Drug points

Purpuric rash with donepezil treatment

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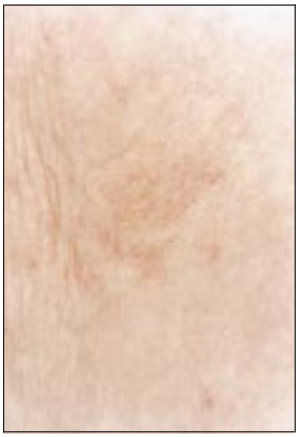
The most commonly reported adverse events with donepezil are gastrointestinal (nausea, diarrhoea, and constipation).[1] Donepezil has been licensed in the United Kingdom since April 1997, and from April to December 1997 only seven adverse reactions affecting the skin were reported through the yellow card adverse drug reaction reporting scheme (Committee on Safety of Medicines, personal communication). To our knowledge, this is the first report of purpuric rash associated with donepezil treatment.

An 82 year old woman was seen with a two year history of memory problems. She was also hypertensive and receiving long term treatment with atenolol and doxazosin. On examination she was normotensive (140/80 mm Hg) and had moderate cognitive impairment (score in mini-mental state examination 15/30 and on the cognitive subscale of the Alzheimer's disease assessment scale 46/75). Routine haematological and biochemical tests gave normal results (platelet count 146×10^9/l), and a computed tomogram of the brain was normal. Probable Alzheimer's disease was diagnosed according to published criteria,[2] and treatment with donepezil 5 mg daily was started. After 4 days she developed diarrhoea and vomiting. On review she had a purpuric rash on her trunk and her arms and legs (figure). Donepezil treatment was stopped, with resolution of the gastrointestinal symptoms, which were thought to be a result of gastroenteritis as another family member was affected. The rash began to fade.



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After discussion with the patient and her carer we cautiously restarted donepezil treatment. On review 16 days later an obvious recurrence of the purpuric rash was noted on her trunk and legs, although she had not had a recurrence of the gastrointestinal symptoms. Donepezil treatment was stopped. Successive platelet counts were 119×10^9/l and 157×10^9/l, and the rash had almost resolved when she was reviewed six weeks after rechallenge with donepezil.

Donepezil was thought to be the cause of this rash because of the temporal association with treatment and its recurrence on rechallenge.

1 Rogers SL, Friedhoff LT. The efficacy and safety of donepezil in patients with Alzheimer's disease: results of a US multicentre, randomized, double-blind, placebo-controlled trial. The Donepezil Study Group. *Dementia* 1996;7:293-303.
2 McKhann G, Drachman D, Folstein M, Katzman R, Price D, Stadlan EM. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of the Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology* 1984; 34:939-44.

Withdrawal reaction associated with venlafaxine

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We report an apparent withdrawal reaction to venlafaxine, a recently introduced serotonin noradrenaline reuptake inhibitor antidepressant whose use is increasing.

A 42 year old man with a first episode of major depression was treated with venlafaxine after unsuccessful trials with fluoxetine and imipramine. He fully recovered over four weeks while taking a dose of 37.5 mg twice daily. This dose was maintained for 6 months and his mental state was stable. The dose was reduced to 37.5 mg once daily, which he tolerated well. However, within 36 hours after stopping venlafaxine treatment he developed positional vertigo, which caused him significant incapacity, in addition to nausea and light headedness. The symptoms resolved rapidly on reintroduction of the drug. The dose was reduced to 18.75 mg daily for three weeks and then discontinued. He had ongoing symptoms of vertigo, which resolved slowly over three weeks. The patient's determination enabled him to discontinue taking the drug, but he did so with difficulty. He had no previous history of adverse drug reactions or withdrawal symptoms.

Other antidepressants have been reported to have withdrawal syndromes. Attention was drawn to withdrawal of tricyclic antidepressants by Dilsalver, who showed that cholinergic and noradrenergic hypersensitivity were important mechanisms for these symptoms.[1] Selective serotonin reuptake inhibitors, particularly paroxetine, also cause withdrawal syndromes, possibly through adaptation to the effects of serotonin reuptake inhibition.[2] Withdrawal of venlafaxine may share a similar mechanism, and its short half life (5 hours) may add to its potential to cause withdrawal symptoms.

At the time of writing, three reports had been published about five similar cases, but the patients in all five cases were taking higher doses of venlafaxine before treatment was discontinued.[3–5] The possibility of a withdrawal reaction is mentioned in the manufacturer's data sheet, but it implies that such reactions are observed with doses of 150 mg daily and above. Given the possibility of a withdrawal reaction with low doses of venlafaxine, we suggest that this drug is used with caution and that care is taken to gradually taper any dose before discontinuing treatment.

1 Dilsalver SC. Withdrawal phenomena associated with antidepressant and antipsychotic agents. *Drug Safety* 1994;10:103-14.
2 Coupland NJ, Bell CJ, Potokar JP. Serotonin reuptake inhibitor withdrawal. *J Clin Psychopharmacol* 1996;16:356-62.
3 Louie AK, Lannon RA, Kirsch MA, Lewis TB. Venlafaxine withdrawal reactions. *Am J Psychiatry* 1996;153:1652.
4 Farah A, Lauer TE. Possible venlafaxine withdrawal syndrome. *Am J Psychiatry* 1996;153:576.
5 Benazzi F. Venlafaxine withdrawal symptoms. *Can J Psychiatry* 1996;41:487.