Sevoflurane in combination with propofol, not thiopental, induces a more robust neuroapoptosis than sevoflurane alone in the neonatal mouse brain

Purpose Sevoflurane is the most widely used volatile anesthetic of general anesthesia. In children and neonates, it is commonly used alone or in combination with thiopental or propofol. A few recent studies reported that sevoflurane induced neuronal death in the developing rodent brain. We measured the neurotoxicity of these anesthetics at clinical doses, alone and in combination, in the developing mouse brain.

Methods Seven-day-old C57BL/6 mice were randomly assigned to 6 treatment groups. Three groups were exposed to 3% sevoflurane for 6 h after injection of saline, thiopental (5 mg/kg), or propofol (10 mg/kg), whereas three groups were exposed to room air for 6 h after injection of equal doses of saline, thiopental, or propofol. Apoptosis in the hippocampal CA1 region (CA1) and retrosplenial cortex (RC) was assessed using caspase-3 immunostaining.

Results Sevoflurane alone caused significantly higher apoptosis in the CA1 compared with saline plus air ($P = 0.04$). Sevoflurane in combination with propofol resulted in significantly greater numbers of apoptotic neurons than sevoflurane alone in both the CA1 and the RC ($P = 0.04$). However, there was no significant difference in apoptotic neuron density in both the regions between the groups treated with sevoflurane alone and in combination with thiopental ($P = 0.683$).

Conclusion Sevoflurane alone can induce neuronal apoptosis, and this effect
is enhanced by propofol. Thiopental did not exacerbate the neurotoxicity of sevoflurane. There is the possibility that the combination of sevoflurane and propofol is more harmful anesthetic technique than sevoflurane alone in pediatric patients.

以上、本論文は新生仔マウス脳においてセボフルランとプロポフォールの併用は、セボフルラン単独より重篤な神経細胞死を引き起こす可能性を示した論文であり、学術上極めて有益であり、学位論文として価値あるものと認めた

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