

Propofol Infusion Syndrome

Propofol (Diprivan®) is a sedative-hypnotic agent that was first introduced in Europe, and later approved by the Food and Drug Administration (FDA) in 1989. Propofol is structurally unrelated to barbiturates or opioids, and is commonly used to provide general anesthesia and sedation because of its rapid onset and offset of action, ease of titration and administration, and shorter time of awakening and extubation.

The adverse effects associated with propofol include hypotension, bradycardia, respiratory depression, infection, hypertriglyceridemia, and most importantly, **propofol infusion syndrome** (also called propofol-related infusion syndrome or PRIS), which is a rare but fatal syndrome. PRIS-related deaths were first reported in a case series of pediatric patients in the United Kingdom in 1992. These patients initially had respiratory tract infections that required intubation and sedation with high dose propofol. All patients experienced metabolic acidosis as an early feature of the adverse event, and death was due to refractory bradyarrhythmia progressing to asystole. In 1996, the first case of PRIS was reported in an adult patient. From 1992-2007, 33 pediatric and 36 adult patients who developed PRIS were reported in the literature. In a case series of critically ill pediatric patients, risk factors for PRIS included a high dose propofol infusion (>4 mg/kg/hr), and a prolonged period of infusion (>48 hours). Lactic acidosis, lipemic serum, and electrocardiography (ECG) abnormalities are the early clinical features of PRIS. Late effects of PRIS include hyperkalemia, cardiac dysrhythmias, renal failure, rhabdomyolysis, and cardiovascular collapse. The exact mechanisms of PRIS are yet to be identified. The proposed pathophysiology in critically ill patients includes enzyme inhibition in the mitochondrial respiratory chain, utilization of fat substrates instead of carbohydrate metabolism, disruption of mitochondrial fatty acid oxidation, and/or presence of an unidentified metabolite.

If PRIS is suspected, the propofol infusion should be discontinued and the patient switched to an alternative agent for sedation management if needed. Management of PRIS relies on cardiopulmonary and symptomatic support. At present, no single effective treatment has been proposed to reverse PRIS.

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DID YOU KNOW THAT... the FDA requires labeling of propofol to advise of the risk of propofol infusion syndrome (PRIS)?

In February 2007, the FDA responded to an increasing number of reports of PRIS by requiring manufacturers to include warnings about the risk of this potentially fatal reaction. The labeling indicates that high-dose infusions of more than 5 mg/kg/hour for longer than 48 hours or that short-term administration of large doses may result in PRIS. Clinicians are advised to use alternative means of sedation in patients who require prolonged sedation or increased amounts of propofol to achieve adequate sedation, and in patients who have increasing vasopressor requirements, cardiac failure, or metabolic acidosis when propofol is administered.

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