Spotlight on Colchicine

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Key Messages

Colchicine is approved for the treatment of acute gout.

Patients should be counselled on the appropriate use of this medicine and the signs of toxicity to ensure its safe and effective use.

Serious adverse effects and toxicity may be potentiated by pharmacokinetic drug interactions.

Adverse effects predominantly affect the gastrointestinal tract, skin, and blood.

This article on colchicine continues the spotlight series where Medsafe reviews the safety information on a specific medicine or class of medicine.

Indication

Colchicine is indicated for the treatment of acute gout when nonsteroidal anti-inflammatory drugs (NSAIDs) are contraindicated, ineffective or not tolerated[1].

Dose

The toxicity of colchicine is directly related to dose and patients should be advised to take the lowest dose they can to provide relief from pain. The approved adult dose of colchicine for acute gout flares is 1 mg (two tablets), followed by 500 micrograms (one tablet) every six hours for the first 24 hours, to a maximum daily dose of 2.5 mg (five

tablets)[1]. After the first 24 hours, the dose should not exceed 1.5 mg (three tablets)[2]. The total dose given in an acute attack should not exceed 6 mg over four days[1].

In elderly patients, patients with renal or hepatic impairment, or patients weighting less than 50 kg, the maximum dose in the first 24 hours should not exceed 1 mg, and the maximum cumulative dose over four days should not exceed 3 mg[1].

A course of colchicine should not be repeated within three days[1].

An alternative dosage regimen has also been recommended by the New Zealand Formulary[2].

Contraindications

Colchicine should not be used in:

patients with severe or combined renal and hepatic impairment

patients with mild to moderate hepatic impairment while taking a P-glycoprotein or strong CYP3A4 inhibitor

patients with serious cardiac or gastrointestinal disorders, or pre-existing blood dyscrasias

children

breastfeeding mothers[1].

Warnings and Precautions

Fatal Overdose

Colchicine has a low toxic threshold and can be fatal in doses as small as 6 mg[1]. Patients should be told to stop taking colchicine and to seek medical advice immediately if signs of toxicity occur, such as nausea, vomiting, diarrhoea (including bloody diarrhoea) or abdominal pain[1]. There is no specific antidote for colchicine toxicity[1].

Renal Impairment

Clearance of colchicine is decreased in renal impairment[1]. Adverse effects should be monitored for and dosage may be reduced, or the interval extended[1].

Blood Dyscrasias

Colchicine can have leukopenic and thrombocytopenic effects[1]. This may result in an increased incidence of microbial infection, delayed healing, or gingival bleeding[1].

Use in the Elerly

Elderly patients, even those with normal renal and hepatic function, may be more susceptible to colchicine toxicity[1]. All patients in this population should be closely monitored for signs of toxicity and doses may need to be reduced[1].

Use in Pregnancy

Colchicine should be avoided in pregnancy and women of child-bearing age should be advised to use effective contraception whilst taking colchicine[1]. In animal studies, colchicine has been shown to have teratogenic effects[1].

Medicine Interactions

Colchicine is a substrate of the efflux transporter, P-glycoprotein, and is metabolised by CYP3A4[1]. If colchicine is administered with medicines that inhibit P-glycoprotein and/or CYP3A4, increased blood concentrations of colchicine are likely[1]. Medicines that interact with colchicine include ciclosporin, macrolide antibiotics, protease inhibitors, lipid lowering agents, calcium channel blockers and digoxin. Fatal medicine interactions have occurred[1].

The leukopenic and thrombocytopenic effects of colchicine may be intensified by concomitant or recent therapy with blood dyscrasia-causing medications, or bone marrow depressants[1].

Adverse Effets

Adverse effects associated with colchicine predominantly affect the gastrointestinal system, skin and blood. Adverse effects are summarised in Table 1.

Table 1: Selected adverse effects associated with colchicine[1]

System Organ Class	Adverse Effects
Blood and lymphatic system	Anaemia, leukopenia, neutropenia, thrombocytopenia, agranulocytosis, pancytopenia, aplastic anaemia and non-thrombocytopenic purpura
Cardiac	Generalised vascular damage
Eye	Corneal ulcers
Endocrine	Hypothyroidism
Gastrointestinal	Nausea, vomiting, abdominal pain, diarrhoea, paralytic ileus, stomatitis, steatorrhoea
Investigations	Blood alkaline phosphatase increased
Metabolism and nutrition	Vitamin B12 absorption decreased
Musculoskeletal and connective tissue	Myopathy, rhabdomyolysis
Renal and urinary	Bladder spasm, anuria, haematuria, oliguria, acute kidney injury
Reproductive system and breast	Azoospermia, oligospermia
Respiratory, thoracic and mediastinal	Acute respiratory distress syndrome
Skin and subcutaneous tissue	Rash, urticaria, dermatosis, dermatitis, alopecia

New Zealand Reports of Adverse Reactions

From 1 January 2013 to 31 December 2017, the Centre for Adverse Reactions Monitoring (CARM) received 13 reports where colchicine was a suspect medicine. The most commonly reported adverse reactions were diarrhoea (4 reports), acute renal failure (3), abdominal pain (2), myopathy (2), and vomiting (2). Ten reports concerned male patients, consistent with the higher prevalence of gout in males[3].

One patient died from acute renal failure and severe metabolic acidosis due to incorrect self-administration of colchicine[4]. This report highlights the importance of counselling patients on the correct use of this medicine.

Health professionals should advise patients to seek medical advice immediately if they show any signs of toxicity. Please continue to report any adverse reactions to colchicine and any other medicine to CARM. Reports can be submitted on paper or electronically (https://nzphvc.otago.ac.nz/).

References

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