INFLUENCE OF THE CHOICE OF VOLATILE ANESTHETICS ON LIVER ENZYMES AFTER SURGICAL LIVER RESECTIONS

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Summary. The purpose of this study was to evaluate the possible superiority in pharmacological protective effect of sevoflurane compared to isoflurane in patients with liver segmental or lobe resections, through examination of postoperative changes in the liver enzymes ALT and AST and the impact of the choice of anesthetic on surgical hospital charges. It is a prospective study based on the examination of surgical patients. A retrospective cost study analysis after approval of local ethics committee was also performed. Patients with surgical liver resections were divided in two groups according to the main volatile anesthetic used – isoflurane (n = 25) and sevoflurane (n = 17) group. All patients were tested for both liver enzymes AST and ALT before and after the surgery. The health care resources used during the anesthesia were collected. Mean time of operation, minimal alveolar concentration (MAC), average anesthetic quantity used, fresh gas flow, and cost for maintaining anesthesia were calculated. The cost for maintaining anesthesia was compared with the surgical hospital charges. No statistically significant difference has been observed between the two groups according to patients' age, type of liver resection, as well as hospital stay ($p > 0.05$). Comparing the postoperative levels of AST and ALT, we found that their levels were higher in the group of patients on isoflurane. Levels of both ALT and AST were significantly lower, and decreased more rapidly in patients receiving sevoflurane than those receiving isoflurane from 1st to 5th postoperative day. The decrease was almost twice faster in the group on sevoflurane and close to normal physiological levels. All hospital costs appear to be equal in both groups except the cost of maintaining anesthesia that represents 1.67 per cent of hospital charges in the group on sevoflurane and 0.41 per cent in the group on isoflurane. In conclusion, for patients that are going to have liver resection, the preferred main anesthetic in the complex of balanced anesthesia should be sevoflurane, which decreases the AST and ALT levels significantly. For both

anesthetics the total cost for maintaining anesthesia is an insignificant part of the surgical hospital charges and the choice of anesthetic should be based on clinical results rather than on economical ones.

Key word: *anesthesia, sevoflurane, isoflurane, anesthesia cost, liver resections, ALT, AST*

INTRODUCTION

Surgical liver resections are related to a high risk of hemorrhage, which has a negative influence on postoperative recovery, overall patient survival, and quality of life [1, 2]. A clamping maneuver (Pringle maneuver) [3] is used as a routine practice to prevent hemorrhage, but it is related to ischemic liver injury, which leads to postoperative increase in liver enzymes and could lead to death or complications [4]. Nowadays, in order to decrease liver stress, liver preconditioning through short preclamping is performed (5-10 minutes) followed by a recovery of the blood stream and consecutive clamping [5, 6].

There are a limited number of studies on the pharmacological protection of the liver during this process. Volatile anesthetics isoflurane and sevoflurane have been studied as protectors of the myocardium in cardiovascular surgery and ultrasound abnormalities after myocardial ischemia. [7, 8]. Beck-Schimmer et al. performed a randomized controlled trial in order to determine the protective effect of sevoflurane and propofol and to confirm this effect in patients with liver resection. [9] In cases of cirrhosis sevoflurane possess a higher protective effect [10], as well as in neurosurgical interventions [11].

The current study aims to evaluate the possible pharmacological better protective effect of sevoflurane compared to isoflurane in patients with liver segmental or lobe resections, through examination of the changes in the liver enzymes ALT and AST and its impact on surgical hospital charges.

Primary endpoints of the study were to examine if a statistically significant difference in the levels of liver enzymes in both groups of patients – using sevoflurane or isoflurane anesthesia will occur, and what is the presumed economic effect of the anesthetic on the hospital charges within the concrete hospital context.

MATERIALS AND METHODS

It is a prospective study based on surgical patients and a retrospective cost study analysis conducted in one hospital in Varna after approval of local ethics committee. All patients with surgical liver resections were observed during the period January 2009 − June 2010. Patients are divided in two groups according to the volatile anesthetic used − isoflurane group (n = 25) and sevoflurane group (n = 17). All patients have been operated by the same surgical and anesthesiological team.

The choice of volatile anesthetic is unintentional. The available at the moment of operation medicinal product was taken.

Both liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were tested in all patients before the operation and at first, second, third, and fifth postoperative days.

The health care resources used during the anesthesia were collected, as well as mean time of operation, minimal alveolar concentration (MAC), average anesthetic quantity used, fresh gas flow, and cost for anesthesia maintenance were calculated. The cost for anesthesia maintenance was compared with the surgical hospital charges.

The descriptive statistics, ANOVA analysis, nonparametric Wilcoxon, and Man Whitney tests were performed for the evaluation of statistically significant differences in the enzyme levels before the operation and after that in the days of follow-up.

RESULTS

Patients' distribution according to gender, age, type of liver resection and average hospital stay is shown on Table 1. According to ASA physical status classification system all patients belonged to 2nd or 3rd category [12]. Pringle maneuver was performed to all patients. No statistically significant difference was found in the patients' age, length of hospital stay or type of liver resection between the two groups ($p > 0.05$) (Table 1). Due to the lack of statistically significant differences in the basic patients' characteristics we can consider both groups of patients as selected unintentionally.

Table 1. Demographic characteristics of the operated patients

Variable	Sevoflurane group	Isoflurane group
N	17	25
Male / Female	6 / 11	11 / 14
Average age in years (SD)	62 (5.3)	62 (5.7)
Hospital length of stay in days (SD)	6.5 (1.12)	6.5 (1.16)
Type of resection		
– lobe	2 Lect[a] / 1 Dect[b]	1 Lect[a] / 2 Dect[b]
– segment	14	22

[a] Lect – left oriented
[b] Dect – right oriented

General anesthesia with endotracheal intubation was used in both groups with either isoflurane or sevoflurane. Induction of anesthesia was conducted with sodium thiopental, the muscles relaxation was ensured with suxametonium, and as depolarizing agent pancuronium bromide was used. The premedication was performed with fentanyl and promethazine hydrochloride, and fentanyl was used

to control the pain during surgery. After the surgery procedure patients were left to spontaneous awakening.

All operations were successful without lethal exits till the moment of hospital discharge. On Table 2 are presented the results of the AST and ALT tests before and after the surgery. No statistically significant difference has been observed among the initial level of AST and ALT. Levels of both ALT and AST were significantly lower, and decreased more rapidly in patients receiving sevoflurane than those receiving isoflurane from 1st to 5th postoperative days. The decrease is almost twice faster in the group on sevoflurane and close to normal physiological levels.

The average duration of the operation was found to be equal in both groups with MAC for sevoflurane varying from 0.7 to 2.5 MAC for isoflurane and from 1.15 to 1.25 MAC respectively. The average supplied anesthetic volume was 0.5% higher in the sevoflurane group (Table 3). According to Table 3 the average volatile concentrations of isoflurane and sevoflurane are 1.5% and 2.0%, respectively and these are the concentrations when the 3rd stage anesthesia has been achieved. Since the anesthetic potency expressed as minimum alveolar concentration (MAC) of these agents are 1.15% and 1.71% respectively [13, 14], average concentrations of isoflurane and sevoflurane expressed as the ratio to MAC are 1.31 and 1.16, respectively, suggesting that the concentration of isoflurane is higher than that of sevoflurane. The possible explanation of this fact is that in this particular study the isoflurane group has required more anesthetic to achieve the 3rd stage anesthesia.

All hospital costs appear to be equal in both groups of patients and thus the cost for maintaining anesthesia was calculated to be four times higher in the group on sevoflurane (Table 3). The cost of anesthesia maintenance as a part of the surgical hospital charges represents 1.67 per cent in the group on sevoflurane and 0.41 per cent in the group on isoflurane.

Table 2. AST and ALT test levels (UL/L)

Enzymes	**Anesthetic**	**Day before the surgery and of follow up – Mean enzymes level (SD)**				
		0 day – before the surgery	1 day after surgery	2 day after surgery	3 day after surgery	5 day after surgery
AST	isoflurane	23.72 (5.84)	411.60* (60.94)	324.40* (65.14)	233.96* (70.67)	126.92* (26.85)
	sevoflurane	22.24 (6.72)	328.24* (39.54)	233.35* (60.18)	141.94 (59.37)	87.94 (10.56)
ALT	isoflurane	22.91 (5.75)	416.56* (40.07)	315.88* (48.45)	222.48* (43.69)	108.24* (12.02)
	sevoflurane	22.24 (6.72)	342.53* (31.02)	238.18* (40,04)	136.235* (23.86)	88.77* (10.33)

*$p < 0.05$

Table 3. The cost of anesthesia

	Mean time of operation in minutes (SD)	Minimal alveolar concentration (%)	Average anesthetic quantity (%)	Fresh gas flow (l/min)	Total cost of anaesthesia maintenance (BGN)	% of surgical hospital charges
Sevoflurane group	180 (SD 90-270)	from 0.7 to 2.5	2.0	3	53.55	1.67
Isoflurane group	180 (SD 90-270)	from 1.15 to 1.25	1.5	3	13.25	0.41

DISCUSSION

Our results clearly show that in the sevoflurane group levels of ALT and AST are recovering faster to acceptable physiological values. The ALT and AST levels are considered as an indicator for liver damage and their faster recovery in the sevoflurane group suggest easier liver recovery in that group. Our results confirm those of Beck-Schimmer Beatrice et al. [9] and Nishiyama et al. [10, 11] for the probable protective effect of sevoflurane in patients with liver resections. In contrast to Nishiyama [10], we are examining patients with different indications for surgical resection and not only cirrhotic ones. We can consider that the probable protective effect does not depend on the initial disease. Also, in contrast with Beck-Schimmer, we do compare the sevoflurane and isoflurane, and not the sevoflurane and propofol, thus confirming sevoflurane as an anesthetic with a potential protective effect on the liver during resection surgery.

The fact that all patients have been operated by the same surgical and anesthesiological team is also important for eliminating the influence of the human factor on the performance of surgery and anesthesia. This confirms the pharmacological protection of sevoflurane [15].

Comparison of these undoubtfully positive clinical results with the relative share of the cost for anesthesia maintenance shows that even higher, sevoflurane cost is almost diminishing compared to total surgical hospital charges. Thus, if sevoflurane is chosen as a preferred anesthetic for patients with surgical liver resections, that will not have a considerable economic impact on total hospital's charges. On the opposite, it will ensure faster achievement of the physiological levels of ALT and AST. Benefit economic results with sevoflurane were previously established for patients with laparoscopic cholecistectomy [16]. The usage of sevofluranee will decrease the unnecessary expenditures due to the higher level of AST and ALT, and will increase patients' quality of life, supporting faster recovery of the liver function.

CONCLUSION

For patients that are going to have liver resection the preferred main anesthetic in the complex of balanced general anesthesia should be sevoflurane which decreases the AST and ALT levels statistically significantly.

For both anesthetics the total cost of anesthesia maintaining is an insignificant part of the surgical hospital charges and the choice of anesthetic should be based on clinical results rather than on economical ones.

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