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Haemangioma of Infancy: Two Case Reports with an Overdose of Propranolol

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Key Words

Dosage · Haemangioma · Overdose · Propranolol

Abstract

An 8-week-old infant was treated with oral propranolol for a haemangioma of infancy. The standard dose (according to protocol) is 2 mg/kg/day but, because of a mistake by the pharmacist, the child was treated with 8 mg/kg/day without any side effects (pulse, blood pressure and glucose stayed normal).

Introduction

Recent publications on the treatment of haemangioma of infancy (HOI) showed that oral propranolol led to quick therapeutic responses to a certain degree [1]. Propranolol, a β -blocker, may have side effects; the most common serious side effects are bradycardia and hypotension but also dyspnoe, cold acra, provocation of decompensatio cordis or hypoglycemia, nightmares and decreased cardiac output [2]. Therefore, important contraindications in children are among others sinusbradycardia, AV-block, hypotension, asthma and decompensatio cordis. Recently, Lawley et al. [3] published 2 cases of propranolol treatment (2 mg/kg/day) in children with HOI with complications of propranolol-induced hypoglycaemia. We present two cases treated with an overdose of propranolol by mistake.

Case Report

Case 1

A healthy female infant was born September 19th, 2009, with a birth weight of 3,460 g after a gestation period of 38 weeks. She developed a HOI of the left philtrum and nose on day 9. At the age of 4 weeks, she had her first visit to our clinic. At the age of almost 8 weeks, she was started on a systemic oral propranolol treatment according to our protocol because of progressive growth with obstruction of the left nostril. Her haemangioma activity score (HAS) [4] was 3.8 (fig. 1). It was already noted that the haemangioma was less swollen after 1 day. Glucose levels, ECG, cardiac ultrasound and vital signs before and after treatment were all normal. She was discharged after 5 days when the HAS was 3 (fig. 2) after having received 3 doses of 3.5 mg/day propranolol treatment (at our hospital: 3.5 ml). According to our protocol, this equals 2 mg/kg/day propranolol.

The HOI was smaller and less active (HAS was 2) at the visit to the out-patient clinic more than one week after being discharged. Her vital signs were normal: RR 79/35, pulse 115 beats/min. Three weeks after discharge, the HOI was noted to be smaller (HAS was unchanged), and vital signs were normal: RR 113/38, pulse 121 beats/min. Four weeks after discharge, we were consulted again because the parents found out that their child had been treated with an overdose of propranolol. She had been given 3 doses of 3.5 mg/day at our hospital = 3.5 ml, but they had received a preparation at a concentration of 4 mg/ml, thus 4 times stronger, from their own pharmacy. Her parents had been giving her 3 doses of 3.5 ml/day = 3 doses of 14 mg/day propranolol for 4 weeks (8 mg/kg/day). Her vital signs were normal at the visit: RR 82/64, pulse 130 beats/min, respiration 36 breaths/min. She was anamnestic asymptomatic, her physical and laboratory examinations (glucose and blood pressure) were normal. Therefore, there was no need for re-admission or monitoring. By lowering the dosage, the now chronic high blood level of propranolol slowly declined to normal with no risk of side effects (e.g. rebound tachycardia). The patient was seen again 8 weeks after discharge and was now on propranolol at a dose of 2 mg/kg/day.

Case 2

An 11-month-old healthy girl, who had been treated with systemic prednisone because of a HOI on the upper right eyelid, was examined at our emergency room because of fever during the second prednisone pulse therapy. She had a viral infection of unknown origin but more importantly she had developed Cushing syndrome. At that time, blood pressure, pulse and glucose levels were all normal. Following our protocol, she was hospitalized in order to start propranolol therapy. Our normal start dose on day 1 is 0.5 mg/kg/day three times, in her case 5 mg/day, thus 3 doses of 1.5 mg/day. Her first dose was 5 mg by mistake. This was discovered quickly, and she was put under observation. Pulse, blood pressure, glucose level and ECG all stayed normal. After 8 h she received the next dose: 1.5 mg. The following days she was given more propranolol according to the protocol. Side effects were not encountered.

Discussion

Propranolol is used in the treatment of HOI at a dose of 2–3 mg/kg/day [5]. We report that even 8 mg/kg/day is without side effects. The pharmacist classified this overdose as ‘mild’ without serious consequences ($t_{1/2} = 6$ h).

We use a very careful protocol for propranolol therapy in HOI, starting with 0.5 mg/kg/day on day 1, then 1 mg/kg/day on day 2 and 2 mg/kg/day on day 3. This is empirically based because there is no literature on the dose of propranolol for HOI. It is not known how careful one has to be at the start of the therapy. Case 2 indicated that an ascending schedule may not be necessary, at least not so stringent; in this case no complications were seen after administering an overdose 3 times the standard (however, it was still 0.8 mg/kg/day).

There are case reports of side effects (particularly hypoglycaemia) from propranolol therapy [6]; but in the cases described above, no complications were noted after an overdose of propranolol. The mechanism of action for propranolol in haemangioma is still not clear, but initially vasoconstriction is most prominent. Propranolol may be an effective and possibly safer therapeutic innovation for treating haemangiomas. However, more well-designed dose-finding studies are necessary to clarify its exact mechanism of action.

Disclosure Statement

None of the authors disclosed any conflicts of interest.



Fig. 1. Image taken just before propranolol was started (day 0).



Fig. 2. After 5 days of propranolol treatment: the swelling is visibly decreased (by almost half) resulting in a reduction of the strong vasoconstrictive effect.

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