Propofol Tolerance in a Pediatric Patient

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Propofol (Diprivan) is a useful intravenous anesthetic agent that features fast onset, quick recovery, and a low incidence of nausea and vomiting. The pediatric dose required to abolish the eyelash reflex and prevent spontaneous movement in 50% of patients (ED50) is 1.3–3.0 mg/kg. There are no reported cases of tolerance to propofol.

CASE REPORT

A 2-yr-old 10-kg boy presented to our outpatient center for radiation therapy treatment for metastatic gluteal rhabdomyosarcoma. In the 15 months before radiation therapy, he had undergone two courses of chemotherapy with cyclophosphamide, Adriamycin, and vincristine. He had also received two general anesthetics for biopsy and staging that included sodium thiopental (3 mg/kg), succinylcholine (2 mg/kg), and halothane (1.5% expired). During the 6-week outpatient radiation therapy course, the patient maintained normal renal, cardiac, and hepatic function and normal dietary intake. Blood counts and chemistries (blood urea nitrogen, creatinine, liver function tests, leukocyte count, hematocrit, and albumin) remained normal and the patient’s weight unchanged.

The outpatient radiation therapy included 23 treatments for which the anesthetic records (seven anesthetics by the authors) were reviewed retrospectively. Anesthesia for the 15-min procedure consisted of intravenous propofol, given through an existing Hickman catheter. The patient was allowed to ventilate spontaneously using supplemental oxygen. Monitors consisted of noninvasive blood pressure, electrocardiography, and pulse oximetry. Induction and maintenance requirements were determined by titration until spontaneous movement ceased and the eyelash reflex was abolished, yet maintaining spontaneous ventilation. Initial propofol induction doses were 1 mg/kg (10 mg) and 100 μg·kg⁻¹·min⁻¹, respectively. Over the next 19 treatments both the induction and maintenance requirements increased dramatically (Figs. 1 and 2). By the third treatment, the induction dose had increased to 3 mg/kg (30 mg) and the maintenance dose increased to 200 μg·kg⁻¹·min⁻¹. By the 14th treatment the doses had increased to 10 mg/kg (100 mg) and 400 μg·kg⁻¹·min⁻¹, respectively, and at the 19th treatment to 16 mg/kg (160 mg) and 500 μg·kg⁻¹·min⁻¹, respectively.

Despite these large doses the patient maintained spontaneous ventilation and was hemodynamically stable. After each treatment the patient opened his eyes and responded to his mother within 10 min upon discontinuation of the propofol. Propofol was discontinued during the 20th treatment, when 18 mg/kg (180 mg) failed to induce anesthesia. Intravenous ketamine (three 1-mg/kg boluses) was substituted, and the final three treatments were completed without difficulty. The same ketamine doses were required for all three anesthetics.

DISCUSSION

Propofol was chosen as the anesthetic agent for this patient because of its rapid onset and recovery time and the ability to discharge ambulatory patients soon after discontinuation of anesthesia. The use of propofol has been reported extensively, however we are not aware of any reported cases of tolerance to propofol. Setlock and Palmisano suggested that propofol tolerance does not develop after multiple exposures in pediatric patients. Performing in a radiation therapy outpatient setting, Setlock and Palmisano’s study involved ten children receiving propofol for a short duration. However, only three patients received 20 or more exposures, and in almost half of the treatments, propofol was combined with ketamine or midazolam.

Tolerance is described as gradually diminishing responses to repeated exposures to a drug. Mechanisms of tolerance have been attributed to altered physical states of neuronal membranes or to alterations in neurotransmitter levels of their receptors. Tolerance has been described for opioids, nitrous oxide, and inhalational agents.

In our patient, the initial induction and maintenance propofol doses required to abolish the eyelash reflex and

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**Fig. 1. Induction dose of propofol versus treatment number.**

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Maternal Esmolol Administration Resulting in Fetal Distress and Cesarean Section in a Term Pregnancy

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Treatment of the pregnant patient for a cardiac dysrhythmia poses a special problem, because maternal drug administration also may affect the fetus. β-Adrenoceptor blocking drugs are accepted treatment for supraventricular tachycardia (SVT) in the nonpregnant patient. However, animal studies suggest that if uterine blood flow is compromised during pregnancy, administration of these agents to the mother may lead to worsening fetal hypoxia.1–4 Fetal cardiovascular and metabolic compensation for reduced placental blood flow also appears to be modulated by β-adrenoreceptors.2,5

Esmolol is a β1-selective adrenergic blocking drug whose greatest advantages are its short duration of action and rapid clearance. This drug has not been evaluated during human pregnancy, although case reports have demonstrated minimal fetal effects when it is administered during the second and third trimesters.5,6 We report the case of a pregnant woman at term who received esmolol to treat SVT and who required an emergency cesarean section shortly thereafter for significant fetal bradycardia.

CASE REPORT

A 29-yr-old woman, gravida 4, para 2, at 38 weeks' gestation was admitted for the sudden onset of palpitations. An ECG revealed a