Drug treatment for winter depression

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Abstract

For patients with winter depression, or seasonal affective disorder (SAD), winter type, when there appears to be no response to bright-light therapy via the eyes, or the patient prefers another mode of treatment, a prescription of an antidepressant drug needs to be considered. Based on the current evidence, the best choice would in these cases be bupropion, sertraline, moclobemide, or fluoxetine. For patients with winter depression, the daily dosages are similar to those used in the treatment of non-seasonal major depressive disorder, but the duration of treatment in patients with winter depression may be shorter than that in other conditions, albeit if aiming at prevention of the subsequent major depressive episodes.

Introduction

The seasonal pattern, or seasonal affective disorder (SAD), is common (1). The first systematic description of this disorder on the basis of 29 patients was published by a U.S. research group at the National Institute of Health in 1984 (2), after which the term SAD was coined and soon became more popular than the initial one, winter depression (3). However, it is of note here that this disorder was originally described in a research article on a sample of 26 male patients living in Finland (4) as well as in another research article on a sample of 4 soldiers fighting in Finland (5). Articles that have been published in *Psychiatria Fennica*, or in a language other than English, might indeed have had a greater impact than they currently have if the publication were to have been more familiar among scientists.

According to the current diagnostic criteria (DSM-5) for mood disorder with the seasonal pattern, that two major depressive episodes have occurred in the last two years, with a regular temporal relationship between the onset of major depressive

episodes in bipolar type 1 or bipolar type 2 disorder or recurrent major depressive disorder and a particular time of the year, and no non-seasonal major depressive episodes have occurred during that same period. Approximately 10-20% of individuals with recurrent major depressive disorder and 15-22% of those with bipolar disorder have the seasonal pattern (6). Among patients with SAD, the clinical course is estimated to be unipolar in 78-88% and bipolar in 12-22%.

Major depressive episodes are highly recurrent both in patients with major depressive disorder and in patients with bipolar disorder, with or without the seasonal pattern. However, those with seasonal major depressive disorder have had on average 13.4 major depressive episodes as compared with the 10.8 episodes in non-seasonal major depressive disorder, and those with seasonal bipolar disorder on average 20.7 episodes as compared with the 11.7 episodes in non-seasonal bipolar disorder (6). Given the average duration of a SAD major depressive episode, individuals with the seasonal pattern experience symptoms 40-50% of the year, usually year after year (1).

Responses to antidepressant medications may be incomplete, and if they are, such treatment failures lead to longer illness durations, reduced recovery rates, and higher relapse rates. Further options for improving responses to medications should be considered for those patients with psychotic symptoms. In these rare cases, however, SAD, whether winter type or not, is likely to be a co-morbid disorder of another condition. Thus, public health and mental health goals need to include effort towards more effective treatments and their combinations, together with preventive measures, of depressive episodes in general, and those of SAD in specific.

Randomized controlled trials

Data from randomized, controlled trials suggest that antidepressants are effective in the treatment of winter depression.

Three double-blind, placebo-controlled trials with the parallel design on 289 patients with winter depression have studied antidepressant drugs (7-9).

Sertraline, a selective serotonin reuptake inhibitor (SSRI), produced a significantly greater response than placebo in a multi-centre, multi-country, flexible-dose (50-200 mg daily) trial of 8-week duration on 187 patients (7).

Fluoxetine (20 mg daily), another SSRI, produced a slightly higher response rate than placebo in a multi-centre, one-country trial of 5-week duration on 68 patients (8).

Moclobemide (400 mg daily), a reversible inhibitor of monoamine oxidase A, seemed to be no more effective than placebo in a one-centre trial of 3-week duration on 34 patients (9).

In addition to these three trials, a double-blind, active-control trial with the parallel design has studied antidepressant drugs (10).

In a trial of 6-week duration with fluoxetine (20-40 mg daily) or with moclobemide (300-450 mg daily) on 32 patients demonstrated good efficacy for both drugs (10). In this multi-centre trial, 581 depressed patients attended psychiatric services in Finland, 183 (32%) patients were eligible, and of these 32 (18%) met the DSM-III-R criteria for mood disorder with the seasonal pattern and 19 (11%) met the original criteria (2) for SAD.

The results of all these 4 aforementioned trials, however, should be accepted cautiously because of their short duration.

To address this caveat and to test the efficacy in prevention of the depressive episode of winter depression, three randomized, double-blind, placebo-controlled trials with the parallel design on 1042 patients were conducted (11). Patients were enrolled during the autumn, started with extended-release bupropion (150-300 mg daily) while still well, used it until "the first week of spring", as the authors put it, and were thereafter followed for 8 weeks up to the first week of June (11). These multi-centre, two-country trials yielded the relative risk reduction of 44% for patients taking bupropion, and survival analyses for the onset of a depressive episode favoured bupropion over placebo (11). After publication of these results, the U.S. Food and Drug Administration approved bupropion for treatment of winter depression as well as for prevention of winter depression.

Other trials

Most of the remaining 45 trials for treatment of winter depression have included relatively few individuals (12-56). In addition, many of these trials, starting with a trial with melatonin in 1985, were not designed a priori as formal pharmacological randomized controlled trials, but instead they analysed the clinical effects during a test of the hypothesized mechanisms of action in the pathogenesis of winter depression. Hence, no evidence-based data can be derived from these trials.

Conclusion

For patients with winter depression, or seasonal affective disorder (SAD), winter type, the first-line treatment of choice is bright-light therapy via the eyes.

When there appears to be no response to bright-light therapy via the eyes, or the patient prefers another mode of treatment, a prescription needs to be considered. Based on the current evidence, the best choice would then be bupropion, moclobemide, or one of the selective serotonin reuptake inhibitors (sertraline or fluoxetine). No harmful drug-light interactions have been reported in the context of bright-light therapy via the eyes.

The daily dosages of antidepressants used for treatment of SAD are similar to those used in the treatment of non-seasonal major depressive disorder or bipolar disorder, but the duration of treatment in patients with winter depression can often be shorter than that required for other conditions. However, considering the prevention of major depressive episodes, an antidepressant may be started while still feeling well in the autumn and continued until the subsequent spring or longer.

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