A CASE REPORT ON FENOFIBRATE AND ATORVASTATIN INDUCED – RHABDOMYOLYSIS

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Abstract

Background: Here we report a unique case study to report evidence of rhabdomyolysis caused by the interaction of fenofibrate and atorvastatin and to learn about a suitable alternative medication.

Methods: Case study as well as a review of the relevant literature.

Findings: A female patient of age 55 years was admitted to the hospital with complaints of cough, breathlessness, mild expectorate, fever, and pain near the chest for three days and a history of weakness. The patient has a past medical history of hypertension [treated with amlodipine] and diabetes mellitus [treated with tab glimepiride 2mg + metformin 500mg]. The patient's lab investigations showed decreased haemoglobin level [8.2gm/dl], packed cell volume [20.6], mean corpuscular volume [73.1], mean corpuscular haemoglobin [25.6], red blood cell [2.5mill/cumm] decreased count.

Implications: The patient had taken Fenofibrate and Atorvastatin, which will enhance the effects of one another through pharmacodynamic synergism. When combined with an optimal statin regimen to lower triglycerides and increase high-density lipoproteins, fenofibrate may increase the risk of rhabdomyolysis. Hence has to be monitored proportionately. As an alternative to Fenofibrate, Ezetimibe was given which resulted in no interactions that were previously seen and reported.

Keywords: Rhabdomyolysis, Hypertension, Fenofibrate, Atorvastatin, Pharmacodynamic synergism.

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INTRODUCTION

Rhabdomyolysis is characterised by a triad of symptoms, including myalgia, weakness, and myoglobinuria, which is manifested as the classically described tea-colored urine;[1] in addition, some people experience decreased urination, nausea, dehydration, and loss of consciousness. It can be fatal if left untreated. Even though it cannot be passed down from one generation to the next, some genetic diseases can make it more likely that a person would acquire the condition. Damaged muscle tissue can undergo a process known as rhabdomyolysis, which results in the release of proteins and electrolytes into the bloodstream.[2] These substances have the potential to render the heart and kidneys permanently inoperable or even result in death and it is the most typical form of abnormality found in patients. It is a serious medical disorder that is characterized by the rapid breakdown of wounded or damaged tissues.[3]

In some cases, Rhabdomyolysis is brought on by a muscle condition that runs in families (muscle dystrophy). It can be triggered by numerous factors like

High-intensity exercise: Beginning an exercise programme too soon can result in rhabdomyolysis, which is a condition that develops when the muscle does not have enough time to repair after strong activity.[4]

Overheating: Extreme heat leads to a more rapid breakdown of muscular tissue, which in turn leads to severe dehydration.[4]

Trauma: Muscle fibres have the potential to break down rapidly in response to traumatic injuries such as severe burns, being struck by lightning, or being crushed.[4–6]

Medication: Some examples of drugs that might cause muscle breakdown include antipsychotics, antidepressants, and antiviral treatments. Rhabdo myolysis is another potential side effect of taking statins, particularly in those who already have diabetes or liver disease.[4,7]

Illegal drugs and alcohol: Heroin, LSD, cocaine, and excessive consumption of alcohol are all toxic to the body and therefore can lead to muscle deterioration.[4,15]

Long periods of inactivity: Rhabdomyolysis can develop in those who fall, faint, and are unable to stand for an extended period of time.[4]

Rhabdomyolysis is a potentially lethal condition that causes the breakdown of muscle tissue and ultimately leads in death. Overuse of muscles, trauma, exposure to harmful substances, and illness are all potential contributors to muscle degeneration. The breakdown of muscle cells results in the release of the myoglobin protein into the bloodstream.[2] The kidneys are responsible for filtering myoglobin out of the blood so that it can be expelled from the body via urine. When present in excessive concentrations, myoglobin is known to be toxic to the kidneys. It is possible for there to be renal failure and mortality as a consequence of the kidneys being unable to eliminate waste in a timely manner.

Table. Laboratory parameters of the patient

Parameters	Results	Normal Range
Haemoglobin	**8.2**	11.6-15g/dL
Packed cell volume	**20.6**	35.5-44.9%
Mean Corpuscular Hemoglobin	**25.6**	27-31pg/cells
Mean Corpuscular Volume	**73.1**	80-100 fL
Mean Corpuscular Hemoglobin Concentration	33.3	32-36g/dL
Red Blood Count	**2.5**	3.8-5.2×10*12 mill/cumm
Total white cell count	5700	4500-11000
Serum Copper	**<25**	62-140 µg/dL
Serum Ceruloplasmin	**0.03**	0.932-2.65 g/L
Fasting blood sugar	**195**	70-100 mg/dL
Post-prandial blood sugar	**384**	140-199 mg/dL
HbA1c	**7.2**	5.7%- 6.4%
Direct bilirubin	**0.41**	0.0-0.40 mg/dL
Total bilirubin	0.63	0.1-1.2 mg/dL
SGPT	33	7-56 U/L
SGOT	**56**	8-45 U/L
Alkaline Phosphatase	**298**	44-147 U/L
Total protein	6.3	6.0-8.3 g/dL
Albumin	**5.9**	3.4-5.4 g/dL

Serum Creatinine	**1.79**	0.59-1.04 mg /dL
Total cholesterol	**78**	200-239 mg/dL
High-density cholesterol	**75`**	50-60 mg/dL
Low-density cholesterol	**46**	100-129 mg/dL
Triglycerides	**30**	<150 mg/dL
Very low-density cholesterol	18	2-30 mg/dL

CASE SUMMARY

A female patient of age 55 years was admitted to the hospital with complaints of breathlessness, cough, mild expectorate, fever, and pain near the chest for three days and a history of weakness. The patient had a past medical history of Hypertension (HTN) (treated with hypertension), Diabetes Mellitus (DM) (treated with Tab. Glimepiride 2mg + Metformin 500mg). Patient's lab investigations showed decreased Hb levels (8.2gm/dl), PCV (20.6), MCV (73.1), MCH (25.6), and RBC count (2.5 mill/Cubic mm).[8]

When combined with an optimal statin regimen to lower triglycerides and raise HDL levels, fenofibrate may increase the risk of rhabdomyolysis.[9] The patient is hypertensive along with diabetes mellitus at a primary health clinic. The patient reported shortness of breath, chest pain, sweating, cough with mild expectorate, and low triglyceride levels due to a low-fat diet [hyperthyroidism], overactive thyroid [malabsorption syndrome], and a history of lack of appetite.[5]

The patient had been given 80 mg OD of atorvastatin and 145 mg OD of Fenofibrate. Her total blood count revealed a Hb level of 8.2gm/dl, RBC count of 2.5 mill/cumm, PCV count of 20.6%, MCV count of 73.1 pg/cells, MCH of 25.6pg/cells, triglycerides levels of 39mg/dl and HDL levels of 75mg/dl.

The physical examination revealed the patient being febrile at 101˚ F blood pressure of 114/70 mmHg heart rate of 89bpm. The patient has a normal heart rate with a respiratory rate of 20 breaths /min.

The patient was treated for reducing sugar levels with 2mg of Glimepiride and 500mg of metformin. One tablet twice daily was given to the patient for diabetes mellitus, tab. Sitagliptin 50mg and metformin 500mg 1 tab once a day at lunchtime, tab. Atorvastatin 80 mg was given to the patient to lower the cholesterol levels. Tab. Fenofibrate 145mg was given to the patient to reduce and treat high cholesterol and triglycerides levels in the body cap. 75mg Clopidogrel 1 capsule daily to prevent blood clots, tab. Aspirin 75mg daily to lower the chance of heart attacks, clot-related strokes, and other blood flow problems, 2.5mg Nitro-glycerine Capsule 1 cap twice daily to treat angina attacks [Pain in the chest], tab. Pantoprazole 40mg 1 tab once daily before breakfast on an empty stomach was given to treat certain conditions where too much acid in the stomach, tab of isosorbide dinitrate 5mg 1 tab if necessary, used to prevent chest pain.

DISCUSSION

Arthralgia, haemorrhagic stroke, diarrhoea, and nasopharyngitis are the atorvastatin adverse effects that have been reported to the medical community the most frequently.[10,11] Myalgia, limb discomfort, insomnia, muscular spasm, musculoskeletal pain, nausea, and urinary tract infections are some of the other undesirable effects.[12]

Fenofibrate is a fibric acid derivative that is used medically to treat high cholesterol (fibrates). Its primary function is to bring about a reduction in the levels of cholesterol and triglycerides (also known as fatty acids) in the blood. It facilitates the removal of triglycerides from the bloodstream as well as their breakdown.[13] If the patient have serious renal illness, liver disease, gallbladder disease, or are breastfeeding a child, it is possible that taking fenofibrate can cause the muscle tissue to break down, which could lead to kidney failure.[8,14] Face or neck may swell up, and the patient may have difficulty breathing, feel pain in the skin, and also may develop a rash that is red or purple that eventually blisters and peels. These are all indications that the patient is having an allergic reaction. These are the adverse effects caused by fenofibrate that occur most frequently.[11]

When both fenofibrate and atorvastatin are taken at the same time, the potential for adverse effects such as rhabdomyolysis and damage to the liver is increased. Rhabdomyolysis is a disorder that affects only a small percentage of people but can have catastrophic consequences. It is characterised by the breakdown of skeletal muscle tissue. The condition demands prompt medical attention if it presents itself with symptoms such as fever, chills, joint pain or swelling, skin rashes, unusual bleeding, itching, exhaustion, loss of appetite,

nausea, vomiting, dark urine, or yellowing of the skin or eyes.[7,14]

CONCLUSION

Substantial interactions between fenofibrate and atorvastatin result in pharmacodynamic synergism, which means that the two drugs either enhance the effects of one another or have the potential to produce new effects. The previously described interaction became apparent after the patient had taken the drug in question. This medicine lowers total cholesterol levels while simultaneously raising HDL levels, which raises the risk of rhabdomyolysis when taken in conjunction with an optimum statin. To find a solution to this problem, we need to adjust the patient's dose and frequency of administration in line with their pharmacokinetic parameter.

In order to overcome the interaction, the medication Ezetimibe can be substituted for Fenofibrate. Ezetimibe is a type of cholesterol absorption inhibitor that raises HDL levels while simultaneously lowering TG levels and bringing down LDL levels. Fenofibrate is categorised as a fibric acid, and its primary effects include lowering total cholesterol and low-density lipoprotein levels while simultaneously raising high-density lipoprotein levels. According to a recent journal, this Atorvastatin is causing the patient's sleep to be disturbed, so we need to adjust the frequency of the patient's doses. The exact mechanism of action that Fenofibrate and Ezetimibe use is the same. However, there was no interaction found between Ezetimibe and Atorvastatin when it was administered together with Atorvastatin. A thorough investigation reveals that the cholesterol-lowering medications ezetimibe and atorvastatin do not interact in any way. Because of this, we are in a position to enhance the quality of life of the inpatients by acting on the conclusion stated above.

CONSENT TO PARTICIPATE

Before the study began, the patient was informed, and a signed consent form was obtained.

DISCLOSURES

The authors declare that there are no conflicts of interest in this study. The authors are responsible for the content and writing of the papers.

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