Newer Antidepressants Differ Mainly in Safety

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PHOENIX — Second-generation antidepressants do not differ significantly from each other in efficacy or effectiveness, a study funded by the federal Agency for Healthcare Research and Quality shows.

There are some differences, however, in the rapidity of drug action and in rates of individual adverse events that may help providers choose among these medications, Dr. Bradley N. Gaynes said at a meeting of the New Clinical Drug Evaluation Unit sponsored by the National Institutes for Mental Health.

Use of the 12 second-generation antidepressants has skyrocketed over the past 15 years, easily eclipsing the use of tricyclic antidepressants in managing major depressive disorder. The retrospective analysis included results from 203 studies culled from the medical literature, online libraries, international pharmaceutical abstracts, and unpublished data from three drug companies.

No significant differences were found between second-generation antidepressants in either efficacy or quality of life measures in 80 head-to-head comparisons that included more than 17,000 adults, noted Dr. Gaynes of the University of North Carolina, Chapel Hill, and his associates.

A meta-analysis of 62 placebo-controlled trials was performed for indirect comparisons between second-generation antidepressants, which showed a few statistically significant differences that were modest and "likely not clinically important," he said.

For example, seven studies comparing escitalopram (Lexapro) with citalopram (Celexa) found a slightly greater response to escitalopram, but the magnitude of difference was about a third of what would be needed to be considered clinically significant. Slightly greater efficacy seen with sertraline compared with fluoxetine, or with venlafaxine (Effexor) compared with fluoxetine, comprised "a small fraction" of what would be needed to show a clinically meaningful difference between drugs, he noted.

Results from three studies of effectiveness under real-world conditions were similar to those from efficacy trials, with no significant differences in effectiveness or quality of life between drugs. "Although efficacy was similar, it didn't mean that all of the antidepressants were the same. They're not identical," Dr. Gaynes said.

Mirtazapine (Remeron), for example, showed a more rapid onset of action than did selective serotonin reuptake inhibitors in seven trials after a week or two of treatment, but the difference between drugs disappeared by 4 weeks of treatment. "Whether this could be extrapolated to other second-generation antidepressants is unclear," he commented.

Analyses of adverse events reported in 80 head-to-head, randomized, controlled trials and 42 other experimental and observational studies showed that about 23% of patients on any second-generation antidepressant discontinue the medication. Patients who were on venlafaxine were more likely to discontinue treatment because of side effects but less likely to stop treatment from lack of efficacy compared with other second-generation antidepressants.

Nausea and vomiting were more common with the serotonin-norepinephrine reuptake inhibitor (SNRI) venlafaxine (33%) than with SSRIs (22%). Diarrhea was more common with sertraline (Zoloft) (11%) than with other medications (8%). Weight gain was more likely with mirtazapine than with SSRIs and ranged from 0.8 to 3 kg after 6-8 weeks.

Trazodone caused more somnolence than did other medications with which it was compared. The SSRIs were more likely than was bupropion to cause sexual dysfunction. Among SSRIs, sexual dysfunction rates were higher with paroxetine (Paxil) (21%) compared with other SSRIs (5%), though the strength of the evidence was mild, he said.

Dr. Gaynes is associated with several companies that make antidepressants. He has been an adviser or consultant to Pfizer and Shire Pharmaceuticals, has received grants from Pfizer and Ovation Pharmaceuticals, and has been a speaker for GlaxoSmithKline.

Pharmaceutical companies funded 69% of the studies included in the analysis. Government or independent sources funded 9%, and the source of funding wasn't clear for 22% of the studies. ■

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