

Selecting the Appropriate Antidepressant

By Stephanie Skinner, Pharm.D. and
Cathy H. Turner, Pharm.D., BCPS

For the 16% of adults who will experience an episode of depression during their lifetime,^{1,2} medication therapy is recommended as first-line treatment. Selecting a depression medication is often a difficult task, however, because several variables influence choice of therapy: efficacy, tolerability, and medication cost.

Currently pharmacologic regimens, first- and second-generation antidepressants, demonstrate similar efficacy.^{3,4} However, the first generation antidepressants (i.e., amitriptyline, nortriptyline, desipramine, etc.) are often associated with intolerable side effects.^{2,3} Second generation antidepressants, including selective serotonin reuptake inhibitors (ex. fluoxetine, sertraline, paroxetine, citalopram) exhibit high efficacy and an improved side effect profile; however, intolerable side effects are still reported with these agents.

The Lancet recently published a meta-analysis of 117 studies comparing the efficacy and acceptability of the second generation antidepressants.⁵ Efficacy was defined as a 50% reduction from baseline in the depression rating scale at eight weeks; the specific rating scale varied according to trial design. Acceptability was measured by the dropout rate at eight weeks. Results were considered statistically significant if the p-values were less than 0.05. Comparative efficacy was evaluated using fluoxetine as the reference drug since it was the first of these agents on the market.

Table 1: Efficacy of 2nd Generation Antidepressants Versus Fluoxetine

Medication	OR	95% CI
Bupropion (Wellbutrin®)	0.93	0.77-1.11
Citalopram (Celexa®)	0.91	0.75-1.08
Duloxetine (Cymbalta®)	1.01	0.81-1.27
Escitalopram (Lexapro®)	0.76*	0.65-0.89
Fluvoxamine (Luvox®)	1.02	0.81-1.30
Milnacipran (Savella™)	0.99	0.74-1.31
Mirtazapine (Remeron®)	0.73*	0.60-0.88
Paroxetine (Paxil®)	0.98	0.86-1.12
Reboxetine †	1.48*	1.16-1.90
Sertraline (Zoloft®)	0.80*	0.69-0.93
Venlafaxine (Effexor®)	0.78*	0.68-0.90

OR=odds ratio, CI= Confidence Interval, *p<0.05,
† indicates medication not available in the US
Note: OR >1 = Fluoxetine superior

Table 2: Acceptability of 2nd Generation Antidepressants Versus Fluoxetine

Medication	OR	95% CI
Bupropion (Wellbutrin®)	1.12	0.92-1.36
Citalopram (Celexa®)	1.11	0.91-1.37
Duloxetine (Cymbalta®)	0.84	0.64-1.10
Escitalopram (Lexapro®)	1.19	0.99-1.44
Fluvoxamine (Luvox®)	0.82	0.62-1.07
Milnacipran (Savella™)	0.97	0.69-1.32
Mirtazapine (Remeron®)	0.97	0.77-1.21
Paroxetine (Paxil®)	0.91	0.79-1.05
Reboxetine †	0.70*	0.53-0.92
Sertraline (Zoloft®)	1.14	0.96-1.36
Venlafaxine (Effexor®)	0.94	0.81-1.09

OR=odds ratio, CI= Confidence Interval, *p<0.05
† indicates medication not available in the US
Note: OR < 1 = Fluoxetine superior

Escitalopram, mirtazapine, sertraline, and venlafaxine demonstrated superior efficacy compared to fluoxetine, while escitalopram, sertraline, bupropion and citalopram demonstrated superior acceptability. If both efficacy and acceptability are considered, escitalopram and sertraline should be used for initial antidepressant therapy. Preference may be given to sertraline since it is

generically available thus reducing cost to the patient.⁵

Commentary

The results of this meta-analysis contradict a long-held belief by many clinicians that all SSRIs are equally effective and tolerable with patient specific variations only. Current treatment protocols recommend initiating SSRI therapy, and if ineffective, switching to another SSRI before using another second generation antidepressant. Now clinicians have evidence to support the use of a specific agent, sertraline, as first-line therapy. This evidence comes without manufacturer bias; the meta-analysis was not supported by any pharmaceutical manufacturer and results of a meta-regression analysis to assess potential sponsorship bias indicated no substantial change in final rankings.

The authors also challenge trial investigators to use sertraline as the new standard against which new antidepressant therapies should be judged in order raise the efficacy bar for new agents and thereby minimize the number of me-too antidepressants on the market that offer little advantage to the patients for a higher price. With current regulatory standards requiring placebo-controlled trials, it is only hoped that the research community will answer this call.

References

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