SNRIs In Geriatric Patients

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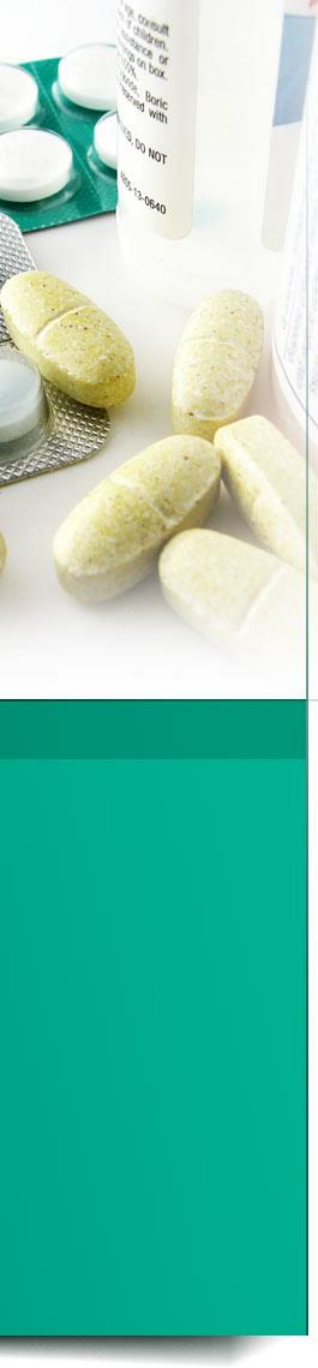


Response to Medications Among Geriatric Patients

- Geriatric patients with psychiatric disorder present clinical challenges not encountered in younger individuals, including a greater incidence of medical comorbidity, higher rates of multiple medication use, changes in drug metabolism due to age or physical illness, and increased sensitivity to antidepressant side effects.

- Geriatric patients with major depression present clinical challenges not encountered in younger individuals, including a greater incidence of medical comorbidity, higher rates of multiple medication use, changes in drug metabolism due to age or physical illness, and increased sensitivity to antidepressant side effects.

CARE

To prevent the emergence of adverse effects, dosages of these medications should not be increased at a rapid pace.

In the elderly, the general prescribing principles described in the acronym CARE are of paramount importance:

C : Caution, Compliance.
A : Adjust dose for Age “to start low and go slow.”
R : Review, Remove, Reduce.
E : Educate, Educate, Educate

Venlafaxine

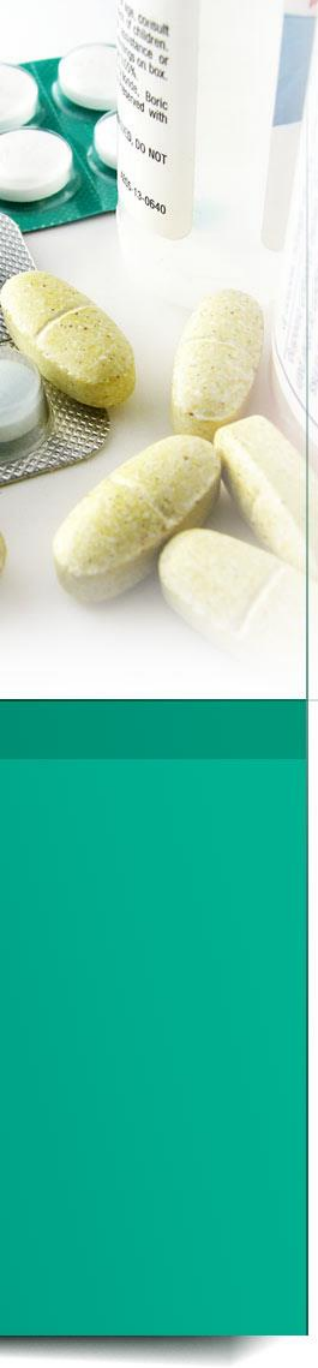
- Among newer antidepressants, venlafaxine has a pharmacological profile that makes it an attractive choice for geriatric patients. It has limited potential to interact with other medications because it only weakly inhibits the cytochrome P450 system and binds to plasma proteins at a low level.
- Dosing may have to be adjusted for patients with renal failure, but typically not for those with liver disease or other medical conditions.
- Data from three double-blind and four open clinical trials support the safety and efficacy of venlafaxine for geriatric depression.

- Patients may experience transient, generally tolerable side effects such as insomnia, nausea, agitation, or dry mouth early in treatment, but more serious problems such as falls or cardiac rhythm disturbances seem to be rare.
- Treatment emergent hypertension occurs in a small percentage of older patients, generally at doses above ***150 mg/day***
- Finally, emerging data suggest that venlafaxine may be effective for conditions such as *stroke, anxiety*, and *neuropathic pain* that frequently accompany depressive disorders in the elderly.

Those with a history of *seizure, stroke, head trauma* are more safely treated with a **venlafaxine** than with TCAs or bupropion.

The safety and tolerability of SNRIs in depressed elderly patients with and without medical comorbidity

- In the last decade, emerging and persuasive evidence reveals that inflammation may play an important role in the pathogenesis of both clinical depression and chronic pain syndromes. This common denominator may partially explain why patients with pain are more prone to develop clinical depression and vice versa.
- Chronic pain and major depression have a shared neurobiology and appear to have a shared neuroanatomy , with similar disturbances to the hypothalamic-pituitary-adrenal (HPA) axis, autonomic nervous system (ANS), and inflammatory cytokines.



Why Antidepressants Act Against Pain?

- Studies have clearly shown that antidepressants act as anti-inflammatory agents in both depression and chronic pain states. Antidepressant therapy improves the clinical symptoms of depression and chronic pain and appears to positively impact immune/cytokine deregulations. Research data indicate that antidepressants can reduce levels of inflammatory cytokines, such as tumor necrosis factor-α and interleukin-6.

- In addition to anti-inflammatory properties, data clearly show that antidepressants (mostly the **tricyclic antidepressants and serotonin–norepinephrine reuptake inhibitors**) have antinociceptive properties. Multiple studies reveal that even in the absence of depression, these antidepressants have efficacy in multiple chronic pain conditions irrespective of comorbid chronic clinical depression.

Drug (Brand)	FDA-approved Indications	Formulations	Usual Dosing Recommendations[a]	Comments
Serotonin–Norepinephrine Reuptake Inhibitors				
Duloxetine (Cymbalta)	Chronic musculoskeletal pain due to chronic osteoarthritis or low back pain, diabetic peripheral neuropathy, fibromyalgia, GAD, MDD	20-, 30-, and 60-mg delayed-release capsules	Chronic musculoskeletal pain: 30 mg/day for 1 week to a target dose of 60 mg/day Diabetic peripheral neuropathy: the initial and target dose is 60 mg/day Fibromyalgia: 30 mg/day for 1 week to a target dose of 60 mg/day	Not recommended for use in patients with CrCl <30 mL/min Not recommended for use in patients with hepatic impairment
Milnacipran (Savella)	Fibromyalgia	12.5-, 25-, 50-, and 100-mg tablets	Fibromyalgia: the dose should be titrated as follows: • Day 1: 12.5 mg • Days 2 and 3: 12.5 mg twice daily • Days 4 to 7: 25 mg twice daily The target dose is 50 mg twice daily	Reduce the dose by 50% in patients with CrCl 5-29 mL/min Not recommended for patients with end-stage renal disease
Venlafaxine[b] (Effexor, Effexor XR, generic)	Effexor: MDD Effexor ER: GAD, MDD, panic disorder, SAD	25-, 37.5-, 50-, 75-, and 100-mg tablets (Effexor, generic) 37.5-, 75-, and 150-mg extended-release capsules (Effexor XR, generic) 37.5-, 75-, 150-, and 225-mg extended-release tablets	Neuropathic pain: initial doses of 37.5 mg once or twice daily titrated by 75 mg weekly to response or a maximum dose of 225 mg/day	Reduce the dose by 25% to 50% in patients with mild to moderate renal impairment Reduce the dose by 50% in patients with mild to moderate hepatic impairment

The safety and tolerability of duloxetine in depressed elderly patients with and without medical comorbidity

- Major depressive disorder is common in elderly patients, with an estimated prevalence of about 3%. It is often associated with physical disability and a high mortality rate.
- Elderly patients are more predisposed to depression than younger patients because of ***concurrent medical disorders***, ***chronic pain, sadness secondary to life-cycle issues and social isolation.***

- A large 4-year prospective study suggested that approximately ***25%*** of patients > 65 years with chronic medical illness suffer from depressive symptomatology . Substantial evidence supports the increased prevalence of depression in several chronic medical illnesses.
- Specifically, patients with ***cardiovascular disease***, ***diabetes mellitus, arthritis*** appear to have approximately 2–3 times the risk for depression.

Unutzer J, Patrick DL, Simon G et al. Depressive symptoms and the cost of health services in HMO patients aged 65 years and older. A 4-year prospective study. JAMA 1997; 277: 1618–23.

Comorbidity of depression and medical illness inelderly patients leads to increased morbidity and mortality, as well as higher healthcare costs.

Therefore, there is a need for a safe, well-tolerated

and effective antidepressant in elderly patients with major depressive disorder , particularly in those suffering from major depressive disorder with chronic medical illness.

Duloxetine

Duloxetine hydrochloride is an antidepressant that inhibits both serotonin (5-HT) and norepinephrine (NE) reuptake. The dual-acting mechanism of duloxetine makes it particularly interesting in the treatment of depression with cognitive impairment, as imbalance or deficiency in either (5-HT) or (NE) systems has been found to contribute to cognitive deficits. Duloxetine has been shown to treat depression effectively in the elderly.

- Results support the efficacy and tolerability of duloxetine in the treatment of elderly patients with MDD with or without common comorbid medical conditions.
- The efficacy and tolerability of duloxetine in the treatment of depression in elderly patients were not largely affected by comorbidity status.

- In older adults, major depression (MDD) and chronic low back pain (CLBP) are frequently comorbid, mutually exacerbating, and risk factors for one another.
- The studies suggest that ***Duloxetine*** at doses of up to ***120 mg/day***, delivered with ***Depression and Pain Care Management*** (DPCM) intervention, may be a rational treatment choice for older adults living with comorbid depression and CLBP.
- Treatment of these linked conditions with duloxetine + DPCM may result in improvement in low back pain before improvement in depression.

Duloxetine is effective and well tolerated in treating elderly patients with MDD.

The duloxetine vs. placebo treatment effect on cognition, depression and quality-of-life in elderly patients with MDD was not largely affected by the presence or absence of one or more of the three medical comorbidities (vascular disease, diabetes ,arthritis) that frequently occur in the elderly population.

Milnacipran

Milnacipran at single doses of up to 100 mg in healthy young volunteers is free from disruptive effects on cognitive function and psychomotor performance.

Milnacipran 75 mg (50+25 mg) appears to be free of negative effects on cognitive function in elderly volunteers, where it seemingly improves performance. In contrast, the tricyclic antidepressant amitriptyline, used here as a positive internal control, significantly impaired performance in the elderly .

This finding not only validated the sensitivity of this current test battery but also indicates the potential behavioural toxicity of amitriptyline in clinical use in the elderly.

Desvenlafaxine for menopausal symptoms (off-label use)

- Desvenlafaxine isn't approved to treat menopausal symptoms, but sometimes it's used off-label to treat menopausal hot flashes.
- Desvenlafaxine can reduce how many hot flashes you have and how severe they are. One review of studies looked at people taking desvenlafaxine ,these people had 55% to 69% fewer hot flashes with treatment than they had prior to treatment.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