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Orginal contribution

Effect of 2 anesthetic techniques on the postoperative proinflammatory and anti-inflammatory cytokine response and cellular immune function to minor surgery

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Abstract

Study Objective: The aim of this study was to investigate the influence of 2 established anesthetic techniques: total intravenous anesthesia and balanced inhalation anesthesia (BAL) on the perioperative-induced changes of peripheral blood mononuclear cells (PBMCs), changes in lymphocyte subsets, and the balance of proinflammatory and anti-inflammatory cytokines.

Design: This is a prospective, randomized, clinical comparison study.

Settings: This study was set at a university hospital.

Patients: This study involved 50 patients with American Society of Anesthesiologists physical status I who were scheduled for elective minimal invasive partial diskectomy.

Interventions: There was no intervention involved in this study.

Measurements: Changes in differential counts, lymphocyte subsets, and proliferation rates were determined before surgery and in the early postoperative period. Plasma concentrations of pro-inflammatory cytokines (IL-2, IL-6, IL-12, interferon γ) and anti-inflammatory cytokines (IL-10, IL-1RA, transforming growth factor β), and plasma concentrations of cortisol, epinephrine, and norepinephrine were measured before, during, and after surgery.

Main Results: Absolute number of $CD3^+$, $CD4^+$, and $CD8^+$, and expression of HLA-DR and activation marker $CD25^+$, $CD26^+$, and $CD69^+$ decreased more in response to surgery after BAL. Changes in distribution of T-lymphocyte cells seem to be in part related to severe postoperative pain. Plasma concentration of IL-6 significantly increased during and after surgery with BAL without relation to pain.

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Conclusion: Anesthetic management may have varying influences on the postoperative immune response. Surgery-induced inflammatory response and alteration in cell-mediated immunity seem to be more pronounced after BAL. These effects were attributed to the enhanced stress response after BAL.

1. Introduction

Surgical procedures initiate inflammatory responses, which are essential for maintaining the homeostatic state during the postoperative course. Severe dysregulation of the inflammatory process may induce complications such as wound healing disorders, increased susceptibility to infections, inadequate stress reactions, multiple organ failure, and an increased incidence of metastasis [1,2]. The balance between immune stimulatory and immune suppressive mechanisms is affected by preoperative health status, extent and duration of surgery, drug treatment, anxiety, and pain. In addition, general anesthesia may impair the inflammatory responses, either directly by disturbing functions of immune cells or indirectly by modulation of the stress response. In contrast to the well-documented in vitro effects of different anesthetic drugs, different in vivo studies suggest only transient effects on the immune response [3,4]. In the present study, balanced inhalation anesthesia (BAL) and total intravenous anesthesia (TIVA) were analyzed in patients undergoing partial diskectomy.

We hypothesized that (1) the choice of anesthetic management and/or (2) differences in the duration of surgery, and (3) postoperative pain may affect postoperative immune competence by modulating the composition of leukocyte subsets, the expression of activation molecules, the cytokine pattern, and the proliferative capacity of mononuclear cells, and that they could be either beneficial or detrimental to the patient.

2. Methods

The study was approved by the local ethics committee of the Otto-von-Guericke-University, Magdeburg. Fifty patients with American Society of Anesthesiologists physical status I undergoing elective partial diskectomy were included in the study after giving their written informed consent to participate. Exclusion criteria were cardiopulmonary, endocrinologic or immunologic diseases, malignancies, or chronic pain management. The patients (range of age, 22-63 years; 15 female and 35 male patients) were prospectively randomized into 2 groups to receive either TIVA (n = 25) or BAL (n = 23) according to standard random procedures in our institution. Two patients were excluded from the BAL group because they either had an anaphylactic reaction to thiopental sodium (n = 1) or had excessive bleeding from a prolonged duration of surgery (n = 1). Thus, 48 patients were finally enrolled into the study.

2.1. Anesthetic management

All patients received an intramuscular dose of midazolam (0.1 mg/kg) 30 minutes before arrival at the operating room. In the TIVA group, anesthesia was induced with propofol (2 mg/kg) and sufentanil (0.3 μg/kg), and maintained with propofol (5 mg/kg per hour) and bolus doses of sufentanil (0.3 μg/kg) given before the start of surgery. In the BAL group, anesthesia was induced with thiopental (5 mg/kg) and fentanyl (2.5 μg/kg), and maintained with sevoflurane (1.0-2.0 vol%, end-tidal concentration) in nitrous oxide/oxygen (fraction of inspired oxygen, 0.3) and fentanyl (2.5 μg/kg) before skin incision. Atracurium (0.5 mg/kg) was given to facilitate orotracheal intubation, followed by a continuous application of atracurium (0.3 mg/kg). Controlled mechanical ventilation (ADU-Systems, Datex-Ohmeda, Freiburg, Germany) was adjusted to achieve normocapnia and an oxyhemoglobin saturation of more than 95%. A continuous infusion of electrolyte solution (5 mL/kg per hour) was given for fluid therapy. Monitoring included heart rate (HR), systolic and diastolic blood pressure, mean arterial pressure, temperature, and measurements of end-expiratory sevoflurane concentrations (integrated Datex-Ohmeda monitor system; Instrumentarium Corp, Helsinki, Finland). Depth of anesthesia was controlled within 20% of preoperative values. In all patients, tracheas were extubated immediately after the end of surgery, and patients were transferred to the recovery room on the ward. Supplemental oxygen was not given postoperatively; however, oxyhemoglobin saturation was constantly greater than 95% in all patients. Pain therapy was provided by intravenous (IV) infusion of 1 g/4 h metamizol supplemented with titrated doses of piritramid or tramadol as required. Patients were interviewed immediately at the end of anesthesia and 2 and 6 hours after surgery on the morning and evening of the first through third postoperative day to obtain a self-assessment of their pain intensity with a 3-point verbal rating scale (1, none or light; 2, moderate; 3, severe).

2.2. Study protocol

Peripheral venous blood samples were collected immediately before induction of anesthesia, before surgery, at the end of surgery, 2 hours after surgery, and on the first and on the third postoperative days using sodium citrate vacutainers (BD Bioscience, Erembogem, Belgium) for assessment of cytokine and hormone concentrations. Cell-free plasma samples were prepared by 2-step centrifugation (15 minutes at 700g, 10 minutes at 900g) within 30 minutes of blood collection. Plasma aliquots were stored at -80°C until assayed. For subpopulation analyses and proliferation studies,