Risk of hyponatraemia with antidepressants

Dear bpac,

I note on reading the article "Pharmacological management of depression in adults" (BPJ Special Edition, July 2009), that there is no mention of hyponatraemia. It is of enough concern in those over 65, or those medically ill, to warrant routine electrolytes after a week or two of treatment on SSRIs, venlafaxine and TCAs.

Dr Peter Miller, Psychiatrist
Christchurch

There has been increasing awareness of the risk of hyponatraemia after starting antidepressants.[1] Many guidelines in primary and secondary care are now being updated to include monitoring advice.

Risk factors for antidepressant-induced hyponatraemia include older age, low body weight, female gender, previous history of hyponatraemia, reduced renal function and concurrent intake of other hyponatraemic medicines, such as diuretics. Most reports have been linked to SSRIs but hyponatraemia can occur with any antidepressant including TCAs and newer agents such as venlafaxine and mirtazapine.

Hyponatraemia due to antidepressants or thiazide diuretics usually occurs in the first four weeks of treatment. All patients taking antidepressants should be observed for signs of hyponatraemia (dizziness, nausea, lethargy, confusion cramps and seizures). Monitoring recommendations vary slightly but a general consensus (especially for high risk patients) is as follows:

- Check baseline sodium level before starting the antidepressant
- Check sodium after two weeks, four weeks and again after three months
- Consider checking sodium after a dose increase of the antidepressant or addition of any other hyponatraemic medicine, e.g. a diuretic
- If possible, avoid the combination of a diuretic and an antidepressant (particularly an SSRI) in people already at higher risk of hyponatraemia. Close monitoring is especially important in such patients.

Prescribers should also be aware of other factors that may exacerbate or promote hyponatraemia in a person already taking an antidepressant and/or a diuretic. For example, fluid replacement (during acute gastrointestinal disturbance) with plain water instead of electrolyte solution may acutely aggravate hyponatraemia to dangerous levels.[2]

References

1. Medsafe. Safety signal – serious hyponatraemia. Medsafe;2009. Available from: www.medsafe.govt.nz keyword - hyponatraemia (Accessed Nov, 2010).

2. Accident Compensation Corporation (ACC). Hyponatraemia resulting in extra pontine myelinolysis. Treatment injury case study. ACC; 2008. Available from: www.acc.org.nz keyword hyponatraemia (Accessed Nov, 2010).

Medicine-induced dystonic reactions

Dear bpac

I recently came across two situations where practical information and guidance was rather sparse:

1. *A patient with a known dystonic reaction to metoclopramide required an alternative option for sea sickness - we are trying cyclizine*

2. *A patient developed trismus, most likely due to citalopram and also got very jittery on a tiny dose of quetiapine - all resolved nicely with a small dose of a benzodiazepine*

Often people who experience a dystonic reaction to one medicine need an alternative, e.g. for travel sickness,

and are very scared about having another reaction. Can you offer any guidance on these issues and the treatment of drug-induced dystonias in general?

Dr Margaret Goodey, GP
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Dystonic reactions are relatively common, occurring in approximately 1% of people receiving metoclopramide or prochlorperazine[1] and in up to one-third of people with acute psychosis who are treated with a typical antipsychotic, such as haloperidol or chlorpromazine. Children, young adults and elderly people seem to be at increased risk. A family history of dystonia and recent alcohol or cocaine use also appear to be risk factors.[2]

Most medicine-induced dystonias are caused by oral or injectable antiemetics or antipsychotics with dopamine blocking activity. A number of other medicines have also been implicated including antidepressants, antihistamines and calcium channel blockers. The mechanism is not always clear and some medicines used to treat dystonic reactions, e.g. antihistamines, have also been reported to cause reactions.

Examples of medicines that can cause dystonic reactions:[1]

- Antiemetics or antipsychotics with dopamine blocking activity, e.g.metoclopramide, prochloperazine, chlorpromazine, haloperidol
- Antihistamines, e.g. promethazine,cyclizine
- Antidepressants – especially SSRIs
- H2 antagonists
- Calcium channel blockers – rare but reported with most medicines in this class

N.B. Although atypical antipsychotics are less commonly associated with dystonic reactions, such reactions still sometimes occur, especially when higher doses are used.

Clinical presentation

Dystonic reactions usually appear soon after the causative medicine is initiated. Approximately 50% of reactions occur within 48 hours and 90% within five days of initiation. Reactions can also occur within minutes of taking a single dose or when the dose is increased. They are characterised by intermittent or sustained involuntary contractions of the muscles in the face, neck, trunk, pelvis or limbs.[2] The typical manifestations can occur alone or in combination. Dystonic reactions are not usually life threatening but can be very distressing for patients and carers. Treatment is usually effective within minutes without long-term consequences.

Manifestations of acute dystonia:[1]

Oculogyric crisis	Spasm of the extraorbital muscles, causing upwards and outwards deviation of the eyes Blepharospasm (twitching of eyelid)
Torticollis	Head held turned on one side
Opisthotonus	Painful forced extension of the neck. When severe the back is involved and the patient arches.
Macroglossia	Tongue does not swell, but protrudes and feels swollen
Buccolingual crisis	May be accompanied by trismus, risus sardonicus (spasm of facial muscles causing grinning appearance), dysarthria and grimacing
Laryngospasm	Uncommon but life-threatening
Spasticity	Trunk muscles and limbs can be affected

Differential diagnosis

The presenting features and a recent history of medicine intake usually give a reliable key to diagnosis. Differential

diagnoses include; tetanus, strychnine poisoning, primary neurological causes such as Wilson's Disease, hypocalcaemia and hypomagnesaemia.[1]

Treatment

The underlying mechanism for most dystonic reactions is thought to involve an imbalance between centrally available dopamine and acetylcholine. Medicines that block dopamine receptors produce a relative excess of acetylcholine which leads to the extrapyramidal-like symptoms. Medicines with anticholinergic properties are effective in controlling most reactions.

The recommended first choice treatment is an injectable anticholinergic agent such as benztropine. However, benztropine is unlikely to be carried or immediately available to most GPs. Promethazine (an antihistamine with anticholinergic properties) or diazepam are suitable alternatives.[1]

Benztropine
1- 2 mg by slow IV injection

Promethazine
25 – 50 mg IV or IM

Diazepam
5 – 10 mg IV

Oral benztropine (1–2 mg daily) can be continued for two to three days after the initial reaction.

There is very little information on cross reactions between medicines that cause dystonic reactions. The precipitating medicine should be avoided in the future and if required, careful use of a medicine from a different class is recommended. For example, if the reaction was caused by metoclopramide, an antihistamine with antiemetic properties, e.g. promethazine or cyclizine, can be tried. If a reaction occurs with an antidepressant such as citalopram, the same principle applies, that is, a careful trial of an antidepressant from a different therapeutic class such as a tricyclic antidepressant.

References

1. Campbell D. The management of acute dystonic reactions. Aust Pres 2001;24(1):19-20.
2. Toxicity, medication-induced dystonic reactions. eMedicine; December, 2009. Available from: www.emedicine.medscape.com/ Keyword: dystonic (Accessed Nov, 2010).

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