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Olanzapine: Review of Case Reports of Obsessive Compulsive Disorders (OCD)

Introduction

Obsessive-compulsive disorder (OCD) has been reported to be induced by olanzapine and clozapine. Risperidone has been reported to both improve and worsen OCD. Olanzapine is an atypical antipsychotic indicated for treatment of schizophrenia. The case reports involving clozapine and OCD have been reviewed in previous in a previous Newsletter (Vol. 20:9, October 1999)

The purpose of this newsletter is to review reported cases of olanzapine associated with OCD.

Induction of OCD

OCD is characterized by obsessive thoughts and/or compulsive behaviours that significantly interfere with normal life. Obsessions are unwanted, recurrent, and disturbing thoughts that a person cannot suppress and that can cause overwhelming anxiety. Compulsions are repetitive, ritualized behaviours that the person feels driven to perform to alleviate the anxiety of the obsessions. The obsessive and compulsive rituals can occupy many hours of each day and seriously impair day-to-day living.

One theory as to a possible cause of OCD relates a deficiency in the neurotransmitter serotonin (5HT) leading to worsening symptoms, however a direct link between a deficiency and OCD has yet to be found. Selective serotonin reuptake inhibitors (SSRIs) which effectively increase serotonin concentrations in the synaptic cleft have been used for the treatment of OCD. Drugs that either lower the concentration of 5HT or block 5HT receptors, such as olanzapine, could therefore, reasonably be expected to worsen symptoms of OCD. There have been several case reports, presented below, of patients experiencing a worsening of their obsessive-

compulsive symptoms (OCS) in response to olanzapine therapy and even reports of patients developing new onset OCD.

Morrison et al (1998) reported a patient with partially responsive schizophrenia and comorbid OCD who had a previous history of worsening OCD symptoms with clozapine and risperidone. Olanzapine was started at 10mg/day while haloperidol was tapered off. Fluvoxamine 200mg/day was continued unchanged. By week three the patient's OCD symptoms had increased, and an increase in fluvoxamine to 400mg/day had no effect. Interestingly, the patient felt subjectively better and elected to stay on the olanzapine.

Al-Mulhim et al (1998) present a patient with major-depression with psychotic features which responded partially to fluvoxamine 200mg/day. Olanzapine was started at 5mg/day for five days and then increased to 10mg/day. Two days later she developed de novo OCS and olanzapine was stopped. Upon rechallenge with olanzapine at 5mg/day, the symptoms recurred within 48 hours. The replacement of fluvoxamine with venlafaxine 300mg/day resolved the OCS, even with an increase in olanzapine to 10mg/day.

Mottard et al (1999) present two cases of schizophrenia without history of OCD. In both cases the addition of olanzapine at 15mg/day and 25mg/day induced de novo OCS in 14 days and 3 months respectively. The addition of fluoxetine in one case and clomipramine in the other resolved the OCS.

Ramasubbu et al (2000) documented a case of schizoaffective disorder with OCD, treated with clomipramine 150mg/day. Within 3 days of starting olanzapine 5mg/day, the patient began to deteriorate, and the OCS worsened when olanzapine was

increased to 10mg/day. Clomipramine was increased to 200mg/day and the OCS returned to baseline within 4 weeks.

Lykouras et al (2000) reported three cases, two patients with schizophrenia with comorbid OCD, and one with OCD alone. In all three, the addition of olanzapine (15, 20, and 10mg/day) exacerbated their OCS. In the first case, sertraline 200mg/day resolved the OCS. Olanzapine was removed in the last two cases and both had their OCD go into remission.

Jonkers et al (2002) presented a bipolar II patient who developed de novo OCS five weeks after starting olanzapine 5mg/day. The symptoms subsided after discontinuing olanzapine.

Mahendron (2002) describes a patient with schizophrenia without a history of OCD. The patient was switched from fluphenazine depot injections to olanzapine up to 20mg/day. After two weeks at this dose, he developed OCS. Olanzapine was reduced to 15mg/day and clomipramine 50mg/day was started but the OCS actually worsened. Stopping olanzapine, increasing clomipramine to 75mg/day, and adding quetiapine 100mg/day significantly reduced, but did not eliminate, the symptoms.

Treatment of OCD

Both behaviour therapy and medication(s) are effective in the treatment of OCD, and it is expected that a combination of the two would likely provide optimal results. Clomipramine, a tricyclic antidepressant (TCA), and the SSRIs, fluvoxamine, fluoxetine, paroxetine and sertraline are all currently approved for the treatment of OCD. All of these agents increase serotonergic transmission, and agents which only increase dopaminergic transmission, such as bupropion, have been found to be ineffective in the treatment of OCD.

Clomipramine

There have been several studies demonstrating the efficacy of clomipramine in the treatment of OCD. Clomipramine, a tricyclic antidepressant, is more potent than other TCAs in its effects on serotonin

reuptake inhibition. Desmethylclomipramine, a major active metabolite, is also a potent inhibitor of norepinephrine reuptake. Clomipramine was previously considered to be superior to the SSRIs in the treatment of OCD, however, there have been direct comparison studies demonstrating comparable efficacies in the two groups. Clomipramine is not as well tolerated as the SSRIs, and patients are more likely to discontinue treatment due to side effects. As a result clomipramine is currently recommended as a second-line treatment option for patients who do not respond adequately to SSRIs.

Selective Serotonin Reuptake Inhibitors

There are well-documented double blind, placebo-controlled studies demonstrating the use of fluvoxamine, fluoxetine, paroxetine, and sertraline in the treatment of OCD. The newer agent citalopram, based on its SSRI activity, may also be effective, however, there is limited information to support its use at this time. Although some patients may respond better to a selective agent, there is no evidence that any one SSRI is more effective than another. Treatment should be initiated at the usual recommended dosages, however, higher doses have been found to be more effective than lower doses (fluvoxamine 200mg/day, fluoxetine 40-60mg/day, paroxetine 40-60mg/day, and sertraline 200mg/day).

Non Pharmacologic Treatments: Cognitive Behaviour Therapy (CBT)

CBT is a valuable component of treatment for OCD and should be incorporated into the initial treatment plan when possible. It is a combination of cognitive therapy, which can modify or eliminate unwanted thoughts and beliefs, and behavioural therapy, which aims to help the individual change their behaviour in response to those thoughts.

CBT is based on the assumption that most unwanted thinking patterns, emotional and behavioural reactions are learned. Cognitive techniques (such as challenging negative automatic thoughts) and behavioural techniques (such as graded exposure and relaxation techniques) are used to relieve symptoms by changing negative thoughts, beliefs and behaviour.

The results achieved with CBT are generally maintained long after its discontinuation, which is an advantage over pharmacotherapy. CBT alone may be appropriate for treating mild OCD or in cases where medication is to be avoided, for example in pregnancy. Although a combination of CBT and medications is generally considered more efficacious to either treatment approach used alone, it can cause anxiety and stress and patients will often refuse to participate in it.

Treatments goals and desired outcomes

The primary goal of treatment in OCD is to decrease obsessions and compulsions to a level at which the person is able to function normally. Complete elimination of symptoms is rarely achieved with currently available OCD treatments, which is different from depression and some other anxiety disorders where full recovery is a common, achievable goal. Most clinical trials in OCD define a clinical response as a 20-35% reduction in Yale-Brown Obsessive Compulsive Symptom Checklist (Y-BOCS) scores. Therefore, even those deemed

responders may be left with 65-80% of their original symptoms and, depending on the initial degree of severity, this may or may not result in significant improvements in functioning or quality of life.

Approximately 60-70% of patients show at least moderate improvements in obsessive-compulsive symptoms during an initial (SSRI or clomipramine) medication trial.

Summary

Olanzapine can worsen OCS or can cause new onset of OCD. Onset of OCD symptoms have been as early as three days after starting olanzapine or as late as three months. Symptoms are reversible upon discontinuation of olanzapine, however, treatment with an SSRI or clomipramine may be necessary if the patient has responded well to olanzapine otherwise.

Switching the patient to quetiapine, which seems less likely to cause these symptoms may be another alternative.

Written by: Ruby Virani, BSc (Pharm)

Edited and Reviewed by: Sylvia Zerjav, Pharm D.

This will be our final mailout of the Riverview **For Your Inpharmation**. The newsletter will continue to be published and it will be available on the Riverview Hospital website. The address is http://www.bcmhs.bc.ca/library/content_handler.asp?content_file=Inpharmation/Inpharmation.asp. If you would like to be notified that a new newsletter is posted on the website, please email sschneider@bcmhs.bc.ca. Please ensure you include your entire email address.

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