Embryonic neural stem cells & propofol-induced neurotoxicity

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Propofol is a widely used anesthetic agent for adults and children. Evidence suggests that propofol induces cell death in developing brain. Acetyl-L-carnitine (ALC) has been reported to prevent neuronal damage from a variety of causes in vitro and in vivo. To evaluate the ability of ALC in protecting propofol-induced neuronal toxicity, a rat embryonic neural stem cell (NSC) model was used.

Brain cortices were collected from fetal rats for NSC isolation and culture. On the 8th day in vitro, confluent NSCs were exposed to propofol or propofol plus ALC for 24 hours. NSCs were identified using anti-nestin antibody. Markers of cellular proliferation (EdU), mitochondrial health (MTT), cell death/damage (LDH) and oxidative damage (8-oxo-dG) were monitored to determine the effects of propofol on NSC proliferation; the nature of propofol-induced neurotoxicity; the degree of protection by ALC; and to explore the underlying mechanisms.

50 µM propofol caused a significant decreased number of dividing cells; affected mitochondrial health dose-dependently as evidenced by decreases in the metabolism of MTT. Propofol did not affect LDH release at concentrations of 10, 50 or 100 µM. 50 µM propofol significantly increased 8-oxo-dG formation and this effect was blocked by ALC.

These data suggest that clinically-relevant concentration (50 µM) of propofol induces rat embryonic NSC damage. The elevated levels of 8-oxo dG and its analogs in the culture medium suggest the occurrence of oxidative damage due to increased generation of reactive oxygen species. Co-administration of ALC effectively blocks at least some of the toxicity of propofol, presumably by scavenging ROS and/or reducing ROS production.

Biography

Fang Liu is a scientist in the Division of Neurotoxicology, National Center for Toxicological Research (NCTR)/United States Food & Drug Administration. Liu has been actively involved in biomedical research for more than ten years and has been an author and a co-author for more than 30 peer-reviewed scientific articles and book chapters in the areas of pharmacology, toxicology and molecular biology. Currently, she focuses her research on developmental neurotoxicity. She is a full member of the Society of Toxicology, Society for Neuroscience and the Arkansas Chapter of the Society for Neuroscience. She is also an editor and a reviewer of several reputed peer-reviewed journals.

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