Propofol and Additives: Please Consider Zebras Besides Horses When You Hear Hooves

To the Editor:

We read with great interest the article by Schilling et al.1 dealing with effects of sevoflurane and desflurane as volatile anesthetics compared with propofol as an intravenous anesthetic and the relationship between pulmonary and systemic inflammation in patients undergoing open thoracic surgery.2 Authors remarked that proinflammatory cytokines increased in the ventilated lung after one lung ventilation. Mediator release was more enhanced during propofol anesthesia compared with desflurane or sevoflurane administration. Postoperatively, the proinflammatory cytokines tumor necrosis factor-α (P < 0.001), interleukin-1β (IL-1β) (P < 0.002), and interleukin 8 (IL-8) (P < 0.025) were more increased in patients during propofol administration compared with both volatile anesthesia groups, and postoperative serum concentration of IL-6 was increased in all patient groups after thoracic surgery (P < 0.001). The authors concluded that one-lung ventilation increases the alveolar concentrations of proinflammatory mediators in the ventilated lung. Both desflurane and sevoflurane suppress the local alveolar, but not the systemic, inflammatory responses to one-lung ventilation and thoracic surgery.

Lung injury after thoracic surgery is a relatively uncommon but major complication with high mortality. Many factors, including cytokine imbalance, ischemia reperfusion injury, and the use of one-lung ventilation, are involved in this process apart from the surgical insult itself.2 In our opinion, a point of this work is not sufficiently clear. EDTA and sulfite might be added as antimicrobial agents to several formulations of propofol, which may have different physiologic responses. Herr et al.3 showed that the patients in the surgical intensive care unit receiving propofol with EDTA had significantly reduced mortality rates at 7 and 28 days compared with those receiving propofol without EDTA. Haitsma et al.4 compared the effects of propofol with EDTA, propofol with sulfite, and ketamine/midazolam on tumor necrosis factor-α, interleukin-6 (IL-6), and macrophage inflammatory protein-2 in an animal study. They showed that bronchoalveolar lavage IL-6 was significantly higher in the propofol with sulfite group compared with both the ketamine/midazolam and the propofol with EDTA groups. They also remarked that pulmonary IL-6 can be modulated by additives in systemic anesthesia.

Accordingly, we think that reporting detailed formula of propofol in studies evaluating the effect of propofol on inflammatory responses would be crucial, and we hope that the previously mentioned comments might add to the value of the manuscript by Schilling et al.1

Saban Yalcin, M.D.,* Harun Aydogan, M.D. Harran University Medical Faculty, Sanliurfa, Turkey. sabanyalcin@yahoo.com

References

In Reply:

We appreciate the great interest of Dr. Yalcin and Dr. Aydogan in reading our article,1 and we would like to thank them for their important comment regarding the different physiologic responses of propofol and its additives. Propofol has become one of the most widely administered drugs for induction and maintenance of anesthesia and for sedation in the intensive care unit. Therefore, we have chosen this substance as well to provide standardized total intravenous anesthesia in the control group of our clinical study. In patients who received total intravenous anesthesia with propofol, release of proinflammatory cytokines into the alveoli of the ventilated lung was more increased after one-lung ventilation and open thoracic surgery, in comparison with the administration of desflurane or sevoflurane in other patient groups. The time course of pulmonary cytokine release confirms previous clinical studies, which demonstrate an enhanced mediator expression during propofol anesthesia for thoracic surgery.2,3 Moreover, highly lipid-soluble drugs such as propofol may also affect the inflammatory response. Propofol decreases granulocyte recruitment and neutrophil activation by reduction of polarization, chemotaxis, and inhibition of the respiratory burst in clinically used concentrations.4 In addition, it exerts antioxidative properties, which may prevent the organism from oxidative stress.5 The pronounced proinflammatory response should therefore not be interpreted as being