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EFFECT OF LURASIDONE ON POSITIVE SYMPTOMS IN SCHIZOPHRENIA PATIENTSIN RURAL SETTING IN INDIA: A LONGITUDANAL STUDY

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ABSTRACT

Background and objectives: New antipsychotics have modified the course of schizophrenia. Not many medications have shown improvement in negative symptoms, and psychological shortages, compounded by unbearable results. Lurasidone is a moderately new participant in the field of schizophrenia in the Indian setting. This investigation assessed the general viability of Lurasidone across positive symptoms of schizophrenia. **Methods:** This is a longitudinal observational investigation. PANSS was administered at the time of admission, first month and following 3 months. An aggregate of 57 patients, analyzed utilizing ICD-10 standards, were selected, from the psychiatry OPD of MVJ Medical College and Research Hospital. 7 patients left because of grievousness. Measurable examination of the information was done on the SPSS (Statistical Package for Social Sciences Software). Utilizing suitable measurable techniques, dimensional examinations were made utilizing the focal propensities like the Mean with Standard Deviations for Lurasidone. T- test was applied for finding out the significance of 'p' values where appropriate. **Results:** In positive scale of PANSS, mean decrease of positive score toward the finish of multi week was 6.13, toward the finish of 3 months the mean positive score was 10.9.The current investigation showed that Lurasidone has impact on certain manifestations of schizophrenia at week 4 and better adequacy at week 12. By and large outcomes show better reaction to positive symptoms. Anyway a more drawn out follow up would help us study the impact of Lurasidone on the course of schizophrenia.

KEYWORDS: Lurasidone; efficacy; Indian population; schizophrenia; positive symptoms.

INTRODUCTION

The management of schizophrenia has seen huge steps in the course of the most recent many years, because of the expanding accessibility of various antipsychotics. However, the low adequacy corresponding to the negative and psychological manifestations of schizophrenia and the upsetting antagonistic responses related with the current antipsychotics, mirror the requirement for better molecules focusing on neglected pathways. Lurasidone is a new contestant in the field of schizophrenia in the Indian setting.

There are not many efficient investigations done in India, about the viability of Lurasidone. Henceforth this investigation is an endeavor to assess the adequacy of the new age antipsychotic Lurasidone, on positive symptoms of schizophrenia.

Lurasidone is a second generation antipsychotic which is now FDA-affirmed for treatment ofschizophrenia. This is certainly not a clinical preliminary and this medication is anything but a trial drug. It is as of now a genuinely settled medication which is cleared for clinical utilization, across the world. The examination includes just clinical assessment of this side effect reaction, with no obtrusive examinations or methods. In that sense it's a serious safe examination. A decent number of schizophrenia patients, would have been put on Lurasidone in any case, in the standard practice, by the senior therapists of this division. This examination is just a deliberate scoring of the enhancements in different side effects and recording those perceptions in an orderly manner, without exposing the patients to any untested or unapproved medicines or without bargaining the patients' prosperity in at any rate. This examination is additionally a little endeavor, utilizing just protected, noninvasive, clinical assessment techniques to add to the heaviness of proof, with respect to whether Lurasidone is successful enough in treating schizophrenia patients in Indian settings.

Lurasidone hydrochloride (HCl) is a novel benzisothiazol substance that has been affirmed by the FDA for the treatment of schizophrenia. Lurasidone has

intense restricting fondness for D2, 5-HT2A and 5HT7 receptors (rival impact), moderate liking for 5HT1A (fractional agonist impact) and α2C receptors (enemy impact), and no obvious liking for H1 and M1 receptors.[1,2,11]

AIMS & OBJECTIVES OF THE STUDY

- This study was designed to evaluate the overall efficacy of Lurasidone across positivesymptoms of schizophrenia

- **METHODOLOGY**
- **Source of data**

Patients determined to have schizophrenia utilizing ICD 10 criteria, on Lurasidone treatment going to the psychiatry OPD at MVJMC and RH which is a tertiary consideration reference clinic

Sample Size ; 57 Patients of schizophrenia

Age b: Patients between 18-60 years were chosen for study, to keep sample morehomogenous and to dodge the false impact old age cognitive derangement

1) Sampling strategy

The cases were selected and the information will be gathered over a time of 1 year 10 months (NOV 2016 – SEP 2018). Choice was made in a sequential continuous manner that agree to take part in the examination.

Permission was gotten from Ethical Committee of our institution.

Inclusion Criteria

1. Newly diagnosed case of schizophrenia.
2. Age groups between 18-60 years are included
3. Written Informed consent.

Exclusion Criteria

1. Other psychiatric disorders except schizophrenia.
2. Patients of schizophrenia receiving treatment previously.
3. Patients who did not show adequate response when put on Lurasidone, even after sufficient amount of time (6 weeks) and adequate dose (60- 120mg) were be switched to other antipsychotics in the best interest of patients. They were considered as dropouts from the study.
4. Patients suffering from severe and debilitating co-morbid medical illness.

4) Instruments: Semi-structured pro- forma was used to record basic socio demographic data.

Modified BG Prasad's socioeconomic class scale

Prasad's financial grouping is generally utilized in Indian clinical writing; it was proposed interestingly by Prasad on per capita pay each month and afterward overhauled by him dependent on average cost for basic items

The revised Classification of Social economic Class - 2016[3]

Classification for 2016. PCI/month in rupees	**Social class**
6277 and above	I
3139 – 6276	II
1883 – 3138	III
942 – 1882	IV
Less than 942	V

Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale (PANSS) is a mental rating scale for estimating manifestation seriousness, in two classes, that is, Positive and Negative sorts inpatients with schizophrenia.

- It was distributed in 1987 by Stanley Kay, Lewis Opler and Abraham Fiszbain. It is generally utilized in assessing result of antipsychotic therapy.[4]
- The PANSS is a moderately concise meeting, requiring 45 to 50 minutes toadminstrate
- Both Positive and Negative scale contains 7 things each. Every thing evaluated between a score of 1-7. Peralta and Cuesta wrote about the between rater unwavering quality of the PANSS from an example of 100 sequentially conceded patients with schizophrenia. Positive and negative scales showed great between rater dependability: interclass connection coefficients (ICC) of 0.72 and 0.80, respectively.[5]

5) Study design

- This is a longitudinal observational study.
- Minimum period of study for each patient is 3 months.

PANSS will be administered at baseline, i.e., before starting the treatment, after 1 month andafter 3 months

6) Assessment at particular visits

First visit with Baseline assessment

- Patients were informed in detail about the purpose and requirements of the study.
- A thorough physical examination was carried out including body mass index and recorded.
- Blood investigations were done; complete blood count, liver function test, renal function test, serum electrolytes, fasting and post prandial blood sugars, thyroid function test and ECG.
- Assessment of positive symptoms schizophrenia was done by applying PANSS.

Second visit

This was done at the end of 1st month, it included

- Re-assessment of severity of positive symptoms of schizophrenia by applying PANSS.
- A thorough physical examination including body mass index was carried outagain and recorded.

Third visit

This was done at the end of 3 rd month, it consisted of

- Re-assessment of severity of positive of schizophrenia by applying PANSS.
- Treatment associated adverse effects of Lurasidone were recorded list.
- A thorough physical examination including body mass index, was carried out andrecorded.

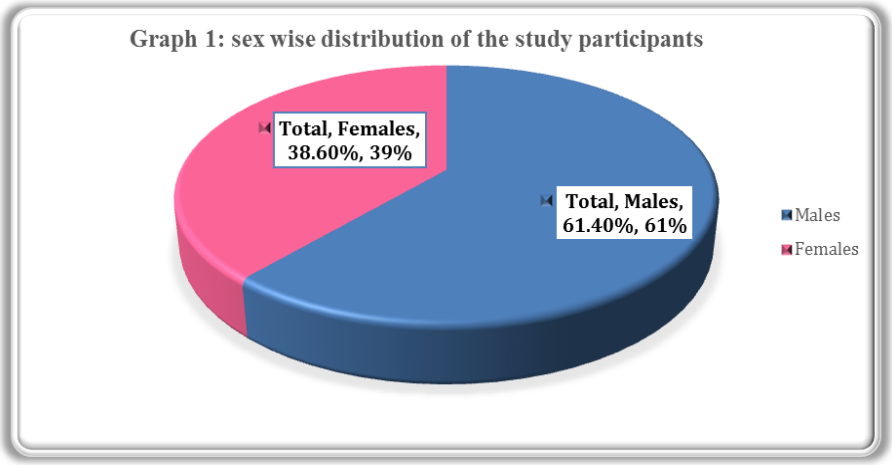
Statistical method used

Statistical analysis of the data was done on the SPSS. Using a statistical methods, dimensional comparisons will be made using the central tendencies like the Means with S.D for Lurasidone before and after treatment.

Paired T- test was applied for finding out the significance of 'p' values where appropriate.

RESULTS

57 patients who fulfilled the inclusion criteria were approached for the current study, 50 were able to complete the study the rest 7 subjects dropped out due to intolerability of Lurasidone.



Graph 1: Shows the sex wise distribution of study participants. Out of 57 of study population, 35 were males (61.4%), 22 were females (38.6%).

Table 1: Distribution of the study participants according to age group.

AGEGROUP	MALE N= 35 (%)	FEMALE N= 22 (%)	TOTAL N= 57 (%)
20-29 Years	24 (68.6%)	17 (77.3%)	41 (71.9%)
30-39 Years	9 (25.7%)	5 (22.7%)	14 (24.6%)
40-49 Years	2 (5.7%)	0	2 (3.5%)

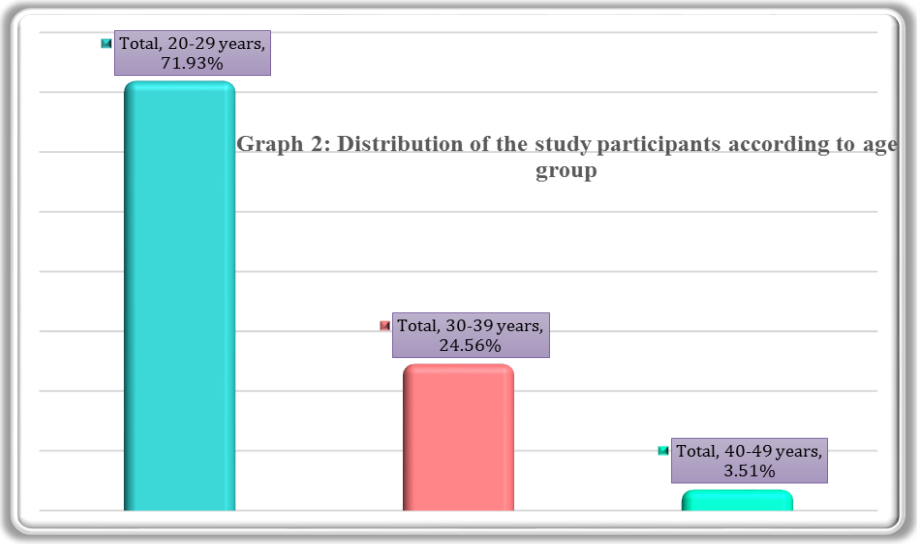


Table 1 and Graph 2 show the age wise distribution of the study participants. The participants were 20 to 49 years of age. Majority of age group were 20 to 29 years (71.93%), where as 30to 39 years was 24.56% and 40 to 49 years was 3.51%.

Table 2: Educational status of the study participants.

Education	Male	Female	Total
	N= 35 (%)	N= 22 (%)	N= 57 (%)
Primary (0-7)	3 (8.6%)	3 (13.6%)	6 (10.5%)
Secondary (8-10)	19 (54.3%)	6 (27.3%)	25 (43.9%)
Intermediate/ PUC	10 (28.6%)	12 (54.5%)	22 (38.6%)
Graduate	3 (8.6%)	1 (4.5%)	4 (7.0%)

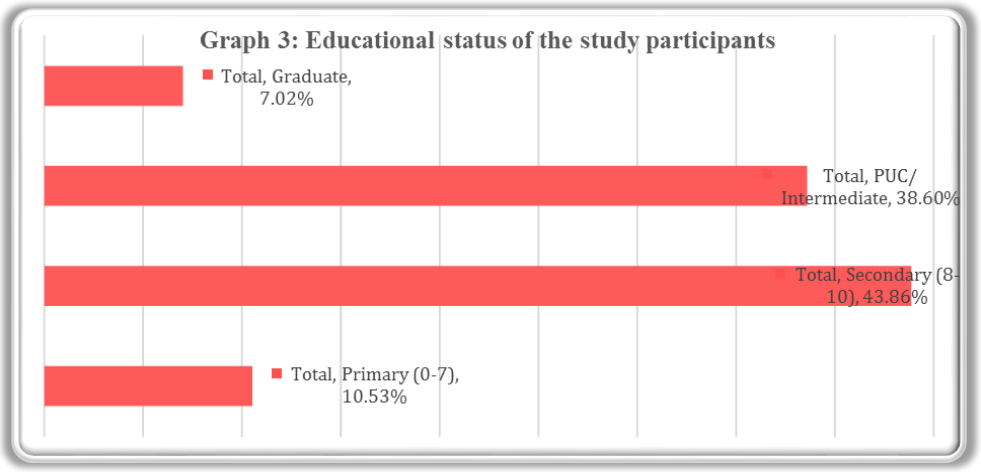


Table 2 and Graph 3 illustrate educational status of study participants from primary to graduate level. Total 6 (10.53%) were educated till primary school (0 to 7); 25 (43.86%) were educated up to secondary school (8 to 10); 22 (38.6%) were educated till PUC or intermediate; 4 (7.02%) were graduates.

Table 3: Distribution of the study participants according to their occupation.

Occupation	Male N= 35 (%)	Female N= 22 (%)	Total N= 57 (%)
Unemployed/ Housewife	0	10 (45.5%)	10 (17.5%)
Unskilled worker	4 (11.4%)	3 (13.6%)	7 (12.3%)
Semiskilled worker	12 (34.3%)	3 (13.6%)	15 (26.3%)
Skilled worker	12 (34.3%)	4 (18.2%)	16 (28.1%)
Clerical, Shopowner	5 (14.3%)	1 (4.5%)	6 (10.5%)
Semi professional	2 (5.7%)	1 (4.5%)	3 (5.3%)

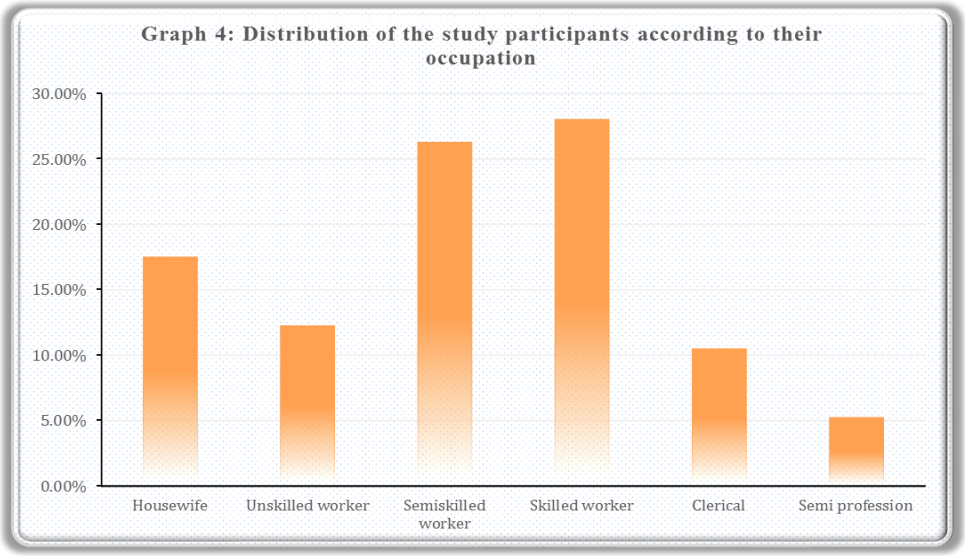


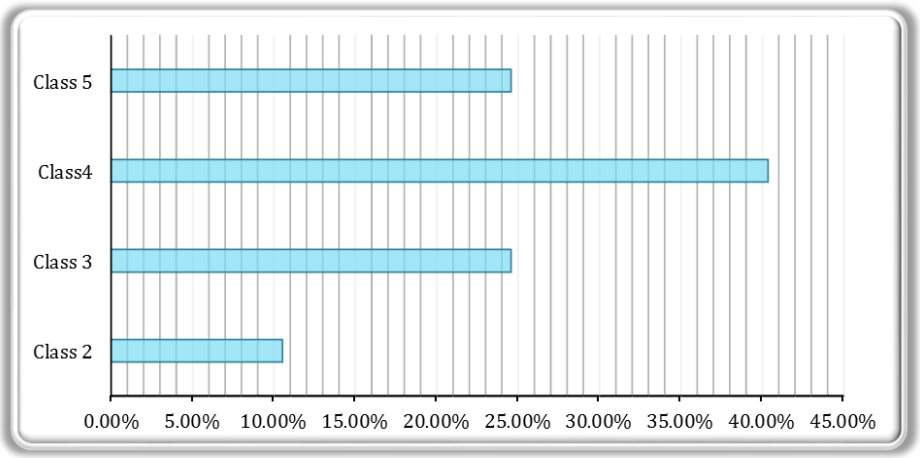
Table 3 and graph 4 show distribution of the study participants according to their occupation, which includes unemployed/ housewife, unskilled workers, semiskilled workers, skilled workers, clerical / shop owners, semi

professional.

Majority of about 16 (28.1%) were skilled workers; 15 (26.3%) were semiskilled workers; 10 (17.5%) were unemployed / housewife; 7(12.3%) were unskilled workers; 6 (10.5%) were clerical / shop owners and 3(5.3%) were semiprofessional.

Table 4: Distribution of the study participants according to their socio-class status.

Socio-Economic Status	Male N= 35 (%)	Female N= 22 (%)	Total N= 57 (%)
Class 2	4 (11.4%)	2 (9.1%)	6 (10.5%)
Class 3	9 (25.7%)	5 (22.7%)	14 (24.6%)
Class 4	16 (45.7%)	7 (31.8%)	23 (40.4%)
Class 5	6 (17.1%)	8 (36.4%)	14 (24.6%)



The sample was categorized in to various socio economic groups based on the Modified B.G. Prasad's classification. Table 4 and graph 5 depicts distribution of the study participants according to their socio-economic status by Modified B.G. Prasad's classification.
Out of which 6 (10.5%) were of Class 2; 14 (24.6%) were of Class 3, majority of about 20(40.4%) belong to Class 4 and Class 5 consist of 14 (24.6%), there was no patient from class 1 Socio-economic status.

Table 5: Distribution of the study participants according to their area of residence

Area of Residence	Male N= 35 (%)	Female N= 22 (%)	Total N= 57 (%)
Rural	24 (68.6%)	14 (63.6%)	38 (66.7%)
Urban	11 (31.4%)	8 (36.4%)	19 (33.3%)

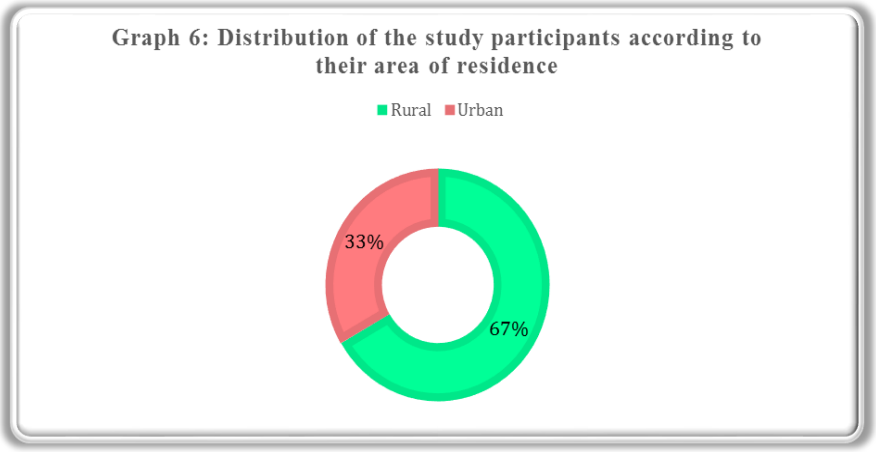


Table 5 and Graph 6 show distribution of study participants according to their area ofresidence.
Rural study participants consist of 24 males and 14 females, total of about 38 (66.7%).Ur ban study participants consist

of 11 males and 8 females, total of about 19 (33.3%).

Table 6: Distribution of the study participants according to their marital status.

Marital Status	Male N= 35 (%)	Female N= 22 (%)	Total N= 57 (%)
Single (Unmarried/ Divorced/ Widowed)	9 (25.7%)	10 (45.5%)	19 (33.3%)
Married	26 (74.3%)	12 (54.5%)	38 (66.7%)

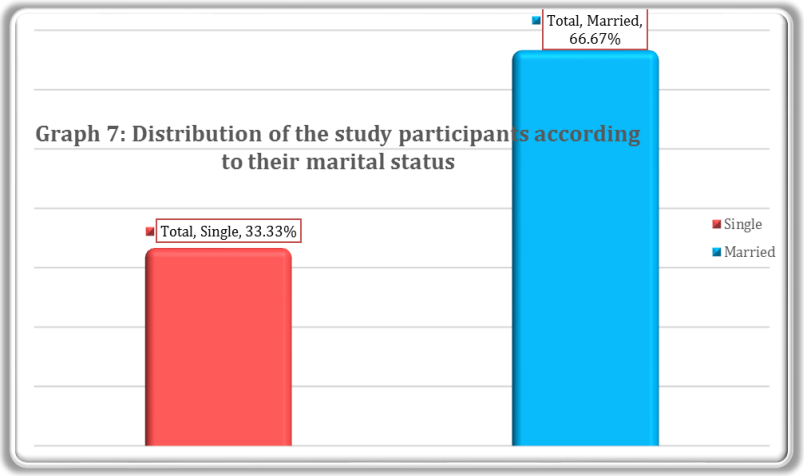


Table 6 and graph 7 shows distribution of the participants according to their married status. Of which 9 males 10 females are Single (unmarried, divorced, widowed) which is about 19 (33.3%) of total study population. 26 males and 12 females were married which is about 38 (66.7%) of total study population.

Table 7: Distribution of the study participants according to the type of family.

Family type	Male N= 35 (%)	Female N= 22 (%)	Total N= 57 (%)
Joint	11 (31.4%)	6 (27.3%)	17 (29.8%)
Nuclear	24 (68.6%)	16 (72.7%)	40 (70.2%)

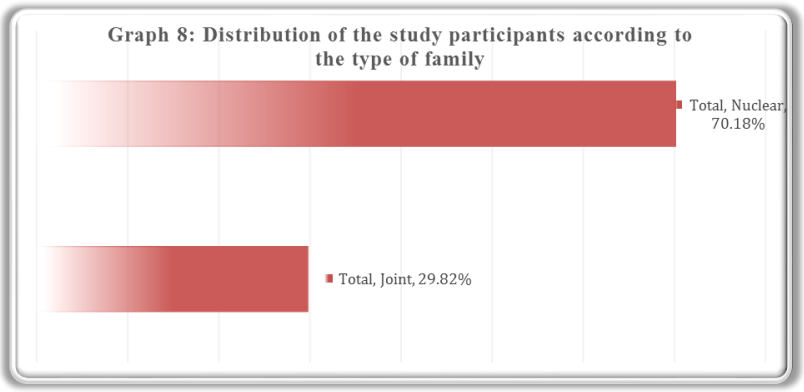


Table 7 and Graph 8 depict distribution of study participants according to types of family. Our study consists of 17 (29.8%) participants belongs to joint family and nearly 70% of the study participants belong to nuclear family.

Table 8: Association between positive scales at different visits.

Sl No	Positivescale at different visits	Mean	N	Std. Deviation	Std. Error Mean	t Value *	df	p Value
1	1st Visit	26.519	52	.9391	.1302	43.503	51	.0001
	2nd Visit	17.000	52	1.0479	.1453			
2	1st Visit	26.560	50	.9293	.1314	74.858	49	.0001
	3rd Visit	10.900	50	1.1473	.1623			
3	2nd Visit	16.900	50	.9313	.1317	35.496	49	.0001
	3rd Visit	10.900	50	1.1473	.1623			

. *Paired 't' test was utilized to test the relationship between various quantitative factors. At 95% CI a likelihood esteem (p estimation) of ≤ 0.05 was considered as measurably significant

The above table (Table 8) shows the association between positive scales at frequent visits.

In this present study at first visit, that is, before giving Lurasidone at baseline there were 57 participants. There is significant improvement in positive scale from first visit to second visit i.e., there was improvement in positive scale after giving the Lurasidone. The mean score at the first visit was 26.519, the mean score at the end of 2nd visit was 17.000 and the mean at the end of 3rd visit was 10.900.

DISCUSSION

1. This examination assessed the general adequacy of Lurasidone across a range of spectrum of schizophrenia. It likewise attempted to assess which manifestation space– positive symptoms - Lurasidone had a higher effect regarding goal.
2. This was a medical clinic based, planned longitudinal observational investigation. The greater part of different investigations, which have assessed the viability of Lurasidone have utilized a randomized, fake treatment controlled techniques. This wasn't possible at our middle since we wished to see the information in a naturalistic way and limit of prepared staff. Eyewitness predisposition is normally experienced in such examinations, this was mostly controlled for at two levels. At the essential examiner level, by monitoring it, and an extra assessment by a specialist was finished. Patients going to the OPD administrations, determined to have schizophrenia dependent on the ICD-10 criterias, who were drug naive, were sequentially accepted into the examination. Patients were analyzed by an expert, who were then alluded to the investigator for evaluation. Patients having other co-bleak mental problems were avoided. Patients were surveyed on PANSS at 3 focuses on schedule - benchmark, toward the finish of multi month and toward the finish of 3 months. Lurasidone showed its greatest impact toward the finish of 3 weeks in preliminaries directed by Meyer JM et al in (2009),[6] in this way patients were reevaluated toward the finish of multi month/4weeks and one more assessment toward the finish of 3 months was done to check whether the impacts accomplished were supported, and if there was any adjustment in bearableness. Comparative exercise was done in investigations led by Loebel AD in (2010).[7] In the underlying examinations directed by Meyer JM, and Cucchiaro J et al in (2009) impacts were read for a lot more limited length going from multi week to 3 weeks.[6] Patients were begun on Lurasidone at 40mg and titrated up to 60 mg to 120 mg relying upon reaction and decency. Lurasidone is second generation antipsychotic which has been endorsed for treatment of schizophrenia at dosages of 40 to 80mg. higher dosages were not discovered solid as indicated by L citrome.[7] However, not many patients showed halfway reaction at 80mg and had the option to endure the portions, in whom the portion was expanded to 120mg. It is feasible to accept that these patients had a variable pace of digestion of the medication and hence required a higher portion. A comparative impact is found in the investigation of different antipsychotics like Risperidone by Feng, Y et al in (2008).[9] Patients were guaranteed that they were not on any drug which may have prompted its degradation. Lurasidone is profoundly protein bound, and expanded absorption is seen with a predefined caloric admission, comparable yet known to be not exactly that needed for Ziprasidone. Since this study was completed on OPD premise, patients' sustenance and different variables influencing the pharmacokinetics couldn't be accounted, for this, has been viewed as a restriction for the investigation and could clarify the requirement for higher than suggested portions of Lurasidone. No particular investigations have been done in independent ethnic bunch, the majority of the examinations were done on Caucasian and Japanese Population. No particular examinations are accessible on Indian populace; to the extent concerned, this is the first investigation in quite a while, considering the viability of Lurasidone on this populace. Further investigations may illuminate issues identified with psycho- pharmaco-genomics and fluctuation in this populace.
3. Fixed portion routine was followed. Measurements utilized were similar with different examinations done by Mitsutaka Nakamura et al (2009), Michael H. Allena et al (2013).[8] However, in the examinations referenced, patient populaces were at that point on some type of antipsychotic, and were changed to Lurasidone with the end goal of study. It can likewise be gathered that the chronicity of sickness in the examinations referenced might have influenced the outcomes regarding reaction and seriousness of negative manifestations. This divergence was not found in our examination and our example, regardless of being drug credulous, we had discovered comparative reaction rates to different investigations, for positive symptoms. Consequently Lurasidone can be perceived to be strong at both beginning and persistent phases of schizophrenia. Reaction is characterized as more than or equivalent to 20% decrease in the PANSS scores. Comparative reaction rate has been utilized for positive manifestation area. Our strategy for computing reaction compares with different investigations like Antony Loebel et al, which have assessed Lurasidone and different antipsychotics for

efficacy.[9,10] Along with PANSS, a total actual assessment and agenda for results of Lurasidone was finished. An aggregate of 57 patients were assessed for this investigation.

4. The current examination showed that Lurasidone has impact on sure manifestations of schizophrenia at week 4 and better viability at week 12. The mean positive score at gauge was 26.519. The early improvement rate in investigation bunch was assessed dependent on the mean decrease of positive score on PANSS from pattern to multi month. In certain size of PANSS, mean decrease of positive score toward the finish ofmulti week was 6.13 which was measurably huge. Toward the finish of 3 months the mean positive score was 10.900, there was a mean decrease of 10 on certain score on PANSS which was genuinely critical. Our outcomes were like past examinations done by M Nakamura et al (2009), A Loebel et al (2010) who presumed that treatment withlurasidone was related with genuinely critical and more noteworthy improvement than fake treatment on the essential viability measure. 8, The PANSS all out score showeda comparative example of measurably huge early and supported improvement with lurasidone. In general decrease in PANSS score was like different investigations referenced above, yet a moderately higher reaction to positive than negative manifestations was noted. Anyway a more extended follow up would help us study the impact of Lurasidone on the course of schizophrenia just as reaction to singular areas and side effects.

CONCLUSION

This examination assesed the general viability of Lurasidone across a range of manifestations of schizophrenia. It likewise attempted to assess space, positive, Lurasidone had a higher effect as far as goal. The current examination showed that Lurasidone has impact on certain manifestations of schizophrenia at week 4 and better adequacy at week 12. Generally decrease in PANSS score was like different examinations done before, yet a moderately higher reaction to positive symptoms was noted. Anyway a more drawn out follow up would help us study the impact of Lurasidone on the course of schizophrenia and side effects.

LIMITATIONS

1. The example size was less, which restricts the generalizability of the outcomes.
2. Study span was not a very long time. A more drawn out planned examination in a naturalistic setting would toss all the more light.
3. Only PANSS was utilized to survey the adequacy of lurasidone on schizophrenia.
4. Sample was taken from a medical clinic setting which doesn't address local area.
5. Patients' nourishment and different components influencing the pharmacokinetics couldn't be accounted

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