Kaohsiung Journal of Medical Sciences (2016) 32, 586–592

Available online at www.sciencedirect.com

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

ORIGINAL ARTICLE

Influence of different menstrual phases on the Bispectral Index during dexmedetomidine sedation

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Received 15 April 2016; accepted 29 August 2016
Available online 19 October 2016

KEYWORDS
Bispectral Index;
Dexmedetomidine;
Menstrual cycle;
Sedation

Abstract To investigate the influence of different menstrual phases on the Bispectral Index (BIS) during dexmedetomidine (Dex) sedation, 40 patients with regular menstrual cycle, American Society of Anesthesiologists I–II, aged 18–40 years, undergoing selective gynecologic laparoscopic surgery, were enrolled. According to different menstrual phases and the serum progesterone concentration, they were divided into two groups: the follicular phase group (Group F) and the luteal phase group (Group L), and each group had 20 patients. Before anesthesia induction, patients were infused with an initial loading dose of Dex (1 μg/kg) for 10 minutes and then 0.5 μg/kg/h for 20 minutes. BIS and the changes in hemodynamic and respiratory parameters were recorded within those 30 minutes. Time to lower BIS to 70 and 60 in Group L was shorter than that in Group F (9.4 ± 1.3 minutes vs. 11.3 ± 2.1 minutes, $p = 0.005$; 11.3 ± 2.4 minutes vs. 14.0 ± 3.6 minutes, $p = 0.021$). The number of patients whose BIS reached 50 in Group L was greater than that in Group F (15 vs. 8, $p < 0.05$). The lowest BIS value in the Group L was lower than that in Group F (46.8 ± 6.3 vs. 55.3 ± 5.5, $p = 0.006$), and the heart rate of patients in both groups showed a decrease ($p < 0.05$). The sedative effect of Dex was more significant in patients during the luteal phase than during the follicular phase.

Conflicts of interest: All authors declare no conflicts of interest.

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http://dx.doi.org/10.1016/j.kjms.2016.09.001

Introduction

Women have higher Bispectral Index (BIS) scores at similar concentrations of anesthetics and emerge faster from general anesthesia than men [1]. In recent years, there is an increased interest in studying sex-based differences in pharmacokinetics and pharmacodynamics [2]. Despite the sex-based differences, different menstrual phases among women may exert a certain influence on anesthesia. Studies have shown that the threshold of pains is lower and postoperative nausea and vomiting are more frequent in the follicular phase than in the luteal phase [3,4]. It was also reported that patients in the follicular phase needed more sevoflurane than those in the luteal phase during the maintenance of general anesthesia and this difference might be caused by the increase of progesterone level in the luteal phase, which reduced the required dosages of anesthetics [5]. Dexmedetomidine (Dex) is a highly selective α_2-adrenergic receptor agonist. It has been reported to provide sedation that parallels natural sleep, anxiolysis, analgesia, and sympatholysis, as well as an anesthetic-sparing effect with minimal respiratory depression [6]. It is a widely used intravenous sedative in clinical anesthesia setting. Different from the sedative mechanism of propofol and midazolam, Dex mainly acts on the α_2-adrenoceptor of locus coeruleus and its sedative effect is similar to that of natural sleepiness [7]. Dex, due to its sympatholytic effects, blunts the hyperdynamic response to laryngoscopy and surgery and maintains a stable hemodynamic profile [8–10]. It also has been found to potentiate the effects of all anesthetic agents, including intravenous and inhalational agents, and has opioid-sparing effects, thereby reducing the doses required [11–13]. Dex has both sympatholytic effects and anesthesia-sparing effects, thus making it an ideal candidate for induction and maintenance.

This prospective observational study was performed to investigate the influence of different menstrual phases on the Dex-sedative effect, which was assessed with BIS. The hypothesis of our study was that for patients in the luteal phase, intravenous administration of Dex results in an increased sedation level, compared with patients in the follicular phase.

Methods

This trial is registered at chictr.org.cn (Trial Registration Number: ChiCTR-IOR-15006092) and is a prospective case–control study, which was approved by the Committee of the Obstetrics and Gynecology Hospital, Fudan University (Shanghai, China). Written informed consent was obtained from all patients. Patients with American Society of Anesthesiologists physical status I or II, aged 18–40 years, with body mass index 21–30 kg/m^2, having regular menstrual cycle, and undergoing selective gynecologic laparoscopic surgery including myomectomy and oophorocystectomy from December 2014 to January 2015 were enrolled ($N = 40$). Regular menstrual cycle is defined as menstrual cycle lasting between 23 days and 35 days with cyclic changes < 2 days [4]. Patients were excluded for the following reasons: taking hormones before surgery, history of alcoholism, antipsychotics, benzodiazepines, anticonvulsant, or opioid drugs. Menstrual cycles of all patients were assessed by experienced gynecologists and peripheral venous blood samples were collected in the morning on the day of the surgery to measure the serum progesterone and estradiol concentrations using the chemiluminescent method. The 40 patients analyzed in this study were divided into two groups: the follicular phase group (Group F) and the luteal phase group (Group L).

All patients underwent routine preoperative preparation. Solid-food intake stopped after supper the day before the operation and all patients fasted for more than 10 hours. No premedication was given. Upon arrival in the operating theater, an intravenous line was set on the back of the left hand for administration of Ringer's lactate solution at 10 mL/kg/h, and standard monitoring measures were applied, including noninvasive arterial pressure, five-lead electrocardiogram, pulse oximetry [peripheral capillary oxygen saturation (SpO_2); Intellivue MP40, Philips, Böblingen, badenia-wirtembergia, Germany], and BIS (BIS VISTA, Covidien, Princeton, New Jersey, USA). After cleaning the forehead and placing the BIS sensor, the electrodes were pressed for 5 seconds. The BIS was calculated with a smoothing rate of 15 seconds. While recording the BIS, movements and talks of other staff members were forbidden. Before the induction of anesthesia, patients were required to close their eyes, wore a four-tailed mask to take in oxygen (6 L/min), and connected to the anesthesia machine (S/5 Avance, Datex-Ohmeda, Inc., Madison, Wisconsin, USA). Dex (4 μg/mL; dexmedetomidine hydrochloride injection, No. 14092732; Hengrui Medicine Co., Ltd, Lianyungang, Jiangsu, China) was prepared using normal sodium chloride injection. Patients were continuously infused initially with a Dex loading dose of 1 μg/kg for 10 minutes and then received 0.5 μg/kg/h Dex for 20 minutes via an infusion pump (Agilia, Fresenius Kabi, Bad Homburg, Baden-Württemberg, Germany). The anesthetists and data recorder were all blind to the menstrual phases of the patients. Following the infusion of Dex, propofol was administered via an infusion pump (Agilia, Fresenius Kabi, Bad Homburg, Baden-Württemberg, Germany), simulating Marsh pharmacokinetic model with a target plasma concentration set at 4.0 μg/mL; then, fentanyl (3 μg/kg) was administered intravenously. After loss of consciousness, rocuronium (0.8 mg/kg) was used for neuromuscular relaxation. Ninety seconds later, tracheal intubation was performed.

The primary outcome measure was the time at which the BIS score decreased to 70 and 60. The secondary outcome measures were heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse oxygen saturation (SpO_2), respiratory rate (RR), and end-tidal CO_2 pressure ($PetCO_2$), which were recorded before the loading dose (T_0) and 5 minutes (T_{5min}), 10 minutes (T_{10min}), 15 minutes (T_{15min}), 20 minutes (T_{20min}), 25 minutes (T_{25min}), and 30 minutes (T_{30min}) after starting Dex infusion.

We also recorded the occurrence, if any, of hypertension, hypotension, bradycardia, apnea after infusion of Dex. Hypertension is defined as an increase of SBP by over 20% of the normal value; hypotension is defined as a decrease of SBP by over 20% of the normal value or SBP lower than 90 mmHg; serious bradycardia is defined as a decrease of HR by over 30% of the normal value or lower than 45 beats/min; and apnea is defined as the stop of spontaneous breathing longer than 20 seconds according to