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## Case Report

### Mirtazapine for Migraine Headaches

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## Abstract

Migraine is one of the most common headache syndromes which occurs almost three times more common in women than men. Due to high prevalence, migraine is considered to be an important cause for living years with disability by World Health Organization. Even considerable effort put in the field, pathophysiology of migraines still remains unclear. On one side interaction between afferent neurons and intracranial vessels takes an important place, however on the other side central nervous system play an important role in trigger of migraine attacks. Furthermore, especially aura of migraine is likely to be caused by cortical spreading depression. Along with genetic predisposition, environmental factors, especially stress is strongly associated with migraine headaches. Our case presentation is a 34 years old single female, who presented to outpatient psychiatry clinic due to prescription refill for Mirtazapine 30 mg. Patient reported that she was prescribed Mirtazapine 6 months ago for migraine headaches

**Keywords:** Migraine, mirtazapine, anxiety, depression

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## Introduction

Migraine is one of the most common headache syndromes which occurs almost three times more common in women than men.<sup>1</sup> Due to high prevalence, migraine is considered to be an important cause for living years with disability by World Health Organization.<sup>2</sup> Even considerable effort put in the field, pathophysiology of migraines still remains unclear. On one side interaction between afferent neurons and intracranial vessels takes an important place, however on the other side central nervous system play an important role in trigger of migraine attacks.

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Furthermore, especially aura of migraine is likely to be caused by cortical spreading depression.<sup>3</sup> Along with genetic predisposition, environmental factors, especially stress is strongly associated with migraine headaches. There is a bidirectional relationship between migraine and depression. Migraine headache is more common in patients who suffer from depression and depressed patients tend to develop migraine headache more frequently.<sup>4</sup> Lanteri-Minet et al. showed that 50.6% of migraine patients had anxiety and/or depression. They also denoted that perceived treatment efficacy and and satisfaction with treatment are lower in migraine patients who are experiencing anxiety or depression.<sup>5</sup> Consistent with that, amitriptyline, which is one of the very first antidepressants in the history, has been shown to have significant beneficial effects in migraine patients. Several randomized controlled trials showed that.<sup>6,7</sup>

Mirtazapine -chemically a tetracyclic antidepressant- is mainly used for treatment of depression with anxiety or decreased sleep. Although Mirtazapine has a unique receptor profile, its mechanism of action had not been fully understood. It blocks serotonergic and adrenergic receptors, in addition has antihistaminergic effects.<sup>8</sup> Along with its antidepressant effects, Mirtazapine is being used for low appetite and underweight, nausea and vomiting, insomnia, itching and headaches and migraine.<sup>9,10,11</sup> Here in this case report, we will discuss a case of migraine headache, which was significantly relieved after starting mirtazapine.

### **Case Report**

Patient is a 34 years old single female, who presented to outpatient psychiatry clinic due to prescription refill for Mirtazapine 30 mg. Patient reported that she was prescribed Mirtazapine 6 months ago for migraine headaches. Patient endorses having sleep problems, some anxiety and feeling nervous prior to prescription of Mirtazapine. Patient was having at least 3 migraine attacks each month, leading to significant distress. At the time of prescription refill, patient said that she has been taking Mirtazapine in the past 6 months, and she had only one migraine attack within last 4 months, and that attack was much less severe than the previous attacks. She also reported significant relief in terms of anxiety and feelings of nervousness, improved sleep. She was prescribed with prescription refill and scheduled for follow up appointments.

### **Discussion**

This case report further indicates that mirtazapine could be a good choice for migraine patient, especially for those, who has comorbid depression and anxiety.

Emmanuelle et al. reported a 25-year-old patient, who was diagnosed with major depressive disorder and received trials of multiple antidepressants. These antidepressant trials ended up with exacerbation of migraine. They gave low dose Mirtazapine to the patient for residual depressive symptoms. Initially at low doses Mirtazapine decreased the severity and frequency of the migraine episodes. Once they increased the dose of Mirtazapine, this effect was lost, and patient started to have severe migraine again. They proposed low doses of Mirtazapine, but not high doses might be helpful for migraine patients with comorbid depression.<sup>12</sup>

Brannon et al. reported a case of 60-year-old male who was suffering from depression for 5 years and also having anxiety. Patient was initially on Paroxetine and Amitriptyline however requested medication change due to side effects. Later patient was started with cognitive behavioral therapy. He was started on Mirtazapine 7.5 mg. His depression improved

with cognitive behavioral therapy and Mirtazapine. Patient noted to be running out Mirtazapine earlier than expected. Further questioning revealed that he was taking extra dose of Mirtazapine whenever he was feeling that migraine is coming on. Moreover, patient reported that frequency of migraine attacks decreased from 4-5 per month to once a month. Later, he was being followed up by a psychiatrist, who discontinued Mirtazapine and started Bupropion, which resulted in increase in frequency of migraine episodes.<sup>13</sup> Comparing our case with the previously reported ones, we propose that not only low dose, but also moderate dose of Mirtazapine could be significantly beneficial for patients who are suffering from comorbid depression and anxiety.

In addition to migraine headaches, Mirtazapine is showed to be helpful for tension type headaches. In a randomized, double blinded, placebo-controlled trial, which included 22 patients. Mirtazapine dose in that study was 15 mg to 30 mg Mirtazapine decreased duration, frequency and intensity of the headaches in a difficult to treat patient population.<sup>14</sup> Another double blind, placebo controlled, parallel trial that included 4 groups as following; Mirtazapine 4.5 mg and Ibuprofen 400 mg, placebo and Mirtazapine 4.5 mg or Ibuprofen 400 mg for 8 weeks. This study found that daily patient who were taking only Ibuprofen had an increase in headache, while combination of mirtazapine and Ibuprofen was ineffective. However, this study included only 4.5 mg of Mirtazapine as an option, which is almost half of the 7.5 mg dose reported by multiple case reports.<sup>15</sup>

Possible mechanisms that explains effectiveness of Mirtazapine in headache syndromes, especially migraine are involvement of emotional stress and serotonergic and noradrenergic changes in the brain during the stress. Activation of 5HT<sub>3</sub> receptor takes place in the pathophysiology of migraine and Mirtazapine blocks this receptor[8]. Activation of serotonergic receptors such as 5HT<sub>1B</sub>, 5HT<sub>1D</sub> and 5HT<sub>1F</sub> by Mirtazapine lead to contraction of intracranial vessels and decrease the neurogenic inflammation.<sup>12</sup>

In conclusion, here we reported a case of migraine, who significantly benefited from Mirtazapine in terms of both frequency and intensity. Mirtazapine dose should be at least 7.5 mg to help with migraine headaches, however doses up to 15 mg or 30 mg is considered as acceptable. Both psychiatrist and neurologists should take into account there is a bidirectional relationship between headache and psychological stress resulting in depression and anxiety.

#### **Author contributions**

MAC, CO took care of the patient and made the literature research. CO, HEW drafted the manuscript and supervised the manuscript. The final version has been read and approved by all authors.

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#### **Conflict of interest**

All authors declare that they have no conflict of interest.

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