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Light therapy for nonseasonal major depressive disorder?

While bright light therapy already has a place in the treatment of seasonal affective disorder, a recent trial spotlights its utility beyond the winter months.

PRACTICE CHANGER

Consider treatment with bright light therapy, alone or in combination with fluoxetine, for patients with nonseasonal major depressive disorder (MDD).[1]

STRENGTH OF RECOMMENDATION

B: Based on a single moderate-quality randomized control trial.

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;73:56-63.

ILLUSTRATIVE CASE

A 38-year-old woman recently diagnosed with MDD without a seasonal pattern comes to see you for her treatment options. Her Hamilton Depression Rating Scale (HAM-D) is 22, and she is not suicidal. Should you consider bright light therapy in addition to pharmacotherapy?

MDD is one of the most common psychiatric illnesses in the United States, affecting approximately one in 5 adults at some point in their lives.[2] Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors are considered effective first-line pharmacotherapy options for MDD.[2,3] Despite their effectiveness, however, studies have shown that only about 40% of patients with MDD achieve remission with first- or second-line drugs.[2] In addition, pharmacologic agents have a higher frequency of treatment-associated adverse effects than fluorescent light therapy.[4]

A Cochrane systematic review of 20 studies (N=620) showed the effectiveness of combined light therapy and pharmacotherapy in treating nonseasonal MDD, but found no benefit to light used as a monotherapy.[5] However, the majority of the studies were of poor quality, occurred in the inpatient setting, and lasted fewer than 4 weeks.

In a 5-week, controlled, double-blind trial not included in the Cochrane review, 102 patients with nonseasonal MDD were randomized to receive either active treatment (bright light therapy) plus sertraline 50 mg daily or sham light treatment (using a dim red light) plus sertraline 50 mg daily. The investigators found a statistically significant larger reduction in depression score in the active treatment group than in the sham light group, based on the HAM-D, the Hamilton 6-Item Subscale, the Melancholia Scale, and the 7 atypical items from the Structured Interview Guide for the Seasonal Affective Disorder version of the HAM-D.[6,7]

STUDY SUMMARY

Light therapy improves depression without a seasonal component

This latest study was an 8-week randomized, double-blind, placebo- and sham-controlled clinical trial evaluating the benefit of light therapy with and without pharma-

cotherapy for nonseasonal MDD.[1] The investigators enrolled 122 adult patients (ages 19-60 years) from outpatient psychiatry clinics with a diagnosis of MDD (as diagnosed by a psychiatrist) and a HAM-D[8] score of at least 20. Subjects had to be off psychotropic medication for at least 2 weeks prior to the first visit and were subsequently monitored for one week to identify spontaneous responders and to give patients time to better regulate their sleep-wake cycle (with the goal of sleeping only between 10:00 pm and 8:00 am daily).

The investigators randomly assigned patients to one of 4 treatment groups: active light monotherapy (10,000-lux fluorescent white light for 30 min/d early in the morning) plus a placebo pill; fluoxetine 20 mg/d plus sham light therapy; placebo pills with sham light therapy; and combined active light therapy with fluoxetine 20 mg daily. Sham light therapy consisted of the use of an inactivated negative ion generator, used in the same fashion as a light box. All patients were analyzed based on modified intention to treat.

The investigators monitored patients for adherence to active and sham treatment by review of their daily logs of device treatment times. Pill counts were used to assess medication adherence. The primary outcome at 8 weeks was the change from baseline in the Montgomery-Asberg Depression Rating Scale (MADRS), a 10-item questionnaire with a worst score of 60.[9] Secondary outcomes were treatment response (≥50% MADRS score reduction) and remission (≤10 MADRS score) at the final 8th-week visit. MADRS scoring was used because of its higher sensitivity to treatment-induced changes and its high correlation with the HAM-D scale.

At the end of 8 weeks, the mean (standard deviation [SD]) changes in MADRS scores from baseline were: light monotherapy 13.4 (7.5), fluoxetine monotherapy 8.8 (9.9), combination therapy 16.9 (9.2), and placebo 6.5 (9.6). The improvement was significant in the light monotherapy treatment group vs the placebo group (P=.006), in the combination treatment group vs the placebo group (P<.001), and in the combination group vs the fluoxetine treatment group (P=.02), but not for the fluoxetine treatment group vs the placebo group (P=.32). The effect sizes vs placebo were: fluoxetine, d=0.24 (95% confidence interval [CI], −0.27 to 0.74); light monotherapy, 0.80 (95% CI, 0.28 to 1.31); and combination therapy, 1.11 (95% CI, 0.54 to 1.64). Effect sizes of more than 0.8 are often considered large.[10]

The treatment response (≥50% MADRS improvement) rate was highest in the combination treatment group (75.9%) with response rates to light monotherapy, placebo, and fluoxetine monotherapy of 50%, 33.3%, and 29%, respectively. There was a significant response effect for the combination vs placebo treatment group (P=.005). Similarly, there was a higher remission rate in the combination treatment group (58.6%) than in the placebo, light monotherapy, or fluoxetine treatment groups (30%, 43.8%, and 19.4%, respectively) with a significant effect for the combination vs placebo treatment group (P=.02).

Combination therapy was superior to placebo in treatment response (≥50% reduction in the MADRS score) and remission (MADRS ≤10) with numbers needed to treat of 2.4 (95% CI, 1.6-5.8) and 3.5 (95% CI, 2.0-29.9), respectively.

By the end of the 8-week study period, 16 of 122 patients had dropped out; 2 reported lack of efficacy, 5 reported adverse effects, and the remainder cited administrative reasons, were lost to follow-up, or withdrew consent.

Seventy-six percent of patients treated with fluoxetine and light therapy saw at least a 50% improvement in their depression scores.

WHAT'S NEW?

New evidence on a not-so-new treatment

We now have evidence that bright light therapy, either alone or in combination with fluoxetine, is efficacious in increasing the remission rate of nonseasonal MDD.

CAVEATS

Choice of SSRI, geography, and trial duration may have affected results

A single SSRI (fluoxetine) was used in this study; other more potent SSRIs might work better. This study was conducted in southern Canada, and light therapy may not demonstrate as large a benefit in regions located farther south. The study excluded pregnant and breastfeeding women.

CONTINUED

The trial duration was relatively short, and the investigators did not attain their preplanned sample size for the study, which limited the power to detect clinically significant seasonal treatment effects and differences between the fluoxetine and placebo groups, regardless of whether they received active phototherapy.

Also, it's worth noting that there were trends for some adverse events (nausea, heartburn, weight gain, agitation, sexual dysfunction, and skin rash) to occur less frequently in the combination group than in the fluoxetine monotherapy group. Possible explanations are that the study had inadequate power, that the sham treatment did not adequately blind patients, or that light therapy can ameliorate some of the adverse effects of fluoxetine.

We now have evidence that bright light therapy, alone or in combination with fluoxetine, is efficacious in increasing the remission rate of nonseasonal major depressive disorder.

CHALLENGES TO IMPLEMENTATION

Commercial insurance doesn't usually cover light therapy

Bright light therapy is fairly safe, and some evidence exists supporting its use in the treatment of nonseasonal MDD; however, the data for its use in this area are limited.[11] Since only a few studies have tested light therapy for nonseasonal MDD, significant uncertainty remains about patient selection, as well as optimal dose, timing, and duration of light therapy in the management of nonseasonal MDD.[12] Although the risks associated with bright light therapy are minimal, the therapy can lead to mania or hypomania,[3] so clinicians need to monitor for such effects when initiating therapy.

Lastly, commercial insurance does not usually cover light therapy. The average price of the bright light devices, which can be found in medical supply stores and online outlets, ranges between $118 and $237.[4,12] However, such devices are reusable, making the amortized cost almost negligible.[13] JFP

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