Kaohsiung Journal of Medical Sciences (2013) 29, 75–81

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: http://www.kjms-online.com

ORIGINAL ARTICLE

Dexmedetomidine did not reduce the effects of tourniquet-induced ischemia-reperfusion injury during general anesthesia

Evrim Bostankolu [a], Hilal Ayoglu [a,*], Serhan Yurtlu [a], Rahsan Dilek Okyay [a], Gülay Erdogan [a], Yeliz Deniz [a], Volkan Hanci [a], Murat Can [b], Isil Ozkocak Turan [a]

[a] *Department of Anesthesiology and Reanimation, Zonguldak Karaelmas University, Zonguldak, Turkey*
[b] *Department of Biochemistry, School of Medicine, Zonguldak Karaelmas University, Zonguldak, Turkey*

Received 4 August 2011; accepted 23 November 2011
Available online 13 October 2012

KEYWORDS
Dexmedetomidine;
Ischemia reperfusion injury;
Malondialdehyde;
Total antioxidant capacity

Abstract Ischemia reperfusion injury causes the release of free oxygen radicals. Free oxygen radicals initiate the production of toxic metabolites, such as malondialdehyde (MDA), through the lipid peroxidation of cellular membranes. Following lipid peroxidation, the antioxidant enzyme system is activated against reactive oxygen species (ROS) and attempts to protect cells from oxidative damage. There is a balance between the scavenging capacity of antioxidant enzymes and ROS. Because of this balance, the total antioxidant capacity (TAC) measurement is a sensitive indicator of the overall protective effects of the antioxidants. Alpha$_2$ receptor agonists are effective in preventing hemodynamic reactions during extremity surgeries by preventing the release of catecholamines secondary to tourniquet application. They have also been shown to possess preventive effects in various ischemia-reperfusion injury models. In our study, we examined the effects of dexmedetomidine on tourniquet-induced ischemia-reperfusion injury in lower extremity surgeries performed under general anesthesia. The effects of dexmedetomidine were measured with serum MDA and TAC levels. We studied 60 adult American Society of Anesthesiologists (ASA) physical status I or II patients undergoing one-sided lower extremity surgery with tourniquet. The patients were randomly divided into two groups. Group D was administered a dexmedetomidine infusion at a rate of 0.1 μg/kg/minute^{-1} for 10 minutes prior to induction and then at 0.7 μg/kg/hour^{-1} until 10 minutes before the end of the operation. The control group (Group C) received a saline infusion of the same amount and for the same period of time. General anesthesia was induced with thiopental, fentanyl, and rocuronium and maintained with nitrous oxide and sevoflurane in both groups. Venous blood samples were obtained before the administration of the study drugs (basal) at 1 minute before tourniquet release and at 5 and 20 minutes after tourniquet release

* Corresponding author. Bahcelievler mah, Gul Sok, Bahadir apt, Da:18, Site, Zonguldak, Turkey.
E-mail address: periayogluzku@yahoo.com (H. Ayoglu).

http://dx.doi.org/10.1016/j.kjms.2012.08.013

(ATR). In both groups, MDA levels decreased at 5 and 20 minutes ATR when compared with the basal values ($p < 0.05$). TAC levels decreased at 1 and 5 minutes ATR and then returned to basal values at 20 minutes ATR ($p < 0.05$). In reference to the prevention of lipid peroxidation in tourniquet-induced ischemia-reperfusion injury, the results from the two groups in our study showed that dexmedetomidine did not have an additional protective role during routine general anesthesia.

Introduction

Tourniquets in the proximal area are widely used in extremity surgeries to control intraoperative bleeding [1]. Ischemia occurs in the extremity following tourniquet inflation, and reperfusion occurs after deflation because of the re-establishment of blood flow [1]. The hemodynamic and metabolic changes that occur with tourniquet placement depend on the tourniquet phase (inflation/deflation), the duration of tourniquet placement, the size of the ischemic area, the type of anesthesia administered, and the cardiovascular condition of the patient [2]. The removal of the tourniquet initiates the event of ischemia reperfusion injury through the sequestration of oxygenated blood cells in the extremity, which leads to the appearance of free oxygen radicals [3]. Reactive oxygen species (ROS) that appear with reperfusion injury damage cellular structures through the process of the lipid peroxidation of cellular membranes and yield toxic metabolites such as malondialdehyde (MDA) [4]. As an important intermediate product in lipid peroxidation, MDA is used as a sensitive marker of ischemia-reperfusion injury [5]. ROS-induced tissue injury is triggered by various defense mechanisms [6]. The first defense mechanisms include the antioxidant enzymes of superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) [6]. These enzymes catalyze ROS into less reactive substances [7,8]. There is a balance between ROS and the scavenging capacity of antioxidant enzymes. Total antioxidant capacity (TAC) is a test that measures all antioxidants rather than measuring them separately and revealing their relationships [9]. TAC is a functional outcome of both the oxidation capacity and the consumption rate of antioxidants during oxidative stress [10]. Both clinical and experimental studies focusing on the reduction of free radical-mediated reperfusion injury due to tourniquet-induced ischemia report that tissue injury may be controlled through the use of immunosuppressives, corticosteroids, anesthetic agents, various anesthesia methods and antioxidants [7,8,11,12]. As a selective alpha$_2$ receptor agonist, dexmedetomidine has high lipid resolution and has analgesic, sedative and anesthetic effects [13]. Alpha$_2$ receptor agonists are effective in preventing hemodynamic reactions in extremity surgeries where a tourniquet is used because they prevent the release of catecholamines and have been shown to possess preventive effects in various ischemia-reperfusion injury studies [13–15].

We hypothesized that dexmedetomidine might protect against ischemia-reperfusion injury in extremity surgeries performed under general anesthesia with the use of a tourniquet. The primary outcome variables were determined with serum MDA and TAC values measured at bsal, at 1 minute before and at 5 and 20 minutes after the release of the tourniquet.

Methods

Ethical approval for this study (Ethical Committee N° 2008/17) was provided by the Ethical Committee of Zonguldak Karaelmas University Hospitals, Zonguldak, Turkey (Chairperson Assoc. Prof. B.D Gun) on November 20, 2008.

After gaining the approval of the university ethics committee, written informed consent was obtained from the study participants. The participants enrolled in our study included patients who were scheduled for an elective lower extremity operation under general anesthesia using a one-sided tourniquet who did not have a previous history of liver and renal disease, diabetes mellitus, smoking, antioxidant treatment or an allergy to any of the drugs used in the study. In the preanesthetic assessment, 60 American Society of Anesthesiologists (ASA) physical status I or II patients 18-65 years of age and weighing 60–100 kg were included in the study. Cases with tourniquet times of less than 60 minutes or longer than 150 minutes were excluded. All patients received 0.07 mg/kg intramuscular midazolam 30 minutes prior to the operation.

In the operating room, standard procedures for monitoring patients under anesthesia were performed. Vascular access from a large cubital vein was achieved with a 16-gauge (G) needle. Basal blood samples were drawn for the determination of serum MDA and TAC levels prior to the administration of study drugs (T0). For the drip infusion, a 20-G needle was used for vascular access in the other arm. Patients were randomly assigned by sealed envelope to one of two groups: Group D ($n = 30$) or Group C ($n = 30$). Group D received dexmedetomidine (Precedex 2 ml/200 μg, Meditera, Izmir, Turkey) at an infusion rate of 0.1 μg/kg/minute^{-1} for 10 minutes prior to induction and at a rate of 0.7 μg/kg/hour^{-1} until 10 minutes before the end of the operation. The control group (Group C; $n = 30$) received a saline solution of the same volume and for the same amount of time. Both groups were administered thiopental 5 mg/kg, fentanyl 1 μg/kg, and rocuronium bromide 0.6 mg/kg at the end of 10 minutes for anesthesia induction. Anesthesia was maintained in both groups with 4 L minute^{-1} 50% N_2O for oxygen and rocuronium maintenance. The end tidal (ET) sevoflurane concentration was 1.5%, and the $ETCO_2$ was 35 mmHg. Following intubation, the affected extremity was elevated and wrapped with an Esmarch bandage, and a tourniquet was