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ATORVASTATIN INDUCED INSOMNIA: A CASE STUDY

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ABSTRACT

Hypercholesteremia is managed and treated with statin medication. They are also used in cardiovascular disease, stroke and are contraindicated in liver disease. This case report describes and highlights a relatively unknown adverse effect of atorvastatin - insomnia.

KEYWORDS: Atorvastatin, Insomnia, Statins, Hypercholesterolemia.

INTRODUCTION

Hypercholesterolemia is one of the leading causes of Coronary Heart disease and cerebrovascular diseases. The clinical benefit is obtained by lowering LDL cholesterol. Statins are being used in cardiovascular diseases even without hypercholesterolemia due to their effect in increasing HDL cholesterol. They are the first line drugs for treatment of hypercholesterolemia The agents are namely atorvastatin, rosuvastatin, simvastatin, lovastatin, fluvastatin etc.

Statins are HMG CoA Reductase inhibitors used widely as lipid lowering agents. They reducecholesterol synthesis in the liver by preventing the conversion of HMGCoA enzyme to mevalonate. Thus they reduce LDL, VLDL, apolipoproteins B, TG and increase HDL. They are well tolerated drugs with rare serious adverse drug reactions reported in the clinical trials and post marketing surveillance.[1] The rare ADRs reported include muscle weakness, liver and kidney damage. CNS effects are also recently being reported nowadays. As lipids being one of the main components of CNS and myelin sheaths and synapses, the risk of CNS effects should be considered. The CNS effects include memory loss, depression, insomnia, suicidal thoughts, anti-social behaviours etc.[2]

Statins act by lowering the plasma cholesterol thus affecting the brain cholesterol mechanism. Lipophilic statins directly affect the brain cholesterol metabolism, crossing the blood-brain barrier and inhibiting the cholesterol synthesis in the nerve cells. According to a theory proposed by Engelberg, lowering the cholesterol level in the brain cell membrane leads to lower lipid microviscosity. This decreases the synaptic binding and exposure thus affecting the neurotransmitter exposure leading to transient cognitive and psychological dysfunction.[3]

CASE REPORT

A 63 year old male patient came to General medicine OPD for regular check up. He was a known case of Systemic hypertension for 1 year. On examining he had normal bowel and bladder, adequate sleep quality and no shortness of breath on exertion. Routine blood check up revealed Deranged Fasting Lipid Profile with elevated total cholesterol (257 mg/dl), triglycerides (361 mg/dl), LDL (143 mg/dl) and VLDL (72 mg/dl). Considering elevated Lipid profile, lipid- lowering drug was initiated. Fenofibrate 145 mg once a day in the evening was given for 3 months. On the next follow up after 3 months, the total cholesterol did not show a decreasing trend and it was still elevated (Total cholesterol - 262 mg/dl). Thus atorvastatin 5 mg was added along with fenofibrate. After 7 days the patient came to the OPD with the complaints of severe sleep disturbances for a few days. Atorvastatin was suspected to be the cause of insomnia. Thus atorvastatin was withdrawn in-view-of severe insomnia and ezetimibe 10 mg was added. The patient was given Melatonin 6 mg at bedtime. On next review, after 1 month, he had improved cholesterol level and sleep was restored after withdrawal of Atorvastatin.

DISCUSSION

Statin medication, which is often safe and well tolerated, is the cornerstone for both primary and secondary prevention of cardiovascular disorders. A growing body of data from the US Food and Drug Administration's Adverse Event Reporting System (FAERS) suggests that using statins increases the risk of sleep disorders, including insomnia.[4] There are studies suggesting that cognitive impairment is mostly associated with moderate or high intensity statin therapy. Among lipophilic statins, atorvastatin and simvastatin have a greater degree of lipophilicity, thus they are mostly associated with more incidence of cognitive impairment. Other lipophilic statins like fluvastatin, lovastatin, and pitavastatin undergo extensive first pass metabolism, and are bound to plasma protein while atorvastatin have a longer half-life of

about 11 - 30 hours. This is thought to be the reason for its highest association with cognitive impairment.[5]

CONCLUSION

Atorvastatin can potentially cause sleep disturbance. Due to the longer half life of atorvastatin, it remains in the body for quite a long time. This may be the reason for it to cause cognitive impairment like insomnia. Further studies are required to establish the correlation between statins and sleep rhythm.

Conflict of interest

There is no conflict of interest.

Abbreviations

LDL - Low density lipoproteinHDL- High density lipoprotein

HMG CoA- Hydroxymethylglutaryl Coenzyme AVLDL- Very low density lipoprotein

TG- Triglyceride

ADR- Adverse drug reaction CNS- Central nervous system

FAERS- Food and Drug Administration's Adverse Event Reporting System

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