

Antioxidant agent ameliorates anesthetic-induced toxicity in rat embryonic neural stem cells

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Propofol is a widely used general anesthetic. Acetyl-L-carnitine (aLc), an anti-oxidant dietary supplement, has been reported to prevent neuronal damage from a variety of causes. To evaluate the ability of aLc to protect against propofol-induced neuronal toxicity, neural stem cells were isolated from gestational day 14 rat fetuses and on the 8th day in culture were exposed for 24 hr to propofol at 10, 50, 100, 300 and 600 μ M, with or without aLc (10 μ M). Markers of cellular proliferation (EdU), mitochondrial health (MTT), cell death/damage (LDH) and oxidative damage (8-oxo-dG) were monitored to determine: 1) the effects of propofol on neural stem cell proliferation; 2) the nature of propofol-induced neurotoxicity; 3) the degree of protection afforded by aLc; and 4) to provide information regarding possible mechanisms underlying protection. After propofol exposure at a clinically-relevant concentration (50 μ M), the number of dividing cells was significantly decreased and oxidative DNA damage was increased. There was also a significant dose-dependent reduction in mitochondrial health as evidenced by decreases in MTT metabolism. No significant effect on LDH release was observed at propofol concentrations up to 100 μ M. The oxidative damage at 50 μ M propofol was blocked by aLc. Thus, clinically-relevant concentrations of propofol induce dose-dependent adverse effects on rat embryonic neural stem cells by slowing or stopping cell division/proliferation and causing cellular damage. Elevated levels of 8-oxo-dG suggest oxidative damage and aLc effectively blocks at least some of the toxicity of propofol, presumably by scavenging oxidative species and/or reducing their production.

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