

RGH Pharmacy E-Bulletin

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A joint initiative of the Patient Services Section and the Drug and Therapeutics Information Service of the Pharmacy Department, Repatriation General Hospital, Daw Park, South Australia. The RGH Pharmacy E-Bulletin is distributed in electronic format on a weekly basis, and aims to present concise, factual information on issues of current interest in therapeutics, drug safety and cost-effective use of medications.

Editor: Assoc. Prof. Chris Alderman, University of South Australia – Director of Pharmacy, RGH
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Drug-induced myopathies

Drug-induced myopathies may present in varying degrees of severity from mild muscle weakness to rhabdomyolysis with acute renal failure. Drugs may cause myopathic symptoms by directly affecting a muscle organelle, inducing immunological or inflammatory myopathy, altering systemic functions leading to electrolyte disturbances or via nutritional deprivation, and this in turn affects muscle function. Many toxic myopathies are reversible, thus prompt detection of the offending agent is essential. These are some common drugs implicated in this condition:

Lipid lowering agents

Statin-induced myopathies range from asymptomatic elevation of the plasma CK, to rhabdomyolysis. The risk is greater with lipophilic statins (simvastatin, atorvastatin, lovastatin) than hydrophilic statins (pravastatin). Co-administration of CYP3A4 substrates that inhibit statin metabolism, (e.g. amiodarone, gemfibrozil, cyclosporine & macrolide antibiotics, increase the incidence. The role of ubiquinone in this myopathy is discussed in E-bulletin Vol 22 (1). Other lipid lowering agents such as fibrates, nicotinic acid & ezetimibe may also cause myopathy, usually in combination with statins.

Glucocorticoids

Patients treated with long term, large doses of glucocorticoids may experience myopathic weakness, through atrophy of type II fibres. This is most likely with 9-a-fluorinated steroids (dexamethasone, betamethasone, triamcinolone) but may also occur with prolonged administration of prednisone (usually at dosages greater > 20mg daily) or prednisolone. However reduction in dose usually reverses this myopathy. Critical care patients receiving high dose corticosteroids in combination with a non-depolarising muscle blocker may experience acute quadriplegic myopathy and aggressive mobilisation and cessation of steroid is required in this setting.

Antirheumatic drugs

Colchicine may induce muscle weakness through interference with normal growth of microtubules. Patients with impaired renal function and organ transplant recipients on cyclosporine are at an elevated risk due to increased plasma concentration of colchicine. Immune-mediated neuromuscular complications have been associated with D-Penicillamine, with the incidence of polymyositis and dermatomyositis at about 0.6%. Myopathy induced by chloroquine or hydroxychloroquine is a rare complication, with symptoms resolving within months after discontinuation of the drug.

Zidovudine and other nucleoside reverse transcriptase inhibitors (NRTIs)

Differences in tissue distribution of NRTIs result in selective tissue toxicity; zidovudine causes mitochondrial myopathy, while other NRTIs can cause neuropathy or a combination of both. The degree of zidovudine-induced myopathy is dependant on the duration and dose of therapy, with 17% of patients receiving long-term zidovudine experiencing some degree of myopathy.

Other drugs

Drugs that cause severe hypokalaemia (thiazide diuretics, amphotericin B and lithium) or hyperkalaemia (such as potassium-sparing diuretics) may induce diffuse muscle weakness. Antipsychotics can increase plasma CK, even in the absence of neuroleptic malignant syndrome. Cocaine, heroin, amphetamines and PCP may induce rhabdomyolysis and sometimes compression syndrome. These illicit drugs usually come in combination with various substances, and thus whether it is the drug itself that induces the toxicity remains unclear. Alcohol can cause either acute myopathy that resolves after cessation (with potential recurrence if consumption resumes), or chronic myopathy, often due to a combination of toxic effects, chronic malnutrition and electrolyte abnormalities.

This E-Bulletin is based on work by Helen Chuah, Clinical Pharmacist, RGH

FOR FURTHER INFORMATION CONTACT THE PHARMACY DEPARTMENT ON 82751763 or email: chris.alderman@health.sa.gov.au
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