Case Report

Bradycardia after pulse methylprednisolone therapy in a child—Uncommon side effect of a frequently used drug: A case report

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Abstract

Corticosteroids are potent anti-inflammatory agents used as a mainstay of therapy in most of the rheumatologic disorders. Common side effects of pulse steroid therapy include hypertension, hyperglycemia, seizure, hypokalemia, and infection. We report a case of an 11-year-old girl with polyarticular Juvenile idiopathic arthritis who developed bradycardia following pulse methylprednisolone therapy. On day 2 of methylprednisolone infusion, she developed bradycardia with a heart rate between 50 and 60/min. ECG was suggestive of sinus bradycardia. There was no evidence of dyselectrolytemia (Na—141 mmol/l, K—3.54 mmol/l, Ca—8.72 mg/l) or sepsis. The patient did not receive methylprednisolone on day 3 and vitals continued to be monitored. Her heart rate improved after 12 hours. In the mid of infusion on day 4, again the patient had bradycardia with a heart rate of 50–60/minute. Since she was hemodynamically stable, we continued the infusion, and bradycardia resolved in the next 8 hours. On follow-up after 2 weeks, she had some improvement in joint symptoms and normal heart rate. As per Naranjo adverse drug reaction probability scale, the adverse reaction in our case was probable with a score of 8. Although bradycardia associated with pulse steroid therapy is benign and is usually reversible following cessation of therapy, a baseline heart rate, ECG, and electrolyte level are suggested before infusion as a cautionary measure to minimize serious adverse events.

Keywords: Bradycardia, methylprednisolone, pulse therapy

Introduction

Corticosteroids are potent anti-inflammatory agents used as a mainstay of therapy in most of the rheumatologic disorders. In addition, corticosteroids are prescribed by primary care physicians for many infectious and inflammatory disorders. High-dose corticosteroid given as intermittent intravenous (i.v.) bolus for a shorter duration of 3–5 days is known as pulse therapy.[1] Common side effects of pulse steroid therapy include hypertension, hyperglycemia, seizure, hypokalemia, and infection. Cardiac adverse events like arrhythmia, cardiac arrest, and death have been reported with high-dose intravenous corticosteroid therapy.[2] With due consent, we report a case of an 11-year-old girl with polyarticular juvenile idiopathic arthritis (JIA) who developed bradycardia following pulse methylprednisolone treatment.

Case Report

An 11-year-old girl presented to our OPD with complaints of pain in multiple joints of the body for the last 4 years. She also had a history of on-and-off low-grade fever for the last 4 years. The patient was not on any current treatment on presentation.

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On examination, she was found to be severely thin with a weight of 17.7 kg, length of 122 cm, and BMI of 12.3 kg/m^2(≈3rd centile as per IAP). Her pulse rate was 86/minute, respiratory rate was 20/minute, temperature was 98.7°F, and BP was 100/66 mm Hg. On musculoskeletal examination, she had active arthritis in multiple joints of upper limb, lower limb, cervical spine, and temporomandibular joints. Baseline investigations revealed hemoglobin of 9.1 gm/dl, total WBC count of 26100/mm^3, and platelet count of 4.99 lakhs/mm^3. Inflammatory markers like ESR (47) and CRP (11O mg/dl) were raised. Liver function tests, renal function tests, electrolytes, and random blood sugar records were essentially normal. Evidence of any acute infection was reasonably excluded. In view of high disease activity measured by juvenile idiopathic arthritis disease activity scoring 71 (JADAS-71 score 79), a decision was taken to give i.v. methylprednisolone pulse therapy for 3 days. She was started with 500 mg (28.25 mg/kg) i.v. infusion over 4 hours on day 1 with vitals and blood sugar monitoring. No significant alteration in vitals was observed. On day 2 of methylprednisolone infusion, she developed bradycardia with a heart rate between 50 and 60/min. toward the end of infusion. The patient was keenly observed with strict cardiac monitoring. ECG and basic investigations like complete hemogram, ESR, CRP, and serum electrolytes (sodium, potassium, and calcium) were ordered. ECG was suggestive of sinus bradycardia. There was no evidence of dyselectrolytemia (Na—141 mmol/l, K—3.54 mmol/l, Ca—8.72 mg/l) or sepsis. Laboratory parameters pre- and post-medication is summarized in Table 1. Although she was clinically and hemodynamically stable, her heart rate continued to remain below 60/minute for the next 12 hours with the nadir at 48 beats/minute. The patient did not receive methylprednisolone on day 3 and vitals continued to be monitored. Echocardiography was normal and the patient was on continuous heart rate monitoring till discharge. Heart rate improved after 12 hours with a sustained rise above 60/minute and returned to a baseline heart rate of 80/minute in the next 6 hours. We were truly clueless about this transient suppression of heart rate and a consensus was taken to complete methylprednisolone pulse on day 4. In the mid of infusion on day 4, again the patient had bradycardia with a heart rate of 50–60/minute. Since the child was hemodynamically stable, we continued the infusion, and bradycardia resolved in the next 8 hours [Figure 1]. She was kept under observation for the next 48 hours and discharged with weekly methotrexate therapy. On follow-up after 2 weeks, she had some improvement in joint symptoms and normal heart rate. As per Naranjo adverse drug reaction probability scale, the adverse reaction in our case was probable with a score of 8 [Table 2].[3]

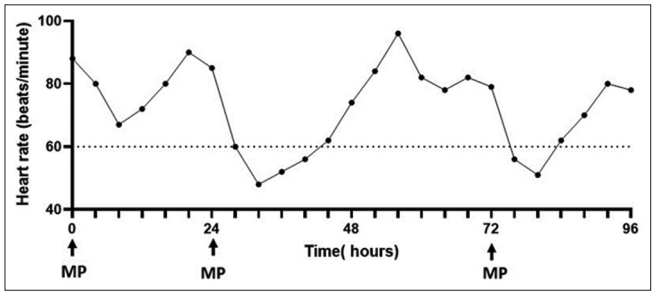

Figure 1: Heart rate variability following pulse methylprednisolone (MP) infusion

Discussion

Corticosteroids are in use for a long time and the expected side effects are well known to the treating physicians. It is a common drug advised for common conditions like asthma, croup, chronic obstructive pulmonary disease (COPD), allergy, anaphylaxis, and chronic rheumatologic conditions. However, there is limited literature on heart rate variability with its use. Albeit rare, case reports of bradycardia following pulse methylprednisolone therapy have been reported in both adults and children.[4] Arrhythmia like atrial fibrillation, ventricular fibrillation, and cardiac arrest has been reported in adults. Even high-dose oral prednisolone and pulse dexamethasone have resulted in slowing heart rate following therapy.[5]

The exact pathophysiology behind corticosteroid-induced bradycardia is still unknown. The proposed mechanisms include; (1) steroid-induced hypertension and volume expansion causing alteration in baroreceptor reflex, (2) mineralocorticoids activity leading to hypokalemia, (3) decreased myocardial sensitivity to catecholamine, and (4) idiosyncratic reaction. The

Table 1: Laboratory findings in patient before and after methylprednisolone treatment

Investigations	Baseline values	Values after methylprednisolone therapy
Hemoglobin (gm/dl)	9.1	8.4
Total leucocyte count (cells/mm^3)	26,110	12,530
Platelet count (cells/mm^3)	4,99,000	5,01,400
ESR (mm/1st hr)	47	40
CRP (mg/l)	110	63.78
Sodium (mmol/l)	140	141
Potassium (mmol/l)	4.32	3.54
Calcium (mg/dl)	8.8	8.72
Random blood sugar (mg/dl)	101	115

Table 2: Naranjo adverse drug reaction probability score*

Questions (1 to 10)	Patient's score (0 to +2)
2. Did the adverse event appear after the suspected drug was administered?	+2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1
4. Did the adverse event reappear when the drug was re-administered?	+2
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	+2
6. Did the reaction reappear when a placebo was given?	+1
Total score	+8

*Adverse reaction probability score: Doubtful: ≤0, possible: 1–4, probable: 5–8, Definite: ≥9, Only positive scores with questions are mentioned

presence of pre-existing cardiac and renal disease and rapid infusion rate are associated risk factors for the development of bradycardia. Documented dyselectrolytemia was reported in a few cases.[6,7] In our case, the patient did not have dyselectrolytemia and infusion was given slowly over 4 hours. Our patient was not also on any other medication during this period.

Bradycardia associated with corticosteroid therapy is usually sinus in rhythm. It is usually benign in nature and asymptomatic.[8] Our patient was also clinically and hemodynamically stable. Common symptoms of bradycardia include dizziness, chest pain, fatigability, and syncope. The onset of bradycardia can occur during methylprednisolone administration to a few days following the last therapy and lasts for hours to days.[7] Our case was unique because the patient developed bradycardia during the second dose of pulse therapy itself in contrast to the existing literature. To our knowledge, early resolution of bradycardia within 12 hours was also distinctive and specific to our case and has not been reported in adults or children.

Conclusion

Due to the widespread use of corticosteroids, primary healthcare providers should be aware of bradycardia as a potential adverse event. Although bradycardia is benign and is usually reversible following cessation of therapy, a baseline heart rate, ECG, and electrolyte level are suggested before infusion as a cautionary measure to minimize serious adverse events.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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