at 24 and 72 hours postoperatively (Fig. 3, 4).

There is certainly proteinuria after low-flow anesthesia with Sevoflurane and Desfluran (Fig. 5, 6).

Discussions

Millions of patients are anesthetized each year with Sevoflurane but there are rare reports of renal injury caused

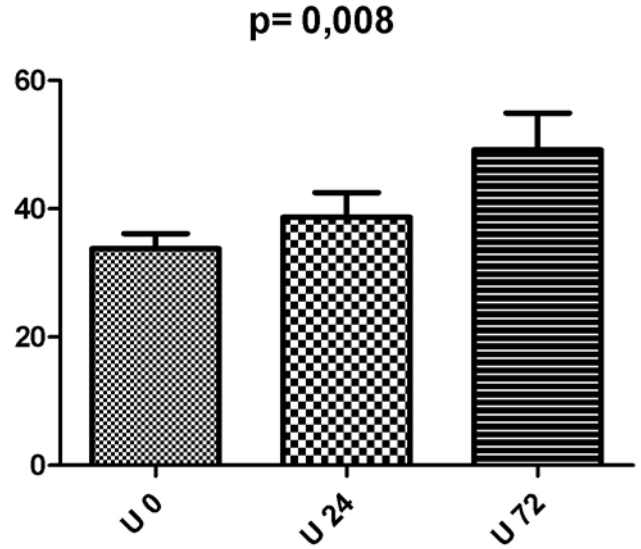

Fig. 3. Blood urea nitrogen level before and after Desfluran anesthesia (U = urea nitrogen (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery, 72 = 72 hours after surgery)

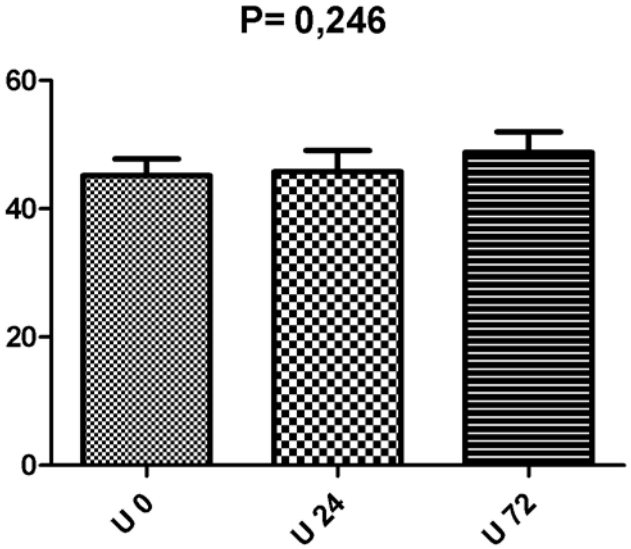

Fig. 4. Blood urea nitrogen level before and after Sevoflurane anesthesia (U = urea nitrogen (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery, 72 = 72 hours after surgery)

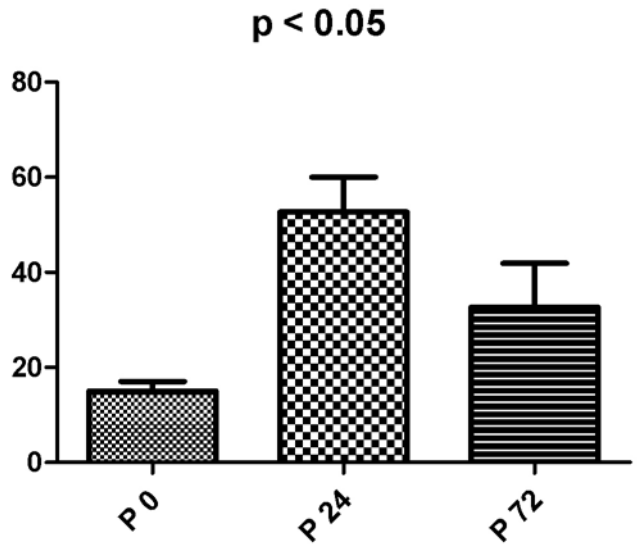

Fig. 5. Proteinuria level before and after Desfluran anesthesia (P = urinary proteins (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery, 72 = 72 hours after surgery)

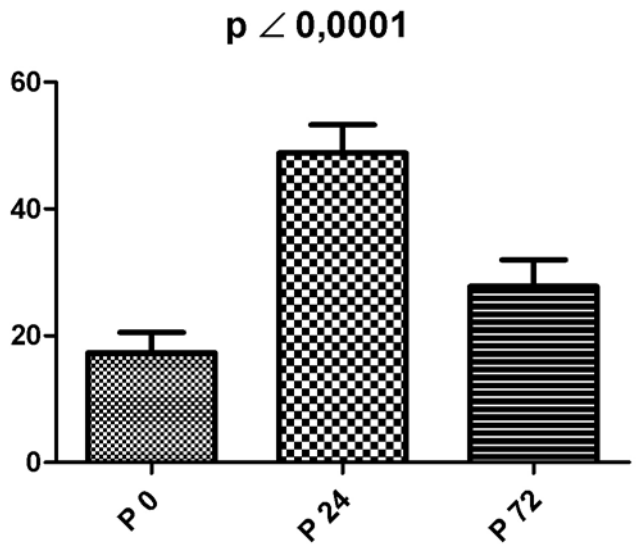

Fig. 6. Proteinuria level before and after Sevofluran anesthesia (P = urinary proteins (mg/dl), 0 = preoperatively, 24 = 24 hours after surgery, 72 = 72 hours after surgery)

by exposure to this anesthetic [19]. Data from literature suggest that fluoride ion production after the exposure to Sevoflurane determines transient renal injury wich is comparable to that produced by Desfluran anesthesia [20–22]. Numerous studies considered that albuminuria and glycosuria are markers of renal toxicity of Compound A but these are not implemented as "gold standard" for the preoperative and postoperative monitoring because of the high cost compared with the cost of serum creatinine determining [23]. Changes in serum creatinine level are insignificant in the two groups surveyed, as other studies found in the literature demonstrated too [24] but there are significant increases in blood nitrogen urea in the group with Desfluran anesthesia. Statistically significant presence of urinary protein in both groups of patients demonstrate another mechanism of renal demage than Compound A.

Conclusions

The results of these investigations show that there is no significant differences between general anesthesia with low-flow Sevoflurane and low-flow Desfluran regarding renal permeability.

By comparing preoperative and postoperative (24 and 72 hours) blood urea nitrogen and serum creatinine levels we found changes in particular cases (obese patients, etc).

We found that renal permeability to proteins was increased in both groups of patients after medium and long term general anesthesia. Our recommendation after analysing the data are to minimize the exposure of patients with the mentioned pathology (obesity, diabetes mellitus, hypertension) who undergo general anesthesia longer than 2 hours, to a low-flow under 2 l/min at a MAC >2%.

Using soda containing $Ca(OH)_2$ leads to a dramatic decrease in the amount of the CO_2 produced.

The results of the investigation does not show significant differences regarding serum creatinine levels but there is significant proteinuria that should be taken into account although it doesn't appears to be related to compound A. We consider that the significant increase of blood urea nitrogen level after Desfluran anesthesia is related to surgical pathology and doesn't represent a side effect of Desfluran.

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