as its use increases. Fauroux et al.[5] demonstrated the improved efficacy of sedation, pain control, and safety of premixed 50% nitrous oxide and oxygen for fiberoptic bronchoscopy in children.

Finally, discharge criteria for children who have been sedated should advance along with the drugs and techniques used for sedation during a procedure. The application of specific criteria in this area is a significant improvement over subjective measures that have been used in the past.

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Arginine-vasopressin in severe forms of septic shock

Dear Editor,

We read with interest the article by Irazuzta et al. on the pharmacological support of infants and children in septic shock.[1] Apart from conventional inotropes, the authors suggest the use of vasopressin in severe forms of septic shock.[1] We agree with the authors that arginine-vasopressin and its long-acting analogue, terlipressin, are potent vasopressors that may be useful rescue agents in the treatment of catecholamine-resistant septic shock.[2] However, there is still no clear concept when to start arginine-vasopressin and terlipressin therapy in catecholamine-resistant shock. Recently, a large clinical study in adults with septic shock demonstrated the beneficial effects of initiating arginine-vasopressin therapy before norepinephrine requirements exceed 0.6 µg /kg/minute.[3] This is in accordance with our own limited experience in preterm neonates.[4] In a small series of extremely low birth weight infants, the surviving infants received norepinephrine and epinephrine in a dosage < 0.6 µg/kg/minute prior to arginine-vasopressin medication.[4] Moreover, there is still no clear concept about the precise (starting) dose of arginine-vasopressin/terlipressin therapy in the pediatric population. Due to the lack of reference values in children, the doses are often extrapolated from adult patient reports.[2] In order to shed more light on these important issues, there is a need for large prospective studies in children on the use of arginine-vasopressin and terlipressin in severe forms of septic shock in children.

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Authors' reply

We agree with the final comments that large protective studies in children are lacking on the use of arginine-vasopressin and terlipressin in septic shock. However, there is a significant amount of pediatric experience utilizing vasopressin as a rescue treatment in septic shock with low sys-

temic vascular resistance. We would be inclined to start vasopressin after the patient has been adequately fluid resuscitated, without hypocalcemia or hypoglycemia, with adequate catecholamine and corticosteroid support. In general, we believe that if there is no significant improvement in systemic vascular resistance with a norepinephrine dose above 1 µg/kg/minute, vasopressin should be considered. A common starting dose is an adjustment of the adult dose at 0.0003 units per kg/min up to 0.002 units/kg/min.

Two authors of our article (Garcia PC & Piva JP) have conducted two studies involving vasopressin infusion in children (data still not published). One study assessed children with septic shock after fluid resuscitation and corticosteroid administration who were refractory to norepinephrine (above 1 µg/kg/min) infusion. We agreed to use a vasopressin dose of 0.0005 U/kg/min (dilution of 200 U/mL), gradually titrating the dose to 0.002 U/kg/min (ideal dose).[1] The maximum dose was defined as 0.008 U/kg/min. The first 12 patients included in this study showed a significant increment in arterial blood pressure and in cardiac output, allowing a reduction in norepinephrine infusion.

We have just ended our second study, a double-blind, randomized controlled trial that assessed the use of low-dose vasopressin in children with severe respiratory disease.[2] Children under mechanical ventilation were randomized (1:1 ratio) to receive either vasopressin (0.0005 U/kg/min) or NaCl 0.9% (0.01 mL/kg/min) infusions for a period of 48 hours. The initial mean arterial pressure (MAP) was similar in both groups, but after the infusions were started, the MAP of children in the vasopressin group was significantly higher ($p < 0.05$). Hyponatremia was more frequent in children in the vasopressin group (58% vs. 8%, $p < 0.01$). Urine output was smaller in children that received vasopressin (2.4 vs. 4.2 mL/kg/hour, $p = 0.033$), and after the end of the infusions, children who received vasopressin had higher urine output than children that received placebo (7.4 vs. 3.8 mL/kg/hour, $p = 0.037$). Low-dose vasopressin infusion increased MAP in children requiring mechanical ventilation. However, vasopressin decreased urine output and sodium concentration, increasing the incidence of hyponatremia.

We want to extend our appreciation to the writer for sharing his own experience with the use of arginine-vasopressin in preterm neonates.

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