Newer Antidepressants Not Always Better

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Old standby Zoloft? Late-model Lexapro? New antidepressants might be no more effective than the best existing drugs, according to two new systematic reviews that compared 12 commonly used medications.

New antidepressants might be no more effective than the best existing drugs, according to two new systematic reviews that compared 12 commonly used medications. “Patients are usually encouraged to take the newest medication,” said lead author Andrea Cipriani, M.D., of the University of Verona, in Italy. “But it’s better to have an old treatment that has been proved with many patients and many years in the market.” The reviews suggest that sertraline — sold under the brand name Zoloft since 1991— could be the best initial choice of antidepressant in people with acute major depression. The generic formulation produced the best balance of effectiveness, tolerability and purchase price, the authors say.

Patients also did well on one of the newest antidepressants, escitalopram (Lexapro), but it is not yet available in lower-cost generic form. The authors note that comprehensive economic studies are necessary to evaluate overall cost-effectiveness of various treatments.

Cipriani said that the review recommendations are for new episodes of depression. “If a patient is taking another drug and doing well, we are not saying he has to change.”

The reviews appear in the most recent issue of *The Cochrane Library*, a publication of The Cochrane Collaboration, an international organization that evaluates medical research. Systematic reviews draw evidence-based

conclusions about medical practice after considering both the content and quality of existing medical trials on a topic.

Depression is the fourth-leading cause of disease burden worldwide and antidepressant drugs are now the mainstay of treatment for moderate to severe cases. The aim of the two reviews was to compare the benefits and side effects of sertraline and escitalopram, respectively, with those of other antidepressants during the first six to 12 weeks of treatment.

Cipriani noted that all of the included studies compared one drug against another — not to a placebo — so the results reveal not the absolute effect, but rather the relative advantages and disadvantages of various medications.

In addition, these reviews rely on summary data from each study, rather than individual patient data. Future studies that go into greater detail can help identify the best medications for various subgroups of patients such as men vs. women, teens vs. adults and so on.

For sertraline, the reviewers included 59 randomized controlled trials totaling about 10,000 participants. Sertraline proved more effective than fluoxetine (Prozac), but less effective than mirtazapine (Remeron). In terms of side effects, bupropion (Wellbutrin) was easier to tolerate than sertraline, while the latter outscored amitriptyline (Elavil), imipramine (Tofranil), paroxetine (Paxil) and mirtazapine (Remeron).

For escitalopram, the reviewers included 22 randomized controlled trials totaling about 4,000 participants. Few statistically significant differences appeared in this review, although escitalopram was more effective than citalopram (Celexa) and fluoxetine (Prozac) and had fewer side effects than duloxetine (Cymbalta). The drug manufacturer sponsored most of the studies in this review, so there may be biases in favor of escitalopram.

Rather than seeking genuine advances in treatment, the review authors say, some pharmaceutical companies seem to be introducing close chemical cousins of generic medications. By gaining patent protection for the “new” drug, a company can market it as a higher-priced brand name product.

Sponsorship bias is a recurring concern in trials of virtually all new medications. In the Cochrane reviews themselves, one of the co-authors has received research funds and speaking fees from the companies Asahi Kasei, Astellas, Dai-Nippon Sumitomo, Eisai, Eli Lilly, GlaxoSmithKline, Janssen, Kyowa Hakko, Meiji, Nikken Kagaku, Organon, Otsuka, Pfizer and Yoshitomi. The Japanese Ministry of Education, Science and Technology, and the Japanese Ministry of Health, Labour and Welfare have also funded some of his research.

However, the co-authors of these Cochrane reviews also published a recent study in The Lancet that was free of any potential funding bias. The study also used a more complex statistical method to analyze data from 117 randomized controlled trials involving 25,928 participants.

The findings support the Cochrane reviews, Cipriani said, with sertraline and escitalopram ranking as the best treatments.

“Such findings have enormous implications,” said Sagar Parikh, M.D., of the University of Toronto, in a commentary published along with The Lancet study. “For the clinician, prudent engagement of the patient in treatment ideally involves giving the patient a choice.… A new gold standard of reliable information has been compiled for patients to review.”

In early studies, new medical treatments are typically compared to sham treatments. Once the effectiveness of certain approaches is well established, new options must be judged against the best existing

treatments.

Cipriani argued that this time has come for antidepressants, and that sertraline is the drug to beat. “We need new treatments in psychiatry, but they have to be proved better than other treatments,” he said. “We should be comparing new drugs to the best available existing drugs.”

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