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Expert Opinion

## The use of ondansetron in psychiatry: An educational article and expert opinion

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### Abstract



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Neuroleptics are anti-psychotics medications that are used in a variety of neuropsychiatric disorders including schizophrenia, anxiety, Tourette syndrome, autism, and mental retardation. The first and second generations of neuroleptics are dopamine 2 receptor blocker and the first generation agents are associated with significant risk of the occurrence of extra-pyramidal side effects in effective doses. Despite the emergence of several generations of neuroleptics, the disadvantages of the relatively high incidence of side effects and treatment resistance continued as challenging problems <sup>1-6</sup>.

It has been suggested that these problems may be solved with use of adjunctive therapies that help in improving responsiveness and reduce the possibility of the occurrence of side effects. The aim of this paper is to provide a relevant educational overview of ondansetron research progress in the field of psychiatry.

**Conclusion:** The current expert opinion suggests that ondansetron has the potential to be the agent which can help in solving the problem associated with use of neuroleptics including the possibility of the occurrence of side effects and treatment resistance. There is preliminary evidence suggesting that ondansetron can be used as an adjunctive therapy in a variety of neuropsychiatric disorders including schizophrenia, Tourette syndrome, and obsessive-compulsive disorder.

**Keywords:** Ondansetron, neuropsychiatric disorders, expert opinion.

## Introduction

Neuroleptics are anti-psychotics medications that are used in a variety of neuropsychiatric disorders including schizophrenia, anxiety, Tourette syndrome, autism, and mental retardation. The first and second generations of neuroleptics are dopamine 2 receptor blocker and the first generation agents are associated with significant risk of the occurrence of extra-pyramidal side effects in effective doses. Despite the emergence of several generations of neuroleptics, the disadvantages of the relatively high incidence of side effects and treatment resistance continued as challenging problems <sup>1-6</sup>.

Non-dopamine neuroleptics include serotonin 5HT<sub>3</sub> antagonists, ondansetron. The use of ondansetron, a serotonin (5-HT<sub>3</sub>) receptor antagonists in anxiety, schizophrenia depression, migraine, and cognitive disorders has been suggested early during the 1990s as it can reduce behavioral abnormalities with affecting normal behavior <sup>6,7,8</sup>.

Sirota et al (1997) reported the treatment of 20 patients with schizophrenia who developed neuroleptic-induced tardive dyskinesia with ondansetron 12 mg daily for 12 weeks. Treatment was associated with significant improvement in psychotic symptoms tardive dyskinesia <sup>6</sup>.

Levkovitz et al (2005) reported a placebo controlled study which included 21 treated schizophrenic patients in remission whom were treated with ondansetron or placebo. The study

showed that ondansetron was associated with significant improvement in visuo-spatial memory <sup>7</sup>.

Zhang et al (2006) from China reported a placebo controlled study which included 121 treatment-resistant patients with schizophrenia. The patients were treated with haloperidol 4-30 mg daily. 58 patients also received ondansetron 8 mg daily, while 63 patients received placebo for three months. The use of ondansetron was associated with a much higher improvement in negative symptoms, general psychopathology, and cognition. Ondansetron also markedly reduced the occurrence and severity of parkinsonism and akathisia.

Therefore, Zhang et al suggested that ondansetron can be a useful adjunctive medication which can increase the effectiveness and reduce some of the side effects of neuroleptics used for chronic, treatment-resistant schizophrenia. Ondansetron is mostly beneficial for negative and cognitive symptoms <sup>8</sup>.

Kulkarni et al (2018) from Australia reported a placebo-controlled study which included 85 patients aged 18-65 years with schizophrenia or schizoaffective disorder. Patients received either adjunctive ondansetron 8 mg a day or placebo. The use of adjunctive ondansetron was associated with marked improvement in the cognitive disorganization symptoms of schizophrenia ( $p < 0.05$ ) <sup>9</sup>.

Faris et al (2000) from the United States reported a study which included patients with bulimia nervosa who were experiencing at least seven coupled binge/vomit attacks every

week. 13 patients were treated with ondansetron 24 mg a day, while 12 patients received placebo for one month. Ondansetron treatment was associated with considerable symptomatic improvement. The reduction in binge-eating and vomiting during ondansetron treatment was attributed to improvement of the physiology of meal termination and satiation control through correction of abnormal vagal neurotransmission <sup>10</sup>.

Hewlett and colleagues (2003) reported a study which included six patients with obsessive-compulsive disorder treated with ondansetron 1 mg 3 times daily for 2 months. Treatment was well tolerated and was associated with marked improvement <sup>11</sup>.

Pallanti et al (2009) reported a study which included 14 patients with obsessive-compulsive disorder who were resistant to treatment with selective serotonin reuptake inhibitor. The patients were treated with ondansetron 0.25 mg twice a day for 6 weeks and ondansetron was then titrated to 0.5 mg twice a day for 6 weeks. Ondansetron reduced symptoms about 25% in 9 of the 14 patients (64.3%) at 12 weeks. Treatment was not associated with important side effects <sup>12</sup>.

Pallanti et al (2010) reported a study which included 21 patients with obsessive-compulsive disorder who were poorly responsive to treatment with selective serotonin reuptake inhibitor. The patients were treated with ondansetron 0.25 mg twice a day for 2 weeks and ondansetron was then titrated to 0.5 mg twice a day for 10 weeks. Ondansetron reduced symptoms about 27% in 12 of the 21 patients (57%) at 12 weeks. Treatment was not associated with important side effects. Discontinuation of ondansetron was associated with worsening of symptoms <sup>13</sup>.

Toren et al (1999) reported a study which included 6 male patients with haloperidol-resistant Tourette syndrome aged 14-48 years. The patients were treated with ondansetron 8-16 mg daily for 3 weeks. The use of ondansetron was associated with a marked reduction in the severity of tics. Two patients experienced a clear-cut improvement and two patients a probable improvement. Two patients did not experience improvement. Side-effects included transient abdominal pain in five patients and constipation in two patients <sup>14</sup>.

Toren et al (2005) reported a placebo-controlled study which included thirty patients aged 12 to 46 years, who had haloperidol resistant Tourette syndrome. The patients were treated with ondansetron 8 mg daily during the first week, 16 mg daily during the second week, and 24 mg daily during the third week. Ondansetron treatment was associated with marked reduction in the severity of the tic disorder. However, mild and transient abdominal pain was reported during treatment.

## Conclusion

The current expert opinion suggests that ondansetron has the potential to be the agent which can help in solving the problem associated with use of neuroleptics including the possibility of the occurrence of side effects and treatment resistance.

There is preliminary evidence suggesting that ondansetron can be used as an adjunctive therapy in a variety of neuropsychiatric disorders including schizophrenia, Tourette syndrome, and obsessive-compulsive disorder.

**Conflict of interest:** None.

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