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CASE REPORT

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Omeprazole was safely reused in a rhabdomyolysis patient associated with proton pump inhibitors: A case report

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Key Clinical Message

Proton pump inhibitors (PPIs) are commonly used in the clinical treatment of abnormal gastric acid secretion and gastric acid related diseases. There are disputes about blood purification and PPIs reuse in patients with PPIs-induced rhabdomyolysis. Herein we reported an 84-year-old woman with a 10-year history of coronary heart disease and gastric acid. After 18 days of omeprazole therapy, the blood myoglobin of the patient rose progressively. Laboratory examination confirmed rhabdomyolysis, and PPIs-induced rhabdomyolysis was considered. Atorvastatin was initially discontinued. Additionally, omeprazole was altered to iprazole. Since blood myoglobin continued to exceed the highest value identified, continuous renal replacement therapy (CRRT) and hemoperfusion (HP) were administrated. When PPIs-induced rhabdomyolysis was considered, iprazole was discontinued. Two days after discontinuation of iprazole, blood myoglobin continuously decreased. After rhabdomyolysis was resolved, omeprazole was reused, and rhabdomyolysis did not reoccur. PPIs in combination with statins increase the risk of rhabdomyolysis. In the present case, switching to another PPIs or CRRT and HP therapy did not alleviate rhabdomyolysis. Rhabdomyolysis caused by statins is countless, but other reasons cannot be overlooked. In any case, the removal of etiology is the primary component of the treatment of rhabdomyolysis. When rhabdomyolysis is alleviated, PPIs can be reused safely under close monitoring.

KEYWORDS

drug adverse reaction, proton pump inhibitor, rhabdomyolysis

1 | INTRODUCTION

Rhabdomyolysis is a clinical disorder characterized by the breakdown of skeletal muscle with the release of intracellular components, such as creatine kinase (CK), myoglobin, lactate dehydrogenase, aldolase, and electrolytes, into the systemic circulation.[1] It can result from multiple disorders, such as trauma and exertion, hypoxic injury, infection, high temperature, and drugs and toxins.[2] Given the recommendations of the American Heart Association Practice Guide, statins are generally prescribed in cardiovascular patients. An increasing number of studies

indicate that rhabdomyolysis is a well-documented side effect of statin therapy, and there was an increased risk when drugs concurrently utilized inhibit cytochrome p450-3A4 (CYP3A4).[3]

Abnormal gastric acid secretion and gastric acid related diseases are common clinical diseases. Proton pump inhibitors (PPIs) alter gastric acid secretion by inhibiting H^+/K^+-ATPase in gastric parietal cells. PPIs have the characteristics of high specificity, strong acid inhibition, and convenient administration. Hence, PPIs are commonly used in the clinical treatment of abnormal gastric acid secretion and gastric acid related diseases. The potential side effects of PPIs include osteoporosis, fracture, infections, impaired absorption of nutrients, dementia, kidney injury, cardiovascular and cerebrovascular diseases, diabetes, and other adverse reactions.[4,5]

It should be noted that there may be drug interaction when PPIs and statins are administered simultaneously. PPIs were reported to inhibit the metabolism of statins metabolized through CYP3A4, thereby enhancing the concentration of statins, and eventually lead to rhabdomyolysis.[6] In previous reports, the evidence linking PPIs therapy to rhabdomyolysis was weak enough to confirm causality.[7] For patients with clear indications of continuous use of PPIs, there is dispute about PPIs reuse in patients with PPIs-induced rhabdomyolysis.[6]

Rhabdomyolysis leads to renal injury through the following mechanisms: oxidative stress, inflammation, apoptosis, vasoconstriction, and tubular obstruction.[8] The initiation of blood purification may be required to control volume overload and remove toxic substances, particularly medium molecular substances such as creatine kinase, lactate dehydrogenase, myoglobin, and other pathogenic substances.[2] So far, it is controversial to use renal replacement therapy in patients with rhabdomyolysis accompanied by AKI.[9]

2 | CASE PRESENTATION

An 84-year-old woman with a 10-year history of coronary heart disease and gastric acid was admitted to the department of general medicine on November 11, 2021. The admission diagnosis was coronary heart disease, reflux esophagitis, pneumonia, hypertension, hyperuricemia, cerebral infarction, lumbar spine compression fracture. The treatment protocol included isosorbide mononitrate [40 mg once daily (QD) via oral administration (PO)], rosuvastatin (10 mg QD via PO), irbesartan (150 mg QD via PO), levamlodipine besylate (2.5 mg QD via PO), metoprolol succinate (47.5 mg QD via PO), febuxostat (40 mg QD via PQ), omeprazole [40 mg twice a day (BID) via intravenous injection], cefminox (1 g BID via intravenous infusion), and percutaneous vertebroplasty.

After the above treatment, the patient's heart function, blood pressure, lung infection, and low back pain improved significantly. On the 18th day of admission, although the patient's serum troponin I had no significant change compared with that at admission, the blood myoglobin of the patient increased to 96 U/L (vs. 61.6 U/L at admission). On the 21st day after admission, blood myoglobin further increased to 419.1 U/L, and the serum creatinine level significantly increased to 98 umol/L (vs. 60 umol/L at admission). Except for mild knee pain, the patient had no general muscle weakness. No rash was found on physical examination. Laboratory tests showed a slight elevation of erythrocyte sedimentation rate (30 mm/h). Hepatitis B, hepatitis C, autoimmune hepatitis indicators were negative. Autoantibody tests including ANA, SS-A, SS-B, Jo-1, RNP, SCL-70, etc. were negative. Since rhabdomyolysis has occurred, atorvastatin was discontinued. To rule out the possibility of rhabdomyolysis caused by omeprazole, omeprazole was changed to iprazole (10 mg QD via intravenous injection). To reduce muscle cell damage, glutathione, magnesium isoglutamic oxalate, and polyene phosphatidylcholine were also used. In addition, Febustat was removed to exclude the possible cause of rhabdomyolysis.

As shown in Figure 1, even after the adoption of continuous renal replacement therapy (CRRT) and

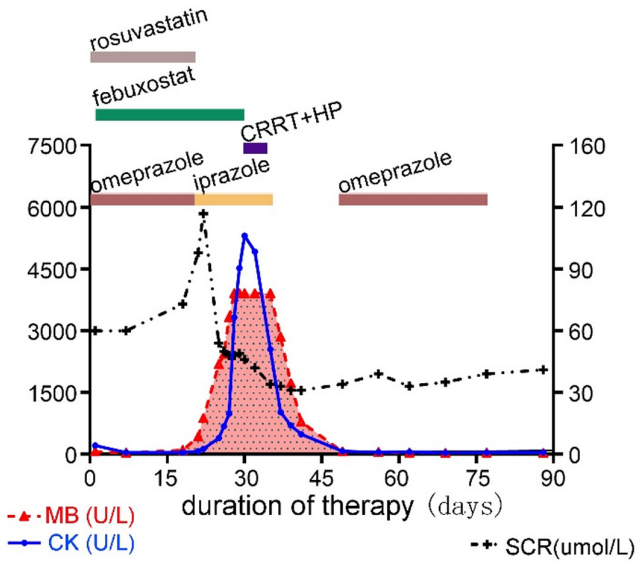

FIGURE 1 Creatine kinase, myoglobin, and serum creatinine relative to the duration of medication administration. CK (blue), creatine kinase; CRRT, continuous renal replacement therapy; HP, hemoperfusion; MB (red), myoglobin; SCR (black), serum creatinine. Since the maximum value of myoglobin detected by the equipment is 3909 U/L, the value greater than 3909 U/L is recorded as 3909 U/L in this legend.

hemoperfusion (HP), blood myoglobin was still not gotten relieved and continued to exceed the highest value detected (3909 U/L). Therefore, we have recognized that there are some factors involved in the rhabdomyolysis of this patient. The possibility of rhabdomyolysis associated with PPIs was considered. The Naranjo adverse drug reaction (ADR) probability scale was used to determine causality.[10] Naranjo ADR scores were found to be 3 (probable) for atorvastatin and 3 (probable) for PPIs. Two days after the discontinuation of iprazole, blood myoglobin, blood creatine kinase, and blood creatine kinase enzymes began to decrease considerably. Even without the help of CRRT and HP treatment, those indicators returned to normal levels. Interestingly, omeprazole was reused after rhabdomyolysis was resolved, and rhabdomyolysis did not reoccur.

3 | DISCUSSION

Various statins are metabolized through the CYP3A4 isozyme into inactive metabolites. It is known that PPI can inhibit the activity of CYP3A4 to differing degrees. PPIs were reported to inhibit the metabolism of statins metabolized through CYP3A4, thereby enhancing the concentration of statins and subsequently leading to rhabdomyolysis.[6] Rhabdomyolysis was reported to be a feature of polymyositis after the use of omeprazole or statins.[11,12] The patients reported above were treated with hormones. The present case was treated with atorvastatin for coronary heart disease and had no previous history of rhabdomyolysis. Omeprazole was prescribed because of reflux esophagitis. At 18 days after the initiation of omeprazole, increased blood myoglobin was noticed. The present patient switched to other PPIs, but rhabdomyolysis was not alleviated. Two days after iprazole was stopped, even without the help of CRRT and HP therapy, the blood myoglobin of the current case steadily dropped and eventually returned to normal. Based on this, rhabdomyolysis provoked by PPIs was implied. Considering the manifestations and relevant examinations of our case, the diagnosis of polymyositis was not considered, and steroids were not applied. In any case, the removal of etiology is the primary component of the treatment of rhabdomyolysis. Though rhabdomyolysis caused by statins is numerous, other reasons should not be overlooked.[2]

Our case demonstrated that rhabdomyolysis might not occur when statins or PPIs were administered exclusively. Nonetheless, when PPIs are used together with statins, the risk of rhabdomyolysis will increase.[6] After rhabdomyolysis was resolved in the current case, omeprazole was reused, and rhabdomyolysis did not occur. Our case signifies that PPIs might be safely reused in the PPIs-induced patients under close monitoring when necessary.

The renal function of the present case improved after traditional treatment. Regarding abnormally elevated blood myoglobin and creatine kinase, CRRT and HP were adopted. Consistent with previous literature, rhabdomyolysis was not alleviated through CRRT and HP therapy. CRRT therapy can shorten the length of hospital stays but cannot decrease mortality or adverse events.[9] Consequently, CRRT was not regularly preferred. Nonetheless, Hemodialysis or CRRT may be required to remove toxic substances, notably medium molecular substances such as creatine kinase, lactate dehydrogenase, myoglobin, and other pathogenic substances.[2]

Taken together, neither switching to another PPIs nor CRRT and HP therapy can ameliorate PPIs-induced rhabdomyolysis. Etiological removal is the essential component of the treatment of rhabdomyolysis anyhow. When rhabdomyolysis is cured, PPIs might be cautiously challenged under strict monitoring. Due to the limitations of the case report, it is impossible to attain a definite conclusion. Prospective studies may be needed to better specify the blood purification and PPIs reuse in patients with PPIs-induced rhabdomyolysis.

AUTHOR CONTRIBUTIONS

Zhen Wang: Conceptualization; data curation; writing – original draft; writing – review and editing. **Jun Shen:** Data curation; investigation; resources. **Lei Zhang:** Investigation; methodology; supervision; validation.

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DATA AVAILABILITY STATEMENT

Data supporting the findings of this report may be obtained from the corresponding author upon rational request.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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