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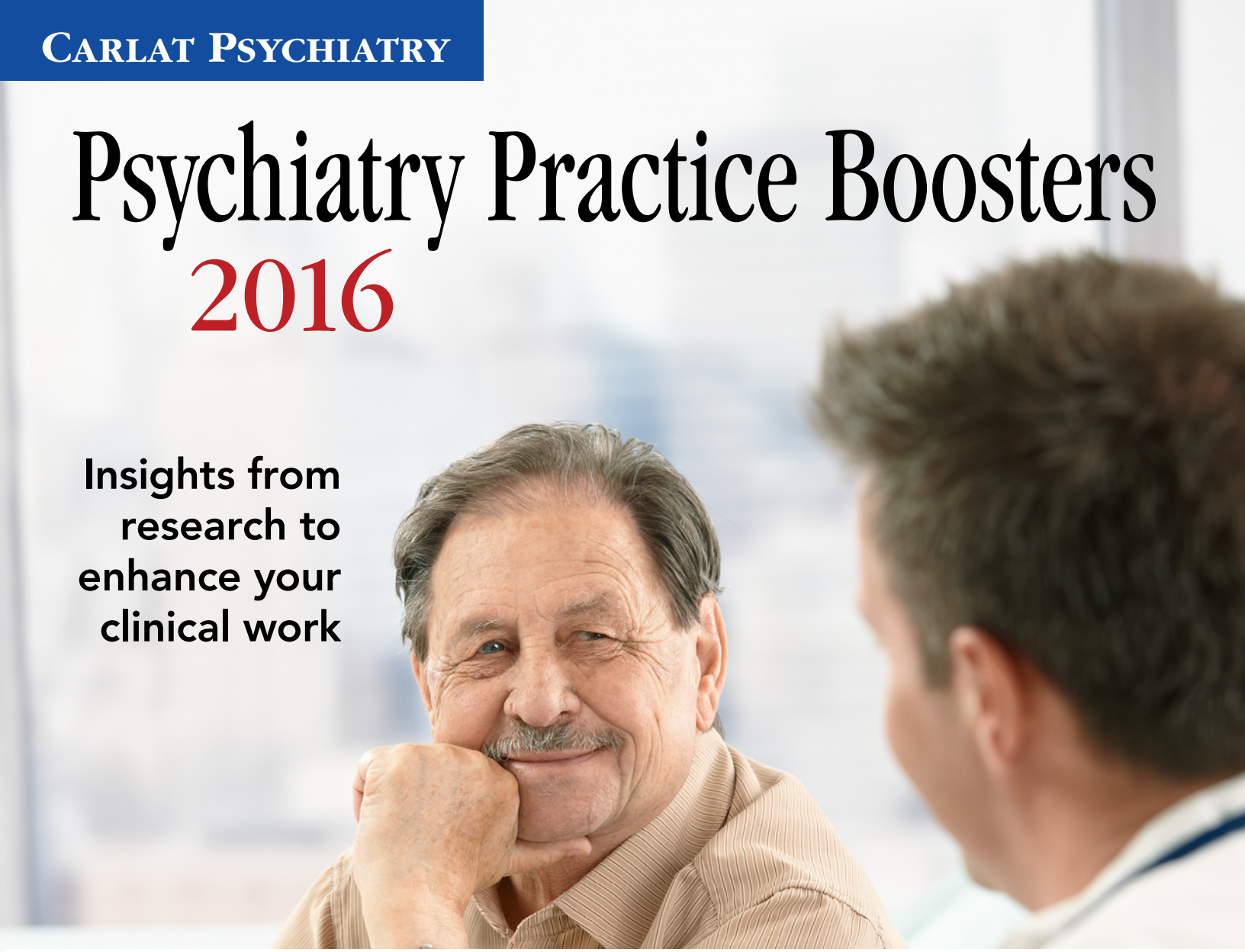

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Light Therapy for Non-Seasonal Depression

REVIEW OF: Lam RW, Levitt AJ, Levitan RD, et al. Efficacy of bright light treatment, fluoxetine, and the combination in patients with nonseasonal major depressive disorder: a randomized clinical trial. *JAMA Psychiatry.* 2016;73(1):56–63. doi:10.1001/jamapsychiatry.2015.2235.

STUDY TYPE: Randomized double-blind placebo-controlled trial

Most of us know that light therapy is effective for seasonal affective disorder (SAD), but does it work for non-seasonal depression?

Recall that SAD is defined as recurrent episodes of depression that occur at a particular time of year (usually winter) and that completely remit at another time (usually the spring). By the way, DSM-5 doesn't use the term SAD, but instead calls it "major depressive disorder with seasonal pattern."

Whether light therapy works for non-seasonal depression is unclear. Systematic reviews have yielded inconclusive results, in part because prior studies have had methodological weaknesses. A new study with a robust design was published in 2016.

Over a 5-year period, researchers recruited 122 adult patients with non-seasonal major depression between the ages of 19 through 60 from three clinics in Canada. The patients were randomized to one of four groups: light therapy alone, fluoxetine 20 mg plus light therapy (combination treatment), fluoxetine 20 mg plus sham negative ion treatment, and double placebo (placebo pills plus negative ion). Light therapy was given with a 10,000-lux fluorescent light box for 30 minutes daily in the early morning. The study lasted 8 weeks, and 106 participants completed it. The primary outcome measure was change in the Montgomery-Åsberg Depression Rating Scale (MADRS); secondary outcomes included response and remission rates.

RESULTS

At study conclusion, both light therapy and combination therapy were superior to placebo; however, combination therapy beat placebo more convincingly. Whereas light therapy alone yielded lower MADRS scores than placebo, combination therapy bested placebo not only on MADRS scores, but also on response rates and remission rates. Surprisingly, fluoxetine was not significantly better than placebo; the authors attributed this to small sample size.

Here are the numbers: Average improvements in MADRS scores were 16.9 (combined fluoxetine and light), 13.4 (light therapy only), 8.8 (fluoxetine and sham light), and 6.5 (placebo). Response rates (defined as ≥ 50% drop in MADRS score) for combined treatment, light, fluoxetine, and placebo were 76%, 50%, 29%, and 33%, respectively. Remission rates (defined as MADRS score ≤ 10) were 59%, 44%, 19%, and 30%.

THE CARLAT TAKE

This is probably the best-designed clinical trial of light therapy for non-seasonal depression to date, and the results endorse both light monotherapy and combination light and fluoxetine, with the combination being possibly more robust. Both combination treatment and light monotherapy beat fluoxetine alone in this trial.

PRACTICE IMPLICATIONS

The bottom line is that, at least for depressed patients in the higher latitudes, we should consider changing our standard practice of prescribing an antidepressant alone. Having patients add light therapy every morning for several weeks may well optimize antidepressant treatment.

The New Three-Month Version of Injectable Paliperidone: Should You Use It?

REVIEW OF: Berwaerts J, Liu Y, Gopal S, et al. Efficacy and safety of the 3-month formulation of paliperidone palmitate vs placebo for relapse prevention of schizophrenia: a randomized clinical trial. *JAMA Psychiatry.* 2015;72(8):830–839. doi:10.1001/jamapsychiatry.2015.0241.

STUDY TYPE: Randomized double-blind placebo-controlled trial

Long-acting injectable antipsychotics (LAI), formerly known as "depot" neuroleptics, are good options for some patients—primarily those who either forget or don't want to take their pills. While studies have not always shown a clear advantage of LAIs over orals, there's no question that they can play a useful role for some. All previously available LAIs (there are 6 options out there) had to be given no less frequently than every 2–4 weeks. Now, a 3-month formulation of paliperidone (Invega Trinza) has been developed and approved by the FDA. What did the pivotal research trial show?

506 patients were recruited from multiple study sites spanning eight countries. For the first 17 weeks, all patients were treated with the standard once-monthly version of injectable paliperidone (Invega Sustenna). After dropouts, 379 patients were left, and all were switched to a 12-week trial of Invega Trinza. After additional dropouts, 305 patients were left, and they were randomly assigned to either continued treatment with Trinza (n = 160) or placebo injectable (n = 145). These patients were followed on average for 6 to 9 months.

RESULTS

The main outcome was percent of patients who relapsed to psychosis. Only 11 patients (7%) relapsed while on Trinza, significantly fewer than the 31 patients (23%) who relapsed on placebo. Because of the large efficacy difference between Trinza and placebo, the study was ended early. Trinza was well-tolerated. The main side effects reported more frequently on Trinza than placebo were headaches (9% vs. 4% on placebo), weight gain (9% vs. 3%), and akathisia (4% vs. 1%). While the study was not designed to compare different doses, patients on the 525 mg dose of paliperidone were more likely to last longer before relapse than those taking the 350 mg dose.

THE CARLAT TAKE

Trinza was more effective than placebo, and the magnitude of the advantage was so large the study was stopped early. Sounds good, but there are a couple of caveats. First, Trinza was contrasted with placebo as opposed to comparable and cheaper active agents, such as oral meds or other LAIs. This means that we don't know whether the new formulation really has an advantage over its competitors.

In fact, the study design inherently favored preparations made with paliperidone. How? The only patients who received Trinza were those who had already done well for 4 months on

paliperidone monthly injectable. This "enriched" sample essentially stacks the deck in favor of Trinza. It would be like doing a consumer taste test of a new version of Coca-Cola, but only including consumers who had been enjoying the older version of Coke. By excluding those who prefer Pepsi from your trial, you'd expect your new version of Coke to be given high marks. Analogously, if you were considering switching a patient from, say, Haldol decanoate to paliperidone, that patient might be less likely to do as well as the patients in this study.

Nonetheless, an antipsychotic preparation that lasts for 3 whole months is a genuine innovation, and we're happy to have another option for patients.

PRACTICE IMPLICATIONS

If you have patients who are noncompliant with oral meds, offer them an LAI, and if insurance will pay, consider going with paliperidone monthly in preparation for an eventual switch to Trinza. If your patient is already on monthly paliperidone, but doesn't like monthly shots, then it's reasonable to try the switch to the 3-month version. But if your patient is stable on any other injectable, we don't know if the switch will be effective.