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Research Article

Preoperative paracetamol infusion reduces sevoflurane consumption during thyroidectomy under general anesthesia with spectral entropy monitoring

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KEYWORDS

Paracetamol;
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Abstract *Background:* Intravenous (IV) paracetamol has a significant opioid-sparing effect. We investigated the effect of paracetamol infusion on sevoflurane consumption during entropy monitored general anesthesia.

Methods: Sixty-two ASA I and II patients undergoing thyroidectomy under general anesthesia were included in a prospective, randomized, double-blind and placebo controlled study. The patients were randomized to receive a slow infusion of either 1 g paracetamol (paracetamol group, $n = 31$) or saline (control group, $n = 31$) just before induction of anesthesia. Sevoflurane concentration was titrated to keep the state entropy value between 40 and 50. End-tidal sevoflurane concentration, sevoflurane consumption, recovery characteristics, time to first analgesic request and meperidine consumption during the first 6 postoperative hours were recorded.

Results: The mean ± SD estimated sevoflurane consumption was significantly lower in the paracetamol treated patients (36.2 ± 15 vs 44.9 ± 13.9 ml, in the control group; $p = 0.021$). Patients receiving paracetamol had a faster post-anesthetic recovery profile (extubation time, time to eye opening to command and time to state name and mention his/her home address) than the other

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group ($p < 0.05$). Mean ± SD time to first analgesic request was significantly prolonged in paracetamol group compared to control group (48.4 ± 14.0 vs 40.7 ± 11.5 min, respectively; $p = 0.021$). Meperidine consumption was higher in control group than in paracetamol group (28.7 ± 10.2 vs 23.1 ± 9.0 mg, respectively; $p = 0.025$).

Conclusion: Preoperative IV paracetamol infusion improved consumption and emergence from entropy monitored sevoflurane anesthesia with enhancement of the early postoperative analgesia.

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1. Introduction

Proper monitoring of the depth of anesthesia is crucial for judicious titration of anesthetics to prevent awareness under general anesthesia as well as the side effects of anesthetic over-dose with the subsequent economic waste and environmental pollution. With awareness, the patient may exhibit symptoms ranging from mild anxiety to post traumatic stress disorder (sleep disturbances, nightmares and social difficulties) [1]. In the standard clinical practice, the depth of anesthesia is judged by the clinical experience of the anesthetist, based on the patient's vital signs and the hemodynamic responses. However, the regular use of certain medications as β-blockers and antihypertensive drugs render the hemodynamic signs unreliable for titration of anesthetics [2].

At present; the electroencephalogram (EEG) based spectral entropy is increasingly being used for monitoring the depth of anesthesia and provides information regarding the cortical state of the patient and the level of hypnosis [3] as well as an indirect measure of the adequacy of analgesia [4]. The monitor uses different algorithms to calculate the level of consciousness index by processing the EEG signal measured over the forehead and drive the numeric index [5]. The spectral entropy has 2 signals: State entropy (SE) which reflects the hypnotic level of the patient; computed from an EEG data from the previous 15 s in the range of 0.8–32 Hz, and shows the value in the range of 0–91 and Response entropy (RE) that includes; in addition to the EEG, a forehead muscle electromyography component and reflects the patient arousal and response to painful stimuli. The latter is computed from an EEG data in the range of 0.8–47 Hz and shows the value in the range of 0–100 [6]. State entropy values between "40–60" are the recommended surgical level of anesthesia while "100" signifies awake state and "0" indicates suppression of the cortical neuronal activity [7].

Intravenous (IV) paracetamol (acetaminophen in USA) is an effective analgesic and antipyretic agent acting at both the central and peripheral components of the pain pathway [8] and devoid of the detrimental effects of opioids and non-steroidal anti-inflammatory drugs (NSAID) with a tolerability profile similar to placebo [9]. The onset of paracetamol analgesia starts rapidly after 5–10 min of IV administration, with peak effect obtained within 1 h and lasting 4–6 h. [10] Thus, IV paracetamol is a suitable medication for the treatment of postoperative pain when used either alone or as a part of a balanced analgesic regimen. Moreover, several studies in the medical literature have demonstrated the opioid-sparing effect of IV paracetamol [11–15]. In view of these reports; we hypothesized that preoperative infusion of IV paracetamol would decrease sevoflurane consumption during general anesthesia. To explore this; we designed a prospective, randomized, double-blind and placebo controlled study to evaluate the effect of the preoperative single-dose administration of IV paracetamol on sevoflurane consumption in patients undergoing thyroidectomy under general anesthesia with an entropy added to the standard intraoperative monitors.

2. Methods

This study took place in king Abdulaziz Naval Base Hospital, Jubail, Kingdom of Saudi Arabia, from May 2011 to April 2013. The protocol was approved by the Hospital Ethics Committee and written informed consent was obtained from each patient. The study was registered at the Australian New Zealand Clinical Trial Registry (ANZCTR). URL and unique identification number: http://www.ANZCTR.org.au/ACTRN12613000485730.aspx. We studied 62 ASA physical status I and II patients of both sex, aged 20–55 years scheduled for subtotal thyroidectomy under general anesthesia. All enrolled patients were euthyroid. Patients were excluded if they had known allergy to paracetamol, neurological or psychological diseases, impaired liver functions (Alanine Transaminase > twice the normal value) and impaired renal function (serum creatinine > 2.0 mg%). Exclusion criteria also included pregnancy and breast feeding, the chronic use of analgesics or drugs affecting the central nervous system (CNS) function, the use of paracetamol within 6 h or any other analgesic medication within 12 h before the operation.

The patients were premedicated with lorazepam 2 mg orally on the evening of operation, and had been fasting for 8 h before surgery. At the operating theatre, all patients had a venous cannula inserted into one of the veins of the dorsum of the hand and IV fluid (lactated Ringer' solution) started at a rate of 7 ml kg h^{-1}. Intraoperative vitals monitoring [electrocardiogram (ECG), noninvasive systolic and diastolic blood pressure (Systolic and Diastolic BP), peripheral oxygen saturation (SpO_2) were applied. After wiping the skin with alcohol, the entropy sensor (Entropy sensor, Disposable. Datex-Ohmeda, Instrumentarium Corp. Helsenki, Finland) was applied to the patient's forehead (approximately 4 cm above the nose) and the temple area (between the corner of the eye and the hairline). The sensor was connected to the Datex-Ohmeda M-Entropy module via the Datex-Ohmeda ENT-3 Entropy sensor cable.

Before the start of anesthesia, the patients were randomized, by using a computer generated random list to one of two groups; the Paracetamol group (Group P) and the Control group (Group C). All patients received a slow IV infusion over 15 min just before induction of anesthesia of either 1 g paracetamol (Perfalgan 10 mg ml^{-1}, 100 ml vial; UPSA, France) (Group P, $n = 31$) or 100 ml of normal saline (Group C, $n = 31$). Blinding was carried out by a technician, not involved

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