SEVERE SINUS BRADYCARDIA SECONDARY TO THE USE OF INTRAVENOUS STEROIDS.

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ABSTRACT

High-dose glucocorticoids are commonly used for a wide variety of childhood diseases. They are known to cause several side-effects by oral administration; nonetheless, side-effects associated with intravenous bolus are not well known[1]. Whereas a rise in blood pressure is a well-known side-effect of corticosteroid treatment, sinus bradycardia has been reported as another adverse effect of high-dose glucocorticoid therapy[2]. This effect mainly occurs in adults and few cases have been described in children. We report two cases of sinus bradycardia due to intravenous methylprednisolone administration in paediatric oncology patients and the approach we adopted for their resolution.

Key words: intravenous glucocorticoids, sinus bradycardia, high-dose glucocorticoid.

INTRODUCTION

High-dose intravenous glucocorticoids are increasingly being used in multiple diseases in childhood; especially in oncological, renal and rheumatological diseases[3]. Numerous well-known side-effects have been described such as hypertension, hyperglycaemia and hyperlipidaemia, among others. At the cardiovascular level, however, their effects on the heart rate are not so well known. Among these effects we may find sinus tachycardia and bradycardia, atrial fibrillation and ventricular tachycardia that can even lead to heart failure or myocardial infarction[4]. These effects on heart rhythm are most frequently described in adults and are associated with the administration of intravenous steroids. Nevertheless, some cases have been observed in paediatric age patients[5]. We present 2 cases of paediatric sinus bradycardia associated with intravenous steroids.

CASE 1

We present the case of a 20-month-old girl diagnosed with acute lymphoblastic leukaemia type B, without a personal medical history of interest, and whom was

starting treatment with intravenous prednisone at 60 mg/m^2/day, due to oral intolerance, according to the SEHOP-PETHEMA 2013 protocol. We observed sustained bradycardia 3 days after beginning the treatment. The bradycardia presented during sleep with a heart rate around 50 bpm, and which was associated with hypertension. The patient was clinically stable at all times, and without ionic alterations. We checked the vital signs from admission and observed a progressive decrease in the heart rate after starting intravenous corticoid administration. Prior to administration, the heart rate was within the normal range. We evaluated the patient in the paediatric cardiology department, but did not detect any cardiac pathology. Thus, we were observing a secondary/ acquired bradycardia, which was probably related to the underlying disease or to the treatment received. We finally decided to modify the treatment and use the oral route and initiate treatment with caffeine. This gave a good result, and was maintained for a total of 9 days. Subsequently, we observed heart rates within the normal range.

CASE 2

We present the case of a 2-year old child that was diagnosed with acute lymphoblastic leukaemia type B, and whom started treatment according to the SEHOP-PETHEMA 2013 protocol with intravenous prednisone at 60 mg/ m^2/day, due to poor tolerance via the oral route resulting from severe impairment of their general health. Within the personal medical history of interest, they had been diagnosed with a dilated cardiomyopathy, which was probably secondary to very severe anaemia, with progressive recovery of heart function. On admission, we recorded a level of 2.7 g/dl haemoglobin. This required numerous transfusions until recovery.

After starting administration of intravenous corticoids, we observed a progressive decrease in heart rate, which led to severe sustained bradycardia on the fourth and fifth days after onset of treatment. We registered heart rates during sleep of between 45-50 bpm, which remained clinically stable. Faced with the situation, and given the improvement in general health, we decided to administer oral steroids, and start intravenous caffeine at 5 mg/kg/day, under close monitoring in the PICU. After starting treatment with caffeine, and after changing steroids to the oral administration route, we saw clinical improvement with a progressive increase in heart rate until this normalised. We maintained treatment with oral caffeine for 25 days, and subsequently suspended the treatment without incident.

In subsequent controls by the paediatric cardiology department, the patient presented cardiac contractility within the normal range, and heart rates within their age range. Therefore, we attributed the bradycardia to the side-effect produced by the administration of intravenous corticoids.

DISCUSSION

Among all the patients receiving treatment with intravenous steroids in the paediatric oncology department at our hospital, we observed sustained moderate-severe sinus bradycardia in two cases. This was reversed after we changed the treatment to the oral route and started caffeine administration. Neither of our patients presented bradycardia prior to treatment onset, and only the patient in “case 2” presented a diagnosis of dilated cardiomyopathy. This resolved after correcting the severe anaemia. Thus, we attributed the severe bradycardia in both cases to the administration of high doses of intravenous corticoids.

The cardiovascular side-effects of treatment with high doses of intravenous corticoids include hypertension, sinus tachycardia, sinus bradycardia, atrial fibrillation and ventricular tachycardia, and even heart failure or myocardial infarction[3]. Nevertheless, bradycardia is a little known side-effect since it has been described in few studies. Arrhythmias can occur in 1% to 82% of patients receiving intravenous steroids[6].

Although various theories have been postulated, the mechanism by which this bradycardia occurs is unknown. One of these theories is that the administration of high doses of steroids lowers the threshold of stimulation of myocardial cells, secondary to alterations of blood potassium and urinary excretion of sodium and potassium. These changes facilitate the existence of ion exchange alterations in these cells[7].

Another theory is that the administration of high doses of intravenous corticosteroids induces changes in the physiology of sodium and water; thus, producing an increase in plasma volume and so triggering reflex bradycardia by the activation of low pressure baroreceptors[7,8]

In a study with paediatric cancer patients conducted in 2008, it was observed that up to 63.9% of patients developed bradycardia at some point secondary to the administration of intravenous corticosteroids in the first 88 hours from treatment onset. In those patients who presented symptoms, an ECG was performed revealing sinus bradycardia. This retrospective study suggested that sinus bradycardia may be an early side-effect of the administration of high-dose intravenous steroids in children and that ECG monitoring is important in these patients[9].

Most patients remain asymptomatic. Among the main symptoms we may find are palpitations, although these can also occur in patients with underlying heart disease, and very rarely, we may find malignant arrhythmias, loss of consciousness and cardiac arrest.

With regard to treatment, this is not necessary in most patients, and the bradycardia resolves spontaneously without incident[7]. In other cases, it is

necessary to initiate treatment with chronotropic or antiarrhythmic drugs, and even fit a transitory pacemaker[3].

CONFLICT OF INTEREST

The authors have no conflicts to disclose.

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