Clinical Interventions in Aging

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LETTER

What Should Clinicians Do for Older Adults with Polypharmacy and Depression? [Letter]

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Dear editor

We have read with great interest the study by Cheng et al,[1] which determined that older adult patients with polypharmacy were at greater risk of developing depression. We would like to share our perspectives based on our experience from an academic medical center hospital with 4000 beds in China with our international peers.

First, clinicians should pay closer attention to drug–drug interactions (DDIs) caused by antidepressants in geriatric patients with polypharmacy and depression. We experienced a case of gastrointestinal bleeding in an 89-year-old polymedicated patient who had been prescribed 18 types of medications in February 2022. Although there were two other causes (ie, lack of using gastrointestinal protective agents, and inappropriate prescribing of rivaroxaban in adult patients aged over 75 years, which is associated with a higher risk of gastrointestinal hemorrhage compared to warfarin, apixaban and edoxaban),[2] the concurrent use of anticoagulant and sertraline was the third culprit. Prescribing information for sertraline requires that patients be warned about the risk of bleeding when sertraline is used in combination with drugs that could affect blood coagulation.

The risk of serotonin syndrome may increase due to DDIs between tramadol and serotonergic antidepressants such as amitriptyline, selective serotonin reuptake inhibitors (SSRIs) (eg, citalopram, escitalopram, fluoxetine, paroxetine, sertraline, fluvoxamine), serotonin and norepinephrine reuptake inhibitors (eg, duloxetine, venlafaxine), and mirtazapine. Buprenorphine and oxycodone are alternatives to tramadol because of their therapeutic advantages (eg, lack of such DDIs and unnecessary dose adjustment in older adults). SSRIs should not be co-administered with monoamine oxidase inhibitors such as linezolid and selegiline. Fluvoxamine, a strong cytochrome P450 enzyme 1A2 (CYP1A2) inhibitor, could seriously affect the pharmacokinetics of tizanidine and increase the intensity and duration of its effects. Other SSRIs are alternatives to fluvoxamine when co-medicating with CYP1A2 substrates commonly used for older adults (eg, clozapine, flutamide, haloperidol, melatonin, mexiletine, olanzapine, riluzole, tacrine, theophylline, and tizanidine). Duloxetine, venlafaxine, paroxetine, and fluoxetine are CYP2D6 inhibitors, and thus may inhibit the drug metabolism of CYP2D6 substrates. For example, the plasma exposure and beta-blocking action of metoprolol may be increased. The conversion of the prodrug tamoxifen into the active metabolite endoxifen via CYP2D6 could be significantly inhibited, resulting in reduced benefits of tamoxifen therapy for breast cancer patients. Non-CYP2D6-inhibitor antidepressants are alternatives, or dose adjustment of CYP2D6 substrates is necessary. St John's Wort is a popular herbal remedy widely prescribed for depression in many countries; however, its herb-drug interaction potential is prominent due to its potent induction of human CYP3A4 and P-glycoprotein.[3] Clinicians must be on high alert when they learn that a patient with polypharmacy is receiving or planning to receive St John's Wort treatment.

Secondly, Chen et al's meaningful finding should inspire the international community to further investigate whether deprescribing in older adults with polypharmacy would help alleviate the occurrence and symptoms of depression. So far, only very few studies have addressed the effectiveness of relevant interventions. For example, deprescription in older

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adults with type 2 diabetes by replacing a hypoglycemic therapeutic scheme with a single drug combination (insulin degludec/liraglutide) may improve the quality of life with a significantly decreased depression score and increased activities of daily living and cognitive function scores.[4] Patients also report lower depression scores 6 months after deprescribing anticholinergic and sedative medicines in residential aged care facilities.[5] More well designed prospective intervention studies investigating deprescription in geriatric patients are needed in the future.

Disclosure

The authors report no conflicts of interest in this communication.

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