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The impact of high dose corticosteroid treatment affect on cardiac abnormalities in patients with multiple sclerosis

Ceyhun Sayman[1], Sena Güneş[1], Oğuzhan Türk[1], Hümeyra Çelik[2], Ece Özdemir Öktem[1], Şeyda Çankaya[1], Ahmet Özşimşek[1], Burak Yuluğ[1]

[1]Department of Neurology, Alaaddin Keykubat University, Alanya Training and Research Hospital, Antalya, Turkiye
[2]Department of Physiology, Alaaddin Keykubat University, Alanya Training and Research Hospital, Antalya, Turkiye

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Corresponding Author: Ceyhun Sayman, ceysayman@yahoo.com.tr

ABSTRACT

Aims: High-dose corticosteroids to control acute relapses of Multiple sclerosis, leveraging their anti-inflammatory effects. However, these treatments can lead to cardiovascular side effects. Understanding the pathophysiology of corticosteroid induced bradycardia is paramount for healthcare providers. Our aim in this study are to identify risk factors for cardiac side effects and assess the timing of cardiac complications relative to treatment.

Methods: Patients who met the McDonald's criteria for definite MS and patients requiring admission for pulse steroid treatment with an acute recurrence were included. Individuals taking cardiac medications, or with a heart illness were excluded. Patients were given 1 g IV methylprednisolone in 2 hours for five to seven days in order to treat acute relapses.

Results: We studied with 23 patients (6 males and 17 females, 26.1/73.9% respectively). The mean±SD age of the patients was 34.6±9.9 (18-43) years and the mean±SD duration of disease was 5.5±4.9 years. Most of the patients were relapsing–remitting MS in 73.9%, primary progressive in 4.4% and secondary progressive in 21.7%.The most common cardiac arhythmia during corticosteroid pulse therapy was sinus bradycradia(n=6).

Conclusion: The combination of direct effects on cardiac myocytes, electrolyte disturbances, autonomic dysfunction, and individual genetic factors can contribute to the development of bradycardia in MS patients treated with high-dose methylprednisolone. Close monitoring and prompt intervention are crucial to manage this adverse effect and optimize patient safety.

Keywords: Multiple sclerosis, pulse corticosteroid, bradicardia

INTRODUCTION

High dose corticosteroid therapy has long been established as a treatment modality for various immune related conditions.[1] It is also a cornerstone in the management of multiple sclerosis (MS) exacerbations, serving to alleviate symptoms and hasten recovery.[2] MS exacerbations represent acute inflammatory demyelinating events in the central nervous system, characterized by patient-reported or objectively observed symptoms lasting at least 24 hours, as defined by the revised McDonald criteria.[3] Typically, involving intravenous administration of doses exceeding 1 gram per day for a duration of 5 to 7 doses, these regimens have proven efficacy in managing acute exacerbations.[4]

However, the use of high dose corticosteroids in MS exacerbations is not without its risks, particularly concerning cardiovascular adverse events.[5] Beyond acute exacerbations, glucocorticoid use has been associated with various cardiovascular risks, including myocardial infarction, stroke, heart failure, and a notable twofold increase in the risk of atrial fibrillation or flutter, as demonstrated in population based case control studies.[6] Moreover, sinus bradycardia following high dose methylprednisolone therapy is considered an uncommon side effect.[7] More details regarding the frequency of this adverse event.

Despite its rarity, the occurrence of sinus bradycardia underscores the importance of vigilance regarding cardiovascular complications associated with corticosteroid therapy in MS exacerbations. Understanding the pathophysiology and clinical implications of corticosteroid induced bradycardia is paramount for healthcare providers involved in optimizing patient safety during treatment.[8]

METHODS

From April 2023 to March 2024, 23 consecutive patients who met the McDonald's criteria for definite MS and patients requiring admission for pulse steroid treatment with an acute recurrence to the Neurology Department at Alanya Alaaddin Keykubat University Hospital were enrolled retrospectively. The study was approved by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Researches Ethics Committee (Date: 19.10.2022, Decision No: 10-04). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. Any worsening of symptoms that lasted more than 24 hours was considered as a relapse. Individuals taking beta blockers or antiarrhythmic medications, or those with a history of heart illness, were not allowed to participate. Patients were given 1 g IV methylprednisolone (diluted in 500 cc of 5% dextrose water) in 2 hours for five to seven days in order to treat acute relapses. For those who experienced symptoms such as vertigo, dizziness, or chest pain, cardiac monitoring was done. Disturbances in cardiac rhythm were identified by a specialist. Patients who have a history of cardiac pathology likes arrhythmia, thyroid disease, hyperlipidemia, diabetes, and autonomic dysfunction were excluded.

RESULTS

We studied with 23 consecutive patients retrospectively (6 males and 17 females, 26.1/73.9%) with acute MS relapse who underwent treatment with corticosteroid pulse therapy at Alanya Alaaddin Keykubat University Hospital. The mean±SD age of the patients was 33.6±8.9 (18-43) years and the mean±SD duration of disease was 3.5±1.9 years. Most of the patients were relapsing–remitting MS in 73.9%, primary progressive in 4.4% and secondary progressive in 21.7%. The most common cardiac arrhythmia during corticosteroid pulse therapy was sinus bradycardia that was detected in 6 patients (shown in Figure 1). The electrocardiogram (ECG) findings had no acute abnormalities. Prior to during and following the bradycardia induced dose reduction of the pulse steroid treatment were shown in Figure 2.

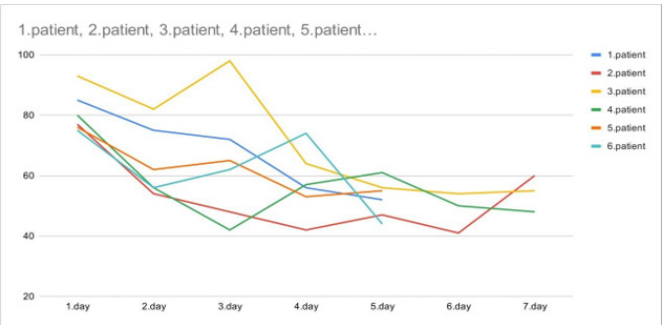


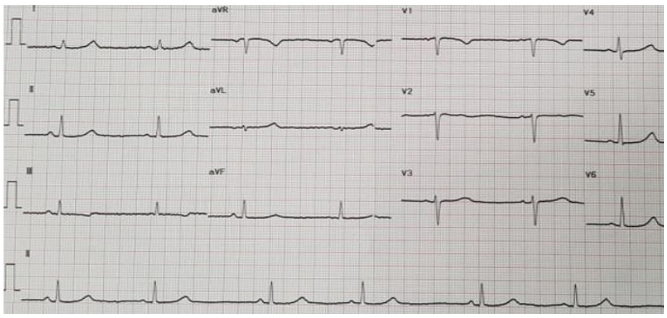
Figure 1. Heart rate changes during pulse steroid treatment

Case 1

A 29 years old woman had a persistent numbness on the right half of her face for a week. She underwent a thorough neurological examination at emergency which revealed hypoesthesia limited to the right side of her face. Routine blood tests showed no abnormalities. Contrast-enhanced MRI scans were revealing: demyelinating plaques were observed in various regions of her brain, indicative of MS exacerbations.

Over a period of 5 days, she received 1000 mg of methylprednisolone daily. While initially, her vital signs

A (Patient 1)



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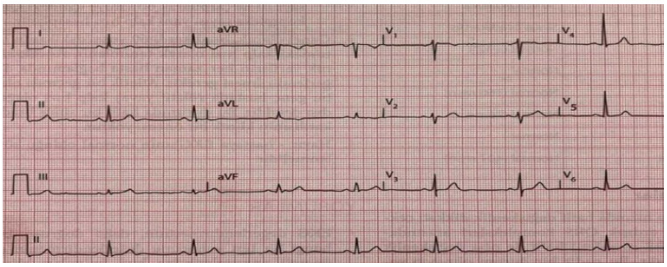

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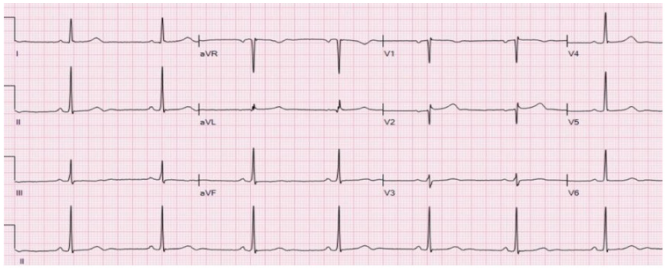
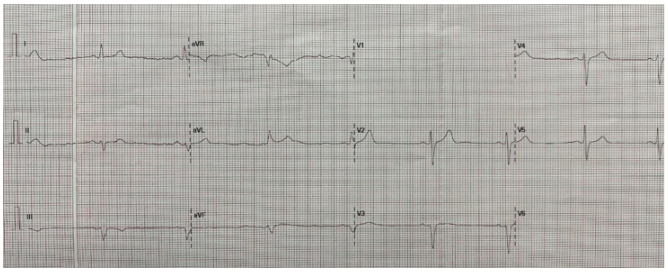
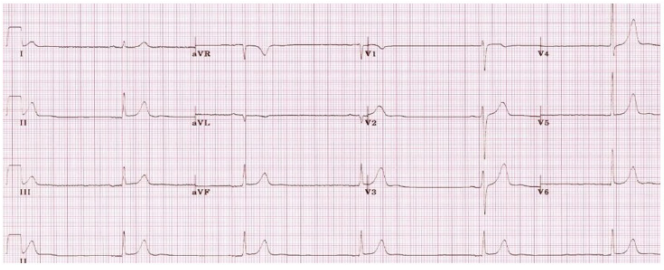


D (Patient 4)



E (Patient 5)



F (Patient 6)

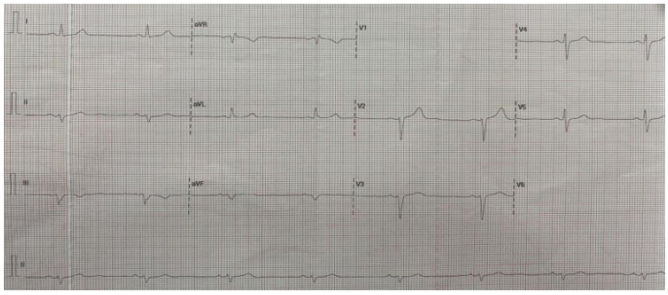


Figure 2. Electrocardiography findings while giving pulse steroid treatment

remained stable, about eight hours after receiving the treatment, her pulse rate dropped to 50 beats per minute, indicating a case of sinus bradycardia. However, she remained asymptomatic, and closely monitoring her condition. Fortunately, as the steroid treatment progressed, her pulse rate gradually normalized, and significant improvement in her symptoms was observed. Following the completion of her 5 day treatment course, her pulse rate returned to its pre-treatment levels, and she was discharged from the hospital with appropriate follow-up plan.

Case 2

A 25 years old woman diagnosed with MS in 2016, presented to the neurology outpatient clinic with complaints of blurred vision in her right eye and weakness in both lower extremities. Contrast-enhanced brain MRI revealed multiple hyperintense lesions within the cerebral white matter, periventricular area, some extending perpendicularly to the callososeptal interface. Peripheral dominant contrast enhancement was observed in lesions located in specific brain regions, indicating active demyelinating plaque formations.

Based on these findings, 7 day course of methylprednisolone treatment was planned. Throughout the treatment period, her vital signs were closely monitored. Similar to other patients, she experienced a temporary decrease in heart rate following steroid administration, which normalized post treatment. After completing the steroid treatment, her symptoms were significantly diminished and her pulse rate returned to baseline levels.

Case 3

A 41 years old man with a five year history of diagnosed MS, presented to the emergency department with complaints of numbness in his legs that had been progressively worsening over the past month. Neurological examination revealed asymmetric motor weakness and hypoesthesia in his lower extremities, prompting further investigations. Imaging studies, including contrast-enhanced brain and spinal MRI scans, confirmed the presence of MS plaques in bilateral periventricular cerebral white matter, the corpus callosum, and the cervical and thoracic spinal cord. Despite the absence of contrast enhancement suggestive of active lesions in some areas, initiating a 7 day course of methylprednisolone treatment to manage his symptoms and potentially prevent further disease progression.

During the course of his steroid treatment, he experienced a sinus bradycardia, which resolved post-treatment. With close monitoring and management, he was discharged from the hospital with plans for ongoing follow-up care.

Case 4

A 33 years old woman with no known prior illnesses, presented to the neurology outpatient clinic with complaints of numbness in her right arm. Contrast-enhanced MRI scans of the brain, cervical, thoracic, and lumbar regions were performed, revealing no significant lesions suggestive of MS.

However, given the clinical suspicion and the possibility of early or subtle disease manifestations, over the course of a 5 day treatment regimen, She received methylprednisolone, closely monitored for any adverse effects. She experienced a temporary decrease in heart rate following steroid administration, which resolved post-treatment. With continued monitoring and management, she was discharged from the hospital with plans for ongoing follow-up care.

Case 5

A 25 years old woman with no known comorbidities, presented to the neurology outpatient clinic with intermittent numbness in her left arm and legs, as well as episodic blurred vision over the past three years. Concerned about the possibility of MS, contrast-enhanced MRI scans of the brain, cervical, and thoracic regions revealed notable appearances of MS plaques, particularly in the cerebral white matter and juxtacortical fibers. Despite the absence of contrast-enhancing lesions, suggestive of active disease, she was initiated a 5-day course of methylprednisolone treatment to manage her symptoms and potentially prevent disease progression.

During the course of her steroid treatment, she experienced a brief episode of bradycardia, which resolved post-treatment. With close monitoring and management, her symptoms were dissappearad ,and she was discharged from the hospital with plans for ongoing follow-up care to monitor her condition and adjust treatment as needed.

Case 6

A 32 years old man with no known comorbidities, presented with a complaint of vision impairment in his right eye for the past three days. Concerned about the possibility of optic neuritis, a comprehensive evaluation, including ophthalmological examination, visual evoked potential (VEP) test, lumbar puncture, and MRI imaging.

VEP testing indicated prolonged p100 wave latency in the right eye, suggestive of optic neuritis. However, MRI scans did not reveal any abnormalities, raising questions about the underlying cause of his symptoms. Despite the absence of definitive imaging findings, he was taken a 5 day course of methylprednisolone treatment to manage his symptoms and potentially prevent further vision loss.

Throughout the course of his steroid treatment, he experienced a sinus bradycardia, which resolved post-treatment. He was discharged from the hospital with plans for ongoing follow-up care to monitor his condition and adjust treatment as needed.

DISCUSSION

In our present study, we observed that methylprednisolone, a commonly used corticosteroid in the management of multiple sclerosis (MS) exacerbations, exhibited the adverse effect of sinus bradycardia. Compared to previous literature, our present findings are consistent with the known cardiovascular side effects of high-dose corticosteroid therapy, which include arrhythmias and sudden death.[9,10]

The common feature of our MS patients showing this adverse effect was the use of intravenous pulse therapy with methylprednisolone. Corticosteroids have been utilized to treat inflammatory illnesses; however, because of differences in dosage, duration, and mode of administration, not all possible side effects have been well understood. The side effects of intravenous pulse therapy that are most frequently reported are infections, behavioral abnormalities, hyperglycemia, hypokalemia, and hypertension. Arrhythmias and sudden death have been documented in the literature as the most severe side effects.[11]

Methylprednisolone, a potent corticosteroid commonly used in the management of MS exacerbations, has been associated

with various cardiovascular adverse effects, including sinus bradycardia. Understanding this phenomenon is crucial for clinicians managing MS patients undergoing corticosteroid therapy Symptomatic bradycardia, characterized by symptoms such as dizziness, chest pain or dyspnea, requires prompt evaluation and intervention to prevent adverse outcomes.[12] Close monitoring of vital signs, including heart rate and telemetry may be warranted during corticosteroid therapy, especially in high-risk patients. Management of methylprednisolone induced bradycardia typically involves conservative measures such as dose reduction or discontinuation of corticosteroid therapy, electrolyte correction if indicated, and supportive care.

The etiology of methylprednisolone induced symptomatic sinus bradycardia in MS patients is multifactorial and not fully elucidated. However, several mechanisms have been proposed to explain the occurrence of bradycardia following corticosteroid therapy. Animal studies suggest that high-dose methylprednisolone can affect cardiac myocytes, altering cardiovascular sensitivity to catecholamines and potentially leading to bradycardia. Changes in the responsiveness of cardiac cells to catecholamines could lead to a decrease in heart rate, manifesting as sinus bradycardia.[13,14]

Additionally, corticosteroids may induce electrolyte imbalances, disrupt normal cardiac rhythm, and contribute to bradycardia. Sudden shifts in electrolyte concentrations, particularly potassium, can disrupt the normal electrical conduction system of the heart, potentially leading to cardiac arrhythmias such as bradycardia. This mechanism is particularly relevant in patients with MS, as they may already have alterations in autonomic function, which can further predispose them to electrolyte imbalances.[15] Corticosteroids may induce physiological changes in sodium and water balance. This can result in the expansion of plasma volume and activation of low-pressure baroreceptors. Baroreceptors are sensors located in blood vessels and the heart that regulate blood pressure and heart rate. Activation of these receptors may lead to reflex bradycardia as a compensatory mechanism to maintain blood pressure homeostasis.[16]

Also some MS patients may have underlying cardiac abnormalities or autonomic dysfunction, which predisposes them to develop bradycardia in response to corticosteroid therapy. Additionally, genetic factors or variations in drug metabolism pathways may influence an individual's susceptibility to cardiac side effects of methylprednisolone.

CONCLUSION

Methylprednisolone induced sinus bradycardia represents a rare but clinically significant complication in MS patients undergoing corticosteroid therapy. Clinicians should maintain a high index of suspicion for this adverse effect, closely monitor patients, and promptly intervene when necessary to ensure optimal outcomes. Further research is warranted to elucidate the underlying mechanisms and refine strategies for managing corticosteroid induced bradycardia in MS patients. While bradycardia associated with corticosteroid therapy is usually transient and resolves spontaneously following end of the treatment, it is essential for clinicians to assess and mitigate potential risks in MS patients, optimizing both therapeutic efficacy and patient safety.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was approved by the Alanya Alaaddin Keykubat University Faculty of Medicine Clinical Researches Ethics Committee (Date:19.10.2022, Decision No: 10-04).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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