Profuse Oral Secretions after Propafenone Administration in Neonates

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Propafenone, an antiarrhythmic drug that is effective for treating supraventricular tachycardias, can induce well-known proarrhythmic and systemic adverse effects. We describe a previously unreported adverse effect in 3 newborns: oral propafenone–induced profuse oral secretions and respiratory distress of sufficient severity to necessitate discontinuation of propafenone. *(J Pediatr 2010;157:856-7)*

Propafenone is an antiarrhythmic drug that has proved effective in treating supraventricular tachycardias (SVT) in children;[1] however, it can induce adverse systemic effects, including neurologic extrapyramidal symptoms (restlessness and headache), gastrointestinal symptoms (nausea, vomiting, anorexia), hepatic effects (increased serum transaminase levels), hematologic effects (eosinophilia), and dermatologic symptoms (rash, itching).[2] These adverse effects are usually reversible on discontinuation of treatment. Propafenone also can be proarrhythmic, worsening an existing arrhythmia or causing cardiac arrest or sudden death.[3,4] We describe a previously unreported propafenone-induced adverse effect—profuse oral secretions and respiratory distress—in 3 newborns admitted to our unit for treatment of SVT.

Patients

Case 1

A newborn girl born at 38 weeks' gestation and weighing 2940 g was transferred to our unit at 5 days of life because of paroxysmal SVT, which was successfully converted to sinus rhythm by inducing the diving reflex with an ice bag. Echocardiography revealed no cardiac abnormalities. The infant was otherwise healthy and was not receiving any medical treatment. Oral therapy with propafenone was started at 10 mg/kg/day. The next day, shortly after drug administration, the infant developed respiratory distress with abundant oral secretions and a decrease in O_2 saturation to 90%. Supplemental oxygen was started. A chest radiograph showed no abnormalities. The infant was suctioned several times. Blood gas analysis and standard electrocardiography (ECG) were normal. The infant's condition slowly improved; after 30 minutes, dyspnea had resolved and O_2 saturation had increased to >98%. Supplemental oxygen was stopped. About 8 hours later, another dose of oral propafenone was administered. Within 20 minutes, the same symptoms appeared, with the infant requiring supplemental oxygen for about 20 minutes. The infant remained symptom-free after she was switched to treatment with another antiarrhythmic drug.

Case 2

A newborn boy born at 36 weeks' gestation and weighing 2665 g was transferred to our unit at 7 days of life for treatment of SVT. Echocardiography showed no cardiac abnormalities. The infant had no other health problems and was not receiving any medical treatment. An ECG documented ventricular preexcitation (Wolff-Parkinson-White syndrome), and oral propafenone at 10 mg/kg/day was started. The next day, within a few minutes after propafenone administration, the infant became agitated and exhibited respiratory distress with abundant dense oral secretions, requiring frequent suctioning, and decreased O_2 saturation. Chest radiography and blood gas analysis findings were normal. An ECG demonstrated sinus rhythm and ventricular preexcitation. The infant's symptoms regressed slowly, but recurred with the next dose. After substitution of another antiarrhythmic drug for propafenone, the infant's respiratory symptoms disappeared.

Case 3

A newborn girl born at 38 weeks' gestation and weighing 2150 g had a cardiac atrioventricular septal defect, left ventricular hypoplasia, total anomalous pulmonary venous return, and paroxysmal SVT at 15 days of life that was successfully converted to sinus rhythm with adenosine (100 μg/kg intravenous bolus). Treatment with oral propafenone 10 mg/kg/day was started. The next day, about 20 minutes after drug administration, the infant exhibited respiratory distress with abundant oral secretions requiring oxygen administration. Chest radiograph, standard ECG, and laboratory values were normal. The infant's respiratory symptoms necessitated frequent suctioning and disappeared after about 30 minutes, but recurred when the next dose was given 8 hours later. These symptoms disappeared after discontinuation of propafenone and initiation of another antiarrhythmic drug.

ECG	Electrocardiogram
SVT	Supraventricular tachycardia

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The authors declare no conflicts of interest.

 10.1016/j.jpeds.2010.06.028

Discussion

To the best our knowledge, the adverse effect that we describe here has not been reported previously. We called these 3 cases to the attention of the Italian drug agency (AIFA). All 3 neonates were admitted to our regional referral unit for congenital heart diseases and arrhythmias of infancy for treatment of SVT between April and December 2008. During the same period, 5 neonates were treated with oral propafenone, our standard first-line drug for preventing SVT recurrence.[1] Propafenone is used because of its efficacy,[4] and treatment is electrophysiologically guided by transesophageal pacing. In neonates with spontaneous SVT recurrence or SVT inducible by transesophageal pacing, our next step is treatment with flecainide. We do not use a beta-blocker alone as first-line therapy, because we prefer to change the conduction and refractoriness of the accessory pathway rather than that of the atrioventricular node.[1]

Although not life-threatening, this adverse effect was sufficiently severe to necessitate discontinuation of propafenone in the 3 neonates. We assessed the causal relationship between propafenone administration and the clinical signs that we observed using the adverse drug reaction probability scale of Naranjo,[5] and a score of >9 (indicating a definite adverse drug reaction) was assigned in each case. We hypothesized that this adverse effect might be related to sialorrhea due to the bitter taste of the medicine, given the rapid appearance of the symptoms after oral drug intake.

Because there is no pediatric formulation of propafenone, we prepare the drug directly in our unit, as follows. First, 150-mg propafenone tablets are crushed, and the powder is suspended in 15 mL of sterile water. Then 1 mL, containing 10 mg, is diluted with 10 mL of sterile water, such that 1 mL contains 1 mg of propafenone. The drug concentration was the same for all 3 neonates. The preparation was uniform and was administered with a syringe, allowing the neonates to swallow the preparation slowly. In all 3 neonates, severe sialorrhea appeared on the second day of therapy, probably after repeated stimulation of the taste receptors. Because we suspected that the reaction could possibly be due to the bitter taste of the medicine, we tried twice to administer the preparation through a nasogastric feeding tube, to circumvent the taste receptors. In both cases, the attempt was successful, and drug administration was uneventful. Starting after December 2008, we have administered the drug with a 33% sucrose solution to diminish the bitter taste. The adverse effect did not occur in 2 subsequent neonates treated with oral propafenone.

The treatment of neonates with antiarrhythmic drugs remains complex, given that none of the available agents is free of adverse effects. In our experience, propafenone remains the first-choice antiarrhythmic for preventing recurrence of SVT in neonates, because of the characteristic physiopathology of SVT in this population. Nonetheless, we recommend diluting the drug with a 33% sucrose solution for oral administration. ■

Submitted for publication Dec 21, 2009; last revision received Apr 19, 2010; accepted Jun 16, 2010.

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