Leucocyte distribution during sevoflurane anaesthesia

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Summary

We have examined if sevoflurane anaesthesia per se modified the number of circulating leucocytes in humans. Fifty-nine patients undergoing elective surgery were anaesthetized with sevoflurane in oxygen. The inhaled concentration was increased gradually to 5% and maintained for 20 min. Arterial blood samples were obtained before induction of anaesthesia and at 20 min. While the total number of leucocytes remained constant, circulating neutrophils decreased (mean 3370 (SD 1030) mm\(^3\); \(P<0.01\)) and lymphocytes increased (1870 (520) mm\(^3\); \(P<0.01\)). We conclude that high concentrations of sevoflurane modified the distribution of leucocytes in anaesthetized patients. (Br. J. Anaesth. 1998; 80: 502–503)

Keywords: anaesthetics volatile, sevoflurane; blood, leucocytes; blood, neutrophils; blood, lymphocytes

Methods and results

Previous studies have demonstrated that major surgical procedures combined with anaesthesia caused marked changes in leucocyte dynamics involving lymphopenia and neutrophilia.\(^1\) However, few clinical reports have examined the effects of anaesthesia per se on leucocyte dynamics. We have recently shown in vivo that 2 MAC of sevoflurane anaesthesia induced leucocyte rolling and adhesion with microvascular endothelium in the rat mesentery via endothelial cell-dependent mechanisms.\(^2\) If such events occur in a clinical situation, circulating leucocyte dynamics may be altered during anaesthesia. Therefore, we have examined if the number of circulating leucocyte subtypes was modified during sevoflurane anaesthesia.

Methods and results

After obtaining approval from our institutional Ethics Committee and informed consent, we studied 59 patients undergoing elective surgery under general anaesthesia. Exclusion criteria were: ASA II or more, patients more than 60 yr of age, those receiving preoperative transfusion or those with malignancy or inflammatory diseases. All patients received ranitidine 150 mg orally on the night before surgery, and hydroxyzine 50 mg and atropine 0.5 mg i.m. as premedication.

On arrival in the operating room, routine monitoring, including arterial pressure, ECG and pulse oximetry, was established. Arterial pressure was measured every 2 min throughout the study. Anaesthesia was induced with sevoflurane, which was increased by 0.5% every 4–5 breath up to 5%, in 100% oxygen (6 litre min\(^{-1}\)), using a semi-closed circle system. Ventilation was assisted at first and then changed gradually to being fully controlled for the next 20 min. Sevoflurane concentration at the Y-piece was confirmed by an anaesthesia gas analyser (Capnomac Ultima; Datex Instrumentation, Helsinki, Finland). During the study, acetated Ringer's solution 50–100 ml was given i.v. to obviate the dilutional effects on subsequent blood cell counting. Blood (2 ml) was obtained from the radial artery before and 20 min after induction of anaesthesia. Blood cells and leucocyte differential counting were performed using an automatic cell counter (SE-7000, Toa Medical Electronics, Tokyo).

Data are expressed as mean (sd), unless otherwise specified. The Student's \(t\) test was used to analyse the data where appropriate. \(P<0.05\) was considered statistically significant.

Mean age of the study population was 31.8 (range 20–25) yr. Exhaled sevoflurane concentrations were within the range 4.3–4.7%. Sevoflurane significantly depressed systemic arterial pressure (from 121 (14) to 100 (14) mm Hg; mean \(-17.4\%\) \((P<0.05)\). No patient required vasopressors to maintain arterial pressure. Similarly, heart rate increased from baseline values (78 (19) to 94 (14) beat min\(^{-1}\); mean \(+20.5\%\) \((P<0.05)\).

Changes in leucocyte numbers during sevoflurane anaesthesia are shown in figure 1. The total number of white blood cells remained constant during sevoflurane anaesthesia. While circulating lymphocytes increased significantly (mean \(+10.3\%\)), the number of neutrophils decreased (\(-5.9\%)\) from baseline values. Monocytes, eosinophils and basophils did not change significantly during the study.

Comment

Immune responses after anaesthesia and surgery are characterized by lymphopenia and granulocytosis, decreased lymphocyte transformation to various antigens and impaired neutrophil function, such as chemotaxis or oxygen radical production.\(^1\) While surgical procedures are considered to play more important roles than anaesthesia per se on the postoperative alterations in immune function, previ
Sevoflurane and circulating leucocytes

in vitro studies demonstrated that leucocyte function was depressed significantly by exposure to anaesthetics in a dose-dependent manner. However, few in vivo studies have examined the effects of anaesthesia per se on circulating leucocyte numbers. We have demonstrated that high concentrations of sevoflurane, even for a short time, decreased the number of circulating neutrophils and increased lymphocyte numbers. Interestingly, this finding is in agreement with a previous report that acupuncture analgesia caused a decrease in neutrophil counts and increased lymphocyte counts.4

There are several explanations for our results. Previous studies demonstrated that adrenal hormones such as corticosteroids were mainly responsible for redistribution of leucocytes between blood and other immune compartments. Although we did not measure such hormones, the adrenosympathetic system during deep anaesthesia could have been depressed. Second, sevoflurane may modify leucocyte volume, resulting in miscounting of leucocyte subtypes by an automatic cell counter. However, even if leucocyte size was altered during sevoflurane anaesthesia, haemolysis before subtype measurements should have restored such changes. Furthermore, the internal density of leucocytes, which was another variable in subtype determination by the automatic counter, is unlikely to be affected by exogenous factors. Third, if neutrophil adhesion with endothelium occurred, as shown in animal studies, the number of circulating neutrophils should have been depressed. Because of the observational data, however, these possibilities cannot elucidate the underlying mechanisms of the discrepancy between neutrophil and lymphocyte dynamics.

Another study showed that fluid loading with crystalloid caused an increase in circulating lymphocytes, suggesting the possibility that lymphocytes are shifted into the intravascular space together with the bulk flow of fluid from the interstitium. As significant depression of systemic perfusion pressure during anaesthesia induces blood redistribution from non-vital to vital organs involving leucocyte dynamics, we did not examine other inhalation anaesthetics, such as halothane, at high concentrations in a clinical setting. Further studies are warranted to clarify the biological implications of such observations.

References