

# Undiagnosed Hypothyroidism: Culprit for Fenofibrate Induced Rhabdomyolysis

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## Abstract

Fenofibrate induced rhabdomyolysis is not very common event. We present a case of muscle pain and generalized weakness following administration of fenofibrate for 10 days in undiagnosed hypothyroidism. Patient gradually improved after stopping the drug. As per our knowledge, this is probably the first case report of fenofibrate induced rhabdomyolysis from Nepal.

**Keyword:** Fenofibrate, hypothyroidism, rhabdomyolysis.

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## Introduction

Hypothyroidism on many occasions may remain undiagnosed as symptoms of hypothyroidism are vague. There are many clinical situations in which patients are taking different medicines in the case of undiagnosed hypothyroidism.

Fibric acid derivatives such as fenofibrate increases high density lipoprotein (HDL) and lowers low density lipoprotein (LDL), total plasma cholesterol, very low-density lipoprotein (VLDL) and triglyceride. Fenofibrate has half-life of about 20 hours, is 99% protein-bound with 80% excretion via urine. One of the most serious side-effect is rhabdomyolysis and myopathy.<sup>1</sup>

Myopathy in hypothyroidism generally present as elevation of serum creatinine phosphokinase (CPK), muscle pain and stiffness, proximal muscle weakness and cramps.<sup>2,3</sup> Rhabdomyolysis is a syndrome involving skeletal muscle necrosis and the consequent release of intracellular muscle proteins and electrolytes into the systemic circulation. Its severity is variable, ranging from asymptomatic elevations in serum muscle enzymes levels to life-threatening electrolyte disturbances and acute renal failure.<sup>4</sup> The typical clinical presentation includes muscle weakness, myalgias and dark-colored urine due to myoglobinuria, and the diagnosis is usually established by elevated serum skeletal muscle enzyme levels.<sup>5</sup> Creatinine phosphokinase is the most sensitive indicator of muscle injury and, although there is no defined serum cut-off level for the diagnosis, many clinicians use five to ten times the upper limit of normal range.<sup>6</sup> Only few articles have been reported on fenofibrate induced rhabdomyolysis in patients of hypothyroidism

in other settings.<sup>1,7</sup> No case have been reported in the settings similar to ours as per our best knowledge. We report a case of 38 years male of undiagnosed hypothyroidism culprit for fenofibrate induces rhabdomyolysis.

## Case report:

A 38 years male, non-smoker, non-alcohol consumer, known case of systemic hypertension under medication, recently diagnosed as hypertriglyceridemia (triglyceride [TG] level of 6.5 mmol/L) and started on fenofibrate 160 mg since last 10 days came with complain of generalized weakness and bilateral pain in arms, thighs and buttocks since last 10 days. He denied any history suggestive of inherited muscle disease. He complained of undue fatigue and difficulty in mobilization. The patient was having inadequate urine output since same duration however there was no history of swelling of limbs. On examination, patient had generalized muscle tenderness and proximal muscle weakness.

The diagnosis of rhabdomyolysis in this patient was established on the basis of myalgia, muscle weakness, prominent elevation of serum levels of CPK, lactate dehydrogenase, aspartate aminotransferase and also creatinine. The fenofibrate was discontinued, thyroid hormone replacement was started with oral levothyroxine (50mcg/day) and intravenous fluid replacement with normal saline was started. The urine output was normalized, and serum urea and creatinine decreased to normal values during hospital stay. The patient's maximal weakness was observed on the seventh day following the onset of weakness. The patient started improving on the tenth day following stoppage of the offending drug.

Investigations at admission, discharge and follow up are shown in Table 1.

**Table 1:** Serial investigations of the patient from admission till follow up.

	At admission	After 1 week	After 1 month	After 3 months
CPK-TOTAL	39463 IU/L	29021 IU/L	474 IU/L	234 IU/L
CREATININE	1.3 mg/dL	1.2 mg/dL	0.9mg/dL	0.9mg/dL
POTASSIUM	4.0 MEQ/L	3.9 MEQ/L	5.1 MEQ/L	4.8 MEQ/L
ALT	501 IU/L	470 IU/L	24 IU/L	71 IU/L
AST	2076 IU/L	859 IU/L	20 IU/L	36 IU/L
TG	2.2 MMOL/L			3.3 MMOL/L
LDL	2.2 MMOL/L			1.6 MMOL/L
TOTAL CHOLESTEROL	4.3 MMOL/L			3.1 MMOL/L
URINE MYOGLOBIN	>12000 MICROGRAM/L			
TSH	137 uIU/ML		70.2 uIU/ML	2.87 uIU/ML

### Discussion:

Hypothyroidism is an established secondary cause of dyslipidemia, but it is also a potential risk factor of myopathy induced by lipid-lowering agents.<sup>8-11</sup> Fenofibrate monotherapy-induced rhabdomyolysis is very rare event. Thus, other risk factor like hypothyroidism should be suspected, in cases of fenofibrate induced rhabdomyolysis.<sup>12</sup> Once diagnosed, it is mandatory to stop fibrates and start IV hydration along with correction of hypothyroidism. Our patient started recovering after 2 days and his myopathy improved after 10 days. In cases of rhabdomyolysis, rechallenge of the treatment is not advised because of the risk of a serious relapse. Treatment of hypothyroidism itself should lower the TG level in these cases.<sup>13</sup> Isolated hypothyroidism leading to rhabdomyolysis is a rare and literatures have recommended to search for other precipitating factors like statin therapy and heavy exercise.<sup>14</sup> Our patient recovered completely after stopping fenofibrate and subsequently adding oral levothyroxine.

The study has few limitations. The demarcation of cause of improvement on the patient could have been contributed by both of the measures of adding levothyroxine and stopping fenofibrate. We didn't consider muscle biopsy and genetic testing in the patient as the patient recovered almost completely in follow up.

### Conclusion:

Hypothyroidism increase the chance of myopathy and should be checked in all patients of dyslipidemia who are planned to be treated with fenofibrate.

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