

2015

Is Lurasidone more safe and effective in the treatment ofschizoffective disorder and schizophrenia than other commonanti-psychotic medications?

Megan M. Sisbarro

Philadelphia College of Osteopathic Medicine, Meganhe@pcom.edu

Follow this and additional works at: http://digitalcommons.pcom.edu/pa_systematic_reviews



Part of the [Medicine and Health Sciences Commons](#)

Recommended Citation

Sisbarro, Megan M., "Is Lurasidone more safe and effective in the treatment ofschizoffective disorder and schizophrenia than other commonanti-psychotic medications?" (2015). *PCOM Physician Assistant Studies Student Scholarship*. Paper 247.

This Selective Evidence-Based Medicine Review is brought to you for free and open access by the Student Dissertations, Theses and Papers at DigitalCommons@PCOM. It has been accepted for inclusion in PCOM Physician Assistant Studies Student Scholarship by an authorized administrator of DigitalCommons@PCOM. For more information, please contact library@pcom.edu.

**Is Lurasidone more safe and effective in the treatment of
schizoaffective disorder and schizophrenia than other common
anti-psychotic medications?**

Megan M. Sisbarro, PA-S

A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, Pennsylvania

December 19, 2014

Abstract

Objective: The objective of this selective EBM review is to determine whether or not Lurasidone is more safe and effective in the treatment of schizoaffective disorder and schizophrenia than other common anti-psychotic medications.

Study Design: Review of two English language randomized double-blinded controlled comparisons and one English language Randomized open-label parallel-group comparison.

Data Sources: The randomized double-blinded controlled comparison studies and the randomized open-label parallel-group comparison were all found using PubMed and EBSCOhost databases. All three articles were published in peer-reviewed journals.

Outcomes Measured: Participant withdrawal due to adverse effects and treatment failure, patient responses to MATRICS consensus cognitive battery, interview responses, and patient responses on the schizophrenia cognition rating scale were all measured to determine the efficacy and safety of Lurasidone.

Results: According to Harvey et. al, the difference between Lurasidone and other common anti-psychotics, such as Ziprasidone, is not statistically significant with a $p=0.058$. Potkin, et. al reported that Lurasidone is more safe and effective compared to other common anti-psychotics with a $p=0.020$. McEvoy et. al demonstrated the safety and efficacy of lurasidone with p values <0.05 .

Conclusion: The results from this review are inconclusive. One study with a p value of 0.020 and another with p values <0.05 indicates that Lurasidone is more safe and effective and, but a p value of 0.058 in the third study does not agree with the findings of the other studies.

Keywords: lurasidone, schizophrenia, schizoaffective disorder

Introduction

Schizophrenia and schizophrenic-type disorders are characterized by disturbances in mood, thought, behavior, and filtering of stimuli of any type.⁴ Schizophrenic patients on anti-psychotic medications experience a high prevalence of side effects, as high as 86.19%, which can lead to non-adherence.⁶ This review evaluates two randomized control trials and a randomized open-label parallel group study to determine whether Lurasidone is more safe and effective than other, more commonly used anti-psychotic medications.

The average age of onset for men is early to mid-20's and late-20's for females. There is no way to predict the course of the disorder for each individual patient, but a decrease of symptoms over the course of the lifetime of a schizophrenic patient has been described in literature and is thought to be due to decreased dopamine activity as patients age. There are both negative and positive symptoms associated with schizophrenia and schizophrenic-type disorders. Some negative symptoms are social withdrawal, anhedonia, avolition, and alogia. Some positive symptoms are hallucinations, delusions, disorganized speech, and psychomotor abnormalities. It is common for patients to experience both types of symptoms in the course of their life with schizophrenia.⁴

Schizophrenia and schizophrenic-type disorders are not the most common psychological disorder encountered in medical practice, but the symptoms of this disorder can be very debilitating, resulting in a disruption of activities of daily living. The lifetime prevalence of schizophrenia in the general population is 0.3-0.7%, and that of schizoaffective disorder is 0.3%.⁴ Patients with these types of disorders can be encountered in all settings of medicine, but particularly in Family Medicine and

Behavioral Medicine. A 2004 study estimated that schizophrenic patients occupied one for every three psychiatric hospital beds in the United States that year.⁵ The cost of care for these patients in 2004 was about \$6.85 billion in both Canada and the U.S. Due to the increase in morbidity and mortality, and decreased productivity associated with this disorder, about \$4.83 billion is spent on healthcare-related issues, while the rest of the estimated expenditures come from non-healthcare related costs.⁵

These disorders are commonly treated with typical and atypical neuroleptics, as well as hospitalization. Typical neuroleptics, such as phenothiazines, thioxanthenes, butyrophenones, dihydroindolones, dibenzoxazepines, and benzisoxazoles, are common neuroleptic anti-psychotics, which work on dopamine (D2) receptors.⁶ These typical anti-psychotics treat only positive symptoms of schizophrenia, and are associated with increased extra-pyramidal symptoms with increasing doses.⁶ Atypical neuroleptics are clozapine, risperidone, olanzapine, quetiapine, aripiprazole, ziprasidone, paliperidone, iloperidone, and lurasidone. Atypical neuroleptics treat both the positive and negative symptoms of schizophrenia, and vary in their mechanism of action. Risperidone blocks D2 receptors and 5-HT₂ receptors, and clozapine blocks D₄ receptors, as well as serotonergic, histaminergic, and alpha noradrenergic blocking capacities.⁶ Hospitalization is often needed when patient's behaviors and delusions become harmful or dangerous to themselves or others. There is no cure for schizophrenia or schizophrenia-type disorders, but neuroleptics are effective in managing symptoms.

Objective

The objective of this review is to determine whether or not lurasidone is more safe and effective in the treatment of schizoaffective disorder and schizophrenia than other common anti-psychotic medications.

Methods

The criteria for selection of the studies in this review were participants 18-years-old and older who have been diagnosed with either schizophrenia or schizoaffective disorder according to the DSM-V. The participants in all of the studies selected took part in interventions involving lurasidone in various doses based on whether lurasidone is being compared to ziprasidone, or randomly assigned based on the patient's use of sedating and non-sedating anti-psychotics previously.

PCOM library databases PubMed and Medline were used to find the data for this review. All of the data was published in English in peer-reviewed journals. Inclusion criteria included randomized control double-blind comparison studies, and a randomized open-label parallel-group study that reported patient-oriented outcomes. Exclusion criteria were patients younger than 18-years-old and research reporting non-patient reported outcomes. Statistics reported in this review include p-values, NNH, ARI, and RRI.

Table 1. Demographics and Characteristics of included studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Harvey ¹ (2011)	Randomized double-blind controlled comparison	301	18-70 years old	Community dwelling patients with schizophrenia or schizoaffective disorder who had never received treatment with Ziprasidone or Lurasidone	Patients younger than 18, schizophrenia disorder that was chronic (at least 6 months) or has been hospitalized/ experienced acute exacerbation of psychosis within last 3 months, history of head traum, substance abuse currently or in the past.	96	Lurasidone 120mg QD Ziprasidone 80mg BID
McEvoy ² (2013)	Randomized Open-label parallel-group comparison	240	18-70 years old	Adults with DSM-IV defined schizophrenia or schizoaffective disorder	Patients younger than 18, in an acute phase of illness	19	Lurasidone: 40-80mg/d over 6 weeks 40-120mg/d over 6 weeks
Potkin ³ (2011)	Double-blind Randomized control comparison	301	18-70 years old	Adults with schizophrenia or schizoaffective disorder that was chronic	Patients younger than 18, patients who weren't stable enough to be treated in outpatient setting	94	Lurasidone 120mg QD Ziprasidone 80mg BID

Outcomes Measured

The outcomes measured in this review were withdrawal from the studies due to adverse effects, participant-based interviews and use of the Schizophrenia Cognition Rating Scale. Investigators also used the MATRICS Consensus Cognitive Battery, Positive and Negative Syndrome Scale, Clinical Global Impressions-severity scale, and Calgary Depression Scale for Schizophrenia.

Results

McEvoy, et. al conducted a randomized, open-label parallel group study consisting of 240 participants aged 18-72 who were diagnosed with schizophrenia or schizoaffective disorder and were not in an acute phase of the illness. These participants were required to partake in a 14-day “wash-out” period, where they tapered their previous medications to 50% over the first 7 days, then tapered down to no medication by the 14th day. The participants then started a 6 week period of lurasidone which started at 40 mg per day, the participants were then broken down into two groups based on whether they were on a sedating (olanzapine or quetiapine) or non-sedating medication (all others) prior to the start of the study. The participants in each were randomly titrated up to either 80 mg or 120 mg over 6 weeks.²

The two groups were 86 participants who were previously on sedating medications, and 154 were treated with non-sedating medications. The study then measured time to treatment failure, which included failure of clinical response to lurasidone, discontinuation due to an adverse effect, or exacerbation of the disorder being treated. In the prior use of sedating medications group, 10 of the 86 participants withdrew

due to treatment failure, and 9 out of 154 of the other group withdrew for treatment failure.²

The effectiveness of lurasidone was measured using three scales valuing patient's experience of symptoms. The three scales were Positive and Negative Syndrome Scale, Clinical Global Impressions-Severity, and Calgary Depression Scale for Schizophrenia. Each participant's change of score within each scale over 6 months was recorded, and the mean change and the p-value was recorded.

Table 2. Results of McEvoy, et al randomized open-label parallel group study

Rating Scale	Mean Change	p-value
Positive and Negative Syndrome Scale	-8.2	<0.0001
Clinical Global Impressions-Severity	-0.39	<0.0001
Calgary Depression Scale for Schizophrenia	-1.2	0.0002

The results from this study demonstrate the efficacy of lurasidone in both groups. All three p-values indicate the overall changes in symptoms experienced by the participants in each group were statistically significant. Thus, the changes the participants experienced were not due to chance, but due to the therapeutic effects of lurasidone.

Potkin, et. al studied 301 patients aged 18-70-years-old with schizophrenia or schizoaffective disorder in a 21-day randomized double-blind controlled comparison trial. The participants in this trial were randomly assigned to either lurasidone 120 mg every day (150 participants), or ziprasidone 80 mg twice per day (151 participants). Among the 301 participants, 94 withdrew from the study. Of the 94 participants who withdrew,

32.5% (31 participants) of them were in the lurasidone treatment group and 30.7% (29 participants) of them were from the ziprasidone treatment group. Of those who withdrew in the lurasidone group, 10.4% (3 participants) were due to adverse effects of the medication compared to 11.1% (3 participants) in the ziprasidone group³.

Table 3. Potkin et. al, double-blind controlled comparison trial

Study	Participants	RRI	ARI	NNH	p-value
Potkin	301	-0.063	-0.7	-142	0.02

Based on the participants who withdrew from the study, a relative risk increase value of -0.063 was determined, and an ARI of -0.7 was then calculated. Number needed to harm in this study was -142, which implies that for every 142 patients exposed to lurasidone, one will discontinue it's use due to adverse events. The p-value of 0.02 signifies that this data is statistically significant, and that the results of this study did not happen due to chance (Table 3).

The main adverse effects experienced in this study were insomnia, vomiting, nausea, headache, somnolence, anxiety, and sedation. Of the 150 lurasidone participants, 85 (56.7%) experienced one adverse effect. Of these, 10 (6.7% of the total population) reported the adverse effect was severe. In the ziprasidone group, 99 participants (65.6%) experienced an adverse effect, and 11 (7.3% of the total population) reported the adverse effects as severe.³

Harvey, et. al conducted a randomized double-blind controlled comparison trial comparing lurasidone 120 mg per day (150 participants) to ziprasidone 80 mg (151 participants) twice per day in 301 participants diagnosed with schizophrenia or

schizoaffective disorder. The participants were 18-70-years-old, who had not been hospitalized in the past 3 months for exacerbations of their schizophrenia or schizoaffective disorder. At the end of the 21-day study, 67.5% of the lurasidone group and 69.3% of the ziprasidone group finished the treatments. Using an interview-based cognitive function tool, Schizophrenia Cognition Rating Scale (SCoRS) and MATRICS Consensus Cognitive Battery (MCCB), efficacy of lurasidone was determined compared to ziprasidone. Participants were evaluated at baseline as well as at week 3 with SCoRS, which included participant answers to interview questions and interviewer's interpretation of the participant according to each question. The overall change in SCoRS and MCCB ratings between the two groups was not statistically significant, but the change from baseline to week 3 in the lurasidone group proved to be statistically significant with a p-value of changes in MCCB scores of 0.026 and SCoRS of <0.001. Compared to the change in MCCB scores in the ziprasidone group $p=0.254$, and the SCoRS changes, $p=0.158$, which proved to not be statistically significant. The difference between the scores in these two groups was found to not be statistically significant with $p=0.058$, indicating that the results found in this study could be attributed to chance. As this data was not dichotomous, between group t-tests were performed by Harvey, et. al¹.

Overall, this data shows that the change in schizophrenic and schizoaffective disorder patients experienced over the first three weeks was significant and not due to chance. However, the p value between the lurasidone and ziprasidone groups was not statistically significant. Therefore, there was no significant difference between the experimental and control groups.

Discussion

Lurasidone was approved for use in treating schizophrenia and schizoaffective disorder in October, 2010.⁷ It is available for use in the United States for treatment of these disorders as well as bipolar disorder more commonly. Lurasidone is a benzoisothiazol derivative and its mechanism of action is believed to be contributed to dopamine type 2 (D2) and serotonin type 2 (5HT2A) receptor antagonism. It is an oral medication that should start treatment at 40mg and titrated up to an appropriate dose for the patient, with 80mg the suggested maximum dose.⁸ It is suggested by the manufacturers that lurasidone be taken with food, at least 350 calories.⁸ The cost of lurasidone can be a limiting factor for patients trying to receive treatment as the cost per unit is about \$18.46/80mg and the cost for a 30-day supply for the maximum dose (80mg) is \$603.60 without insurance.⁶

Lurasidone has two black box warnings associated with adverse effects in certain populations. One of the black box warnings pertains to increase mortality risk due to cardiovascular or infectious events in patients using the medication for dementia-related psychosis. The other black box warning is an increased risk of suicide in children, adolescents, and young adults with major depressive symptoms as well as psychotic symptoms.⁹

Some limitations encountered in searching for information for this review was the lack of studies that not only evaluated participants diagnosed with schizophrenia, but schizoaffective disorder as well. While both disorders have similar symptoms, they are not identical and more information could have been gathered comparing more medications to lurasidone to determine true efficacy compared to other treatments.

Conclusion

The results of the data in this review are inconclusive as to whether lurasidone is more safe and effective than other common anti-psychotic medications in the treatment of schizophrenia and schizoaffective disorder. Many participants experienced adverse side effects in all of the experiments, but the number of participants who withdrew due to the severity of adverse effects varied. In the study performed by McEvoy, et al demonstrated an improvement in the participant's symptoms when switching from either non-sedating or sedating antipsychotics, supporting the idea that it is safe and effective to switch to lurasidone from other antipsychotics. Harvey, et al showed that the changes experienced by the participants of that study were not statistically significant, so the decrease in symptoms in that study cannot be attributed solely to the medication. More conclusive results could be attained if the studies used could have compared lurasidone to either atypical or typical anti-psychotics, so a distinct difference could be made between the two classes of anti-psychotics and lurasidone. The results of this review could also be improved if a larger population was used, as the two randomized double blind controlled comparison studies contained the same number of participants and the same interventions, but were conducted by two different researchers. These two studies could also be improved if they were to observe the participants on lurasidone for longer than 21 days. There were many factors that were not controlled in these studies, such as: diet, only comparing lurasidone to one other medication, and the medications the participants were on before starting the studies. Diet could affect absorption of the drug and therefore the efficacy, and the lack of comparison of more medications in these studies made it impossible to compare the treatment of lurasidone with more than just ziprasidone. The amount of time patients were off prior medications before starting the studies, as one of

the studies had a 14 day “wash-out” period, may not have been long enough for the medications to completely be out of the participants systems. More research is necessary to determine a definitive answer to the objective of this review, and to provide more knowledge regarding the use of lurasidone in schizophrenia and schizoaffective disorder.

References

1. Harvey PD, Ogasa M, Cucchiaro J, Loebel A, Keefe RS. Performance and interview-based assessments of cognitive change in a randomized, double-blind comparison of lurasidone vs. ziprasidone. *Schizophr Res.* 2011;127(1-3):188-194. Accessed 1/31/2014 3:30:58 PM.
2. McEvoy JP, Citrome L, Hernandez D, et al. Effectiveness of lurasidone in patients with schizophrenia or schizoaffective disorder switched from other antipsychotics: A randomized, 6-week, open-label study. *J Clin Psychiatry.* 2013;74(2):170-179. Accessed 1/31/2014 3:30:58 PM.
3. Potkin SG, Ogasa M, Cucchiaro J, Loebel A. Double-blind comparison of the safety and efficacy of lurasidone and ziprasidone in clinically stable outpatients with schizophrenia or schizoaffective disorder. *Schizophr Res.* 2011;132(2-3):101-107. Accessed 1/31/2014 3:30:58 PM
4. American Psychiatric Association. Schizophrenia spectrum and other psychotic disorders. *Diagnostic and Statistical manual of mental disorders* (5th ed.). Washington, DC. Psychiatry Online.
<http://dsm.psychiatryonline.org.ezproxy.pcom.edu:2048/content.aspx?bookid=556§ionid=41101758&resultclick=24#103437013>
5. The Internet Mental Health Initiative. Schizophrenia Facts and Statistics. (2010, January 1). <http://schizophrenia.com/szfacts.htm>
6. A Lange Medical Book, *Current Medical Diagnosis and Treatment 2014* New York : 53rd ed , Digital book, Schizophrenia and other Psychotic Disorders, pages 3,569-3,700;New York ; 2014.
7. *FDA approves Latuda to treat schizophrenia in adults* October ;2010 ; Available from:
<http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm231512.htm> (Accessed August 2014).
8. Latuda (lurasidone) October ;2010 ; Available from:
<https://www.centerwatch.com/drug-information/fda-approved-drugs/drug/1124/latuda-lurasidone> (Accessed October 2014).
9. *Important Safety Information and Indications for Latuda* October ;2010 ; Available from: <http://www.latuda.com/sz/important-safety-information.html> (Accessed October 2014).