# HYPOTHYROIDISM IS A PREDISPOSING FACTOR FOR FENOFIBRATE-INDUCED RHABDOMYOLYSIS - PATIENT REPORT AND LITERATURE REVIEW

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**SUMMARY**

A literature survey reveals that both lipid lowering drugs - statins and fibrates - and hypothyroidism are documented causes of muscle disorders including rhabdomyolysis leading to acute renal failure. We describe a case of fenofibrate monotherapy (Lipicard®) induced dialysis dependent acute renal failure in an undiagnosed hypothyroid patient which is the first case to be reported from Sri Lanka. We strongly recommend that all patients who are receiving statins and/or fibrates should be screened for occult hypothyroidism which seems to aggravate the muscle damage due to the above drugs, with or without other risk factors.

**KEY WORDS**

hypothyroidsm, rhabdomyolysis, predisposing factor

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## INTRODUCTION

Fenofibrate, a fibric acid derivative, is currently recommended to treat diabetic dyslipidaemia and hypertriglyceridaemia. Fenofibrate, which has replaced older fibrates such as gemfibrozil and bezafibrate, is generally presumed to be a fairly safe drug in comparison to the former group. The British National Formulary warns that fibrates could cause a myositis-like syndrome, especially in those with impaired renal functions /1/. Both fenofibrate and hypothyroidism are well known causes of muscle damage and rhabdomyolysis. A literature survey did not reveal any documented instances of fenofibrate monotherapy-related rhabdomyolysis in hypothyroidism leading to dialysis dependant acute real failure, and the following report is probably the first of its kind.

## PATIENT REPORT

A 70 year-old man with a past medical history of hypertension and hyperlipidaemia presented with recent onset bilateral lower limb pain, weakness and backache of one week duration. There were no other significant symptoms except for lethargy, loss of appetite and reduced urine output. There was no history of a viral illness or alcohol consumption. His drug history revealed that he had been on nefidipine-SR 20 mg bid and fenofibrate (Lipicard®) 200 mg daily, prescribed by his general practitioner, which he had been continuing unsupervised for the last three months prior to presentation. Physical examination revealed clinical features of hypothyroidism and generalized muscle tenderness. The important abnormal laboratory parameters were as follows: creatinine phosphokinase (CPK) >7,500 units, blood urea 232 $mg.dl^{-1}$, serum creatinine 988 $\mu mol.l^{-1}$, TSH >75 $mlU.ml^{-1}$, and myoglobinaemia. A clinical diagnosis of severe rhabdomyolysis due to fenofibrate and hypothyroidism was made, and was treated accordingly including haemodialysis. His CPK level became normal within one month while the renal functions took several months to reach normal values, and the patient currently remains euthyroid on L-thyroxine.

## DISCUSSION

Hypothyroidism is a known endocrine cause of muscle disorders. The symptoms are often limited to myalgia, muscle stiffness and cramps, with elevated levels of muscle enzymes at times. Myxoedema and myopathy are well recognized, and severe rhabdomyolysis leading to acute renal failure had also being described /2-7/. Similarly, lipid lowering agents, both statins and fibrates, either as monotherapy or combined therapy, have also been found to cause myopathies and rhabdomyolysis /8-13/. In the USA, a study by Graham *et al.* found that the rhabdomyolysis risk was similar and low for monotherapy with atorvastatin, provastatin and simvastatin /14/. The use of combined statin and fibrates increased the risk, especially in older patients with diabetes mellitus /14/. Similarly, clofibrate induced myopathy in primary hypothyroidism /15/, and rhabdomyolysis-induced acute renal failure secondary to statin-fibrate combination in hypothyroidism has been documented /8,16,17/.

The exact mechanism of fenofibrate-induced muscle damage is unclear. An increased risk for adverse events was observed with gemfibrozil relative to fenofibrate, predominantly driven by an increased rate of rhabdomyolysis, which was particularly noticeable in patients who were taking a statin in addition /18/. Gliclazide may potentiate rabdomyolysis by fenofibrate /19/. Furthermore, fenofibrate induced rhabdomyolysis has been documented in haemodialysed patients with hypothyroidsm /20/. It seems that co-existing hypothyroidism predisposes to the potentiation of muscle damage by fenofibrate. In fact, hyperlipidemia itself could be a manifestation of occult hypothyroidism.

The present report describes fibrate monotherapy-induced severe rhabdomyolysis in a undiagnosed hypothyroid patient who previously had no documented renal disease. With the evidence available we recommend that hypothyroidism be listed as a predisposing cause for enhanced statin- and fibrate-induced muscle damage.

## CONCLUSION

This case is the first to be documented in Sri Lanka in which fenofibrate (Lipicard®) monotherapy caused severe rhabdomyolysis leading to dialysis dependent acute renal failure in an undiagnosed

hypothyroid patient who previously had no apparent renal disease, and to our knowledge there are no similar reported instances in the literature to date. As evident from our literature search, we strongly recommend that thyroid status be routinely assessed in all patients receiving lipid lowering drugs to minimize such catastrophes, particularly with patients who have other risk factors for fenofibrate induced muscle damage.

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