ejpmr, 2025, 12(1), 292-294

SJIF Impact Factor 7.065

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Case Study

ISSN 2394-3211

EJPMR

AMIODARONE AND ITS NEUROTOXICITIES: A CASE STUDY ON DRUG INDUCED PROXIMAL MYOPATHY

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Article Received on 23/11/2024 **Article Revised on 13/12/2024** **Article Accepted on 02/01/2025**

ABSTRACT

Amiodarone is an anti-arrhythmic drug widely known for its effectiveness in the management of life-threatening ventricular tachyarrhythmias. Treatment using this drug is often limited to ventricular arrhythmias due to its numerous side effects. Neurotoxicity is one such serious adverse effect of amiodarone in which patients are presented with ataxia, tremor or in rare instances proximal myopathy which is characterised by symmetrical weakness of proximal upper or lower limbs. We report a case of amiodarone-induced proximal myopathy in an adult female with a history of type 1 diabetes mellitus who presented with difficulty in walking and progressive weakness after being on amiodarone therapy for atrial fibrillation. The patient's symptoms resolved with the reduction in amiodarone dose and physiotherapy to further improve mobility and strength.

KEYWORDS: Amiodarone, anti-arrhytmics, atrial fibrillation, proximal myopathy.

INTRODUCTION

Amiodarone is a class III anti arrhythmic drug which has shown its efficacy in the treatment of ventricular arrhythmias especially in recurrent life threatening conditions and also in treatment of supraventricular arrhythmias such as atrial fibrillation. Although it's benefit in rhythm control, amiodarone shows several adverse reactions. Neuromyopathy is a rare neuromuscular side effect that occurs in patient characterized by significant proximal and distal muscle weakness, dysphagia, ataxia and poly myoclonus. This rare side effect is said to be caused by the amphiphilic cationic nature of amiodarone that interacts with anionic phospholipids of organelles. This causes formation of autophagic vacuoles that are seen in muscle biopsies. Desethyl – amiodarone obtained after hepatic metabolism may also accumulate in muscle tissue causing further damage to the tissues.[1]

CASE DESCRIPTION

A 20 year old female patient who is a known case of type 1 Diabetes Mellitus and Atrial fibrillation on amiodarone was presented with difficulty in walking since 2 months, showing progressive weakness initially. She had difficulty in climbing stairs and also had frequent episodes of buckling while walking. She required support from getting up from chairs since 1 month and had difficulty in getting up from bed.

Her past medical history was taken which revealed that the patient was known case of type 1 diabetes mellitus, diagnosed with atrial fibrillation with fast ventricular rate 9 months back and was prescribed amiodarone (Cordarone) 200 mg thrice daily during her course of hospital stay which was reduced to 100mg twice daily on discharge. On follow up amiodarone therapy was changed to 100mg /200mg once daily on alternate day dosing to be continued. Patient started showing weakness after 7 months of amiodarone therapy.

During initial examination, the patient was conscious and had Glasgow coma scale score of 15/15. Her vitals were found to be stable and extra ocular movements were full with no ptosis. On physical examination power in upper limb was 5/5. Lower limb bilateral hip flexion/extension 1/5 with hip abduction and adduction 5/5 and 2/5 respectively. Knee extension and knee flexion were 4/5 and 3/5. Ankle dorsal flexion and plantar flexion were 4+/5 and 5/5 respectively. Neck flexion/extension were found to be strong and all DTR (deep tendon reflexes) were sluggish. Her sensory system were found to be normal and she had waddling gait.

For further assessment, she was admitted and her neuroelectrophysiology study done which showed evidence for mild demyelinating polyneuropathy affecting both limbs. MRI LS spine with whole spine screening was performed which showed normal lumbar

spine with no significant bulges. There was a T2 hyperintensive lesion in posterior half of D7 vertebral body-possibly vertebral hemangioma. Straightening of cervical spine with disc dessication at multiple levels. Disc osteophyte complexin the C3/C4, C4/C5, C5/C6 levels causing less than 50% narrowing of anterior thecal space no significant spinal canal stenosis was reported. Her laboratory investigation showed normal CPK value of 88 IU/L (normal range: 25-200 IU/L) and vitamin B12 value of 258 pg/mL (normal range: 190-950 pg/mL). Investigations also revealed significantly decreased vitamin D levels of 7.09 ng/ml (normal range: 20 -29 ng/ml). Her HbA1c (glycosylated hemoglobin) levels showed significant increase with a value of 12% (normal range: 4%-6%). Arterial Doppler study was done for both lower limbs and showed no evidence of arterial obstruction. In view of pure proximal weakness involving only lower limbs she was advised clinical exome sequencing and muscle biopsy to bystanders which was refused.

MANAGEMENT AND OUTCOME

After initial assessments, the patient was started on vitamin supplementation with IV Rexite Plus (Pyridoxine HCl, Mecobalamin and Nicotianmide combination) given on day 1 and switched to oral vitamin supplementation for the remainder of hospital stay. Decreased vitamin D levels were managed with IM. Arachitol injection (vitamin D3 60k) given stat and then supplemented orally with weekly once dosing. Elevated blood sugar levels were managed with insulin therapy which was administered according to GRBS. Upon endocrinology consultation, patient was also administered oral hypoglycemics to further control glycemic levels.

In view of suspicion of amiodarone induced proximal myopathy, physiotherapy was started and Amiodarone dosing was reduced to 100mg once daily according to the ECG findings. Physiotherapy of grade 1 that used small movements of the spine performed within the spines resistance was done and by the second day of physiotherapy, the patient's power improved with her right flexion 3/5 and knee extension 4+/5. She was symptomatically better and discharged with vitamin D supplements and instructions to continue past medications along with physiotherapy and follow up after 2 weeks. Physiotherapy was done for the next 2 weeks after discharge with exercise therapy grade 1 along with gait training. By the end of 2 weeks, the patient's condition further improved and was able to perform 'sit to stand' with mild to moderate support. On the following outpatient visits, the patient showed significant improvement in her condition and was seen to perform activities like climbing stairs without support.

DISCUSSION

Amiodarone is a highly effective anti-arrhythmic drug but its numerous adverse effects often limits its use in clinical setting. Adverse effects such as discoloration of skin, thyroid dysfunction, hepatitis and pulmonary fibrosis have been documented.[2] Amiodarone-related neurotoxicities commonly reported are ataxia, tremor and peripheral neuropathy. A study conducted by Palakurthy and colleagues reported approximately 45 % of its study population showing amiodarone-related neurotoxicities of which 4 patients showed proximal myopathy. Development of neurotoxicity due to amiodarone can neither be related to age or cumulating drug dose.[3] According to a case reported by Michael Stanton et al of the University of Calgary (Canada), a female patient with significant atrial fibrillation presented with signs of weakness related to amiodarone therapy. Her symptoms resolved after discontinuation of offending drug.[4] Similarly, another case reported by K Itoh et al of the Nagoya University (Japan) described a male patient with sustained ventricular tachycardia on amiodarone 400mg/day presented with symptoms of severe myolysis and elevated CPK values. His symptoms gradually decreased after the dose was reduced to 250mg/day.[5] The majority of amiodarone induced side effects reported resolves after either discontinuation of drug or by decreasing its dose and frequency of administration. Evidences we have provided show lower limb neuropathy was not secondary to diabetes mellitus type 1. Vitamin B12 deficiency was also ruled out. Unusual features of this case were the decreased vitamin D levels and normal CPK levels along with short duration of amiodarone therapy. The degree of myopathy may not always correlate with CPK levels in amiodarone induced cases. In this case patient was initially treated with vitamin supplementation and hypoglycemic drugs to rule out other possible causes of myopathy and prevent further complications. The short duration of amiodarone therapy also does not exclude amiodarone induced myopathies. It is optimal to perform a muscle biopsy to confirm the causal relationship between drug and reaction but often avoided due to risk associated with the procedure.

CONCLUSION

Amiodarone induced neurological manifestations are often manageable with discontinuation of drug or by decreasing its dosage. Fewer cases has been reported that have caused neurological disabling in certain patients and in some cases were the adverse effects were not reversible even after withdrawal of drug. This is a non-fatal case in which patient showed recovery following vitamin supplementation and short term physiotherapy. The patient further recovered from her condition and showed better improvement in muscle power and mobility when amiodarone dosage was reduced. Thus, Amiodarone even with its significant cardiac benefits, also presents a variety of side effects, which if identified and managed at early stages can prevent further complications and help improve patient's overall life quality.

ACKNOWLEDGEMENTS
The authors would like to thank the management of Lourdes hospital and St Joseph's College of Pharmacy for their support and encouragement.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

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