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Abstract

Obsessive compulsive disorder (OCD) is a psychiatric disorder characterized by recurrent intrusive thoughts (obsessions) that cause significant anxiety and distress, leading to repetitive behaviors (compulsions) that an individual feels driven to perform. The symptoms of OCD can range from mild to so severe that it can be incapacitating to an individual's life. Treatment is often prescribed, including both pharmacological and behavioral therapy. Overall, 70% of patients starting treatment experience a significant improvement; however, there is still a portion of patients with severe OCD that do not respond to first and second-line treatment plans. We present the case of a 62-year-old-male who was admitted to inpatient psychiatry for severe OCD. The patient failed to respond to first- and second-line treatment options and was prescribed ondansetron for his obsessive thoughts. Ondansetron is a 5-HT_3 receptor antagonist indicated for the treatment and prevention of nausea and vomiting. Our patient successfully responded to an off-label use of ondansetron for obsessive thoughts in OCD.

Introduction

Obsessive-Compulsive Disorder (OCD) is a relatively common psychiatric disorder that causes significant distress and impairment in function. OCD is characterized by recurrent intrusive thoughts that typically causes significant anxiety and distress that leads to repetitive behavioral acts. The treatment for OCD includes both behavioral therapy and pharmacological treatment options. Most patients respond to the standard treatment options; when first- and second-line treatment options fail, the chronicity and severity of the disease can be debilitating to a patient's life. Presented is a case in which first- and second-line

treatment options failed when prescribed. Ondansetron (Zofran®), a $5HT_3$ antagonist, is a common medication used for the treatment and prevention of nausea and vomiting. This medication was prescribed to our patient as an off-label attempt to treat obsessive thoughts. The treatment options for OCD, including the use of ondansetron and other $5\text{-}HT_3$ antagonists as alternative or augmentative treatment options, will be discussed.

Case Synopsis

A 62-year-old male was admitted to inpatient psychiatry with suicidal ideations due to severe anxiety. The patient had a significant past medical history of OCD, diagnosed at 22 years of age. He complained of severe anxiety rated 10/10 and suicidal ideations without a plan. During the hospital stay, the patient reported that 10 hours per day, he thought about washing his hands to avoid contamination because of his obsession with cleanliness. He refused to shake hands or touch door knobs without compulsively washing his hands afterwards. He reported that these obsessions and compulsions made it impossible for him to have any enjoyment in life. The patient appeared to be very anxious upon physical examination, with noticeable hand tremors and an erythematous dry flaky rash noted on his hands due to excessive washing.

The patient was taking a tricyclic antidepressant, clomipramine, 50 mg orally at night for his obsessive thoughts; a serotonin reuptake inhibitor, fluoxetine, 40 mg orally daily and a benzodiazepine, clonazepam, 2 mg orally daily for his anxiety for years prior to admission. This treatment plan was only providing minimal improvement in his symptoms. It was decided to add an anxiolytic, buspirone, 10 mg by mouth twice daily, to help control his anxiety, which was only minimally effective. Due to the development of severe hypotension

from the clomipramine, the medication was switched to an atypical antipsychotic, lurasidone, 40 mg by mouth daily for his obsessive thoughts. Hypotension again developed, and the medication was discontinued. At this point, the patient was started on an antiemetic, ondansetron, 0.25 mg twice daily orally, as an off-label attempt to treat the patient's obsessive thoughts. After two weeks of being on this medication, the patient responded well to the ondansetron, reporting a better mood, fewer compulsions to wash his hands, and a decrease in anxiety which he rated 6/10. He denied any suicidal ideations, intent or plan.

The patient was no longer an imminent threat to himself or others and was discharged from the hospital with prescriptions for ondansetron 0.5mg by mouth twice daily, fluoxetine 40mg by mouth once daily, and clonazepam 1mg by mouth twice daily, as needed for anxiety.

Literature Review

Obsessive compulsive disorder (OCD) is a psychiatric disorder characterized by recurrent intrusive thoughts (obsessions) that cause significant anxiety and distress that leads to repetitive behaviors (compulsions) that individuals feel driven to perform to relieve that anxiety. OCD typically starts in childhood, persists throughout a lifetime, and can cause significant impairment in function due to the severity and chronicity of the disorder.[1] Treatment options include both pharmacologic and behavioral therapies. Most patients starting treatment for OCD respond well, however about 30% of patients fail first and second-line treatment options. These patients with moderate to severe OCD who fail standard treatment options may be significantly debilitated due to the chronicity and severity of the disease.

Selective serotonin reuptake inhibitors (SSRIs) are the first line of treatment for OCD.[1] Tricyclic antidepressants and atypical antipsychotics are the second line of treatment in patients where SSRIs are ineffective; however, ondansetron holds promise as a new alternative when first- and second-line treatment options fail. OCD is linked to decreased levels of serotonin and increased levels of dopamine in the brain, which implies two possible mechanisms for how ondansetron may be beneficial in the treatment of OCD. Ondansetron blocks the 5-HT_3 receptor, which, in combination with the blockade of serotonin reuptake, allows for higher-than-normal serotonin levels in the brain. In addition, 5-HT_3 blockage may have a weak, downstream inhibitory effect on dopaminergic neurotransmission; as 5-HT_3 receptors act indirectly by inhibiting cortico-mesolimbic dopamine release, thus decreasing dopamine levels.[2,3] In addition, inhibition of the 5-HT_3 receptor with a genetic variant related to the "washing" phenotype expressed with OCD could limit activity of the ion channel controlled by the 5-HT_3 receptor.[2]

Although numerous studies have shown inconclusive results, several studies show that 5-HT_3 antagonists are efficacious and are proven to be safe in patients with OCD.[4,5,6] In the work of Heidari et al, the 5-HT_3 antagonist, ondansetron, was shown to be beneficial when used as an augmentative agent to fluvoxamine, an SSRI, in the treatment of patients with moderate to severe OCD with no significant adverse events reported.[7] Neda et al showed similar results augmenting fluvoxamine, an SSRI, with granisetron, a 5-HT_3 receptor antagonist. Patients in the study responded successfully to granisetron as an adjunct to fluvoxamine.[4] Even though the results from the mentioned studies are inconclusive, they display promise for the use of ondansetron in the treatment of OCD without significant adverse effects. Thus, ondansetron may be beneficial as an alternative treatment option in

patients with moderate to severe OCD who have failed to respond first and/or second line treatment options.[2,4,5]

Discussion

Obsessive compulsive disorder can be incapacitating to an individual's life if left untreated or symptoms are unresponsive to standard treatment options. Typically, about 70% of patients starting pharmacologic treatment respond positively and can continue their lives without any impairment. However, some patients do not respond to first and second-line treatment options, which can cause significant impairment in daily function. Our patient failed all traditional options for the treatment of OCD. When admitted to the inpatient psychiatric unit, the patient was on an SSRI, fluoxetine, which is first line for the treatment of OCD. He was also on clomipramine, a tricyclic antidepressant, which is a second line treatment option for patients with OCD. Unfortunately, the patient did not respond to the medications he was originally prescribed. Other second line treatment options such buspirone and lurasidone were prescribed in attempt to treat his symptoms, however, the attempts were unsuccessful. Our patient failed to respond to first and second line treatment options, leaving his symptoms uncontrolled. It is important to recognize that the patient's quality of life may be affected due to the severity and treatment failures in OCD. These patients may benefit from other treatment options such as ondansetron and other 5-HT3 antagonists as alternative treatment options.

According to recent literature, ondansetron, and other $5HT_3$ antagonists, may be beneficial in the treatment of obsessive compulsive disorder and is proving to be safe in these patients.[2,3,4] Heidari, Zarei , Hosseini et al, displayed evidence that ondansetron was shown to provide a beneficial effect when used in conjunction with fluvoxamine in the treatment of

patients with moderate to severe OCD, without any adverse effects.[7] Likewise, our patient was prescribed fluoxetine, an SSRI similar to fluvoxamine, and showed significant improvement in OCD symptoms with the addition of ondansetron. Neda, Mahdieh, Mohammad et al showed similar results augmenting fluvoxamine with granisetron, another 5-HT_3 receptor antagonist similar to ondansetron.[4] Patients in the study responded successfully to granisetron as an adjunct to fluvoxamine, comparable to how our patient responded to ondansetron as an adjunctive treatment to a similar SSRI.

When trying to understand the role of ondansetron in the treatment of obsessive thoughts, it is important to recognize the pathophysiology of OCD. OCD is linked to decreased levels of serotonin and increased levels of dopamine, two common neurotransmitters found in the brain.[3] This implies that there may be two possible mechanisms for how ondansetron may be beneficial in the treatment of OCD. Ondansetron blocks the 5-HT_3 receptor, which, in combination with the blockade of serotonin reuptake via inhibition by the SSRIs, allows for an increase in the serotonin levels in the brain. The addition of ondansetron allows for greater increase in serotonin levels, than would an SSRI alone. This provides evidence that when ondansetron is added in combination with a selective serotonin reuptake inhibitor, better treatment of obsessive thoughts may be achieved.[3] This parallels the treatment regimen our patient was trialed on. He was taking fluoxetine, and, with the addition of ondansetron, he showed significant improvement in his symptoms.

Another proposed mechanism explaining the use of ondansetron in the treatment of OCD is through the inhibition and thus downfield effects of dopamine. Through 5-HT_3 blockage, ondansetron has a weak, downstream inhibitory effect on dopaminergic neurotransmission; 5-HT_3 receptors act indirectly by inhibiting cortico-mesolimbic dopamine

release, thus decreasing dopamine levels in the brain.[3] A further possibility is the inhibition of the 5-HT_3 receptor with a noted genetic variant linked to OCD. In a study published by Lennertz and colleagues, the *HTR3E* genetic variant p.T86A was found to have a significant association with the "washing" obsession found primarily in males. The phenotypic expression of this genetic variant was not directly discussed, but administration of 5-HT_3 antagonists like ondansetron were found to diminish the "washing" action of OCD patients expressing this *HTR3E* variant. More evidence would be needed for our specific patient to identify this genetic variant possibly being present.[2]

Although numerous studies have shown inconclusive results, several studies show that 5-HT_3 antagonists are efficacious and are proven to be safe in patients with OCD.[4,5,6] Our patient provides an example of the severity obsessive compulsive disorder can progress to if left untreated or is unresponsive to standard treatment options. This case supports the current literature on the use of ondansetron, and other 5-HT_3 receptor antagonists, in the treatment of obsessive thoughts. Our patient successfully responded to this off-label attempt to treat OCD. The patient was discharged home to his family on a low dose of ondansetron in addition to fluoxetine and clonazepam. Although more research needs to be done for ondansetron to formally receive this indication, 5 -HT_3 receptor antagonist are showing promise as an alternative treatment option in the patients with moderate to severe OCD, refractory to current standard medication treatment options.

Conclusion

Obsessive-compulsive disorder is a very common psychiatric condition. Most patients respond to pharmacological treatment options, however, when first- and second-line treatment options fail, the chronicity and severity of the disease can be debilitating to a patient's life.

Ondansetron, a 5-HT3 receptor antagonist classically used for the treatment and prevention of nausea and vomiting, may be beneficial as an off-label use in OCD. Our patient successfully responded to ondansetron after failing first and second line treatment options. Considering that results from studies are inconclusive but are showing promise with the use of ondansetron in the treatment of OCD without significant adverse effects, the use of ondansetron should be considered as an off-label attempt for treatment of obsessive thoughts in moderate to severe OCD when first- and second-line treatment options fail.

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