

The management of acute dystonic reactions

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Introduction

Drug-induced acute dystonic reactions are a common presentation to the emergency department. They occur in 0.5% to 1% of patients given metoclopramide or prochlorperazine.¹ Up to 33% of acutely psychotic patients will have some sort of drug-induced movement disorder within the first few days of treatment with a typical antipsychotic drug. Younger men are at higher risk of acute extrapyramidal symptoms.

Although there are case reports of oculogyric crises from other classes of drugs, including H₂ antagonists, erythromycin and antihistamines, the majority of patients will have received an antiemetic or an antipsychotic drug.

Differential diagnosis

The manifestations of acute dystonia can appear alone, or in any combination (Table 1).

Patients and carers find these reactions alarming. The diagnosis is not always obvious, and in one particularly challenging fortnight last year I saw four patients who were initially misdiagnosed as:

- a 'dislocated jaw' from prochlorperazine given for labyrinthitis
- an 'allergy with swollen tongue' which was a dystonic reaction to metoclopramide
- a 'hyperventilation' who was exhibiting a classic oculogyric reaction
- increasingly 'strange behaviour' caused by the overdose of trifluoperazine for which a young man had been admitted two days previously.

These were all acute dystonic reactions. Upper airway obstruction from pharyngeal muscle spasm or laryngospasm is a rare but potentially life-threatening complication.

The differential diagnosis includes:

- tetanus and strychnine poisoning
- hyperventilation (carpopedal spasm is usually more prominent than it is in acute dystonic reactions)
- hypocalcaemia and hypomagnesaemia
- primary neurological causes such as Wilson's disease.

If there is any doubt, it is reasonable to treat as an acute dystonic reaction in the first instance, and investigate further if there is no response.

Treatment

Dystonia responds promptly to the anticholinergic benzotropine 1–2 mg by slow intravenous injection. Most patients respond within 5 minutes and are symptom-free by 15 minutes. If there is no response the dose can be repeated after 10 minutes, but if that does not work then the diagnosis is probably wrong.

The alternatives are antihistamines. Popular American texts^{2,3} recommend diphenhydramine 1–2 mg/kg up to 100 mg by slow intravenous injection, and the current Oxford Handbook of Clinical Medicine⁴ suggests procyclidine, but neither of these drugs is available in Australia as a parenteral preparation.

Promethazine, 25–50 mg intravenously or intramuscularly, has been used less frequently but it works and it is readily available in most emergency departments and doctors' bags. It may be a useful alternative for the uncommon patient who has both dystonia and significant anticholinergic symptoms from antipsychotic drugs.

Diazepam, 5–10 mg intravenously, has been used for the rare patient who does not completely respond to the more specific antidotes. Unlike the other antidotes, it cannot be given intramuscularly.

There are rare case reports of dystonia **caused** by all of these treatments, including diazepam.

Children should be given parenteral benzotropine, 0.02 mg/kg

Table 1

Manifestations of acute dystonia

Oculogyric crisis	Spasm of the extraorbital muscles, causing upwards and outwards deviation of the eyes Blephorospasm
Torticollis	Head held turned to one side
Opisthotonus	Painful forced extension of the neck. When severe the back is involved and the patient arches off the bed.
Macroglossia	The tongue does not swell, but it protrudes and feels swollen
Buccolingual crisis	May be accompanied by trismus, risus sardonicus, dysarthria and grimacing
Laryngospasm	Uncommon but frightening
Spasticity	Trunk muscles and less commonly limbs can be affected

to a maximum of 1 mg, either intramuscularly or intravenously. This can be repeated once, but if the intramuscular route is chosen, allow 30 minutes to elapse before repeating. The same dose should be given orally, twice daily for the next 24–48 hours to prevent recurrence. Benztrapine comes in a 2 mg tablet, so the dose needs to be approximated to the nearest 0.5 mg, or quarter tablet.

Avoiding recurrences

After initial treatment, patients should be given oral medication for two or three days, usually benztrapine 1–2 mg twice daily. In general practice, most reactions will have been caused by antiemetics. Fortunately benztrapine, diphenhydramine and promethazine all have antiemetic effects so the causative agent can be safely discontinued.

The best predictor of an acute dystonic reaction is a previous history of having had one. Patients should avoid exposure to the precipitating drug, but they are also at higher than average risk if exposed to another drug which causes dystonic reactions. It may be possible to find a substitute which does not cause dystonia.

Antiemetics are usually avoided in children and need not be given for short-term problems such as gastroenteritis. If an antiemetic is necessary, then antihistamines such as promethazine have a long established place.

Conclusion

Acute dystonic reactions are a common and distressing complication of antiemetic and antipsychotic drugs. Treatment with intravenous benztrapine is safe and produces rapid relief. Patients who have a possible acute dystonic reaction should initially be treated with benztrapine. If they do not respond less common disorders may be considered.

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FURTHER READING

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New drugs

Some of the views expressed in the following notes on newly approved products should be regarded as tentative, as there may have been little experience in Australia of their safety or efficacy. However, the Editorial Board believes that comments made in good faith at an early stage may still be of value. As a result of fuller experience, initial comments may need to be modified. The Board is prepared to do this. Before new drugs are prescribed, the Board believes it is important that full information is obtained either from the manufacturer's approved product information, a drug information centre or some other appropriate source.

Bupropion

Zyban (Glaxo Wellcome)

150 mg sustained-release tablets

Approved indication: nicotine dependence

Australian Medicines Handbook Section 18.6.2

Bupropion is not a new drug. It was approved in the USA for the treatment of depression more than 10 years ago. The antidepressant effect probably involves the drug's action on neurotransmitters. These actions may also help smokers to quit; depressed smokers gave up smoking during the clinical trials of bupropion.

To study the usefulness of bupropion in assisting smoking cessation, 615 smokers were enrolled in a randomised placebo-controlled trial. All the participants were given counselling in addition to drug treatment. After seven weeks of treatment, 19% of the placebo group had given up smoking. In the bupropion group the success rate increased with the dose. Approximately 29% of those taking 100 mg daily gave up, compared with 39% of those taking 150 mg and 44% of those taking 300 mg. All the participants put on weight, but the least

weight gain (1.5 kg) was in the patients taking the highest (300 mg) dose of bupropion.¹

Bupropion has also been compared with nicotine patches. In this trial 244 people were randomised to take bupropion, 244 used a nicotine patch, 245 used both medications and 160 were given placebos. During the nine weeks of treatment the participants were also counselled. When the participants were reviewed after six months, 35% of the bupropion group had stopped smoking compared with 21% of those using the nicotine patch and 19% of the placebo group. In the combined treatment group, 39% had stopped smoking. Treatment with bupropion alone, or in combination with a nicotine patch, was significantly better than treatment with the patch alone.²

Patients begin bupropion when they are still smoking. They start with 150 mg once a day, and after three days they take 150 mg twice a day. Smoking should stop in the second week of treatment. If the patient is still smoking after seven weeks they are unlikely to benefit by continuing bupropion.

There is extensive first-pass metabolism and metabolism is the main method of clearance. Less than 1% of the drug is