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Original Contribution

Effect of dexmedetomidine on intraocular pressure in patients undergoing robot-assisted laparoscopic radical prostatectomy under total intravenous anesthesia: A randomized, double blinded placebo controlled clinical trial

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ABSTRACT

Study objective: To study the effects of intraoperative dexmedetomidine on the intraocular pressure (IOP) in patients undergoing robot-assisted laparoscopic radical prostatectomy (RALRP) under propofol–remifentanil anesthesia.
Design: Double-blind, randomized controlled trial.
Setting: Operating room.
Patients: Forty consenting male patients aged ≥20 to < 80 years with American Society of Anesthesiologists physical status classes I and II.
Interventions: The patients were randomly assigned to either dexmedetomidine (DEX) (n = 20) or control (n = 20) group. Anesthesia was induced and maintained using propofol, remifentanil, and rocuronium. In the dexmedetomidine group, dexmedetomidine was administered at 0.4 μg/kg/h immediately after anesthesia induction until the end of the surgery, whereas normal saline was administered as placebo in the control group.
Measurements: IOP was measured using a rebound tonometer. Time points of measuring IOP were as follows: T1: before anesthesia induction, T2: 5 min after intubation, T3: 60 min after placing patient in the Trendelenburg position, T4: 120 min after placing patient in the Trendelenburg position, T5: 180 min after placing patient in the Trendelenburg position, T6: 5 min after placing patient in a horizontal position, T7: 5 min after extubation, and T8: 30 min after extubation.
Main results: A linear mixed model analysis demonstrated a significant intergroup difference in IOP over time and during pneumoperitoneum in the steep Trendelenburg position. IOP at T5 was significantly lower in the dexmedetomidine group than in the control group even after post-hoc analysis in the steep Trendelenburg position periods with Bonferroni correction.
Conclusions: Dexmedetomidine combined with propofol decreases IOP in the steep Trendelenburg position during RALRP.

1. Introduction

Robot-assisted laparoscopic radical prostatectomy (RALRP) requires the pneumoperitoneum in the steep Trendelenburg position [1,2]. The procedure increases intraocular pressure (IOP) to 30–40 mm Hg [3]; this degree of IOP may not cause cessation of blood flow in the optic nerve head [4], but ophthalmologic injuries such as ischemic optic neuropathy and transient visual loss have been reported in patients undergoing RALRP [5,6]. These ocular complications may occur secondary to the physiologic changes caused by pneumoperitoneum and the steep Trendelenburg position. Studies have reported that increased IOP is not directly related to the development of posterior ischemic optic neuropathy; however, it is likely to be a risk factor for ophthalmic complications, including ischemic optic neuropathy, retinal artery occlusion, and deterioration of preoperative glaucoma [7,8]. Patients undergoing RALRP are elderly males and are likely to be at risk for dysfunctional autoregulation of ocular blood flow [9]; moreover, the incidence of glaucoma is increased in these patients [10]. Sometimes anesthesiologists may hesitate to determine the indication for RALRP in glaucoma patients [11]. Anesthesiologists need to monitor any increase

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in IOP and control the magnitude of increase in IOP, if possible, in patients undergoing RALRP.

There is limited knowledge on using pharmacological interventions as adjuncts to anesthesia for alleviating IOP elevation during RALRP. Dexmedetomidine, a highly selective α_2-receptor agonist, may be one of the pharmacological agents with favorable pharmacological properties for decreasing IOP [12,13]. A previous study demonstrated that additional continuous infusions of dexmedetomidine inhibit the IOP increase during RALRP performed under sevoflurane anesthesia [14,15]. Propofol-based anesthesia has also been reported to reduce IOP during RALRP compared with sevoflurane-based anesthesia [16].

The present study aimed to evaluate the effects of continuous dexmedetomidine infusion combined with propofol-based anesthesia on IOP in patients undergoing RALRP.

2. Materials and methods

This was a prospective, randomized, double-blind controlled study conducted at the Ehime University Hospital in Toon, Japan. Study approval was obtained from the Institutional Review Board (registration number 1405013). The study was registered with the UMIN Clinical Trials Registry (000014432).

2.1. Study subjects

Adult male patients with American Society of Anesthesiologists physical status (ASA-PS) classes I and II who were scheduled for RALRP at the Ehime University Hospital were consecutively enrolled from June 2014 to June 2015. All patients gave their signed and written consent. Exclusion criteria included patients with a history of drug allergy to dexmedetomidine, patients with glaucoma, and patients with a history of ophthalmic surgery as well as those who had received any medication known to alter IOP and those with body mass index > 35. The details regarding the participants have been presented in a Consolidated Standards of Reporting Trials (CONSORT) flow diagram (Fig. 1).

2.2. Procedure

Forty patients were enrolled and randomly allocated to either dexmedetomidine group (n = 20) or control group (n = 20) according to a predetermined randomization sequence generated on www.random.org. All study medications were prepared by an independent investigator who was not associated with IOP measurements or anesthetic management of patients. The patients, surgical team, research team, and anesthesiologists were all blinded to group allocation.

IOP measurements were performed on patients' left eyes using a rebound tonometer (Icare PRO®; Icare, Espoo, Finland). Rebound tonometer allows downward measurement of the eye in a supine patient as well as standard measurements in the normal upright position. Measurement of IOP using rebound tonometry does not require topical anesthetics and has a good correlation with Goldmann applanation tonometry [17].

A standard anesthetic technique was used. On arrival in the operating room, noninvasive arterial blood pressure, electrocardiogram (ECG), and oxygen saturation (SpO2) were routinely evaluated.

Anesthesia was induced and maintained using a target-controlled infusion of propofol at the target blood concentration 3–4 μg/ml and continuous infusions of remifentanil (0.15–0.3 μg/kg/min). Rocuronium bromide (50 mg) was used for tracheal intubation. After induction of anesthesia, rocuronium bromide (7 μg/kg/min) was administered continuously during the surgery to improve surgical conditions and facilitate RALRP at low IAP levels. Sugammadex sodium that suggested no prominent negative effect on IOP was used to reverse the muscle relaxant effects at the end of the surgery [18].

The ventilator was set at tidal volume 8–10 ml/kg, respiratory rate 12–16 breaths/min, inspiratory:expiratory ratio 1:2, FiO_2 0.4 with air, and an inspiratory fresh gas flow of 2 l/min. The ventilator was adjusted to keep the end-tidal CO_2 ($ETCO_2$) between 30 and 40 mm Hg, and positive end-expiratory pressure was not applied. After anesthesia induction, a radial artery catheter was inserted for continuous arterial pressure monitoring and blood sampling. The mean arterial pressure was maintained over 60 mm Hg. A bispectral index (BIS) monitor (BIS processor QE-910P, Aspect Medical System Inc., Newton, MA, USA) was used to monitor the anesthesia level, and BIS values were maintained between 40 and 50. Neuromuscular monitoring could not be performed because patients' arms were partially covered in drapes, which hindered their observation and ultimately the accurate monitoring.

In the dexmedetomidine group, dexmedetomidine was administered at 0.4 μg/kg/h immediately after anesthesia induction until the end of surgery, whereas in the control group, normal saline was administered as placebo at the same rate as the treatment group. We determined the

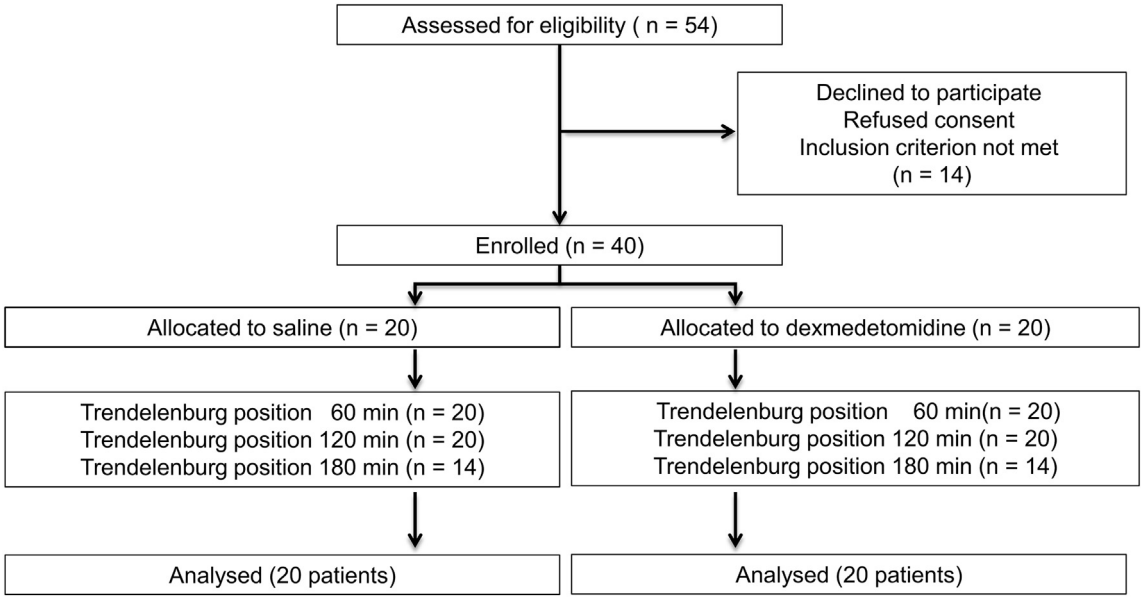

Fig. 1. CONSORT flow diagram.