Fenofibrate-induced myopathy

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Fenofibrate induced myopathy is a rare adverse event. We present a case of muscle pain and quadriplegia following administration of 200mg of fenofibrate for 35 days. Patient gradually improved after stopping the drug. As per our knowledge, this is probably the first case report of fenofibrate induced myopathy from India.

**Key Words:** Drug induced myopathy, Fenofibrate

**Introduction**

Drug-induced myopathies are rare adverse drug reactions (ADR) seen more regularly after the introduction of modern lipid-lowering drugs. We present a case of myopathy following treatment of hyperlipidemia with fenofibrate. As per our knowledge, this is the first case report of fenofibrate-induced myopathy from India.

**Case Report**

A 58-year-old male suffering from ischemic heart disease and hypertriglyceridemia was prescribed isosorbide mononitrate 30 mg daily and fenofibrate 200 mg daily. He noticed severe pain in the calves associated with weakness after 5 weeks. Fenofibrate was stopped after four days of onset of pain. His symptoms progressed requiring admission six days after onset of symptoms. He denied history of sensory symptoms and bowel bladder disturbances. His pain increased in intensity and ascended to involve the thigh, hip, shoulders, and elbow. There was history suggestive of weakness of the small muscles of the upper and lower limbs and mild tenderness of the proximal muscles. His maximal weakness was observed on the ninth day following the onset of weakness and five days after the discontinuation of fenofibrate. There was no history of swelling, redness, flier of muscles or atrophy. There was no history suggestive of any weakness in the muscles supplied by the cranial nerves, alteration of higher mental function, seizure, headache, vomiting. There was no history of fever; no history of passage of “cola”-colored urine. He was non-hypertensive, non-diabetic. There was no history of similar muscle weakness in the past. There was no family history of similar illness. There was no history of concomitant administration of drugs like gemfibrozil, erythromycin, etoposide, ketoconazole, and high-dose corticosteroids. There was no history of ingestion of organophosphorus compounds or alcohol intake.

On clinical examination he had no abnormality in general survey. There was no postural hypotension. Neurological examination revealed no abnormality in higher mental function and cranial nerves. Motor system examination did not reveal any obvious wasting or fasciculations in any muscle. There was tenderness over proximal muscles. The tone in both the upper and lower limbs was reduced. Power in the upper limbs was Grade 2 and in the lower limbs Grade 1. There was severe weakness in the small muscles of both the upper and lower limbs. There was some differential involvement as evidenced by his ability to flex the fingers with difficulty but inability to open them at all. He also had weakness of the truncal muscles. Sensoric system examination was normal. Examination of the reflexes showed absent jaw jerk. Biceps, supinator and triceps jerks were diminished. Knee and ankle jerks were absent. Abdominal, cremasteric reflexes were normal. Plantars were flexors. Coordination in the upper limbs was normal. In the lower limbs it could not be tested. Investigations showed; serum creatinine phosphokinase (CPK) 1129 U/L (normal 25-90 U/L); serum aldolase 24 U/L (normal up to 6 U/L); serum potassium 4.5 meq/L; serum cholesterol 203mg/dL; serum triglyceride 334mg/dL; serum TSH 0.8u/L; urine for myoglobinuria – negative. EMG and NCV study of all the four limbs suggested myopathy.

The patient’s maximal weakness was observed on the ninth day following the onset of weakness and five days after the discontinuation of fenofibrate. The patient started improving on the seventh day following stoppage of the offending drug. His CPK and aldolase started declining from the seventh day. They reached the baseline after one month following maximal weakness and his muscle power at that time was Grade 4+.

**Discussion**

Fenofibrate is a derivative of fibric acid. It reduces very low density lipoprotein (VLDL) and triglyceride, while increasing high density lipoprotein (HDL) and lowering low density lipoprotein (LDL) as well as total plasma cholesterol. Fenofibrate is 99% protein-bound with a half-life of about 20 hours and 80% is excreted in the urine. One of the most serious side-effects of the drug is myopathy and rhabdomyolysis. Our patient developed myopathy after taking fenofibrate 200mg for 35 days. Rapid improvement of the patient’s weakness and decrease in muscle enzymes following stoppage of fenofibrate suggested that the patient was suffering from drug induced myopathy. Also, there was no other discernable cause for myopathy. The exact cause of fribrate myopathy is unknown.
But several clinical features mark fenofibrate myopathy as toxic in nature: lack of pre-existing muscular symptoms, delay in onset of symptoms after exposure to fenofibrate, lack of any other cause for myopathy and almost complete resolution of symptoms after stoppage of fenofibrate. Basic pathological changes are noted as necrosis and regeneration. Fibrates usually produce painful myopathy without polymyositis. Endocrine, metabolic and genetic factors might play a role in the pathophysiology. There are case reports of hypothyroidism and rhabdomyolysis by a fibrate, mainly fenofibrate. Fenofibrate-induced rhabdomyolysis in two dialysis patients with hypothyroidism has been reported. Hypothyroidism as well as increased plasma level of fenofibrate due to renal failure have been implicated as precipitating factors in these cases. Myoglobinuria depends upon the rapidity and degree of muscle necrosis. Our patient did not complain of “cola”-colored urine and urine for myoglobin was negative.

The most important issue is the early diagnosis of the condition and stoppage of the drug, so that the patient recovers early. Our patient started recovering seven days following the stoppage of the drug. Any volume depletion should be corrected. Alkalization of the urine is required if there is myoglobinuria. Rechallenge of the treatment is not advisable because of the risk of a serious relapse. Thyroid and renal dysfunction increase the chance of myopathy and should be checked in patients to be treated with fenofibrate. One should be very cautious while using fenofibrate in conditions predisposed to rhabdomyolysis like severe infection, major surgery, hypotension, volume depletion, trauma, severe metabolic or electrolyte imbalance. Similar care should be taken when fenofibrate is co-administered with statins, erythromycin, ketoconazole, and cyclosporin. The patient should be asked to stop the intake of fenofibrate and report immediately if muscle pain/weakness develops.

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References


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