THE EFFECT OF HALOTHANE, ISOFLURANE, SEVOFLURANE AND PROPOFOL INFUSION ON RENAL FUNCTION AFTER CORONARY ARTERY BYPASS SURGERY

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Abstract

Renal insufficiency after cardiac surgery is associated with increased mortality, morbidity, and length of stay in the intensive care unit. We investigated the effect of isoflurane, halothane, sevoflurane and propofol anesthesia on perioperative renal function following elective coronary artery surgery.

The medical records of 224 patients, in the Hacettepe University Medical Faculty Hospital who had undergone cardiac surgery in one year, were retrospectively reviewed. 65 (29%) patients received isoflurane, 68 (30%) patients received halothane, 64 (29%) patients received sevoflurane, and 27 (12%) patients received propofol infusion as part of maintenance anesthesia for coronary artery bypass surgery.

Patient characteristics (age, sex, preoperative ejection fraction), operative data (duration of CPB, duration of operation, number of distal anastomoses, usage of diuretic, intraoperative crystalloid and blood

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transfusion), intraoperative urinary output, preoperative and postoperative (6^{th} hours and 24^{th} hours) BUN and plasma creatinine levels, were not statistically significant between and within groups.

Intraoperative inotropic agent (dopamine) was used in 8 (12.3%) patients in the isoflurane group, in 10 (14.7%) patients in the halothane group, in 11 (17.2%) patients in sevoflurane group and in 9 (33.3%) patients in the propofol group.

Postoperatively fluid and blood transfusion, postoperative drainage, urinary output, diuretic usage were smiliar between the four groups (p>0,05). Inotropic agent was used in 8 (12.3%) patients in the isoflurane group, in 9 (13.2%) patients in the halothane group, in 16 (25%) patients in the sevoflurane group and in 7 (25.9%) patients in the propofol group.

It is concluded that, halothane, isoflurane, sevoflurane and propofol infusion anesthesia as part of anesthesia maintenance for elective coronary artery bypass surgery does not affect early postoperative renal functions.

Key Words: Renal dysfunction, anesthetic agent; isoflurane, sevoflurane, halothane, propofol, cardiopulmonary bypass.

Introduction

Despite improvements in surgical techniques the cardiopulmonary bypass (CPB) circuit and postoperative patient care, renal failure is still a major complication in patients undergoing cardiac surgery with CPB[1]. It has been reported that acute renal failure requiring dialysis develops in 2-7% of cardiac surgery patients and is strongly associated with postoperative morbidity and mortality[2]. The cause is multifactorial depending on patient's clinical status and CPB related events, (hypotension, hypoperfusion, loss of pulsality, hemolysis and release of proinflammatory substances)[3]. To date, it is less well known whether anesthetic agents used in

maintenance of anesthesia, effect perioperative renal dysfunction. A retrospective study was therefore conducted to evaluate the influences of these agents on clinical outcome. The effect of anesthetic agents; isoflurane, halothane, sevoflurane and propofol infusion anesthesia on the perioperative and early postoperative renal functions after elective coronary artery bypass surgery, were investigated.

Methods

A one year cardiac surgery data base was used which had been collected for the postoperative days concerning items that might influence patient outcome. 224 consecutive adult patients (age 48-68, male/female 167/57) who underwent CABG surgery were retrospectively studied. Comprehensive preoperative data were collected from cardiac and medical histories for all patients. They were divided into 4 group for the maintenance of anesthesia; Group H (n = 68) halothane, Group I (n = 65) isoflurane, Group S (n = 64) sevoflurane, Group P (n = 27) propofol infusion.

General anesthesia was induced with etomidate and fentanyl and norcuron was used to facilitate endotracheal intubation. After tracheal intubation, ventilation was controlled to ensure normal blood gases by using an inspired oxygen concentration of 50% and 50% N_2O before CPB, and 100% after separation from bypass.

In all patients, a peripheral vein was cannulated before anesthesia and an arterial radial catheter was inserted after induction of anesthesia for continuos monitoring of mean arterial pressure.

Before CPB, hypertension and hypotension were defined as an increase or a decrease in mean arterial pressure of 20% from baseline respectively. Hypertension was treated with additional doses of fentanyl (100-150 μg). Hypotension was treated with rapid i.v. administration of lactated Ringer's solution. Phenylephrine (bolus of 250 μg; vasopressor support) could be used when mean arterial pressure was 60 mmHg.

After aortic and right atrium cannulation, CPB was instituted with a membrane oxygenator primed with 1,5 L of crystalloid and body temperature was decreased to 27-29°C.

After aortic clamping, a cardioplegic solution (hypercalemic crystalloid solution) was infused into the aortic root until myocardial temperature decreased to 15°C. A nonpulsatile pump flow rate >1.6 L $min^{-1}m^2$ was maintained during hypothermia and increased up to 2.6 L $min^{-1}m^2$ during rewarming. After completion of surgical procedure and systemic rewarming, patients were weaned from CPB when the rectal temperature of 36°C had been reached. Inotropic support (dopamine, dobutamine or epinephrine) was used in case of low cardiac output at the time of CPB weaning or later.

In the ICU repeated boluses of morphine were used to keep patients pain free. Weaning from ventilator was started during of emergence of anesthesia and when stable hemodynamics and normothermia had been maintained.

The following demographic variables were collected for each patient: age, body weight, height, sex. Other preoperative variables were also evaluated: history of hypotension, diabetes mellitus, peripheral vascular disease, myocardial infarction, ASA class, left ventricular ejection fraction. Preoperative renal function was assessed by baseline serum creatinine levels, blood urea nitrogen and urea levels. Intraoperative variables evaluated were CPB and aortic cross clamping duration, packed red cell transfusion, MAP, urine output during surgery and post-CPB catecholamine infusion. Postoperative bleeding was assessed by total chest drainage and administration of blood units.

Chi-square test was used to compare the categorical variables between the groups. For the parametric data, ANOVA was used. For analyzing the changes of laboratory values over time, repeated measures ANOVA was used. SPSS software was used for statistical analysis. $P<0.05$ was considered as statistically significant.

Results

A total of 224 patients were studied. The majority of the patients were men (167) with a mean age of 57. There were 65 (29%), 68 (30%), 64 (29%), 27 (12%) patients in isoflurane, halothane, sevoflurane and propofol respectively. There were no statistically significant difference in demographic data (age, sex, number of bypass, diabetes mellitus and pre operative ejection fraction) (Table 1).

Table 1

Demographical data of patients (patient number or median ± SD)

	Isoflurane (n = 65)	**Halothane (n = 68)**	**Sevoflurane (n = 64)**	**Propofol (n = 27)**	**p**
Age (y)	56 ± 12	54 ± 11	57 ± 10	55 ± 8	0,306
Sex (F/M)	17/48	15/53	19/45	6/21	0,937
Bypass no (1/2/3/4/5/6)	14/21/16/11/3/0	11/17/18/18/3/1	11/18/18/10/7/0	3/13/8/3/0/0	0,910
Diabetes mellitus	13	18	14	4	0,676
Preoperative ejection fraction	61 ± 10	63 ± 8	62 ± 7	60 ± 10	0,595

There were also no significant differences in CPB and aortic cross clamp (ACC) duration and anesthesia, surgery duration between the four groups. Intraoperative blood transfusion, diuretic administration,urine output, the lowest intropeative MAP and CVP were similar between groups. The patient number that had inotropic support (Dopamine) was significantly different between groups; 8 (12,3%), 10 (14,7%), 11 (17,2%), 9 (33%) in isoflurane, halothane, sevoflurane, propofol respectively ($p<0.05$). There was not significant difference in postoperative fluid administration, blood transfusion, drainage,urine output and furosemide administration between groups. The number of patient requiring inotropic support had significant difference in the postoperative period; 8 (12,3%), 9 (13,2%), 16 (25%), 7 (25,9%) in isoflurane, halothane, sevoflurane and propofol group respectively ($p<0.05$) (Table 2).

Table 2

Perioperative clinical demographics of the patients (patient number or median ± SD)

	Isoflurane (n = 65)	**Halothane (n = 68)**	**Sevoflurane (n = 64)**	**Propofol (n = 27)**	**P**
Aortic clamping duration (min)	39 ± 20	41 ± 18	40 ± 16	39 ± 11	0,832
CPB duration (min)	69 ± 28	75 ± 30	71 ± 22	70 ± 23	0,562
Operation duration (min)	190 ± 42	196 ± 53	202 ± 48	193 ± 47	0,526
Anesthesia duration (min)	225 ± 44	238 ± 59	237 ± 48	227 ± 46	0,406
Intraoperative fluid administration (mL)	2532 ± 845	2572 ± 681	2623 ± 724	2672 ± 542	0,822
Intraoperative blood administration (unit)	1,3 ± 0,9	1,4 ± 1,1	1,6 ± 1,2	1,8 ± 1,4	0,150
Intraoperative urine output (mL)	695 ± 340	866 ± 530	891 ± 492	780 ± 430	0,07
Intraoperative inotropic support	8	10	11	9	0,033 *
Intraoperative furosemide administration	13	14	10	5	0,616
Intraoperative lowest MAP	87 ± 15	88 ± 11	89 ± 11	85 ± 18	0,552
Intraoperative lowest CVP	11 ± 4	11 ± 3	11 ± 5	9 ± 5	0,120
Postoperative fluid administration (mL)	2760 ± 300	2755 ± 307	2765 ± 460	2677 ± 320	0,732
Blood administration at postoperative 24 h (mL)	800 ± 530	660 ± 280	700 ± 280	860 ± 525	0,066
Urine output at postoperatifve 24 h (mL)	2980 ± 1065	2970 ± 1000	2690 ± 1160	3340 ± 1120	0,069
Furosemide administration at postoperatifve 24 h	23	19	24	9	0,859
Postoperative drainage	565 ± 300	588 ± 300	699 ± 300	594 ± 220	0,05
Postoperative inotropic support	8	9	16	7	0,029 *

There was not any significant difference between groups in preoperative, postoperative (after 6 and 24 hour) hemoglobin, hematocrit, and platelet concentration ($p>0.05$). There was not any significant difference between the groups in the preoperative, postoperative (after 6 and 24 hour) urea, BUN and creatinine values ($p>0.05$) (Table 3).

Table 3
Pre- and postoperative laboratory values of the patients (patient number or median ± SD)

	Isoflurane (n = 65)	**Halothane (n = 68)**	**Sevoflurane (n = 64)**	**Propofol (n = 27)**	**p**
Preoperative hemoglobin (gr/dL)	13,6 ± 1,6	13,9 ± 1,5	13,9 ± 1,4	13,9 ± 1,3	0,559
Postoperative hemoglobin (T1)	11,5 ± 1,3	11,5 ± 1,5	10,9 ± 1,7	11,2 ± 1,5	0,105
Postoperative hemoglobin (T2)	11,7 ± 1,2	12,0 ± 1,3	11,5 ± 1,5	11,9 ± 1,5	0,256
Postoperative hemoglobin (T3)	11,9 ± 1,2	12,4 ± 1,3	11,9 ± 1,3	12,5 ± 1,6	0,05
Preoperative hematocrit (%)	40,7 ± 5,8	41,8 ± 5,6	41,5 ± 4,4	41,1 ± 3,9	0,555
Postoperative hematocrit (T1)	34,2 ± 4,1	34,2 ± 4,4	32,6 ± 5,1	33,1 ± 4,6	0,123
Postoperative hematocrit (T2)	35,0 ± 3,4	36,6 ± 3,6	34,5 ± 4,7	36,3 ± 4,4	0,140
Postoperative hematocrit(T3)	35,2 ± 3,3	37,2 ± 3,6	34,8 ± 4,3	37,1 ± 5,9	0,05
Preoperative platelet	250 ± 82	272 ± 97	252 ± 72	251 ± 101	0,424
Postoperative platelet (T1)	155 ± 46	166 ± 75	158 ± 77	145 ± 59	0,521
Postoperative platelet (T2)	155 ± 48	158 ± 75	164 ± 79	140 ± 55	0,495
Postoperative platelet (T3)	164 ± 50	171 ± 62	165 ± 76	165 ± 57	0,916
Preoperative urea	5,2 ± 1,6	5,5 ± 1,6	4,8 ± 1,9	5,7 ± 1,8	0,05
Preoperative BUN	16,5 ± 6,4	16,7 ± 5,8	14,6 ± 6,6	16,9 ± 4,7	0,186
Postoperative BUN (T1)	16,0 ± 6,0	15,0 ± 4,5	16,3 ± 4,3	15,5 ± 3,2	0,381
Postoperative BUN (T2)	15,4 ± 6,0	15,4 ± 5,0	17,2 ± 5,0	16,7 ± 6,7	0,180
Postoperative BUN (T3)	15,4 ± 6,3	15,0 ± 4,9	16,4 ± 4,4	15,4 ± 3,9	0,497
Preoperative creatinine (mg/dl)	1,0 ± 0,2	1,0 ± 0,3	0,9 ± 0,3	1,1 ± 0,2	0.05
Postoperative creatinine (T1)	0,9 ± 0,3	1 ± 0,2	0,8 ± 0,3	1,0 ± 0,3	0.05
Postoperative creatinine (T2)	0,9 ± 0,2	1,0 ± 0,3	1,1 ± 0,4	1,1 ± 0,3	0.05
Postoperative creatinine (T3)	1,0 ± 0,3	1,0 ± 0,3	1,1 ± 0,3	1,0 ± 0,2	0.05

T1: after operation, T2: 6 hours after operation T3: 24 hour after operation.

Discussion

The retrospective study on 244 patients undergoing elective coronary artery surgery using anesthesia either with isoflurane, halothane, sevoflurane or propofol revealed that the changes in plasma creatinine, BUN and urea concentrations before and after surgery were similar in the four groups. In the four groups there was no patient who demonstrated important increases in creatinine of more than 44 μm (0.5 mg/dl)[4].

These results suggest that comparing isoflurane, halothane, sevoflurane and propofol, did not produce greater increases in creatinine after elective coronary artery surgery. An increase in plasma creatinine of >20% from preoperative value has a good specificity (0.99) to detect a decrease in creatinine clearance of 20% but has a slow sensitivity (0.46)[4].

BUN is frequently used in routine clinical chemistry. However, BUN concentration is less reliable than creatinine as measure of renal functions[5]. However, BUN levels support the creatinine results, and showed no important differences between the four groups.

Renal dysfunction is therefore a potential postoperative complication and may appear as a marker rather than a factor of high death risk[6]. Through a large scale study including 42,773 patients, Chertow et al[2]. demonstrated a statistically significant relationship between acute renal failure and early mortality after cardiac surgery. Ryckwaert et al[7], reported that postoperative 20% increase in plasma creatinine after cardiac surgery is not rare and has a significant impact on postoperative outcome, mainly when multiple organ dysfunction occurs. There were not any clinically important increase in our creatinine results and no mortality in our series.

In a 2002 we had studied the effects of sevoflurane and isoflurane anesthesia on renal tubular function via determining the inorganic florid and urinary N-Acetyl-B- Glukozaminidase (NAG) levels in coronary artery bypass surgery. Blood and urine florid levels were significantly

higher in sevoflurane group but there were no statistically significant difference in NAG levels. It was concluded that, sevoflurane did not cause tubular damage in cardiac surgery for short term, although it increased fluoride levels[8].

Two recent studies have compared changes in creatinine after sevoflurane anesthesia and other agents for noncardiac surgery. Both had smilar findings to ours. Mazze et al[9] analyzed 22 studies comparing sevoflurane with isoflurane, enflurane and propofol. With almost 3500 patients, they found no differences in postoperative changes in creatinine and urea between the anesthetic agents. Groudine et al[10], conducted a randomized trial comparing sevoflurane and isoflurane in 188 patients and found no differences in postoperative creatinine, urea, albuminuria, and glycosuria.

We studied the effect of anesthetic agents on renal functions and investigated whether there are risk factors for renal dysfunction at coronary artery bypass surgery. Like other recent studies (randomized trial or retrospective), we found no differences in renal functions and no early renal dysfunctions for the four groups studied.

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