Arab Journal of Nephrology and Transplantation. 2012 Jan;5(1):47-9

Case Report

Bradycardia Following Oral Corticosteroid Use: Case Report and Literature Review

Amar Al Shibli[1*], Ibrahim Al Attrach[2], Mohammad A. Hamdan[3]

Divisions of General Pediatrics[1], Nephrology[2] and Cardiology[3], Department of Pediatrics, Tawam Hospital Al-Ain, United Arab Emirates

Abstract

Introduction: Corticosteroids are used in various clinical conditions that include many immune-mediated inflammatory diseases. Different side effects were described including cardiac arrhythmias. Most of those arrhythmias were in the form of bradycardia which usually occurs with high intravenous steroid doses. More significant arrhythmias and cardiac arrest were also described. In this report we describe a case of bradycardia that developed after the use of oral corticosteroids.

Case report: We report a case of bradycardia that developed in a 14 year-old male after receiving oral prednisone. The patient had steroid-sensitive nephrotic syndrome and presented with anasarca that started to develop few days prior to hospitalization. He had no underlying heart disease. Vitals was normal. Investigations confirmed a new nephrotic relapse. Oral prednisone 80 mg / day divided into three doses was started. Albumin infusions were initially given with intravenous furosemide to control the edema. Seven days after hospitalization, he developed bradycardia with a pulse rate of 50-60 per minute, which was less than 50% of the baseline heart rate. He didn't develop significant symptoms and he had no other apparent corticosteroids side effects. Cardiac evaluation and echocardiography were normal. Electrocardiogram revealed only sinus bradycardia.The bradycardia recovered after decreasing the dose of steroids to 60 mg PO every other day and he was discharged in stable condition a few days later.

Conclusion: Cardiac arrhythmias may develop with all forms of steroids including oral prednisone. Bradyarrhythmias can occur even with standard doses of oral prednisone.

* Correspondence author: Amar Al Shibli, MD Consultant Pediatrician, Department of Pediatrics, Tawam Hospital,UAE University POBox: 15258; Al Ain, United Arab Emirates,E mail: ashibli@tawamhospital.ae

Keywords: Bradycardia; Pediatrics; Steroids ; Prednisolone

Introduction

Corticosteroids are used in various clinical conditions and have established therapeutic benefits in children affected by several autoimmune or rheumatic diseases. They have several cardiovascular adverse reactions, which are more common in adults than in children. The exact etiology of such reactions is unknown, but several mechanisms have been proposed.

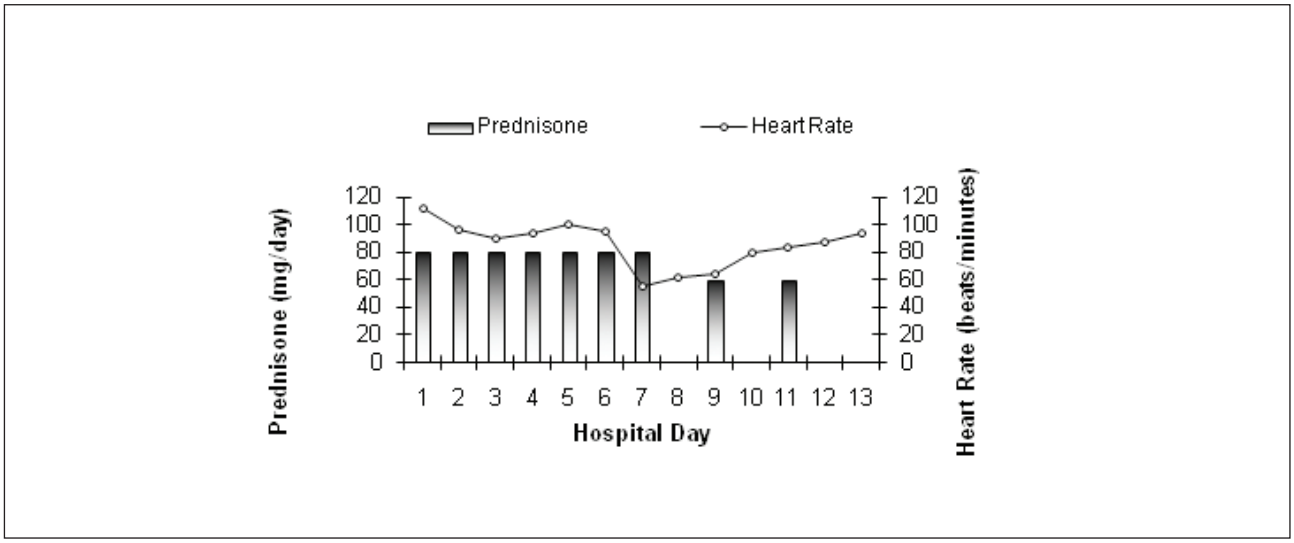
Tachy- or brady-arrhythmias occur in 1-82% of adults and children taking steroids [1, 2]. Intravenous methylprednisolone (IVMP) in adults was reported to cause atrial fibrillation, supraventricular tachycardia, ventricular tachycardia, bradycardia, asystole and even death [3-8]. In children, such adverse reactions are less frequent. They were reported with various types, routes, and dosages of steroids. Ueda *et al* reported atrial fibrillation in two children within 24 hours after receiving a pulse therapy of IVMP [9], while bradycardia developed in 82% of children who received IVMP for refractory Kawasaki disease [2]. Dexamethasone was reported to cause bradycardia and hypertension in premature infants treated for bronchopulmonary dysplasia [10].

Despite numerous previous reports of steroid induced bradycardia when given through the intravenous or intramuscular route, using the standard dose (2 mg/ kg/ day up to 80 mg) of oral prednisone was not previously reported to cause bradycardia.

Case Report

A 14 year-old adolescent who suffered from steroid sensitive nephrotic syndrome was admitted with a relapse. He presented with anasarca that was started to develop few days prior to hospitalization. On admission, the blood pressure was 120/80 mmHg, Heart rate was 112 beats per minute (bpm) and respiratory rate was 19 per minute. Weight was 53kg and his height was 149 cm body surface

Figure 1:Heart rate in relation to the dose of oral prednisone in reported patient



area of 1.5 m^2. Investigations showed nephrotic-range proteinuria, hypoalbuminemia, hypercholesterolemia. Hemoglobin level was 11.2 g/dL. He was treated with oral prednisone 80 mg/day divided into three doses. He was also given albumin 20% infusion and intravenous furosemide to control his edema. Three days later he showed clinical and laboratory remission.

Seven days after hospitalization, he developed bradycardia with a pulse rate of 50-60 bpm (50% less than the baseline heart rate) (Figure 1). He was asymptomatic apart from mild dizziness. His blood pressure was 115/80 mmHg and peripheral perfusion was normal. Cardiovascular examination and echocardiogram were normal. Electrocardiogram revealed sinus bradycardia. Serum electrolytes, calcium and magnesium levels were normal. Prednisone dose was subsequently reduced to 60 mg PO every other day. The patient's heart rate returned to baseline 48 hours after reducing prednisolone dose. He was discharged in stable condition a few days later.

Discussion

The exact etiology of steroid induced bradycardia is not known, but several mechanisms have been proposed. Severe bradycardia with or without hypotension was attributed to underlying heart disease [11], or rapid rate of infusion [7, 12]. Our patient had no evidence of underlying heart disease. Dexamethasone can cause bradycardia and hypertension in premature infants treated for bronchopulmonary dysplasia [11]. It has been suggested that alteration in the baroreceptor reflex could explain the association with the change in blood pressure seen in dexamethasone treated patients [10, 13]. However, it is also possible that bradycardia occurs as an idiosyncratic reaction to dexamethasone similar to what was described by Lucas *et al* [12].

Stimulation threshold of myocardial cells can be reduced secondary to direct inhibitory effect of the myocardium, altered sensitivity of adrenergic receptors, or abnormal serum electrolytes [6, 14]. Pudil *et al* showed diffuse accumulation of technetium Tc-99m pyrophosphate in the myocardium of two adults who developed bradycardia secondary to IVMP [6]. This may indicate a direct damage to the myocardium which may cause alteration in the electrolyte flux across the cell membrane. There was no evidence of myocardial inflammation by echocardiogram in our patient, although cardiac-specific inflammatory markers were not tested. Hall *et al* showed depression of cardiovascular alpha- and beta-1 adrenergic receptor sensitivity in animals receiving IVMP [14]. This may result in reduced myocardial sensitivity to catecholamines and altered urinary excretion of potassium and sodium [14]. Although our patient had normal serum electrolytes, he had significant hypoalbuminemia which reduces total calcium concentration in the serum and may lead to altered myocardial sensitivity. Abnormal serum electrolytes were also observed in two out of five children who developed bradycardia after receiving IVMP for refractory Kawasaki disease [2].

Bradycardia is usually asymptomatic; though palpitations, loss of consciousness and even cardiac arrest were described [1, 3, 7-9, 12]. It will usually resolve spontaneously after hours to days of withdrawing or reducing the dose of the offending drug, as happened with our patient. However, the need for administration of

chronotropic or antiarrhythmic agents [5, 15] or temporary cardiac pacing [9] was described in the literature.

Conclusion

Bradycardia may complicate high dose oral prednisone therapy. It is advisable to obtain a baseline heart rate, an electrocardiogram and serum electrolytes before starting high dose steroid therapy in children. Monitoring the patient in hospital for a few days may also be considered.

References

1. Klein-Gitelman MS, Pachman LM. Intravenous corticosteroids: adverse reactions are more variable than expected in children. J Rheumatol. 1998 Oct;25(10):1995-2002.

2. Miura M, Ohki H, Yoshiba S, Ueda H, Sugaya A, Satoh M, Yamagishi H. Adverse effects of methylprednisolone pulse therapy in refractory Kawasaki disease. Arch Dis Child. 2005 Oct;90(10):1096-7.

3. McLuckie AE, Savage RW. Atrial fibrillation following pulse methylprednisolone therapy in an adult. Chest. 1993 Aug;104(2):622-3.

4. Kumari R, Uppal SS. First report of supraventricular tachycardia after intravenous pulse methylprednisolone therapy, with a brief review of the literature. Rheumatol Int. 2005 Nov;26(1):70-3.

5. Belmonte MA, Cequiere A, Roig-Escofet D. Severe ventricular arrhythmia after methylprednisolone pulse therapy in rheumatoid arthritis. J Rheumatol. 1986 Apr;13(2):477-9.

6. Pudil R, Hrncir Z. Severe bradycardia after a methylprednisolone "minipulse" treatment. Arch Intern Med. 2001 Jul 23;161(14):1778-9.

7. Guillen EL, Ruiz AM, Bugallo JB. Hypotension, bradycardia, and asystole after high-dose intravenous methylprednisolone in a monitored patient. Am J Kidney Dis. 1998;32(2):E4.

8. Gardiner PV, Griffiths ID. Sudden death after treatment with pulsed methylprednisolone. BMJ. 1990 Jan 13;300(6717):125.

9. Ueda N, Yoshikawa T, Chihara M, Kawaguchi S, Niinomi Y, Yasaki T. Atrial fibrillation following methylprednisolone pulse therapy. Pediatr Nephrol. 1988 Jan;2(1):29-31.

10.Lenclen R, Karam T, Gajdos V, Mourdie J, Hoenn E, Campot K, Paupe A. Early cardiovascular effects of corticotherapy for bronchopulmonary dysplasia. Arch Pediatr. 2001 Jan;8(1):32-8

11. Jin DK, Choi Y, Cheong HI, Ko KW. Intravenous methylprednisolone. Pediatr Nephrol. 1990 Sep;4(5):576-7.

12. Lucas KG, Howrie DL, Phebus CK. Cardiorespiratory decompensation following methylprednisolone administration. Pediatr Hematol Oncol. 1993 Jul-Sep;10(3):249-55.

13. Ohlsson A, Heyman E. Dexamethasone-induced bradycardia. Lancet. 1988 Nov 5;2(8619):1074.

14. Hall ED, Plaster M, Braughler JM. Acute cardiovascular response to a single large intravenous dose of methylprednisolone and its effects on the responses to norepinephrine and isoproterenol. Proc Soc Exp Biol Med. 1983;173:338-43.

15. Tvede N, Nielsen LP, Andersen V. Bradycardia after high-dose intravenous methylprednisolone therapy. Scand J Rheumatol. 1986;15(3):302-4.