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Case Report

Pulse methylprednisolone therapy triggered sinus bradycardia in two children

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ABSTRACT

Intravenous methylprednisolone is an important therapeutic modality in many conditions, owing to their anti-inflammatory and immune-modulating properties. Along with other side-effects of corticosteroids, cardiovascular side-effects are also seen in varying degree in children. Sinus bradycardia is reported uncommonly in children following high dose intravenous methylprednisolone. We report two paediatric cases without any underlying cardiac problems with asymptomatic bradycardia following high dose intravenous methylprednisolone. Heart rate reduction was seen from 30-40% compared to the baseline heart rate, which returned to its normal value after 24-36 hours of stoppage of the offending drug. A high index of suspicion along with strict cardiovascular monitoring is necessary in patients receiving high dose of methylprednisolone.

Keywords: Steroid, Bradycardia, Cardiovascular side-effects, Autoimmune encephalitis

INTRODUCTION

High dose intravenous methylprednisolone (IV MP) is an important therapeutic modality in many conditions, owing to their anti-inflammatory and immune-modulating properties. The common side-effects of pulse therapy are hyperglycemia, gastrointestinal disturbances, minor infections, and psychiatric manifestations. Cardiovascular side effects include hypertension, hypotension, and cardiac arrhythmias, mainly atrial fibrillation, atrial flutter, ventricular tachycardia, and sinus bradycardia.[1] Sinus bradycardia is uncommonly reported in pediatric patients following high dose IV MP. Here we report two cases of sinus bradycardia during therapy with high dose IV MP, which recovered following cessation of therapy.

CASE REPORTS

Case 1

A 6-year-old boy was admitted with provisional diagnosis of seronegative autoimmune encephalitis. He presented with developmental regression and evolving dyskinesias following an acute febrile seizure. All the routine tests including complete blood counts, renal and liver function tests, vitamin B12 assay, creatine kinase, thyroid profile, electroencephalography, computed tomography brain, magnetic resonance imaging brain, cerebrospinal fluid analysis (cytological/biochemical/malignant cells/NMDA panel), serum for paraneoplastic panel were all negative. In view of the gradual progression of the disease, suspecting seronegative autoimmune encephalitis, the child was admitted for a course of IV MP pulse dose at 30 mg/kg/day for 5 days. On the fourth day of the steroids, the child developed sinus bradycardia with minimum heart rate up to 44/min, which was 33-40% reduction in heart rate compared to the baseline heart rate. Clinically, his blood pressure and cardiovascular examination were normal. His serum potassium was 3.7 meq/dl, and serum calcium was 9.2 mg/dl. Electrocardiography (ECG) showed sinus bradycardia. Methylprednisolone was suspected to be the cause of the bradycardia and hence was witheld. He was hemodynamically stable and bradycardia persisted for 24 hours after the last dose of the steroids,

then he recovered. He was put on low-dose oral prednisolone and discharged with advice to continue for 2 weeks.

Case 2

A 13-years old girl diagnosed HbE trait with systemic juvenile idiopathic arthritis (JIA) girl with Macrophage activation syndrome (MAS). She presented with a history of fever, pain abdomen and body aches with severe pallor. Physical examination revealed pallor, joint swelling involving the ankle joints and right first metacarpophalangeal joint, no organomegaly was clinically appreciated. Initial investigations revealed a TLC of 12,200/ul, platelets >1,00,000/ul, erythrocyte sedimentation rate (ESR) 140 mm AEFH, C-reactive protein (CRP) - 207 mg/dl, serum ferritin >1000 ng/ml, aspartate aminotransferase (AST) - 104 U/l, and triglycerides 224 mg/dl. Considering diagnosis of MAS, bone marrow biopsy was sent and pulse IV MP was started @30 mg/kg/day for 5 days. On the third day of steroids, the child developed sinus bradycardia with lowest heart rate up to 59 beats per minute. There was 39-42% reduction in heart rate compared to the baseline heart rate. She developed pitting pedal edema and her blood pressure records were between 90th and 95th percentiles. The five days' course of IV MP course was completed with strict heart rate monitoring. Bradycardia persisted for next 36 hours after stopping the pulse steroid dose and gradually improved to normal rates.

DISCUSSION

Methylprednisolone is an important treatment modality for treating many acute life-threatening conditions. The exact mechanism of development of bradycardia following IV MP is not known, though many mechanisms are proposed like intravascular volume expansion with hypertension causing altered baroreceptor reflex; mineralocorticoids activity leading to hypokalaemia; altered myocardial sensitivity to catecholamine; and reaction to excipients in the steroid preparation. Our case 2 had hypertension, bilateral ankle oedema and sinus bradycardia probably due to intravascular volume expansion with hypertension causing altered baroreceptor reflex.

Sinus bradycardia following methylprednisolone was first reported in 1986 among five patients who received high dose methylprednisolone for rheumatoid arthritis.[2] It may be dose dependent, although both the cases received 30 mg/kg and developed bradycardia on day 3 or day 4 of infusion.[3,4] Risk of bradycardia is more with increasing dose of steroid, more frequent in older patients and with underlying cardiac defects or with autonomic disturbances.[5] Though incidence of side effects is more with higher doses of methylprednisolone or prednisolone, reports of sinus bradycardia is also reported as a side effect of low-dose-steroid also.[6] Incidence of sinus bradycardia in children was reported to be higher after repeated administrations of pulse methylprednisolone.[7] Though methylprednisolone induced bradycardia is rare, but case reports are available in both pediatric and adult patients.[8,9] Symptomatic sinus bradycardia with acute hypotension was reported in a two years old child with primitive neuroectodermal tumour on multiple chemotherapy following rapid high-dose IV MP.[10]

CONCLUSION

Cardiovascular outcomes secondary to methylprednisolone, particularly sinus bradycardia is a rare consequence. The present report highlights asymptomatic bradycardia in two children following pulse IV MP which had a spontaneous recovery upon stoppage. Hence a high index of suspicion along with strict cardiovascular monitoring is necessary in patients receiving high dose of methylprednisolone.

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