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From the Clinic

Colchicine-induced rhabdomyolysis following a concomitant use of clarithromycin in a haemodialysis patient with familial Mediterranean fever

Sir,

Renal amyloidosis secondary to familial Mediterranean fever (FMF) is one of the common causes of nephrotic syndrome and chronic kidney disease in Turkey [1].

Colchicine is a microtubule-depolymerizing drug widely used for the treatment of gout which may prevent the development of secondary amyloidosis. In end-stage renal disease (ESRD), although the dose of colchicine is suggested to be reduced, there is limited information on efficacy and safety [2]. Inappropriately high doses or coprescription of CYP3A4 or P-glycoprotein inhibitors have been reported to cause serious adverse effects, including death [3–7]. Herein, we present a case of colchicine-induced rhabdomyolysis after using clarithromycin, a macrolide antibiotic and a potent inhibitor of CYP3A4 and P-glycoprotein ABCB1.

A 40-year old male patient on maintenance haemodialysis was admitted with recently developed fatigue, anorexia, headache, dizziness, diffuse myalgia and gastrointestinal symptoms including epigastric pain, diarrhoea and bloating. He presented with FMF in childhood (with frequent attacks of fever and abdominal pain with arthritis) and had developed secondary amyloidosis 10 years previously and ESRD 6 months previously. His long-term medication was colchicine 0.5 mg twice daily, doxazosin 4 mg once daily and 40 mg furosemide on non-dialysis days and sevelamer 1600 mg three times a day.

A further history revealed that the patient had recently been diagnosed with acute sinusitis and was prescribed clarithromycin 500 mg twice daily in another hospital a week beofore. On his initial examination the patient's blood pressure was 100/60 mmHg, he was in a euvolaemic state and had no significant finding except diffuse tenderness, but there was no rebound on abdominal palpation. In his biochemistry, his creatine kinase (CK)(5732 U/L-9035 U/L) and transaminase levels (ALT:110 U/L, AST:309 U/L) were elevated and raised upon follow-up. Due to high CK and transaminases, colchicine-induced rhabdomyolysis was diagnosed and colchicine discontinued. The patient's pain subsided 3 days after discontinuation of colchicine. An EMG was performed because of high levels of CK to exclude the diseases causing myopathie. During outpatient follow-up, the patient's transaminases and CK returned to normal levels and his EMG was normal. After complete recovery, the patient started colchicine 0.5 mg/day again without recurrence of symptoms.

Discussion

After development of ESRD due to amyloidosis secondary to FMF, most patients still need to continue colchicine to prevent FMF attacks and also retard the progression of amyloid deposition in the tissues, especially of the kidneys. The usual prophylactic dose is 0.5 mg once to thrice daily, and dose reductions are suggested for elderly, children and liver and renal failure patients [3]. Colchicine is mainly metabolized in the liver by CYP3A4 and is a substrate for the P-glycoprotein transporter (also known as multidrug transporter 1 and ATP-binding cassette B1 transporter). P-glycoprotein is associated with drug efflux from cells and colchicine excretion is largely dependent on P-glycoprotein. Urinary excretion of colchicine is about 10–20%, and a routine dose reduction is recommended for renal failure patients [2–4]. Therefore, many clinicians reduce the dose of colchicine for dialysis patients to avoid toxicity without complete cessation. Inhibitors of CYP3A4 (such as diltiazem, macrolide antibiotics, triazoles, etc.) increase the toxicity of colchicine [2–4]. Macrolides are also inhibitors of P-glycoproteins which can further impair colchicine elimination which is well reported [5–7]. Moreover, severe interactions have also been reported in patients using a combination of colchicine and HMG-CoA reductase inhibitors in which muscle symptoms, including weakness and pain, are the main initial findings [6].

In our case, a combination of clarithromycin and colchicine resulted in colchicine toxicity which was presented as rhabdomyolysis. Therefore, the patients using colchicine in chronic dialysis should not be prescribed the drugs inhibiting CYP3A4 or P-glycoproteins. The combination can cause severe toxicity and, if unnoticed, can be catastrophic for these patients.

Authors' contribution

All authors participated in interpretation of data, drafting and revising the article, and provided intellectual content of critical importance to the work described.

Conflict of interest statement. None declared.

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