Case Report

Drug Related Crisis in Myasthenia Gravis

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Abstract

Myasthenia gravis is an autoimmune disorder where antibodies against the nicotinic Ach receptor resulting in impaired transmission at the NM junction. A number of drugs have been reported to cause neuromuscular blockade and / or to increase weakness in myasthenia gravis. We report a case of myasthenia gravis in which the calcium channel blocker-nifedipine caused the worsening of the symptoms. ©

Introduction

Myasthenia gravis is an autoimmune disorder with an antibody-mediated pathogenesis. Antibodies directed against the nicotinic Ach receptor on skeletal muscle are responsible for impaired transmission at the NM junction, resulting in muscle fatigability and weakness. The hallmark clinical features of myasthenia are weakness and muscle fatigability. Symptoms include diplopia, ptosis, difficulty in chewing and swallowing, dysarthria, proximal muscle weakness and shortness of breath. The most common muscle involved in descending order of frequency, are the extra ocular muscles and levators of eyelids, proximal limb muscles (especially deltoid, and triceps) muscles of facial expression, mastication, and speech and neck extensors. Treatment mainly consists of Acetyl cholinesterase agents. These include pyridostigmine and neostigmine. These drugs prolong the action of acetyl choline by slowing its degradation at the neuromuscular junction, there by enhancing neuromuscular transmission.

Case Report

Mr S 40 year old from Chennai, admitted with complaints of difficulty in breathing and difficulty in swallowing. Patient was apparently normal 2 years back and he developed gradual onset of bilateral drooping of eyelids. He was evaluated and diagnosed as myasthenia gravis. Patient was prescribed Tab. Pyridostigmine 60mg thrice daily and Tab. neostigmine 7.5 mg bd. Patient was showing improvement of symptoms. Patient was recently diagnosed to have hypertension and started on nifedipine 10 mg bd.

On admission patient had dysphagia, slurred speech, nasal regurgitation, diplopia and fluctuating muscle weakness. On general examination, patient was dyspnoeic, had bilateral ptosis. Pupils were normally reacting and 3mm in size. No evidence of increased salivation or lacrimation. His pulse was 108 / m and, BP 140 / 100mm of Hg, respiratory rate was 36 / mt, and the temperature was normal. Systemic examination: cardiovascular system and abdomen were clinically normal. Respiratory system revealed decreased chest movement with no adventitious sounds. Single breath count was 7 / mt. CNS examination showed IIIrd, IVth and VIth cranial nerve weakness. Abduction and adduction movements were affected more than elevation and depression. Left eye is more affected than the right eye. Other cranial nerves were clinically normal. On examination of the spinomotor system, the bulk, tone, and tendon reflexes were normal. Power was 3/5 shoulder flexion and extension. Repeated injections of neostigmine along with atropine resulted in adequate improvement of signs and symptoms. Investigation showed, normal haemogram, blood sugar, urea, creatinine and electrolytes, CPK, ECG were within normal limits. CT scan chest and MRI of the patient done earlier were normal and showed no thymus enlargement. EMG was done and showed decremental response to repetitive nerve stimulation. Thyroid test function, RA factor, ANA were within normal limits. Lung function test showed decrease in FEV_1 and forced vital capacity.

After the initial improvement, patient began to show decline in respiratory effort and started deteriorating on the second day. The dose of T. pyridostigmine and Neostigmine was stepped up (60 mg qid and 15 mg tds respectively) along with nifedipine for control of hypertension. Despite the increase in the dose of pyridostigmine and injection neostigmine patient did not show adequate improvement. Considering the earlier reports that calcium channel blockers can worsen the symptoms we elicited the history. Patient felt that there was worsening of the symptoms since he was started on antihypertensive drug. Hence Nifedipine was withdrawn and substituted with ACE inhibitors. The

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Drugs known to exacerbate myasthenia gravis

1. D-Penicillamine should never be used in myasthenic patients.
2. The following drugs produce worsening of myasthenic weakness in most patients who receive them.

Succinylcholine, D-tuborcurarine, or other neuromuscular blocking agents
Quinine, quinidine, and procainamide
Aminoglycoside antibiotics, particularly gentamycin, kanamycin, neomycin, and streptomycin
Beta blockers : propranolol, timolol maleate eyedrops
Calcium channel blockers
Magnesium salts (including laxatives and antacids with high Mg concentrations)
Iodinated contrast agents

patient showed remarkable improvement within 12 hrs. His ventilatory function and his symptom improved dramatically. His requirement of pyridostigmine (30 mg bd) and Neostigmine (7.5 mg od) also came down. Since there was an earlier report of worsening of MG symptoms and death with nifedipine we did not reintroduce nifedipine to the patient. Patient completely recovered and was discharged.

Discussion

Myasthenia gravis is a common problem if not adequately treated patient may land up in a crisis. There are various precipitating factors, which can adversely affect the outcome of the disease, in particular, drugs. Drugs that worsen myasthenia gravis include neuromuscular blocking agents such as D-tubocurarine and pancuronium. Depolarizing agents such as succinyl choline, antibiotics like, aminoglycosides, quinine, procainamide, β blockers also increase the weakness. Calcium channel blockers also known to exacerbate the weakness in myasthenia gravis.[1]

Swash[2] *et al* has reported a case of myasthenia gravis exacerbated by taking verapamil[2] and later was substantiated by Lee and Ho with evoked electromyographic response in myasthenia patients. Nogues[3] reported worsening of the myasthenic symptoms and death in a patient due to nifedipine.[3] This was not accepted by Swash who believed the nifedipine could not have caused the exacerbation but by the steroids.[4] Pina latorre[6] *et al* reported another 2 cases of myasthenia gravis exacerbated by nifedipine and felodipine both belonging to dihydropyridine group.[6]

In our case, the case is diagnosed as myasthenia gravis. Starting the patient on nifedipine for hypertension worsened the symptoms gradually. Withdrawal of nifedipine without beginning any specific treatment with azathioprine or prednisolone led to an obvious improvement in symptoms. The mechanism by which calcium antagonist produce neuromuscular blockade has not been well defined. These drugs act at the neuromuscular plaque at both presynaptic and postsynaptic levels. At the presynaptic level, calcium antagonists through interaction with "L" type channels could reduce the nervous transmission without affecting "N" type channels.[5] The post-synaptic effect could be similar to that of acetylcholine receptor blockers. The safety margin at neuromuscular junction is decreased in known cases where CCB are used.

Although we believe that more research is needed on the relationship between calcium channel blockers on neuromuscular transmission, we feel that calcium channel blockers are better avoided in patients with myasthenia gravis.

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