Isoflurane Decreases Interleukin-2 Production by Increasing c-Cbl and Cbl-b Expression in Rat Peripheral Blood Mononuclear Cells

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Introduction

Isoflurane modulates the immune response. In addition to regulating immune-system homeostasis, interleukin (IL)-2 is considered an indicator of functional suppression of T cells because decreased production of IL-2 is associated with increased expression of Casitas B-lineage lymphoma proto-oncogene (c-Cbl) and Cbl-b in T cells. To evaluate the effect of the inhalational anesthetic agent, isoflurane, on T-cell function, we assayed IL-2 production and c-Cbl and Cbl-b expression in rat peripheral blood mononuclear cells (PBMCs).

Materials and Methods

Adult male Sprague–Dawley rats weighing 300–350 g were randomly allocated to the control group (C group), 4 h of isoflurane general anesthesia group (4I group), or 1 day after 4 h of isoflurane general anesthesia group (1D 4I group). Blood was collected by cardiac puncture and PBMCs were isolated. IL-1, IL-2, and IL-6 mRNA levels and c-Cbl, Cbl-b, protein kinase C (PKC) θ , and phospholipase C- γ 1 (PLC- γ 1) protein levels in PBMCs were determined by quantitative reverse transcription polymerase chain reaction and immunoblotting, respectively. Moreover, ubiquitination of PKC θ and PLC- γ 1 in PBMCs was assessed by immunoprecipitation.

Results

The mRNA level of IL-2 in rat PBMCs was significantly decreased in the 4I and 1D 4I groups compared with the control group. c-Cbl, Cbl-b, and ubiquitin expression was significantly increased and the zeta-chain-associated protein kinase 70 (ZAP70), PLC- γ 1, and PKC θ protein levels were significantly decreased in the 4I group. Ubiquitination of PLC- γ 1 and PKC θ were also significantly increased in the 4I group.

Conclusion

Isoflurane influences the expression of ubiquitin, c-Cbl, and Cbl-b in rat PBMCs, which indicates suppression of receptor tyrosine kinase signaling pathways. These results suggest that isoflurane suppresses T-cell function.

Figure 1.

Figure 2.

References

- [1] Homburger JA, Meiler SE: Anesthesia drugs, immunity, and long-term outcome. *Curr Opin Anaesthesiol* 2006; 19:423–8
- [2] Snyder GL, Greenberg S: Effect of anaesthetic technique and other perioperative factors on cancer recurrence. *Br J Anaesth* 2010; 105:106–15.