CURRENT PROBLEMS OF PSYCHIATRY 2010; 11(4): 294-295

Are dual action antidepressants superior than selective antidepressants? Part II

Andrzej Czernikiewicz MD, Ph.D.

Professor and Chair of Department of Psychiatry at Medical University in Lublin, Poland

Summary

Depression is a complex disease with some psychiatric comorbidities, especially anxiety disorders and some comorbid physical symptoms.During the past few years, there has been a strong interest in the development of dual-action antidepressants with a better side effect profile. There are interesting pharmacological reasons why an antidepressant that act on more that one neurotransmitter system might have superior efficacy than antidepressant with single action. There also is an increasing body of evidence for an efficacy advantage in some patients with selective dual-action antidepressants, especially in large group of patients with high manifestation of physical symptoms of depression. Dual-acting antidepressants that inhibit reuptake of both serotonin and norepinephrine (SNRIs) treat a wider array of depressive symptoms (psychological and physical) than antidepressants that target either neurotransmitter alone. SNRIs such as venlafaxine, and duloxetine, may have an earlier onset of action, superior remission abilities, and better efficacy in treating anxiety symptoms of depression than the SSRIs. The remission rates of the patients taking venlafaxine were significantly higher than those of the patients taking SSRIs, regardless of age or gender. Overall, dual-acting agents appear to be more effective than single-acting agents in improving mood, reducing pain, and increasing the chance of remission.

Key words: antidepressants – SNRIs - SSRIs– treatment guidelines

Therapeutic choices of antidepressants according depressive disorders

These therapeutic choices of antidepressants are based on guidelines presented in book "Treating depression effectively" [2].

MAJOR DEPRESSIVE DISORDER

SSRIs and SNRIs have superior side-effect profiles and in most cases at least comparable efficacy to TCAs. Thase has resulted in their adoption as first-line antidepressants for the treatment of major depressive disorder. As it was mentioned above recent evidence has been presented to support higher rates of remission for dual-action antidepressants compared with SSRIs [1] (Table 1).

MDD WITH MELANCHOLIC FEATURES

There are conflicting claims about treatment superiority of antidepressants in depression with melancholic feature. Clomipramine was associated with higher remission rates than two drugs from SSRI class (sertraline and paroxetine) and moclobemide in some individual trials and meta-analysis confirmed that TCAs were superior than SSRIs in the treatment of depression with melancholic features but produces worse side-effects. Venlafaxine, as it was mentioned above, produced higher remission rates compared with fluoxetine. On the other hand, in another meta-analysis paroxetine, venlafaxine, and moclobemide were found to be comparable to TCAs [1] (Table 2).

Table 1. Recommendations for treatment of MDD

Therapeutic choice	Recommendations	Evidence level
First	SSRI, SNRI	1
Second	AMITRYPTYLINE, CLOMIPRAMINE	2
Third	other TLPD, MAOI	2

Table 2. Recommendations for treatment of MDD with melancholic features

Therapeutic choice	Recommendations	Evidence level
First	PAROXETINE, VENLAFAXINE	1
Second	TCAS, especially CLOMIPRAMINE	1
Third	CITALOPRAM, FLUOXETINE, MOCLOBEMIDE	2

Tolerance of selective and dual action antidepressants

From tolerance point of view, the SSRIs are generally better tolerated than the TCAs because of their low affinity for the histaminergic, cholinergic, and alpha-adrenergic receptors. The most common adverse effects include nausea, headache, nervousness, incoordination, insomnia, fatigue, sexual dysfunction, and tremor. Nausea and headache usually resolve with continued treatment (within 1-2 weeks) or dosage reduction. Jitteriness and insomnia early in treatment can be minimized by initiating lower doses or adding a benzodiazepine. Paroxetine often has mild anticholinergic effects. Sexual dysfunction is manifested as ejaculatory delay and impotence in men and anorgasmia in women [1,2].

Most adverse effects associated with venlafaxine are mild to moderate, occur early in the course of treatment, and resolve with continued therapy. Nausea occurs most commonly and is dose-related. It can be minimized by starting therapy with lower dosages (25 mg) and titrating upward gradually. Nausea diminishes with time once the maintenance dose is reached. Sweating, tremor, and agitation occur only at higher doses. Significant dose-dependent increases in blood pressure have been reported at dosages greater than 75 mg/day and limit use in patients with borderline or existing hypertension [1,2].

Use of dual action antidepressants for the treatment of anxiety disorders

80 to 90% of individuals with Major Depressive Disorder also have anxiety symptoms (e.g., anxiety, obsessive preoccupations, panic attacks, phobias, and excessive health concerns). About one third of individuals with Major Depressive Disorder also have a full-blown anxiety disorder (usually either Panic Disorder, Obsessive-Compulsive Disorder, or Social Phobia). Anxiety in a person with major depression leads to a poorer response to treatment, poorer social and work function, greater likelihood of chronicity and an increased risk of suicidal behavior. Most SSRIs and venlafaxine have proven efficacy in the treatment of different subtypes of anxiety disorders. Venlafaxine were found to be comparable to SSRI with anxiolitic properties – paroxetine [3].

Conclusions

1. Depression is a complex disease with some psychiatric comorbidities, especially anxiety disorders and some comorbid physical symptomsDual-acting antidepressants that inhibit reuptake of both serotonin and norepinephrine (SNRIs) treat a wider array of depressive symptoms (psychological and physical) than antidepressants that target either neurotransmitter alone.
3. SNRIs such as venlafaxine, and duloxetine may have an earlier onset of action, superior remission abilities, and better efficacy in treating anxiety symptoms of depression than the SSRIs.

References

1. Kennedy S.H., Lam R.W., Nutt D.J., Thase M.E. Treating depression effectively. Applying clinical guidelines. Martin Dunitz; London-New York: 2007.
2. Smith D., Dempster C., Glanville J., Freemantle N., Anderson I. Efficacy and tolerability of venlafaxine compared with selective serotonin reuptake inhibitors and other antidepressants: a meta-analysis. Br. J. Psychiatry, 2002; 180: 396-404.
3. Feetam C. Depression with anxiety symptoms. In: Taylor D., Paton C. eds., Clinical studies in psychopharmacology: The use of drugs in psychiatry. Martin Dunitz; New York-London: 2002.

Correspondence address

Andrzej Czernikiewicz MD, Ph.D.
Professor and Chair of Department of Psychiatry at Medical University in Lublin, Poland