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Original contribution

Neuroendocrine stress response in gynecological laparoscopy: TIVA with propofol versus sevoflurane anesthesia

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Abstract

Study Objective: To compare intraoperative and postoperative neuroendocrine stress responses during total intravenous anesthesia (TIVA) using propofol and remifentanil versus sevoflurane anesthesia, during laparoscopic surgery.

Design: Prospective, randomized study.

Setting: Tertiary-care university hospital.

Patients: 46 ASA physical status I patients undergoing laparoscopic surgery for benign ovarian cysts.

Intervention: Patients were randomly allocated to two groups to receive either TIVA (Group A = 23) or sevoflurane anesthesia (Group B = 23).

Measurements: Perioperative plasma levels of norepinephrine (NE), epinephrine (E), adrenocorticotropic hormone (ACTH), cortisol, growth hormone (GH), prolactin (PRL), and thyroid hormones (TSH, FT_3, FT_4) were measured. Blood samples were collected preoperatively, 30 minutes after the beginning of surgery, after extubation, and two and 4 hours after the end of surgery (times 0, 1, 2, 3, and 4).

Main Results: In Group A, perioperative levels of NE, E, ACTH, cortisol, and GH compared with preoperative values significantly decreased; in Group B they increased (Groups A vs. B: time 1, $P < 0.001$ for all markers; time *2,* $P < 0.001$ for E, ACTH, cortisol, and GH; time 3, $P < 0.01$ for cortisol, NE, and E, and $P < 0.05$ for ACTH and GH). Perioperative PRL levels were significantly enhanced in both groups versus preoperative values. In both groups, TSH levels increased while FT_3 levels decreased significantly relative to basal values. In both groups, perioperative FT_4 levels significantly increased compared with preoperative values.

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Conclusions: TIVA inhibited the ACTH-cortisol axis and reduced NE, E, and GH levels, but it enhanced PRL and had a weak effect on thyroid hormone concentrations as compared to sevoflurane anesthesia.

1. Introduction

Surgery induces a complex stress response characterized by neurohumoral, immunologic, and metabolic changes. The hypothalamus receives afferent neural and humoral signals from the injured area and integrates this input to provide an adequate response, which includes pituitary and sympathetic stimulation [1]. The magnitude of this stress response depends on a variety of factors such as severity [2] and duration of surgical trauma [3,4], patient age [5], intraoperative blood loss [6], postoperative pain [7], anesthetic method [8], and surgical technique [9].

Although the surgical stress response represents a defense mechanism, the stress-induced changes in postoperative organ function also may be implicated in the development of perioperative complications [4].

Abolition of the stress response by removing some of its negative neuroendocrine components may reduce perioperative morbidity and mortality, improve outcome, and decrease length of hospital stay, thus reducing the total cost of patient care [10,11].

An important goal of current anesthetic research is to find the "stress-free anesthetic method" that can limit activation of the neuroendocrine, inflammatory, and immune responses [12,13]. Many studies suggest that the choice of anesthetic technique can influence the stress response by stimulating, inhibiting, or modulating the pathophysiologic pathways that cause neurohumoral and immunologic changes [11,13-15].

The effects of inhalational anesthesia [14,16,17], propofol anesthesia [18,19], and total intravenous anesthesia (TIVA) [15,20] on modulation of neurohumoral response to surgical trauma have been studied, but some aspects are still unclear. The effect of TIVA with propofol and remifentanil on the hypothalamopituitary-adrenal response, on prolactin, growth hormone, and catecholamine release, and on the hypothalamopituitary-thyroid axis has not been assessed. This study was undertaken to compare the neuroendocrine stress response using TIVA versus inhalational anesthesia with sevoflurane in a surgical model associated with a low stress level, laparoscopic surgery for benign pelvic pathology.

2. Materials and methods

This prospective, randomized, single-blinded study was approved by the Hospital of the Catholic University of the Sacred Heart Ethics Committee, and written, informed consent was obtained from all patients. A total of 46 Caucasian women undergoing laparoscopic surgery at this tertiary-care hospital in Rome, were enrolled. We excluded patients receiving drugs known to affect sympathetic response or hormonal secretions; those with a history of cardiovascular or nervous system diseases; those with diabetes, endocrine disorders, obesity (body mass index $> 25\ kg/m^2$); and those with drug/alcohol abuse. All patients were ASA physical status I.

Patients were randomly allocated to receive total intravenous anesthesia using propofol and remifentanil (Group A, n = 23) or inhalational anesthesia with sevoflurane (Group B, n = 23) using a computer-generated random numbers list. All patients were operated on by the same surgeon according to standard techniques [21]; surgery started between 8:30 and 9:00 a.m. Thirty minutes before surgery, all patients were premedicated with oral diazepam 0.5% 0.2 $mL \cdot kg^{-1}$.

As soon as venous access was established, all patients received 5 $mL \cdot kg^{-1}$ of intravenous (IV) normal saline and they were preoxygenated with oxygen [inspired oxygen concentration (FIO_2) = 1.0]. In the TIVA group, a second venous cannula was inserted in the same arm to administer additional propofol and vecuronium, while the first venous catheter was used for propofol and remifentanil infusions using separate continuous infusion devices (Easyline; Unicare, Arezzo, Italy).

In both groups, a continuous remifentanil infusion of one $\mu g \cdot kg^{-1} \cdot min^{-1}$ was administered for one minute, then decreased to 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In Group A, anesthesia was induced with propofol 1.5 $mg \cdot kg^{-1}$ followed by a constant infusion of 150 $\mu g \cdot kg^{-1} \cdot min^{-1}$ until tracheal intubation; afterward, the propofol infusion rate was reduced to 100 $\mu g \cdot kg^{-1} \cdot min^{-1}$. In Group B, anesthesia was induced with sodium thiopental 5 $mg \cdot kg^{-1}$and then sevoflurane was administered at one minimum alveolar concentration (MAC) to end-tidal concentrations of 1.8% to 2%. After loss of consciousness, all patients received vecuronium 0.1 $mg \cdot kg^{-1}$ and their lungs were manually ventilated for at least three minutes with a FIO_2 of 0.5 before intubation. After pneumoperitoneum, the remifentanil infusion rate was reduced to 0.3 to 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ to maintain blood pressure (BP) and heart rate (HR) within 15% of preoperative values; it was stopped when surgeons removed the surgical instruments in both groups. Propofol and sevoflurane were discontinued at the end of skin closure.

Measurements of inspired and end-tidal concentration of oxygen, carbon dioxide, and sevoflurane were performed continuously by infrared spectrometry (Capnomac Ultima; Datex-Ohmeda, Inc., Milwaukee, WI, USA) calibrated