



Comparison of Lurasidone and Olanzapine in Schizophrenia- A Open label study

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Abstract

The study was conducted at RIMS general Hospital Psychiatry OP and study evaluated comparative efficacy and safety Lurasidone in comparison to Olanzapine in first episode schizophrenia diagnosed based on ICD-10.126 first episode schizophrenia patients participated in the study out of which 60 patients were in olanzapine group and 66 patients Lurasidone group. PANSS and CGI-I were used to assess and compare efficacy. Lurasidone was non inferior to olanzapine in decreasing PANSS score from baseline to end of study at 12th week (95% CI: -8.9 to 4.5). Lurasidone and Olanzapine were equally effective in treating the first episode schizophrenia.

Conclusion: In our study after analysis Lurasidone was equally efficacious in treating first episode of schizophrenia.

Keywords: Lurasidone, Olanzapine, first episode schizophrenia, response rates, PANSS, CGI-I.

Open Label comparative study of Lurasidone and Olanzapine treating first episode of Schizophrenia

Schizophrenia is a chronic psychiatric disorder affecting 1% of population^{1,2,3}. The incidence of schizophrenia 0.1-0.4 per 1000 in 10 (WHO)². The main stay of treatment for schizophrenia is antipsychotics and currently the first choice is second generation antipsychotics⁴ and in them Olanzapine is the frequent choice of psychiatrists. Recently Lurasidone has been introduced in the Indian market which has a different receptor profile

and hence a comparative study would establish any clinical relevance of the unique receptor profile of Lurasidone. Lurasidone is a 2nd generation antipsychotic that strongly binds to D2, D3, D4, 5HT (2A) and 5HT⁽⁷⁾. Lurasidone showed a preferential effect on the ventral striatum and prefrontal cortex. Based on its receptor profile, Lurasidone possesses antipsychotic, antidepressant, and anxiolytic effects with reduced liability to produce EPS and CNS side effects⁵. Olanzapine has high antagonist affinity to D1, D2, D3, D4 and 5HT 2A/2C.

Olanzapine was superior than Aripiprazole, risperidone, ziprasidone where as there was no efficacy difference. amisulpride and clozapine were better than olanzapine in clinical efficacy^{6,7}.

Design & Study Population

This study is conducted in RIMS Psychiatry OP department from march 2016 to feb 2017. The study population included first episode schizophrenia male and female participant who have been diagnosed based on ICD-10 criteria. The therapeutic effects of olanzapine(5mg-30mg) and Lurasidone (40-120mg) were compared in these participants. The participants first episode schizophrenia patients 18-40 of subtypes Paranoid and Hebephrenic schizophrenia. They were administered PANSS scale⁷, CGI-S⁸, SAS scale during first evaluation, 6th week and 12th week of study. The Simpson Angus scale was administered on every visit of the patient.

Inclusion Criteria

- 1) First episode schizophrenia either Hebephrenic or Paranoid subtype
- 2) Consent for interview
- 3) Consent to be linked to olanzapine or Lurasidone study group
- 4) Patients who can be managed on OP basis

Exclusion Criteria

- 1) Presence of any co-morbid psychiatry disorder
- 2) Use of any antipsychotics prior to study
- 3) Use of injectable depot antipsychotics prior to study
- 4) Pregnant, lactating women of child bearing who are not using adequate contraception.
- 5) Violent patients requiring injectable haloperidol or injectable benzodiazepine on high dose to control agitation.

Ethics committee approval: The study got approval from local ethics committee and was conducted according Good Clinical Practice guidelines by the Declaration of Helsinki

Treatment

Patients were allotted to olanzapine or Lurasidone group in alternate way i.e first diagnosed patient gets olanzapine and second diagnosed patient gets Lurasidone. The doses Olanzapine (10-20/day) and Lurasidone 40-120mg /day. The dose olanzapine was started 5mg and slowly titrated in the first week to 10 mg and Lurasidone was titrated from 20 mg to 40 mg in the first week. For every raise of 5mg of olanzapine dose the dose of Lurasidone was raised by 40mg. The maximum dose of olanzapine used in study was 20 mg and Lurasidone 120 mg. Trihexyphenidyl was allowed to address extrapyramidal symptoms. Benzodiazepines were also allowed to alleviate anxiety and sleep symptoms while their usage was limited diazepam of dose not greater than 40mg which was down titrated by the end of 3rd week

Assessment: Efficacy of treatment was measure change in baseline scores of PANSS and CGI-I to scores calculated at the end of study (12th week).

The main goal of the study was to compare the efficacy of olanzapine and Lurasidone. A decline more than 50% of baseline score was considered improvement¹⁰. The primary endpoint was analysed to intent to treat (ITT) patients (patients who completed at least on evaluation) and completer patients are patients who completed all evaluations. The patient who dropped in the middle of study their last observation was carried forward (LOCF)

Statistical Analysis

Comparing clinical efficacy of Lurasidone to that Olanzapine in treating first episode was goal of statistical analysis. PANSS score baseline, change of score and score at end point were primary variables of analysis. All patient who were examined at treated at least once (Intent to treat ITT) and patient who attended the entire study were analysed with Last observation carried forward for ITT population and entire scores for completer population. Patient safety was observed throughout the study

The primary efficacy variable, the PANSS total score absolute change from baseline, was analysed according to null hypothesis and non-inferiority hypothesis; non-inferiority was considered confirmed if the 95% 2-sided confidence interval calculated for the difference. Lurasidone minus olanzapine had an upper limit less than 8

points, corresponding to the non-inferiority margin defined in the protocol. a non-inferiority limit set at 8 points considered clinically relevant with regards to the placebo-active drug difference generally observed¹¹. The variables age, height, weight and subtype of Schizophrenia were compared.

Results

Table 1 Demographic data:

Demographic data	Olanzapine Mean(SD)	Lurasidone Mean(SD)	Chi ²	df	p
Age ^a	36(8)	36(9)		124	0.19
Height(a)	160(12) cm	162(10)cm		124	0.30
Weight (a)	70(10)kg	72(9)kg		124	0.23
SEX					
Male (b)	37	40		1	0.9
Female(b)	23	26			
Paranoid (b)	46	54		1	0.62
Hebephrenic(b)	14	12			

a – independent 't' test. b- Chi² tes

The demographic data of the participants is given in table 1. The data has been evaluated using independent sample 't' test and chi² test wherever

applicable. The olanzapine and Lurasidone sample did not differ significantly with respect to demographic data

Table 2: Attrition and Non-improvement (PANNS reduction <50 %)

Distributon	Olanzapine	Lurasidone
Total (N) at entry	60	66
Lost in 6 th week	4	6
Lost in 12 th week	5	8
Stopped treatment due side effects	0	0
Total lost 6 th and 12 th week	9	14
Total at end of study	51	52
Attrition(a)	15%	21%

.a -chi2 test.

Attrition rate did not differ significantly in Olanzapine and Lurasidone study group

Table 3: PANSS, CGI-I, AND SAS

Scale	Olanzapine			Lurasidone			F	p	C.I At 95 %
	Baseline Mean (S.D)	Endpoint Mean (S.D)	Change (S.D)	Baseline Mean (S.D)	End point Mean (S.D)	change (S.D)			
PANSS	147.8 (17.9)	75.2 (8.4)	72.6 (18.8)	149.4 (17.5)	75.1 (9.2)	74.88 (19.1)	0.65	0.513	-8.9+4.5
CGI-I	5.2 (1.1)	3.1 (1.1)	2.1 (1.2)	5.3 (1.1)	2.8 (1.1)	2.5 (1.2)	1.8	0.06	-.82 + 1.9
SIMS	48.4 (19.2)	32.5 (17.2)	14.9 (7.6)	49.8 (19.8)	31.4 (14.2)	18.4 (9.1)	1.6	0.09	-5.4 + .47

Independent 't' test was done in all three measurements PANSS, CGI-I and SAS scale. Olanzapine and Lurasidone group did not differ significantly.

Results

The participants in both groups were matched in age, height, weight and sex. The Schizophrenia subtype in both group did not differ significantly all the majority subtype is Paranoid Schizophrenia. The drop out in the Olanzapine group 15% and Lurasidone groups 21% which did not differ significantly. Efficacy measured through change in PANSS score and CGI-I group was around 50% in both groups and when compared on independent 't' test and found the change of scores was similar in both groups ($p > 0.05$ at 95% CI). The side effects were measured on Simpson Angus scale the initial ratings, baseline ratings and change in score from baseline to endpoint did not differ statistically in a significant way ($p > 0.05$ and CI of 95%).

Efficacy

The study wanted to compare the efficacy of newly introduced Lurasidone in Indian population with already existing standard drug olanzapine. The attrition rate in the study ranged from 15-21% which is well below the accepted norm of 20%¹⁵ PANSS which measures positive, negative and global psychopathology and CGI-I were used to measure the change and significance. Both groups

showed decrease in symptoms severity in PANSS by 50%.

These 50% decrease in symptom severity in both groups indicate both drug are effective in reducing the symptoms severity in Schizophrenia. The change in PANSS score was compared using independent 't' test and the both groups did not differ significantly in quantitative improvement in both group suggesting Lurasidone is as effective as Olanzapine. The mean dose of Lurasidone was 80mg/day and that Olanzapine was 10mg/day. After disproving the null hypothesis, the non-inferiority as described in protocol was done. Its found that Lurasidone is non inferior to Olanzapine in reducing the symptoms^{15,16,17}

CGI-I score also indicated both drugs caused marked improvement in reducing the severity of illness.

The Simpson Angus score which measures the motor side effects of antipsychotics has been similar in both groups did not show increase the score at end point of study. The neuromuscular side effects by both drugs were similar intensity in both groups.

Conclusion

Lurasidone is as efficacious as Olanzapine in treatment of first episode Schizophrenia. Side effect profile of Lurasidone was similar to Olanzapine

Limitations of the study

- 1) Open label study result do not form a good qualitative evidence.
- 2) Hospital based study cannot generalized natural population.
- 3) Shorter duration of study would have resulted initial larger gains in improvement.
- 4) Sample size small to extrapolate the results of study
- 5) Another scale along with PANSS should have been used like BPRS.
- 6) Quality of life measurements should also have been made.

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