

Atorvastatin Induced Constipation

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Abstract

A 72-year-old with high cholesterol levels (Hypercholesteremia) was advised to take Atorvastatin 20 mg (Atorva-20 mg) which led to constipation and abdominal discomfort. As management, the Atorvastatin was discontinued and replaced with Rosuvastatin. The symptoms of constipation were reduced after cessation of the suspect drug Atorvastatin. The possible mechanisms for the event were unknown but has some proposed mechanisms like 1. Levels of Nitric oxide 2. Inhibiting the production of melvonic acid 3. Decrease in coenzyme Q10.

Keywords: Atorvastatin; adverse event; Constipation; Naranjo scale, Melvonic acid, Coenzyme Q10

Abbreviations

HMG-CO A reductase: 3-hydroxy-3-methyl-glutaryl-coenzyme a reductase.

NO: Nitric oxide.

Introduction

Atorvastatin is an Anti-lipidemic drug that belongs to HMG-CoA reductase class of drugs [1]. Atorvastatin inhibits an enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. This inhibition prevents the conversion of HMG-CO A to mevalonate. Thus, helps in decreasing the production of Cholesterol in the Liver [2]. The adverse events associated with Atorvastatin are Myopathy, Rhabdomyolysis, and Liver enzyme abnormalities [3]. Other common side effects of atorvastatin include diarrhoea, constipation, joint pain, nausea, heart burn fatigue [4].

According to NCI Dictionary, Constipation is a condition in which stool becomes dry, hard, difficult to pass, and bowel movements don't happen very often. It may also include painful bowel movements, feeling bloated, uncomfortable [5].

Case Report

A 72-year-old was advised to take Atorvastatin 20 mg (Atorva-20 mg) for high cholesterol levels (Hypercholesteremia) which led to constipation and abdominal discomfort. The past medical history includes Diabetes mellitus for 10 years and Hypertension for 10 years. The concomitant medications include a combination of Chlorthalidone-12.5 mg, Olmesartan-20 mg, and Amlodipine 5 mg for Hypertension and for Diabetes mellitus she was on Metformin-500 mg and Glibenclamide 5 mg. As on a normal body checkup the patient was found to have higher cholesterol levels for which atorvastatin 20 mg was prescribed but after using it for 2-3 days patient found difficulty in passing stools and had an abdominal discomfort and the patient discontinued the atorvastatin. After two months

when visiting the hospital for a normal checkup patient informed that she discontinued Atorvastatin and she informed that symptoms of constipation were reduced after cessation of Atorvastatin. As a management Atorvastatin was replaced with Rosuvastatin-20 mg by the physician.

Discussion

As per the patient, the atorvastatin has caused constipation, there is no actual mechanism for this event but has some proposed mechanisms which are.

1. Levels of Nitric oxide
2. Inhibiting Production of melvonic acid
3. Decrease in coenzyme Q10 [6].
1. R Tomita et al performed on physiological nerve study on the human colon and concluded that Nitric Oxide plays an important role as a neurotransmitter in nonadrenergic noncholinergic inhibitory nerves of the human colon [7]. Nitric oxide synthase activity is increased by Atorvastatin [8]. Hence this might be one of the reasons for the Atorvastatin induced constipation.
2. The melvonic acid leads to the production of cholesterol. The cholesterol synthesis pathway includes the conversion of HMG-CO A to mevalonate with HMGR enzyme which ultimately leads to the production of Cholesterol in humans. This step is blocked by Statin which causes decreased production of cholesterol [9]. According to some studies and proposals stating that cholesterol is important for bile production [10]. Thus, decreased cholesterol production may cause low bile. Hence low bile production may cause decreased bowel movements and constipation [11].
3. Atorvastatin will also cause a decrease in coenzyme Q10 [12]. Q10 is an antioxidant and co-enzyme which helps in almost all body processes like digestion of food, muscle, cell repair, etc. hence depletion in this coenzyme due to atorvastatin may also cause constipation [13].

Naranjo scale

The assessment for the event is assessed below in the Naranjo Adverse Drug Reaction Probability scale:

Naranjo Adverse Drug Reaction Probability Scale				
Question	Yes	No	Do Not Know	Score
1. Are there previous <i>conclusive</i> reports on this reaction?	+1	0	0	0
2. Did the adverse event appear after the suspected drug was administered?	+2	-1	0	2
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was administered?	+1	0	0	1
4. Did the adverse event reappear when the drug was re-administered?	+2	-1	0	0
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	+2	0	2
6. Did the reaction reappear when a placebo was given?	-1	+1	0	0
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	0	0
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	+1	0	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0	1
TOTAL SCORE:				06

Modified from: Naranjo CA et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther 1981; 30: 239-245.

Figure 1: The Naranjo scale.

According to the Naranjo scale (Figure 01), the total score obtained was 06 for which event can be interpreted as Probable [14].

Conclusion

Hence from the report, atorvastatin has caused constipation due to discussed possible mechanisms, and the event was interpreted as Probable.

Precautions/Things to consider while taking Statins

The precautions to be followed while taking atorvastatin were as follows:

- Avoid taking high cholesterol foods.
- Drink plenty of water and fluids to maintain bowel movements.
- Avoid caffeine-related foods.
- Avoid alcohol and grapefruit [15].
- Add CQ10 Supplements to daily routine [16].

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