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Influence of Dexmedetomidine on the Tourniquet Related Responses in Hypertension Patients Receiving Unilateral Knee Arthroplasty under General Anesthesia

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ABSTRACT

This study aimed to investigate the influence of dexmedetomidine (DEX) on the tourniquet related responses in hypertension patients receiving unilateral knee arthroplasty (UKA) under general anesthesia. Results showed that the incidence of tourniquet induced hypertension (TIH), hemodynamics, MAC and EtSEV in DEX group were significantly lower than those in control group, regardless of hypertension. However, significant differences in TIH, hemodynamics, minimum alveolar concentration (MAC) and end-tidal sevoflurane (EtSEV) were not observed between hypertension patients and non-hypertension patients in both control group and DEX group. Moreover, oxygen index (OI) and respiratory index (RI) remained unchanged after deflation and DEX failed to affect OI and RI within 30 min after deflation, regardless of hypertension. Taken together, DEX may significantly improve the hemodynamics, which is independent of pre-existing hypertension.

Surgery of the extremities is frequently performed after exsanguination of the limb followed by inflation of a tourniquet, aiming to obtain bloodless operating conditions and to prevent unnecessary blood loss. However, prolonged tourniquet inflation may cause a gradual rise in blood pressure, which is also known as tourniquet induced hypertension (TIH). TIH occurs more frequently in patients receiving general anesthesia and/or lower limb surgery [1]. There is no consensus on the definition of TIH. In previous studies, TIH was defined as a rise of more than 30% in systolic or diastolic blood pressure [2,3]. According to this definition, the incidence of TIH in general anesthesia varies among studies and patients receiving different types of anesthesia. Kaufman and Walts reported that the frequency of TIH was 11% in a group of 500 patients whose operations involved the use of a tourniquet in lower limbs surgery [2]. In a retrospective study on 699 patients receiving orthopedic surgery using prolonged tourniquet inflation with a minimum of one hour of anesthesia, hypertension was found in 67% of patients receiving general anesthesia, 18.6% of the patients receiving intravenous regional anesthesia (IVRA), 2.7% of the patients operated under spinal anesthesia and 2.5% of the patients receiving a brachial plexus anesthetic [4]. TIH during the surgery may increase the risk for cardiovascular events (such as coronary ischemia and arrhythmia), especially in patients with advanced age, concomitant hypertension, ischemic heart disease and atherosclerosis [5]. Moreover, tourniquet inflation–deflation induced ischemia and reperfusion may cause damage to the lung, leading to the impairment to the gas exchange of the lung [6]. Thus, to deeply investigate the tourniquet related hemodynamic responses and ischemia–reperfusion injury is important for patients receiving limb surgery under general anesthesia.

Dexmedetomidine (DEX), an imidazole compound, is the pharmacologically active dextroisomer of medetomidine [7], which displays specific and selective α_2-adrenoceptor agonism. Since its release in the US market in late 1999, it has gained remarkable attention in the adult, pediatric and geriatric populations, predominantly because of its minimal respiratory depression. Besides the sedative, analgesic and anxiolytic properties [8], studies in recent years also reveal that DEX has its potential in many other clinical scenarios, including neuroprotection, cardioprotection and renoprotection, with promising results [9].

Theoretically, DEX may exert significant effects on attenuating tourniquet-induced hyperdynamic responses including TIH, which has been confirmed in several studies [10,11]. In addition, pre-operative use of DEX is also helpful to reduce the dose of anesthetics [12]. However, in hypertension patients, the impact of DEX is still unclear because hypertension patients were usually excluded from some studies [10,11]. In the present study, patients with or without hypertension receiving elective unilateral knee arthroplasty (UKA) were recruited to investigate

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Table 1
Demographic Data in Control Group and DEX Group.

Variable	Control Group (n = 39)	DEX Group (n = 41)
Age (years)	66.1 ± 7.5	65.0 ± 7.9
Height (cm)	160.3 ± 6.9	159.7 ± 6.6
Body weight (kg)	65.2 ± 10.2	67.7 ± 11.0
BMI (kg/cm^2)	25.3 ± 3.4	26.4 ± 3.5
Gender (M/F)	10/29	9/32
Tourniquet time (min)	76.3 ± 13.8	79.7 ± 11.3
History of hypertension (yes/no)	18/21	25/16

whether hypertension may influence the hemodynamics and inhaled anesthesia related parameters following pre-operative use of DEX.

Materials and Methods

Inclusion of patients

A total of 80 patients (ASA grade I-III) receiving elective unilateral knee arthroplasty were recruited from the Department of Joint Surgery from July 2011 to January 2012. The mean age was 65.4 ± 7.8 years (range: 46–75 years). There were 19 males and 61 females. In addition, 43 patients had a history of doctor diagnosed hypertension. Hypertension was diagnosed according to the Guideline for the Prevention and Treatment of Hypertension in China [13].

Exclusion criteria: (1) Patients were allergic to DEX or other drugs used in the present study; (2) patients had respiratory infections recently, chronic cough, asthma and chronic obstructive lung disease; (3) patients had severe liver and/or kidney dysfunction; (4) patients had severe sinus bradycardia (<50 beats/min); (5) patients had type II second-degree atrioventricular block.

This study was registered in Chinese Clinical Trial Register (ChiCTR-TRC-11001714) and informed consent was obtained from each patient before study. The whole protocol was approved by the Ethics Committee of Chinese Clinical Trial Register (ChiECRCT-2011044).

Treatments

Patients were randomly divided into control group and DEX group. All the patients received food and water deprivation for 8 h before surgery. Before anesthesia, an access to the upper limb vein was prepared for the fluid infusion and detection of bispectral index (BIS). The heart rate (HR) was routinely monitored and the blood pressure (BP; systolic blood pressure, SBP) was measured invasively via the left radial artery. End-tidal concentration of sevoflurane (EtSEV) and minimal alveolar concentration (MAC) were recorded during anesthesia.

Before anesthesia induction, Ringer's acetate was infused at 5 ml/kg. For anesthesia induction, midazolam at 0.05 mg/kg, propofol at 1 mg/kg, fentanyl at 3 μg/kg and cis-atracurium at 0.3 mg/kg were injected, followed by tracheal intubation and subsequent mechanical ventilation via an anesthesia machine when the BIS reduced to lower than 60. The tidal volume was 10 ml/kg and respiratory rate was 12 breaths/min. Anesthesia was maintained with sevoflurane, and all patients' lungs were mechanically ventilated with 1 L/min fresh gas. The anesthesia depth was adjusted to maintain the BIS at 40–60. The liquid crystal was infused at 6 ml/kg/h via a micropump during surgery.

Table 2
Demographics of Hypertension Patients and Non-Hypertension Patients.

Variable	Hypertension (n = 43)	Non-Hypertension (n = 37)
Age (years)	66.0 ± 6.8	64.8 ± 8.8
Height (cm)	160.4 ± 6.4	159.7 ± 7.4
Body weight (kg)	69.2 ± 11.6	68.1 ± 9.0
BMI (kg/cm^2)	26.7 ± 3.4	26.9 ± 3.3
Gender (M/F)	11/32	8/29
Tourniquet time (min)	78.7 ± 12.8	77.2 ± 12.9

Table 3
Incidence of TIH in Different Groups (n, %).

Group	Control	DEX	Total
Non-hypertension	14 (66.7%)	2 (12.5%)	16 (43.2%)
Hypertension	14 (77.8%)	12 (48.0%)	26 (60.5%)
Total	28 (71.8%)	14 (34.1%)	

Following anesthesia induction, DEX at a loading dose of 1 μg/kg was injected via a pump within 20 min, and maintenance was done with DEX at 0.4 μg/kg/h until tourniquet deflation. In control group, normal saline of equal volume was injected. Adequate muscle relaxation was maintained during surgery to avoid the changes in BP and HR. TIH was defined as invasive SBP higher than 160 mmHg for at least 1 min at 20 min after tourniquet inflation. In addition, the rate pressure product (RPP) was also calculated.

Application of Tourniquet

ZJ-1 numerical control pneumatic tourniquet (width: 71 mm) was used. Following anesthesia, the tourniquet was wrapped at the root of thigh. Mechanical limb exsanguination was performed with an elastic bandage prior to commencing surgery, followed by inflation.

Observations

Demographics including age, gender, height and body weight as well as the history of doctor diagnosed hypertension were recorded.

The hemodynamic parameters (HR, SBP, mean arterial pressure [MAP], cardiac index [CI], stroke volume index [SVI] and systemic vascular resistance index [SVRI]) were detected or calculated before anesthesia induction (T_0) and at different time points (0 [T_1], 20 [T_2], 30 [T_3], 40 [T_4], 50 [T_5] and 60 min [T_6]) after inflation. In addition, the EtSEV and MAC of sevoflurane were also recorded.

One minute before and within 30 min after deflation (5, 15 and 30 min), the arterial partial pressure of oxygen (PaO_2), fraction of inspired oxygen (FiO_2) and alveolo-arterial oxygen partial pressure difference ($P_{(A\text{-}a)}O_2$) were measured, followed by calculation of oxygenation index (OI) and respiratory index (RI).

Statistical Analysis

Quantitative data are expressed as mean ± standard deviation (SD). Comparisons were done with repeated-measures analysis of variance of variance for data collected at different time points and with analysis of variance for those in a specific group. Qualitative data were compared with chi square test. Statistical analysis was performed with SPSS version 18.0, and a value of $P < 0.05$ was considered statistically significant.

Results

General Information

There were no marked differences in the gender, age, body weight, height, BMI, tourniquet time and history of hypertension between control group and DEX group ($P > 0.05$; Table 1), and hypertension patients and non-hypertension also matched in the gender, age, body weight, height, BMI and tourniquet time ($P > 0.05$; Table 2). There were no marked differences in the use of Ringer's acetate and liquid crystal. Loading dose (1 μg/kg) of DEX was injected via a pump for 20 min, and no patients had the heart rate of <45 bpm. Patients were closely monitored, and there were no complications related to hypertension.