Chest pain as a possible side effect of pitavastatin (Livalo)

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Abstract:
Coronary heart disease is a serious complication of dyslipidemia. Pitavastatin is a more commonly prescribed medication for the treatment of dyslipidemia. Here, we report the case of a 37-year-old female, a known patient with well-controlled bronchial asthma. She was recently found to be dyslipidemic and started on pitavastatin calcium 4 mg once a day (OD). On the 10th day of treatment, she began to have crushing chest pain and was admitted to the hospital. All investigations for coronary heart disease came out negative. Her symptoms improved dramatically when pitavastatin was stopped. Pitavastatin is reported to cause myalgia and muscle spasm, especially at higher doses. There is evidence in literature that this medication might cause chest pain in old obese ladies if taken at high doses. We report this case as a possibility of chest pain even in younger females.

Keywords:
Chest pain, dyslipidemia, pitavastatin

Introduction

Pitavastatin is a synthetic hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitor (HMG-CoA inhibitor) used to lower serum levels of total cholesterol, low-density lipoprotein cholesterol (LDL-C), apolipoprotein B, and triglycerides and raise levels of high-density lipoprotein cholesterol (HDL-C).[1] It was introduced into the market in Japan in September 2003 (Livalo Effectiveness and Safety study[2] and approved by The US Food and Drug Administration (USFDA) in August 2009 for the treatment of primary hyperlipidemia and mixed dyslipidemia. Pitavastatin calcium (Livalo-Kowa pharmaceutical) is available as an oral tablet in different strengths: 1, 2, and 4 mg.

Statins inhibit HMG-CoA as a rate-limiting step in cholesterol biosynthesis. Statin therapy has been shown to be effective in lowering LDL-C levels by 20%–50%, as well as lowering triglyceride levels by 10%–20% and causing a possible rise in serum HDL-C levels by 5%–10%.[3] These types of statins have been one of the most widely prescribed groups of drugs in the world since their introduction into the market more than 20 years ago.

Although pitavastatin, like many medications, has many adverse side effects enumerated by the manufacturer, muscle pain is not one of them. The manufacturing company reports that it could cause myopathy and rhabdomyolysis in an old female if taken at a higher dose. We report the case of a 37-year-old female who presented with genuine chest pain as an adverse effect of this medicine.

Case Report

A 37-year-old female, a known case of bronchial asthma since childhood and who was on inhalers, was diagnosed about 2 months ago as hyperlipidemia and started on pitavastatin calcium 4 mg once daily, by her cardiologist 7 weeks ago.

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She presented to the emergency room complaining of chest pain, a characteristic chest wall pain which was crushing in nature but with no cardiac origin. It had begun gradually 10 days before, was retro-ternal, was non-radiating, was severe 10/10 (visual analog pain scale), was aggravated by minimal exertion, and was relieved by rest. It was associated with shortness of breathing on exertion. There were no palpitations, syncopal attacks, nor fever. There was no past medical history of a similar condition and no previous hospitalization. Her bronchial asthma was well controlled on inhalers. She had no family history of similar condition and not known to have any other comorbidities. She is not a smoker and does not drink alcohol. She is a medical staff by profession and unmarried. On examination, she looked anxious, not distressed, fully conscious, and oriented.

The patient noticed that she had put on about 10 kg of weight in the previous 6 weeks. Before taking pitavastatin, she weighed 85 kg, and her height was 163 cm. Her weight had risen to 95 kg after she began pitavastatin. Her body mass index (BMI) was 35.8.

Her blood pressure was 130/80 and heart rate was 86/min, regular. Cardiovascular examination was uneventful. Respiratory system was normal apart from a drop in oxygen saturation from 99% to 94% on walking a short distance. Abdomen was soft, not tender, and no mass was detected. There was no dependent edema.

One month before presentation, the lipid profile was as follows: serum cholesterol 8.2 mmol/L, LDL 6.24 mmol/L, HDL 1.63 mmol/L, and triglyceride 1.14 mmol/L, then dropped after 1-month treatment with pitavastatin to serum cholesterol 5.8 mmol/L, LDL 3.43 mmol/L, KDL 1.80 mmol/L, and triglyceride 0.85 mmol/L. Hemoglobin concentration: 12.7 g/dl, white blood cells: 11.2 x 10^9/µl, platelets: 164 x 10^3/µl, serum urea: 3.6/µl, creatinine: 0.7 µmol/L, serum sodium: 139 mmol/L, serum potassium: 3.9 mmol/L, serum osmolality: 281 mosm/kg, total protein: 73 g/L, albumin: 41.3 g/L, aspartate aminotransferase: 23 µmol/L, alanine transaminase: 23 U/L, Vitamin D: 65, and troponin: 0.0004. Repeated serial troponin was normal as well creatinine kinase and creatinine kinase-muscle/brain. She had a normal thyroid function test. Electrocardiogram revealed normal sinus rhythm. Echocardiogram, chest X-ray, and ultrasound abdomen were all normal.

Computed tomography (CT) pulmonary angiogram showed no pulmonary embolism. CT coronary angiography showed normal coronary arteries, no coronary arteries atherosclerosis, and no stenosis.

The patient was admitted to the cardiac ward and started on telemetry observation. Arterial blood gas analysis was normal, and a 6-min walk test revealed a drop in oxygen saturation from 98% to 91% in room air, associated with severe crushing chest pain which affected her breathing. Pulmonary function test and sleep study were normal.

Although rapid weight gain was to blame for all of these symptoms, all the investigations were negative. The patient was reassured that it was neither an acute coronary syndrome nor coronary artery disease and was discharged after 4 days of admission with full investigation and assessment of her chest pain.

The patient stopped pitavastatin on her own as a trial as she had read about its side effects especially with regard to chest pain. After 3 days, her chest pain and all symptoms such as insomnia subsided and completely disappeared. Accordingly, a final diagnosis of pitavastatin-induced chest pain was made, as a rare side effect of the medication.

**Discussion**

Pitavastatin has many side effects as most of the statin medications do. The manufacturer gives warning of many adverse reactions of this medication. The list of all side effects and their percentage is shown in Table 1.[4] Back pain and pain in the extremities are indicated, but are not dose related; however, myalgia is reported as a dose-related side effect. Previous studies have shown that some side effects such as myalgia and muscle spasm can occur at high doses.

USFDA has reported that until March 2018, the incidence of chest pain in people taking this medication has been 1.99%.[5] Moreover, USFDA reports that chest

**Table 1: Adverse reactions* reported by patients treated with Livalo and placebo in short-term controlled studies**

| Adverse reaction | Placebo (n=208) | Livalo 1 mg (n=309) | Livalo 2 mg (n=951) | Livalo 4 mg (n=1540) |
|------------------|-----------------|---------------------|---------------------|---------------------|
|                  | %               | %                   | %                   | %                   |
| Constipation     | 1.9             | 3.6                 | 1.5                 | 2.2                 |
| Myalgia          | 1.4             | 1.9                 | 2.8                 | 3.1                 |
| Weight gain      | -               | -                   | -                   | 14.71               |
| Extremity pain   | 1.9             | 2/3                 | 0.6                 | 0.9                 |
| Chest pain/dyspnea | -             | -                   | -                   | 11.76               |

*Adverse reactions by MedDRA preferred term*
pain is a recognized side effect of pitavastatin (Livalo), especially in obese females above 60 years of age, taking this medicine at the maximum dose for <1 month. Our case, although young, had most of the above-mentioned aggravating factors. Her BMI was 35, and she went on a high dose to reduce her cholesterol blood level. This case shows a strong association between the removal of this medication from blood and the cessation of chest pain. It illustrates the importance of pitavastatin as a cause of chest pain which can present with varying degrees of severity that demand admission and investigation.

Conclusion

Chest pain can be related to high doses of pitavastatin in middle-aged obese female patients. The causality of this side effect needs further studies.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understood that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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