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SHORT COMMUNICATION

Comparison of arterial lactate levels during sevoflurane versus spinal anesthesia in elderly females undergoing total knee arthroplasty

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Abstract Prolonged tourniquet inflation during total knee arthroplasty (TKR) could lead to ischemic muscle injury. The aim of this study was to investigate the effects of spinal and sevoflurane anesthesia on arterial lactate levels, acid–base status, and on hemodynamic variables in elderly women undergoing TKR. Forty women more than 65 years of age scheduled for elective TKR were enrolled in this study. Patients were allocated to receiving either sevoflurane anesthesia (sevoflurane group, $n = 20$) or spinal anesthesia (spinal group, $n = 20$) according to the patient's decision. Arterial lactate levels were significantly higher in the sevoflurane group than in the spinal group at 5 and 65 min after tourniquet deflation ($P < 0.001$ and $P = 0.033$, respectively), but there were no intergroup differences in the increment of arterial glucose levels at any time point. Mean arterial pressure and heart rate were significantly higher at 5 min before tourniquet inflation ($P < 0.001$, $P = 0.029$, respectively) and lower at 65 min after tourniquet deflation ($P = 0.009$, $P = 0.033$, respectively) in the spinal group than in the sevoflurane group. Our results suggest that spinal anesthesia is associated with lower production of ischemic metabolites than sevoflurane anesthesia after pneumatic tourniquet deflation in elderly women undergoing TKR.

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Although spinal anesthesia for total knee arthroplasty (TKR) is known to reduce oxidative stress compared to sevoflurane anesthesia [1], use of sevoflurane before tourniquet inflation optimizes the interstitial release of substrates required for energy metabolism [2]. Despite the many reports on the complications associated with regional versus general anesthesia for orthopedic surgery [2–4], no previous study has compared anesthetic techniques with respect to blood lactate levels during TKR. The aim of this study was to investigate and compare the effects of spinal and sevoflurane anesthesia on arterial lactate level, acid–base status, and hemodynamic variables in elderly female patients undergoing TKR.

Forty female patients of ASA class I or II and aged more than 65 years scheduled for elective TKR were enrolled in this study. The following exclusion criteria were applied: history of uncontrolled diabetes mellitus, known neuromuscular pathology, severe cardiovascular or respiratory disease, or any contraindication to one of the two anesthetic protocols. Patients were allocated to receive sevoflurane anesthesia (sevoflurane group, $n = 20$) or spinal anesthesia (spinal group, $n = 20$). The groups were determined by the patient's selection of anesthetic method and therefore were not randomized.

Patients were not premedicated. On arrival at the operating room, standard monitors were applied and a 20 G catheter was inserted into the radial artery under local anesthesia. All patients received a fluid preload of 300 ml saline solution. In the sevoflurane group, anesthesia was induced with propofol, rocuronium, and remifentanil. After tracheal intubation, anesthesia was maintained with

sevoflurane and remifentanil. In the spinal group, patients were administered 0.5 % hyperbaric bupivacaine 10 mg intrathecally. Midazolam (0.02 mg/kg) was administered before inflating the tourniquet at patient request. In both groups, when the SBP fell to 20 % below baseline or to lower than 90 mmHg, phenylephrine or ephedrine was given. Normal saline was infused at a constant rate of 6 ml/kg/h. An injection of 6 % hydroxyethyl starch 130/0.4 0.9 % sodium chloride (Voluven; FresiniusKabi, Bad Homberg, Germany) was infused when blood loss exceeded 500 ml. Allogenic packed red blood cells were transfused when the hematocrit level was below 25 %. In both groups, a pneumatic tourniquet (300 mmHg) was applied. Hemodynamic data and oximeter readings were recorded before anesthetic induction (T_0, baseline), 5 min after anesthetic induction (T_1), 5 min before tourniquet inflation (T_2), 5 min after tourniquet inflation (T_3), 5 min after tourniquet deflation (T_4), and 1 h after T_4 (T_5). Arterial blood samples were analyzed at T_1, T_4, and T_5. T_1 and T_4 were selected to compare the values before and after deflation of the tourniquet, and T_5 was selected for determining the clearance of lactate between groups.

In a preliminary study, when the mean difference and SD of arterial lactate values of the two anesthetic techniques were considered to be 0.7 and 1.0 mmol/l, respectively, 17 subjects per group were required for an α value of 0.05 and a power of 80 %. Thus, 20 subjects were included per group to account for expected losses. Statistical analysis was performed using PASW Statistics 13 (SPSS, Chicago, IL, USA). Data are expressed as mean ± SD, median (interquartile range), or numbers of patients. Patient characteristics were compared using the Student's *t* test or Fisher's exact test as appropriate. Repeated-measures analysis of variance (ANOVA) with Bonferroni's correction was used for the intragroup analysis. Statistical significance was accepted for P values <0.05.

No significant differences were found between the sevoflurane and spinal groups in terms of patient characteristics or total operative and tourniquet times. Total infused fluid and estimated blood loss were similar in the groups. The requirements of phenylephrine or ephedrine was similar between groups (spinal vs. sevoflurane: 5/20 vs. 8/20, $P = 0.311$). However, urine output was significantly greater in the spinal group (317 ± 293 vs. 723 ± 488, $P = 0.008$). The incidences of packed red blood cell transfusion in the sevoflurane and spinal groups were 7/20 and 3/20, respectively, which were not significantly different ($P = 0.114$) (Table1). Midazolam was administered in the five patients in the spinal group.

Arterial blood gas analysis results are summarized in Table 2. Mean arterial lactate was significantly higher in the sevoflurane group at T_4 and T_5 ($P < 0.001$ and $P = 0.033$, respectively). As compared with baseline values, arterial lactate increased significantly in both groups at T_4 and T_5. Arterial glucose levels were increased in both groups at T_4 and T_5 compared to baseline value without an intergroup difference.

Observed changes in mean arterial pressure (MAP) and heart rate (HR) are shown in Fig. 1. MAP and HR were significantly higher at T_2 ($P < 0.001$, $P = 0.029$, respectively) and significantly lower at T_5 ($P = 0.009$, $P = 0.033$, respectively) in the spinal group. As compared with baseline values, MAP was significantly lower in the spinal group throughout the study period and was significantly lower in the sevoflurane group at T_1–T_4.

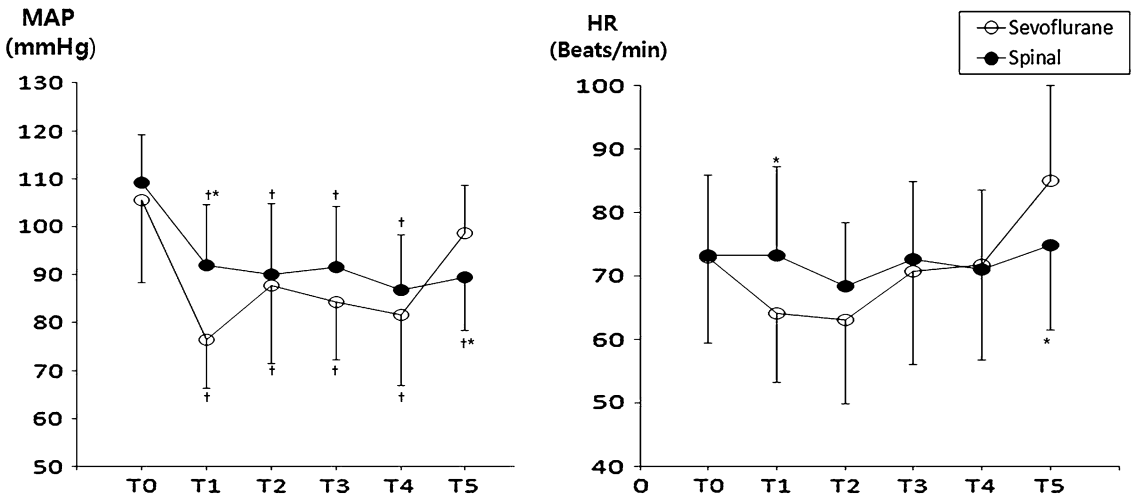

Fig. 1 Hemodynamic parameters. T_0 before anesthetic induction, T_1 5 min after anesthetic induction, T_2 5 min before tourniquet inflation, T_3 5 min after tourniquet inflation, T_4 5 min after tourniquet deflation, T_5 1 h after T4, *MAP* mean arterial pressure, *HR* heartrate. $P < 0.05$ vs. sevoflurane group, $^{\dagger}P < 0.05$ vs. value before induction within groups

Table 1 Patients characteristics and perioperative data

	Sevoflurane ($n = 20$)	Spinal ($n = 20$)	P value
Age (year)	66 ± 9	68 ± 7	0.453
Weight (kg)	61 ± 11	66 ± 13	0.245
Unilateral total knee arthroplasty	15	16	0.705
Bilateral total knee arthroplasty	5	4	
Height (cm)	154 ± 7	156 ± 7	0.493
Diabetes mellitus (n)	2	3	0.633
Hypertension (n)	11	12	0.749
Operation time (min)	258 ± 74	233 ± 68	0.282
Tourniquet time (min)	149 ± 40	138 ± 61	0.537
Total infused fluid (ml)	2023 ± 701	1750 ± 596	0.267
Estimated blood loss (ml)	464 ± 86	408 ± 113	0.101
Urine output (ml)	317 ± 293	723 ± 488	0.008
Packed red blood cell transfusion (pint)	7	3	0.144
1-h lactate clearance	0.2 ± 1.1	0.6 ± 0.5	0.286

Values are mean ± SD or numbers of patients. Lactate clearance, (values of arterial lactate at 5 min after tourniquet deflation minus values of arterial lactate at 65 min after tourniquet deflation)/1 h

Table 2 Arterial blood gas analysis

	Before induction	5 min after tourniquet off	65 min after tourniquet off
pH			
Sevoflurane	7.44 ± 0.02	7.43 ± 0.07	7.40 ± 0.06
Spinal	7.44 ± 0.03	7.41 ± 0.03	7.43 ± 0.04
PCO_2 (mmHg)			
Sevoflurane	40 ± 3	36 ± 4†	40 ± 5
Spinal	39 ± 4	43 ± 11*	40 ± 5
HCO_3^- (mmol/l)			
Sevoflurane	27 ± 2	24 ± 2†	25 ± 2†
Spinal	27 ± 2	24 ± 6	26 ± 2
Base excess (mmol/l)			
Sevoflurane	2.7 ± 2.1	−0.2 ± 2.8†	0.3 ± 2.6†
Spinal	2.5 ± 2.1	0.8 ± 2.2	1.8 ± 1.8
Lactate (mmol/l)			
Sevoflurane	1.0 ± 0.4	2.9 ± 1.6†	2.9 ± 1.4†
Spinal	0.8 ± 0.4	1.6 ± 1.0*†	1.6 ± 1.0*†
Hematocrit (%)			
Sevoflurane	39 ± 5	32 ± 10†	32 ± 4†
Spinal	35 ± 6*	36 ± 13	31 ± 2
Glucose (mg/dl)			
Sevoflurane	102 ± 22	141 ± 30†	176 ± 47†
Spinal	105 ± 29	130 ± 37	148 ± 35†

Values are means ± SDs

* $P < 0.05$ vs. sevoflurane group

† $P < 0.05$ vs. the before-induction value within groups

Four patients in the sevoflurane group and none in the spinal group were administered rescue analgesics during 1 h observation in the postanesthetic care unit ($P = 0.106$).

This study shows that spinal anesthesia is associated with lower arterial lactate levels than sevoflurane anesthesia after pneumatic tourniquet deflation. Ischemia–reperfusion injury induced by prolonged tourniquet inflation could lead to muscle and nerve injury accompanied by anaerobic glycolysis, neutrophil activation, the formation of reactive oxygen species, and the release of vasoactive factors [3]. Although nerves are susceptible to reperfusion injury, muscles are more susceptible to ischemic damage, and muscle injury is caused by ischemia beneath and distal to the cuff; the extent of injury is related to duration of ischemia and patient age [5]. In this study, we only obtained values of arterial lactate and glucose but not reactive oxygen species or inflammatory cytokines; thus, we could not predict the possibility of reperfusion injury but might be able to predict ischemic damage of muscle tissue. In a previous report [2], spinal anesthesia was found to be associated with a higher interstitial lactate and a lower glucose level than sevoflurane anesthesia, and the authors suggested that glucose availability for glycolysis is better preserved by sevoflurane. However, in the present study, although a greater increase in lactate was observed in the sevoflurane group, arterial glucose levels were increased to similar extents in both groups, which we surmise might be caused by age-related alterations in skeletal muscle carbohydrate metabolism. With aging, changes in lactate production and transport other than lactate oxidation and reduced fatigue resistance is observed in aged skeletal muscles [6]. In a previous animal study, it was demonstrated that exercise muscle glycogenolysis is accelerated in old rats, and the authors suggested that this might occur secondary to an age-related reduction in muscle oxidative capacity and blood flow during contractile activity [7].

Several experimental and clinical studies have shown that regional anesthesia might improve tissue perfusion through sympathetic blockade and prevent pain [8–11]. Demirag et al. [9] demonstrated that epidural anesthesia leads to vasodilatation because of sympathetic block of nerve roots and that this prevents vasospasm during surgery. In the present study, we found significantly higher urine output with low arterial lactate levels in the spinal anesthesia group, suggesting relatively well preserved tissue perfusion. Also, significant higher MAP at T_5 (values in the postanesthetic care unit) and lower requirements of analgesics might reflect the superior postoperative analgesic effect.

Several reports demonstrated that in addition to sevoflurane, propofol and remifentanil also have been shown to have protective effect against ischemia/reperfusion injury [2, 12, 13]. We used all these drugs for anesthetic induction and maintenance, and thus we could not exclude the possibility of interactions of the anesthetic drugs. Although there were no significant differences in lower MAP and HR in the sevoflurane group, tourniquet inflation could lead to tissue hypoperfusion and higher arterial lactate levels. Some of the spinal group were administered small doses of midazolam, which might not be a significant factor for modifying glucose metabolite in this study [14].

The present study has several limitations that warrant consideration. First, samples were not collected using a microdialysis method; we only analyzed arterial blood gas, because our focus was on clinical usefulness during perioperative care. Accordingly, we did not determine changes in metabolic substances or inflammatory cytokine levels other than arterial lactate level during ischemic reperfusion. Second, the study was conducted on older women for reasons of availability because the prevalence of TKR is much higher in women and peak lactate concentrations show a curvilinear decline with age, which suggests that anaerobic energy production from glycolysis declines in later years [15, 16]. Thus, our results apply to this population. Finally, because the method of this study was not randomized controlled, the level of evidence is not as high, and therefore, further study may be required.

We conclude that spinal anesthesia is associated with lower arterial lactate levels than sevoflurane anesthesia after pneumatic tourniquet deflation. Furthermore, arterial glucose levels were increased in both groups without an intergroup difference, presumably as the result of age-related alterations in skeletal muscle carbohydrate metabolism. We believe that spinal anesthesia has positive effects on tissue perfusion during the use of a tourniquet in the elderly population.

Conflict of interest No external funding was provided for this study, and the authors have no competing interests to declare.

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