The Role of Ondansetron in the Treatment of Schizophrenia

Allison C Bennett and Tania M Vila

Request

What role does ondansetron play in the treatment of schizophrenia?

Response

BACKGROUND

Schizophrenia is a chronic psychiatric disorder, characterized by a high risk of relapse, that significantly impairs cognitive and social abilities and affects approximately 2.4 million Americans.¹ The onset of schizophrenia typically occurs during early adulthood, between the ages of 20 and 39 years, with men being affected earlier than women.² Genetic and environmental factors both appear to play a role in the etiology of schizophrenia.² According to the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV), schizophrenia is diagnosed in part on the presence of positive and negative symptoms.³ Negative symptoms include social and cognitive disorders such as affective flattening, alogia, and avolition. Positive symptoms include delusions, hallucinations, disorganized speech/thinking, grossly disorganized behavior, and catatonic behaviors.³ Additionally, cognitive impairment, including decreased attention span and memory functioning, is common in patients with schizophrenia.³ Levels of cognitive impairment range from problems with attention span and learning to memory deficits.⁵

OBJECTIVE: To evaluate the efficacy of ondansetron for the treatment of schizophrenia.

DATA SOURCES: Searches of MEDLINE (1950–March 2010) and Google Scholar were performed. Key search terms included ondansetron, Zofran, serotonin antagonists, 5-HT₃ receptor antagonist, and schizophrenia.

STUDY SELECTION AND DATA EXTRACTION: All articles published in English identified from the data sources were evaluated. All studies and case reports evaluating ondansetron for the treatment of schizophrenia were reviewed.

DATA SYNTHESIS: Six clinical trials, including 3 double-blind, randomized trials, and 2 case reports pertinent to ondansetron use in schizophrenia, were identified. Ondansetron daily doses ranged from 4 to 16 mg, with doses administered once or twice daily. Ondansetron was used as monotherapy in 3 trials and as an adjunct to therapy with clozapine, haloperidol, or risperidone, respectively, in 3 trials. Studies were of varying durations, ranging from a single-dose study with a 3-hour follow-up to three 12-week studies. Most studies evaluated ondansetron’s efficacy in treating schizophrenia as measured with changes in Positive and Negative Syndrome Scale (PANSS), Brief Psychiatric Rating Scale, and Clinical Global Impression scale scores. In the 2 largest trials, with a combined patient population of 151, treatment with adjunctive ondansetron resulted in statistically significant improvement in negative symptoms as assessed with PANSS. In all studies, ondansetron was well tolerated, with no severe adverse reactions reported.

CONCLUSIONS: Ondansetron may be effective as an adjunct to antipsychotics for the treatment of schizophrenia, specifically negative symptoms, as assessed with PANSS. Due to the variation in concurrent therapies and dosing regimens, it is difficult to establish an optimal dose from the reviewed trials. Further large, randomized, double-blind, active-controlled studies would be helpful in determining the role of ondansetron in the treatment of schizophrenia.

KEY WORDS: 5-HT₃ receptor antagonist, ondansetron, schizophrenia, serotonin antagonists, Zofran.


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The primary mechanism of action for first-generation antipsychotics is antagonism of dopamine, specifically of D₂ receptors.⁴ Traditional antipsychotics possess D₂ antagonistic properties and appear to exert their antipsychotic properties through a blockade of dopamine. Increased activity of dopamine is at least partly responsible for the
symptoms of schizophrenia. Administration of these agents generally results in partial response; however, a complete response, if attainable, may not be seen for up to 8 weeks. These agents are associated with higher rates of neurologic adverse events, including potentially irreversible tardive dyskinesia, acute dystonia, and Parkinson’s-like symptoms. Second-generation antipsychotics, such as aripiprazole, asenapine, clozapine, olanzapine, paliperidone, quetiapine, risperidone, and ziprasidone, are characterized by having antagonistic properties at both dopamine and serotoninergic receptors. The adverse effect profile of second-generation antipsychotics is primarily metabolic related and includes hyperglycemia, hypercholesterolemia, weight gain, and comparatively fewer extrapyramidal symptoms (EPS) than those associated with first-generation antipsychotics. Schizophrenia is associated with high nonadherence and relapse rates; following maintenance antipsychotic treatment, up to 40% of treated patients may relapse each year. Concerns about both clinical efficacy and tolerability of currently available agents and the finding that drugs with serotonergic antagonistic properties are efficacious in treating schizophrenia led to the investigation of serotonin 5-HT3 receptor antagonists as adjunctive treatment for schizophrenia.

### The Role of Serotonin 5-HT3, Antagonists

More than 2 decades ago, researchers observed that in animal brain studies, 5-HT3 receptor antagonists effectively reversed dopamine-associated hyperactivity and possibly decreased the adverse behaviors associated with a hyperactive dopaminergic state. Further research demonstrated that long-term administration of 5-HT3 receptor antagonists did not lead to D2 receptor upregulation. In the US, currently available 5-HT3 receptor antagonists include ondansetron, granisetron, dolasetron, and palonosetron. Currently approved antipsychotics that are thought to have moderate affinity for 5-HT3 include clozapine, quetiapine, and olanzapine.

### Overview of Ondansetron

Ondansetron is a selective 5-HT3 receptor antagonist currently approved for prevention of nausea and vomiting associated with moderate to highly emetogenic cancer chemotherapy and radiotherapy as well as prevention and treatment of postoperative nausea and vomiting. Recommended adult daily doses range from 8 to 24 mg. Adverse events seen in greater than 10% of patients in clinical trials included headache, malaise/fatigue, wound problems, and drowsiness/sedation.

### LITERATURE REVIEW

A search of MEDLINE (1950–March 2010) and Google Scholar was performed with the search terms ondansetron, Zofran, serotonin antagonists, 5-HT3 serotonin receptor, and schizophrenia. Citations of returned articles were used to evaluate additional references. Six clinical studies5,7,14-17 and 2 case reports18,19 pertinent to ondansetron use in schizophrenia were identified. Ondansetron is the only 5-HT3 receptor antagonist available in the US with studies examining its use in schizophrenia. Ondansetron has been studied for the treatment of tardive dyskinesia,14,17 memory impairment,15 and P50 auditory gating deficits,16 and as an adjunctive treatment for chronic schizophrenia (Table 1).

In trials evaluating the use of ondansetron in tardive dyskinesia, memory impairment, and P50 auditory gating in patients with schizophrenia, ondansetron was well tolerated, with no severe adverse events reported.12 In each of these studies, patients showed improvement in measured outcomes. Two of these trials showed improvement in Positive and Negative Syndrome Scale (PANSS) scores,14,17 leading to the evaluation of ondansetron’s use as adjunctive therapy in the treatment of schizophrenia. This review focuses on the literature evaluating the efficacy of ondansetron as adjunctive treatment for chronic schizophrenia. Two case reports found that ondansetron improved symptoms in patients with schizophrenia who had undergone previous antipsychotic trials.

A case report of successful ondansetron treatment of a 33-year-old male with schizophrenia was published in 1991.18 This patient had received extensive trials of multiple antipsychotics, mood stabilizers, and even electroconvulsive therapy. During treatment, the patient became mute and experienced anorexia. After 1 year of improvement with clozapine treatment, the patient began experiencing treatment-limiting adverse events including seizures and leukopenia, and clozapine was switched to ondansetron 4 mg daily, resulting in an improvement characterized as being similar to his initial response to clozapine. The ondansetron dosage was then increased to 8 mg daily, eliciting no further improvement. Following initiation of ondansetron 4 mg daily, the patient’s mental state and social behavior both improved, while his preexisting antipsychotic regimen was simplified.

A 31-year-old male with schizophrenia, Hodgkin’s lymphoma, diabetes, hypertension, and gastroesophageal reflux disease received intravenous and oral ondansetron for treatment of nausea and vomiting associated with his chemotherapy regimen.19 Although his schizophrenia was partially controlled by multiple antipsychotics, he continued to exhibit positive symptoms. Delusions and hallucinations decreased during treatment with ondansetron; however, psychotic symptoms returned to baseline following discontinuation of chemotherapy and associated ondansetron therapy. Oral ondansetron was reinitiated at a dosage of 4 mg twice daily. Subjective improvement was seen 3 days later, with a reduction in the Brief Psychiatric Rating Scale score reported at 2 weeks, with a continual decrease through week 10.
Zhang et al.\textsuperscript{5} evaluated the clinical efficacy and effect on drug-induced adverse events of the addition of ondansetron to haloperidol in the first double-blind, multicenter, randomized, placebo-controlled study evaluating ondansetron for chronic, treatment-resistant schizophrenia. Chinese Han adult inpatients (N = 121) with confirmed DSM-IV diagnoses of schizophrenia for at least 3 years were included in the study. Eligible patients were treatment-resistant, defined as lack of improvement following treatment with 2 or more antipsychotics for 6 weeks at a dose equivalent to 800 mg/day of chlorpromazine, and were required to exhibit negative symptoms or significant cognitive dysfunction demonstrated on the PANSS and Clinical Global Impression-Severity (CGI-S) scale. Exclusion criteria included chronic or uncontrolled clinical conditions and a recent history of alcohol or substance abuse. Baseline characteristics were similar between the treatment groups. Mean duration of illness was 16.2 years for the entire study population. After initial screening, patients underwent a washout period before being randomly assigned to augment haloperidol 4–30 mg daily with either placebo or ondansetron 8 mg daily for 12 weeks. Subjects were assessed at baseline and at 4-week intervals for changes in positive and negative symptoms, general psychopathology, and cognition. To be categorized as having a clinical response at trial completion, a patient must have demonstrated a 30% or greater decrease in overall PANSS score. Adverse events were classified with the Treatment Emergent Symptom Scale and the Extrapyramidal Symptom Rating Scale (ESRS). Adherence was assessed by monitoring daily medication use. Only subjects taking greater than 80% of daily medications were allowed to continue the study. Eighty-four percent of subjects completed the trial, with both treatment arms having similar discontinuation rates.

### Table 1. Studies Evaluating the Use of Ondansetron in Schizophrenia Patients

<table>
<thead>
<tr>
<th>Reference</th>
<th>Design</th>
<th>Dose</th>
<th>Concomitant Antipsychotic Therapy</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sirota (2000)\textsuperscript{14}</td>
<td>12-wk open-label (N = 20)</td>
<td>OND 8 mg daily in the morning for 1 wk</td>
<td>Stable psychotropic regimens at study entry; doses were unchanged during study</td>
<td>AIMS\textsuperscript{a} mean total scores\textsuperscript{a} and severity\textsuperscript{a}; PANSS\textsuperscript{b} total score\textsuperscript{b} and positive,\textsuperscript{c} negative,\textsuperscript{d} general psychopathology\textsuperscript{e} subscales; and CGI\textsuperscript{f} severity\textsuperscript{f} subscale were all significantly decreased in OND from baseline to 12 wk</td>
</tr>
<tr>
<td>Sirota (2001)\textsuperscript{17}</td>
<td>4-wk open-label (N = 10)</td>
<td>OND 4–8 mg daily</td>
<td>Stable psychotropic regimens at study entry; doses were unchanged during study</td>
<td>AIMS\textsuperscript{a} mean total scores\textsuperscript{a} and severity\textsuperscript{a}; PANSS\textsuperscript{b} total score\textsuperscript{b} and positive,\textsuperscript{c} negative,\textsuperscript{d} general psychopathology\textsuperscript{e} subscales; and CGI\textsuperscript{f} severity\textsuperscript{f} subscale were all significantly decreased in OND from baseline to 12 wk</td>
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<tr>
<td>Levkovitz (2005)\textsuperscript{15}</td>
<td>14-day crossover (two 7-day periods) (N = 21)</td>
<td>OND 8 mg daily (4 mg po bid) + clozapine (mean 360 mg daily ± 160 mg) for 7 days</td>
<td>Clozapine</td>
<td>No significant changes in ESRS,\textsuperscript{a} PANSS,\textsuperscript{a} and CGI,\textsuperscript{f} statistically significantly greater improvement with OND than with placebo in Rey-Osterich Complex Figure Test\textsuperscript{a,\textsuperscript{a}}</td>
</tr>
<tr>
<td>Adler (2005)\textsuperscript{16}</td>
<td>Single-dose (N = 8)</td>
<td>OND 16 mg Placebo</td>
<td>None</td>
<td>OND had significantly better effects on P50 auditory gating\textsuperscript{a} than placebo; no significant changes in BPRS total score, positive or negative symptoms, or anxiety</td>
</tr>
<tr>
<td>Zhang (2006)\textsuperscript{5}</td>
<td>12-wk, randomized double-blind, placebo-controlled (N = 121)</td>
<td>OND 8 mg daily + haloperidol 4–30 mg daily</td>
<td>Haloperidol</td>
<td>Statistically significant improvement in total PANSS,\textsuperscript{a} negative PANSS,\textsuperscript{a} general psychopathology,\textsuperscript{c} cognition,\textsuperscript{c} and clinical response rates\textsuperscript{a}; 7/15 ESRS\textsuperscript{a} measured symptoms; no significant differences in positive or CGI-severity\textsuperscript{f} scores</td>
</tr>
<tr>
<td>Azhondzadeh (2009)\textsuperscript{7}</td>
<td>12-wk randomized, double-blind, placebo-controlled (N = 30)</td>
<td>OND 8 mg daily + risperidone 4–6 mg daily</td>
<td>Risperidone</td>
<td>Statistically significant improvement in PANSS negative symptoms,\textsuperscript{a} general psychopathological symptoms,\textsuperscript{e} PANSS\textsuperscript{a} total scores\textsuperscript{a}</td>
</tr>
</tbody>
</table>

AIMS = Abnormal Involuntary Movement Scale; BPRS = Brief Psychiatric Rating Scale; CGI = Clinical Global Impression; ESRS = Extrapyramidal Symptom Rating Scale; OND = ondansetron; PANSS = Positive And Negative Syndrome Scale.

*Primary outcome.
\textsuperscript{a}p < 0.0001.
\textsuperscript{b}p = 0.01.
\textsuperscript{c}p < 0.001.
\textsuperscript{d}p = 0.02.
\textsuperscript{e}p < 0.0002.
\textsuperscript{f}p = 0.04.
\textsuperscript{g}p < 0.002.
\textsuperscript{h}p = 0.003.
\textsuperscript{i}p < 0.003.
\textsuperscript{j}p = 0.003.
\textsuperscript{k}p < 0.01.
\textsuperscript{l}p ≤ 0.05.
Compared with those receiving placebo, patients receiving ondansetron experienced significantly greater improvement from baseline to endpoint in total PANSS scores (−31.9 ± 20.5 vs placebo group, −21.6 ± 20.8), negative symptoms (−9.1 ± 7.3 vs −5.3 ± 6.0), general psychopathology (−13.9 ± 10.2 vs −9.2 ± 10.8), and cognition (−6.4 ± 4.7 vs −3.7 ± 5.0) (all p ≤ 0.05; last observation carried forward). The clinical response rate was also significantly greater in patients receiving ondansetron (62.5%) than in those receiving placebo (40.3%; p = 0.03). Decreases in positive symptoms and CGI-S scores were not statistically significant.

Over three quarters of patients experienced adverse events, including muscle rigidity, which was reported for more than half of all patients. Patients randomized to receive haloperidol plus ondansetron had significantly lower rates of hyperactivity, muscle rigidity, tremor, akathisia, nausea and vomiting, heart pounding, and ESRS scores of severe, while their rates of milder ESRS scores were higher (p < 0.05 for all comparisons) than scores of those receiving haloperidol plus placebo. The incidence of adverse events in the group treated with haloperidol plus ondansetron was similar to that experienced in those receiving haloperidol plus placebo. Although the majority of patients experienced adverse events, they were not major and may have been mild and transient, leading to the conclusion that the medication was well tolerated.

The authors concluded that the use of ondansetron in combination with haloperidol in patients with treatment-resistant schizophrenia resulted in significant improvement in total PANSS score, negative symptoms, general psychopathology, and cognition. The greatest improvements were seen in negative and cognitive symptoms.

Akhondzadeh et al. evaluated the use of ondansetron in 30 patients (28 outpatients, 2 inpatients) with chronic schizophrenia in a 12-week, double-blind, parallel-group study. Subjects had DSM-IV–classified schizophrenia, had been previously treated with risperidone for a minimum of 8 weeks, and were clinically stable for at least 4 weeks. Exclusion criteria included disorders or medication use that may have affected cognition. Additional antipsychotics were not allowed during the trial. Subjects received risperidone 4–6 mg daily with adjunctive ondansetron or placebo. Primary outcomes measures included PANSS scores and change in cognitive performance. PANSS assessments were completed at baseline, 8 weeks, and study completion. Fourteen cognitive function tests were each performed twice throughout the trial to assess attention, working memory, executive function, verbal memory, visual memory, and construction. EPS were assessed throughout the study with ESRS criteria. Adherence was assessed with tablet counts performed at 4-week intervals.

At study completion, all 30 patients were still enrolled. Mean PANSS scores for positive symptoms were not significantly different at endpoint between groups, but changes in scores for negative symptoms were greater (more improved) in the ondansetron adjunctive treatment arm (−2.66 ± 1.44 with risperidone plus ondansetron) than in the placebo arm (−0.80 ± 1.01 with risperidone plus placebo) (p < 0.001). PANSS score changes from baseline in general psychopathological symptoms showed a significant difference at trial completion: −3.33 ± 1.39 with risperidone plus ondansetron and −0.73 ± 0.96 with risperidone plus placebo (p < 0.001). Evaluation of total PANSS scores showed a difference in score change from baseline to week 12 between the 2 groups, with the group receiving risperidone plus ondansetron showing a change of −6.66 ± 1.91 and the adjunctive placebo arm showing a change of −2.00 ± 1.92 (p < 0.001). There was also a decrease in ESRS score from baseline to trial completion in the ondansetron arm (p = 0.002), but not in the placebo arm. ESRS is a measurement of EPS, which are often associated with many medications used in the treatment of schizophrenia; a decreased ESRS score indicates one of the potential benefits of using ondansetron. The rates of adverse effects were similar between treatment groups and included constipation, insomnia, dizziness, muscle cramps, diarrhea, dry mouth, and vomiting.

The authors concluded that the use of ondansetron in patients with chronic schizophrenia resulted in significant improvement in negative symptoms and cognitive functioning, and fewer adverse events.

**Discussion**

The studies of Zhang et al. and Akhondzadeh et al. are the only 2 trials to date that have evaluated ondansetron’s efficacy in the treatment of schizophrenia, enrolling a combined population of 151 patients. Both evaluated the effects of ondansetron on symptoms and involuntary movements. In the 2 studies, ondansetron was used as adjunctive therapy in patients with chronic schizophrenia, 1 as add-on to haloperidol and 1 as add-on to risperidone. These studies reported that ondansetron led to significantly greater improvements in negative symptoms. Although improvements in positive symptoms were observed in a single case report and 2 small tardive dyskinesia studies, no significant changes were reported in these 2 larger studies.

In the Zhang et al. trial, less than 10% of patients had previously taken haloperidol. Patients in the group who were receiving haloperidol plus ondansetron initiated treatment with 2 new medications simultaneously, impeding the ability to draw inferences about the association between a single medication and outcomes measures. This trial also varied from previous studies and reports in that in a majority of the subjects, negative symptoms and cognitive impairments were dominant, whereas in many previous studies patients exhibited positive symptoms more prominently. The trial included...
only patients who had persistent negative symptoms (score of >20 on the PANSS negative symptom subscale). This could have inflated the perceived benefit since these patients stood the most to gain in symptom scoring.

The first dose of ondansetron is administered approximately 30 minutes prior to treatment with emetogenic chemotherapy agents, suggesting a 30-minute onset of action. However, no literature identified to date has evaluated the time to onset for effects of symptoms of schizophrenia. It is known that medications that act on dopaminergic and serotonergic receptors often take up to 8 weeks to elicit a complete response. A trial lasting greater than 12 weeks would be helpful in evaluating whether ondansetron may be helpful as long-term therapy.

Ondansetron was well tolerated, with no severe adverse reactions reported. Akhondzadeh et al.7 reported similar rates of constipation, insomnia, muscle rigidity/cramp, dry mouth, and vomiting in both treatment arms. Zhang et al.⁵ reported a similar incidence of adverse events overall between the haloperidol plus ondansetron arm and the haloperidol plus placebo arm; however, patients randomized to receive haloperidol plus ondansetron had significantly lower rates of hyperactivity, muscle rigidity, tremor, akathisia, nausea and vomiting, heart pounding, and ESRS scores of severe, and those randomized to haloperidol plus placebo had a significantly lower rate of ESRS scores of mild.

Summary

Ondansetron may be effective as an adjunct to second- or first-generation antipsychotics for the treatment of schizophrenia, specifically negative symptoms, as assessed with the PANSS. However, 2 small trials evaluating the use of ondansetron for tardive dyskinesia showed a significant improvement in the positive symptoms of schizophrenia, as assessed with the PANSS. Ondansetron dosing varied among the trials and ranged from 4 to 16 mg. Due to the variation in concurrent therapies and dosing regimens, it is difficult to establish an optimal dose from the reviewed trials. Safety and tolerability do not appear to be concerns with the use of ondansetron, as adverse events did not limit use. Treatment with ondansetron for greater than 12 weeks has yet to be evaluated.

In the reviewed trials, ondansetron was used in combination with haloperidol and risperidone. The drug or drugs that ondansetron can most effectively augment has not yet been evaluated and could be determined only through head-to-head comparator trials. Although both Zhang et al. and Akhondzadeh et al. concluded that ondansetron has potential to be used as adjunctive therapy in schizophrenia, the small benefit, although statistically significant, is not clinically meaningful enough to change treatment guidelines at this time. For a patient with chronic schizophrenia and treatment-refractory negative symptoms or cognitive impairment, ondansetron may be a reasonable add-on therapy with a low risk for adverse events. Further studies of ondansetron or other 5-HT₃ receptor antagonists would be helpful in determining its role in the treatment of schizophrenia.

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References


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El Rol de Ondansetrón en el Tratamiento de Esquizofrenia
AC Bennett y TM Vila

EXTRACTO
OBJETIVO: Evaluar la eficacia de ondansetrón para el tratamiento de esquizofrenia.
SELECCIÓN DE ESTUDIOS Y EXTRACCIÓN DE DATOS: Todos los artículos en inglés identificados de las fuentes fueron evaluados. Todos los estudios y reportes de casos evaluando ondansetrón para el tratamiento de esquizofrenia fueron revisados.
SÍNTESIS DE DATOS: Seis ensayos clínicos, incluyendo 3 ensayos aleatorios doble ciegos, y 2 reportes de casos pertinentes al uso de ondansetrón en esquizofrenia fueron identificados. Las dosis diarias de ondansetrón fueron de 4 a 16 mg, con dosis administradas 1 o 2 veces al día. Ondansetrón fue usado como monoterapia en 3 ensayos y en otros 3 ensayos como terapia adjunta con clozapina, haloperidol, y risperidona, respectivamente. Los estudios fueron de duración variable, desde un estudio de una dosis con seguimiento de 3 horas hasta 3 estudios de 12 semanas. La mayoría de los estudios evaluaron la eficacia de ondansetrón para tratar esquizofrenia medido por cambios en PANSS, BPRS, y CGI. En los 2 ensayos mayores, con una población combinada de 151, tratamiento adyunto con ondansetrón resultó en mejoramiento estadísticamente significativo de los síntomas negativos como evaluados con la escala PANSS. En todos los estudios, ondansetrón fue bien tolerado, sin que se reportaran efectos adversos severos.
CONCLUSIONES: Ondansetrón puede ser efectivo como terapia adjunta a antipsicóticos para el tratamiento de esquizofrenia, específicamente para síntomas negativos, según evaluado con PANSS. Dada la variación en terapias concurrentes y regímenes de dosificación, es difícil establecer una dosis óptima de los ensayos revisados. Estudios más grandes, aleatorios, doble ciegos, control activo, ayudarían a determinar el rol de ondansetrón en el tratamiento de esquizofrenia.

Traducido por Sonia I Lugo

Le Rôle de l’Ondansetron dans le Traitement de la Schizophrénie
AC Bennett et TM Vila

RÉSUMÉ
OBJECTIF: Evaluer l’efficacité de l’ondansetron dans le traitement de la schizophrénie.
SÉLECTION DE L’ÉTUDE ET SÉLECTION DE L’INFORMATION: Tout article en langue anglaise identifié de sources d’informations a été évalué. Tous les articles et les rapports de cas évaluant l’ondansetron dans le traitement de la schizophrénie ont été analysés. La majorité des études ont évalué l’efficacité de l’ondansetron dans le traitement de la schizophrénie comme mesurée dans les changements des paramètres (PANSS, BPRS, et CGI). Dans les 2 plus larges études avec une population de patients combinée d’un total de 151, le traitement d’appoint avec l’ondansetron a résulé dans une amélioration statistiquement significative des symptômes négatifs comme évalués avec l’échelle PANSS. Dans toutes les études, l’ondansetron a été bien toléré et aucune réaction secondaire sévère ne fut rapportée.
RÉSUMÉ: Six essais cliniques comprenant trois essais randomisés à double aveugle et 2 rapports de cas pertinents pour l’ondansetron dans le traitement de la schizophrénie ont été identifiés. Les doses journalières sont allées de 4 à 16 mg, avec des doses administrées une ou 2 fois par jour. L’ondansetron fut utilisé en monothérapie dans 3 essais et dans 3 autres essais comme traitement d’appoint avec respectivement la clozapine, l’halopéridol et la risperidone. Les études furent de durées variées: une étude à dose unique avec un suivi de traitement de 3 heures et des études de 12 semaines.
CONCLUSIONS: L’ondansetron peut être efficace comme appoint thérapeutique aux antipsychotiques dans le traitement de la schizophrénie, et plus spécifiquement les symptômes négatifs comme évalués dans l’échelle PANSS. En raison des variations dans les traitements concomitants et dans les schémas posologiques, il est difficile d’établir une dose optimale par rapport aux essais analysés. Des études plus amples, randomisées, en double aveugle et contrôlées apporteraient une aide pour déterminer le rôle de l’ondansetron dans le traitement de la schizophrénie.

Traduit par Thierry Youmbi