Reminder of important clinical lesson

Antidepressants and unresponsive episodes in the elderly

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Summary

We present a case where initiation of antidepressant therapy was associated with an episode of unresponsiveness. Providing the opportunity to examine the possible pitfalls in geriatric prescribing.

BACKGROUND

The risk of adverse outcomes secondary to antidepressant use in the elderly has recently been examined by Coupland *et al.*¹ Antidepressants are very commonly prescribed medications,² with therapeutic indications ranging from treatment of depression to management of neuropathic pain. They are associated with numerous well-recognised adverse effects, including weight gain, cardiovascular effects and anticholinergic effects.³ Another important adverse effect is sedation.

CASE PRESENTATION

In March 2011, an 87-year-old man was admitted to the local Geriatric Hospital with a general decline in functional status. A comprehensive geriatric assessment revealed low mood with no evidence of cognitive impairment, the diagnosis of depression was made and he was started on mirtazapine at a dose of 15 mg at night. The following day he became increasingly unsteady on his feet. He was found unresponsive in bed 3 days later. There was no history of observed seizure activity or head trauma. On assessment, the vital signs were unremarkable, cardiovascular and respiratory examinations were normal and neurological examination revealed a diminished mental status, with a response to a deep painful stimulus but no eye opening or verbal response. The deep tendon reflexes were brisk and plantar reflexes extensor. Blood results (including urea and electrolytes, glucose, calcium, magnesium, thyroid function tests, B12 and folate levels, C-reactive protein and full blood count) were normal, an electrocardiogram displayed rate-controlled atrial fibrillation and an urgent magnetic resonance brain scan demonstrated no acute intracranial pathology. His level of consciousness gradually returned to normal after a few hours. The introduction of mirtazapine was suspected to be the cause and was stopped. We found no subjective improvement in mood, after withdrawal of mirtazapine.

OUTCOME AND FOLLOW-UP

He did not have any more episodes of unresponsiveness during the in-patient admission.

DISCUSSION

Depression is the most frequent psychiatric pathology in the elderly population, with a prevalence of 13.5% in the community.⁴ According to Beekman *et al.*,⁵ disability is an important determinant in the prevalence of depression in the elderly, with patients with long-term conditions and people living within institutions having higher rates of prevalence than people living in the community.

We are unable to conclusively prove that the introduction of antidepressant medications caused the episode of unresponsiveness in this patient, principally because the medication was not reintroduced to replicate the sedative effect. However, the circumstantial evidence of this episode in relation to the introduction of an antidepressant, coupled to the long recovery phase, leads us to believe that the antidepressants were the main culprits.

The sedating effect of antidepressants is hardly a new topic of discussion. However, it offers the opportunity to highlight the importance of depression in this population, the mechanisms of action relating to antidepressants involved and the generalities of safe prescribing in the elderly. According to the NHS Grampian formulary, which is developed according to guidance by the National Institute for Clinical Excellence, citalopram and mirtazapine are both first-line treatments for depression in older people.^{6 7}

Mirtazapine is a noradrenergic and specific serotonergic antidepressant that works at a presynaptic α_2 -adrenoreceptor antagonist level, increasing central noradrenergic and serotonergic neurotransmission.⁸ This increase in norepinephrine and serotonin transmission has few anti-muscarinic effects, but can cause sedation during initial treatment, a property that can be exploited in patients where this effect is desirable. It is usually given at night due to its sedating effect.⁹ In addition, it is useful in patients on warfarin therapy, as it does not affect the international normalised ratio.

We have also experienced a similar episode after the introduction of citalopram. Citalopram is a selective serotonin-reuptake inhibitor that works via the inhibition of the reuptake of the monoamine serotonin (5-HT). It may also cause drowsiness.⁹ In clinical trials versus placebo, citalopram has been found to be effective in the treatment of depression in the elderly.^{4 10 11}

Older people are often more sensitive to drugs and therefore at increased risk of experiencing adverse effects. This is due to the pharmacokinetic changes that occur with ageing, including increase in body fat composition, decreased lean mass, decreased P450 enzyme system activity and decreased renal excretion of drugs. These factors are especially important when the drug involved has a narrow therapeutic range.^{9–12} Adverse drug reactions are a common cause of hospital admission in the elderly.^{12–16} According to one study, adverse drug reactions are seven times more frequent in those aged 70–79 years than in those aged 20–29 years.¹⁴ In general, prescribing in the elderly should follow the pattern of ‘start low, go slow’, and the dosage should be reviewed regularly. Polypharmacy is very common in older people due to the presence of multiple comorbidities.^{9–12} It is therefore vital that medications are reviewed regularly, adverse effects actively sought and medications which do not provide significant clinical benefit discontinued.

Inappropriate prescribing in older people is highly prevalent. A review article by Gallagher *et al*¹⁵ estimates that inappropriate medications are prescribed in 12% of community-dwelling older people, increasing to 40% in Nursing Home residents in Europe and the USA. Given this high prevalence, the review recommends the use of drug utilisation tools that are developed in conjunction with each country’s national formulary.¹⁶

Learning points

- ▶ Weigh the risk–benefit ratio of each medication in the older patient.
- ▶ Actively look out for and recognise adverse drug reactions.
- ▶ Seek expert advice regarding the discontinuation of potentially inappropriate medications.

Competing interests None.

Patient consent Obtained.

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