

# Recurrence of Major Depressive Disorder Following a Switch from Escitalopram to St. John's Wort: A Case Report

Erhan Ertekin<sup>1</sup>

## ÖZET:

Majör depresif bozuklukta essitalopram'dan sarı kantaron'a geçilmesini izleyen yineleme: Bir olgu sunumu

Ülkemizde daha çok sarı kantaron, yurt dışında ise St. John's wort olarak bilinen hypericum perforatum bitkisinden elde edilen ekstreler, özellikle Almanca konuşulan ülkelerde majör depresyon tedavisinde yaygın olarak kullanılmaktadır. Bu maddelerin majör depresyonun idame tedavisindeki etkinliği hakkındaki veriler sınırlıdır. Bu olgu sunumunda yineleyici majör depresif bozukluğu olup, ötimik dönemde iken idame tedavisi olarak kullandığı essitalopramın yerine sarı kantaron kullanmaya başlamasının ardından depresyonu yineleyen bir kadın hasta bildirilmektedir.

**Anahtar sözcükler:** Sarı kantaron, St. John's wort, majör depresyon, idame tedavisi-essitalopram

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## ABSTRACT:

Recurrence of major depressive disorder following a switch from escitalopram to St. John's Wort: a case report

Hypericum perforatum extracts, popularly known as St. John's wort (known as "sarı kantaron" in Turkish) are widely used for the treatment of major depression, especially in German speaking countries. Data on the effectiveness of such extracts for the maintenance treatment of major depression is limited. In this case report, a female patient who was euthymic under escitalopram treatment and experienced a recurrence of depression following a switch to St. John's wort will be described.

**Keywords:** St. John's wort, major depression, maintenance treatment, escitalopram

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<sup>1</sup>M.D., Istanbul University, Istanbul Medical Faculty, Department of Psychiatry, Istanbul - Turkey

Address reprint requests to: Dr. Erhan Ertekin, Istanbul University, Istanbul Medical Faculty, Department of Psychiatry, Istanbul - Turkey

E-mail address: erhanert76@yahoo.com

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## INTRODUCTION

Major depressive disorder (MDD) is a common mental disorder with a lifetime prevalence of 10% to 15%<sup>1</sup>. Even when treated successfully, it still imposes a considerable burden on patients, their families, and society<sup>1</sup>. MDD is a recurrent mental disorder and this is the main reason for its significant contribution to increased disability and health care costs<sup>2</sup>. A recent review reported that the number of previous episodes and subclinical residual symptoms appear to be the most important predictors of recurrence of MDD<sup>3</sup>. Therefore, efforts to reduce the disabling effects of depression should include recurrence prevention strategies, especially

in patients at high risk of recurrence<sup>4</sup>. Maintenance treatment, which aims to ensure a return to baseline function and quality of life and to prevent recurrence of symptoms<sup>5</sup>, can be considered to be the main recurrence prevention strategy.

As in the case of acute treatment, psychotherapy (cognitive behavioral or interpersonal) and/or antidepressant medications are the most highly recommended and well-established treatments for relapse/recurrence prevention in patients with MDD. However, complementary and alternative medicine treatments including dietary and herbal supplements are commonly used by people with depression<sup>6</sup>.

One of the most widely used medicinal plants by

patients with MDD is popularly called St. John's wort (botanical name *Hypericum perforatum*). St. John's wort is a medicinal herb that has been used for a variety of medical purposes for centuries. This plant's extracts contains a number of compounds that are candidates for its active ingredients, including hypericin and hyperforin. Although serotonergic and dopaminergic effects have been proposed, its exact mechanism of action in MDD is unknown<sup>6</sup>.

St. John's wort has been studied mostly in short-term trials for acute treatment of MDD. A meta-analysis that included 29 double blind trials found St. John's wort to be as effective as tri- or tetracyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs) in mild to moderate MDD<sup>7</sup>. In another review, four different *Hypericum* extracts have been shown to be significantly more effective than placebo with at least similar efficacy and better tolerability compared to standard antidepressant drugs<sup>8</sup>. However, it has been suggested that studies that support the efficacy of St. John's wort in mild to moderate depression have limitations that may affect the accuracy of their conclusions<sup>9</sup>. In addition, such trials usually have observation periods between 6 and 12 weeks and only a limited number of continuation studies are available in the literature<sup>10</sup>.

Here I describe a case whose symptoms reappeared following a switch from escitalopram to St. John's wort during maintenance treatment of MDD.

## CASE

Ms. O., a single, 55-year-old college professor first presented to a psychiatry unit in 2006, when she was diagnosed as having nasopharyngeal carcinoma. A few months earlier, she had lost her mother whom she had taken care of for two years. Her psychiatrist diagnosed her with first episode MDD and started treatment with escitalopram 10 mg/day. Both her cancer and MDD treatments were successful and the patient reported that her MDD symptoms were fully remitted with the antidepressant medication. She said that she had used escitalopram for more than a year during that

period.

The patient first presented to the Psychiatry Department of Istanbul University, Istanbul Medical Faculty in 2010. At that time, she reported some problems with her siblings and complained about feelings of emptiness and loneliness. Her mood was depressed, she was anhedonic and she reported passive suicidal ideation. She was experiencing neurovegetative symptoms as well, such as insomnia and loss of appetite. Although she could still give her lessons at the college, she reported concentration problems in the classroom. She was easily fatigued and her friends had told her that she appeared "slow" and withdrawn. Her cancer had been remitted with radiotherapy and chemotherapy in 2006 and she was not taking any pharmacotherapeutic agent for any medical condition. Her laboratory work-up was unremarkable and she denied the use of alcohol or any illicit drugs. She had no family history of MDD or any other psychiatric illness. She was diagnosed as having recurrent MDD since that was her second major depressive episode. Her Hamilton Depression Rating Scale (HDRS) score was 23.

Treatment with escitalopram was initiated again at a dose of 10 mg/day. She responded well and her HDRS score dropped to 12 in four weeks. After titrating escitalopram up to 20 mg/day, she continued to do even better. All her depressive symptoms were relieved gradually. At the eighth week of escitalopram treatment, her HDRS score was 2 and her depression was considered as fully remitted. Since that was her second episode of MDD, the need for maintenance treatment for MDD was discussed and a consensus was reached. The patient was fully asymptomatic for two years in which she took escitalopram 20 mg/day for the first year, and 10 mg/day for the second year of maintenance treatment.

In November 2012, the patient decided that she no longer wanted to use an antidepressant and expressed her wish to continue with St. John's wort instead, because she thought it would provide "a safer prophylaxis". She was informed that although this herb might be an option for acute mild to moderate depression, the limited data on its

effectiveness as a prophylactic agent for MDD did not justify her decision. She said that she would not change her mind and declared that she would discontinue escitalopram and start on St. John's wort. After that interview, she started to take 300 mg capsules of St. John's wort three times a day.

In February 2013, the patient reported a recurrence of her depressive symptoms. In contrast to her two previous episodes, there were no identifiable traumatic events or life stressors before the onset of this episode. She reported depressed mood, anhedonia, irregular sleep pattern, loss of appetite, fatigue, concentration difficulties, and thoughts of worthlessness for the previous 25 days. Her HDRS score was 20. She was diagnosed as having recurrent MDD and she agreed to switch back from St. John's wort to escitalopram. During the interviews conducted three and six weeks later, her depressive symptoms were fully remitted with a HDRS score of 4 at the sixth week.

## DISCUSSION

Despite the increasing number of randomized controlled trials (RCTs) for complementary and alternative medicine treatments for MDD, the quality of many RCTs remains an issue. Much of the evidence from those studies is limited by small sample sizes, problems with blinding, and short durations<sup>6</sup>. Among herbal remedies, St. John's wort has the largest data in term of effectiveness for mild to moderate major depressive episodes. However, it has not been extensively studied for maintenance treatment of MDD.

In an open multi centre study with 440 patients suffering from mild to moderate depression, patients were treated for up to 1 year with St. John's wort extract. The results have suggested that St. John's wort is safe and effective for mild to moderate depression over long periods. The author concluded that St. John's wort seemed especially suitable for relapse prevention<sup>11</sup>. By reanalyzing data from a controlled clinical trial, Singer et al. evaluated the duration of response and occurrence of relapse/recurrence in 154 patients who responded in a randomized placebo controlled study to 6 weeks of

treatment for moderate depression with either 20 mg citalopram or 900 mg St. John's wort. The authors concluded that the Hypericum extract STW 3-VI was more efficient in lowering the relapse and recurrence rates when compared to citalopram and placebo<sup>12</sup>.

In another multicenter trial, Kasper et al. evaluated the efficacy of St John's wort during 6 months continuation and 12 months long-term maintenance treatment after recovery from an acute episode of recurrent depression in 426 patients. They reported that St John's wort showed a beneficial effect in preventing relapse<sup>13</sup>.

However, the aforementioned studies may have limitations. The first study is an open study and open studies are prone to bias and are more likely to show an effect than RCT's. In the second study, a relapse occurred in only 30 patients and relapse rates of 14.8% and 17.4% were found for St John's wort and placebo, respectively. In Kasper et al.'s study, St. John's wort failed to differ from placebo on the primary outcome measure, relapse rates.

Another interesting bias about studies on St. John's wort is that trials from German speaking countries reported significantly higher response rates than trials from other countries. In Germany, St John's wort is an approved medication for the treatment of depression whereas in Turkey and much of the rest of the world, it is available as a dietary supplement. St. John's wort has a long tradition in the treatment of depression in German speaking countries and the reason for this "country effect" is not clear<sup>10</sup>.

When Ms. O. reported that she would replace her antidepressant medication with St. John's wort, she was given information about limited data on relapse prevention for MDD by this herb. She said she had found evidence that supports her opinion on the internet and did not change her decision. About 75 days after she switched treatment to St. John's wort, her depressive symptoms relapsed. Contrary to her two previous episodes, this episode did not seem to be related to any identifiable stressor. Her relapse was considered to be a result of the failure of St. John's wort as a prophylactic treatment. Her depressive symptoms resolved after switching back

to escitalopram.

According to the American Psychiatric Association, patients who have had three or more prior major depressive episodes should receive maintenance treatment<sup>14</sup>. The risk of MDD recurrence increases with each successive episode<sup>14</sup> and each successive episode may require longer maintenance treatment. The duration of the maintenance phase varies depending on the frequency and severity of prior major depressive episodes, tolerability of treatments, and patient preferences. For many patients, it may be required indefinitely<sup>14</sup>. Accordingly, a joint decision was made by the patient and the psychiatrist that maintenance treatment with escitalopram should

be continued at least for the next five years.

In conclusion, although it might be considered as an alternative treatment for acute mild or moderate depression, data on the long term use of St. John's wort in MDD is scarce and controversial. Although patient decision typically has to be respected in individual cases, practicing clinicians should make efforts to follow treatment guidelines shaped by evidence-based medicine. Keeping this principle in mind, an evidence-based treatment should be continued as maintenance treatment for recurrent MDD. This case report suggests that St. John's wort may not be such an ideal option, especially when replacing a successful antidepressant treatment.

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