



INDO AMERICAN JOURNAL OF PHARMACEUTICAL RESEARCH



“A COMPARITIVE STUDY ON NEUROCOGNITIVE EFFECTS OF TYPICAL AND ATYPICAL ANTIPSYCHOTICS AMONG PATIENTS IN REFERENCE TO SCHIZOPHRENIA”

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ARTICLE INFO

Article history

Received 19/08/2020

Available online
20/10/2020

Keywords

Schizophrenia,
Neurocognition,
Drug Effects,
Antipsychotics,
Quality Of Life.

ABSTRACT

AIM: To compare the Neurocognitive effects of typical and atypical antipsychotics among schizophrenic patients. **PURPOSE:** Schizophrenia is a mental disorder that is characterized by hallucinations, delusions and other cognitive difficulties; it can often be a lifelong struggle. Although it can be treated very effectively, acute aggravations often occur. Antipsychotic drug therapies are fairly effective for decreasing the rate of relapses and neurocognitive difficulties in patients with schizophrenia. This study aimed to compare the typical and atypical antipsychotics used to treat patients with schizophrenia in terms of neurocognitive effects and Quality of life. **METHODS:** A cross-sectional comparative study is proposed to be conducted in 6 months. All the patients were administered the Morisky Medication Adherence Scale, to evaluate cognitive function by the Mini-Mental State Examination (MMSE). Short Form 36, and the Schedule for Assessing the Neurocognition (Attention, Memory, and Intelligence). **SETTING:** The study was conducted in the government general hospital, Guntur; an 1170 bedded tertiary care teaching hospital. **PARTICIPANTS:** The study included 75 patients who were taking typical antipsychotics and 75 patients taking atypical antipsychotics for the treatment of schizophrenia. **RESULTS:** The medication adherence was similar in both groups of patients and perceived scores of the patients treated with atypical antipsychotics were significantly higher than those of the patients treated with typical antipsychotics in terms of neurocognition and quality of life. **CONCLUSIONS:** Neurocognitive dysfunction is a core feature of schizophrenia and is related to the functional outcome of the illness. In our study, it reveals that atypical antipsychotics therapy was associated with more favourable results of neurocognition and quality of life compared with typical antipsychotics. So Finally, Our study concluded that Patients of Schizophrenia who are taking atypical antipsychotics showed positive results than typical antipsychotics in terms of Neurocognition and Overall patients Quality of Life.

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Please cite this article in press as **Srujana Birudu et al.** “A Comparitive Study on Neurocognitive Effects of Typical and Atypical Antipsychotics Among Patients in Reference To Schizophrenia”. *Indo American Journal of Pharmaceutical Research*.2020;10(09).

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INTRODUCTION

Schizophrenia is described as “the worst disease affecting mankind” where approximately 1% of the world’s population is directly affected by this debilitating disease during their lifetime, affecting men and women equally⁽¹⁾. The word Schizophrenia is less than 100 years old. However, the disease was first identified as a mental illness by Dr.Emile Kraepelin in 1887. In the beginning, he used the term “dementia praecox” for the individuals who had symptoms that were associated with schizophrenia.^(2, 3)It had the symptoms associated with Positive and Negative along with Cognitive Impairment.

It is marked by severe cognitive dysfunction or impairment of persons with schizophrenia are unable to think as they have problems with memory, critical thinking and problem-solving.⁽⁴⁾Schizophrenic patients experience problems in living because they are divided against themselves, out of touch with reality, and disorganized⁽⁵⁾. So in this Study we aimed to compare the treatment of schizophrenia in terms of mainly neurocognitive effects and Quality of life.

Here the main purpose of this study was to know the best therapy in Schizophrenic patients in terms of Neurocognition .As in present scenario; Society was facing many cognitive issues as that it is main place in everyone’s life to perform their daily activities. As per that our Study research main objectives are

Primary Objective

- To compare the Neurocognitive effects of typical and atypical antipsychotics among schizophrenic patients.
- To assess the Attention and Concentration.
- To assess Memory levels in Patients.
- To assess the IQ levels of the patient.

Secondary Objective

- To compare and assess the improvement of Quality Of Life (QOL) of patients using typical and atypical antipsychotics.

In patients with schizophrenia, neurocognitive deficits have been established as an important symptom domain associated with long-term outcomes. On average, these patients perform one to two standard deviations below healthy individuals on neurocognitive measures, such as those assessing attention, memory, and processing speed^(6,7)

Cognitive functions are the mental processes that refer to a person’s ability to carry out any task. They allow the subject to have an active role in the processes of receiving, choosing, transforming, storing, processing and retrieval of information, allowing the subject to navigate the world around him.⁽⁶⁾ Cognitive function is involved in daily activities, such as communicating with a friend or seeking a job or working with colleagues.⁽⁸⁾

In this Work we are mainly focusing on Attention, Memory and Intelligence in Schizophrenic Patients

Attention and Concentration:

Attention is the capacity to attend to a stimulus in an integral part of consciousness, it is the process of directing cognitive resources towards certain aspects of the environment, or towards the execution of certain actions that seem most appropriate. It refers to the state of observation and alertness that allows awareness of what is happening in the environment^(8,9). Concentration is the ability to sustain the focus over an extended period⁽⁸⁾.This was assessed by using Digit Span test or Trail making test and also by using questionnaire.

Memory:

Memory is the ability to encode, store, and effectively retrieve previously learned information or past experiences. It is observed by any difficulty in remembering day to day events while taking the history of the patient.⁽¹⁰⁾

In Mental Status Examination(MSE) Memory get assessed by

✚ Immediate memory as tested by digit span test and to by animal naming.

✚ Recent memory (new learning ability) is assessed by:-

- Recall of the events of the last 24-48hrs
- Recent verbal memory is tested by interviewer introducing himself carefully and asking the patient to repeat his name for 2-3 times, by repeating it get registered then continue the interview for 3-5mins and then ask to repeat his name.
- Recent Visual memory is tested by presenting 3 or 5 unrelated objects and ask the patient to name all those and then hide those objects and after 5mins ask the patient to tell and take out the objects from respective places

✚ Remote memory is tested by asking the patient about:

- Personal events and impersonal events⁽¹¹⁾

Intelligence:

- Intelligence is the ability to think and act logically and rationally
- This is to be interpreted from education, occupational history, clinical behavior and test performance on abstraction, judgment, general information and calculation

As Schizophrenia develops in patients it shows that there is a significant decline in Cognition⁽⁸⁾ that was found to affect many domains including attention, concentration, language, social cognition, executive function, memory and Intelligence^(6,12)

Cognitive Impairment is a common and sturdy feature of schizophrenia.^(13,14,15) as it has been observed in a wide range in patients^(17,18), these abnormalities were noted in early investigations along with positive and negative symptoms^(5,16,24).

In first-episode schizophrenia (FES) it seems that many of the cognitive deficits were observed^(19,20) because Neurocognitive impairments are central and the core feature of schizophrenia^(21,22) in a broad range⁽²³⁾. In most of the patients about 75-85%, we observe cognitive impairment⁽²¹⁾. In many reviews most frequently it was cited that the cognitive impairments present in schizophrenia include impairments of attention, concentration, language, working memory, executive functions, verbal fluency and disturbances in the selection and processing of information^(17,25,26).

TREATMENT OF NEUROCOGNITION

A variety of antipsychotic medications were used in the treatment of positive and negative psychotic symptoms in schizophrenic patients. However, the cognitive effects of antipsychotics remain more poorly understood⁽⁵⁾ but this cognitive impairment is treated by the antipsychotic treatment^(16, 18, 24)

The prototypical atypical neuroleptics are using to dissociate symptoms from cognition⁽⁵⁾. Individual drugs or a combination of drugs in conjunction with various cognitive rehabilitation techniques should be used against the impairments, because certain cognitive functions are necessary for even rudimentary successes in modern life⁽⁵⁾.

Cognitive deficits that are present in schizophrenia are especially debilitating, as they lead to poor clinical, social, and functional outcomes. Moreover, these deficits are present throughout the patient's lifetime and are not the result of the positive or negative symptoms of the disorder, or antipsychotic treatment and appear to be stable and heritable features of schizophrenia^(23,27)

MATERIALS AND METHODS**Patient Selection:**

Between October 2019 and March 2020, Total we consulted 160 patients of Schizophrenia who are on their medication presented to psychiatry department of Government General Hospital, Guntur. Based on information received from the psychiatrists and file reviews, total of 156 patients diagnosed with schizophrenia attending at least 3 consecutive months of appointment. For their follow up medication continuously had been treated with either Typical and atypical antipsychotics. We assessed the patients randomly as 77 of patients taking typical antipsychotics and 77 of patients taking atypical antipsychotics in last 1-2 years who are in maintenance phase.

Patients were accepted in maintenance phase as psychotic symptoms are well controlled. All patients gave written informed consent to participate in the study, which was approved positively by the local ethics committee. Patients were selected on the basis of the following inclusion criteria: (1) Age 30-50 yrs of both genders. (2) Patients using Antipsychotics for ≥ 6 months. (3) Patients diagnosed with schizophrenia for at least 6 months back. (4) Patients who have medication adherence. Exclusion criteria for testing were (1) Patients of newly diagnosed Schizophrenia. (2) If the patient had a diagnosis of affective disorders. (3) Neurologic disease or damage. (4) Mental retardation (IQ below 80 according to MWT-B). (5) Medical illness. (6) History of head injury with loss of consciousness > 5 minutes. (7) Lifetime history of substance dependence or Substance abuse. (8) Pregnancy and lactating mother.

After informing the participating patients about study and taking consent from them, their Sociodemographic characteristics were recorded. All Patients were administered Demographic questionnaire, MMAS (Morisky Medication Adherence Scale), MMSE (Mini Mental Status Examination) to assess Neurocognition, SF 36 (Short form 36) to evaluate Quality of life and Related questions for Attention, Memory and Intelligence.

MMAS Scale results were confirmed with the information from relatives of the patients. And also we confirmed the regular intake of medications by questioning the patient relatives and also by the follow-up medical records. MMSE were taken from the patients and categorised by scoring the results and grouped them accordingly as mild, moderate and severe. And Other questionnaire simplified and categorised as by giving scores according to patients response.

This Study commenced after obtaining the approval of the Institutional Human Ethics Committee (IHEC) for new experiments or extensions of ongoing experiments, using human subjects of Government General Hospital, Guntur.

ASSESSMENT:-**SOCIODEMOGRAPHIC QUESTIONNAIRE:-**

The form was prepared by the authors of the study to assess the participant's sociodemographic data (age, sex, marital status, employment, etc) and clinical characteristics (age at the onset of disease, total duration of disease, etc)

POSITIVE AND NEGATIVE SYNDROME SCALE:-

The PANSS which was developed by Stanley Kay, Lewis Opler, and Abraham Fiszbein in 1987. It is a semi structured interview scale involving of 30 items and a 7 point severity assessment tool. Out of the 30 psychiatric parameters, 7 belong to the positive symptoms subscale, 7 belong to negative symptoms subscale and the remaining 16 to the general psychopathology subscale.

MORISKY MEDICATION ADHERENCE SCALE:-

It is a self reported scale that measures adherence to medication. The MMAS was developed by Morisky. It consists of the 4 closed ended questions with 2 response options(yes or no). medication adherence is considered high if all questions are answered no, moderate if 1 or 2 questions are answered yes. And low if 3 or 4 questions are answered yes.

MINI MENTAL STATE EXAMINATION (OR) FOLSTEIN TEST:-

It was first introduced by Folstein et al. in 1975. It is a 30 – point questionnaire that is used extensively in the clinical and research setting to measure cognitive impairment. Administration of the test takes between 5 and 10 minutes and examines functions including registration, attention, calculation, language, recall, ability to follow simple commands and orientation.

TRAIL MAKING TEST:-

It is a neuropsychological test of visual attention and task switching. It consists of two parts in which the subject is instructed to connect set of 25 dots as quickly as possible while still maintaining the accuracy. This test can provide the information regarding visual search speed, scanning, mental flexibility as well as the executive functioning. The task requires a subject to connect sequence of 25 consecutive targets on a sheet of paper or a computer screen. There are two parts of the test: in the first the targets are all numbers (1, 2, 3) and the subject need to connect them in a sequential order. In the second part the subject alternates between the numbers and letters (1 A, 2 B etc.) and the time taken to join them was recorded.

SHORT FORM 36:-

It is used to assess the quality of life. This tool was developed and put into the use by Rand Corporation. It was translated into Turkish, and its validity and reliability have been confirmed. The SF-36 is a self assessment scale designed to examine general health-related quality of life. It consists of 36 items that measure quality of life in 8 domains.

- Physical functioning
- Social functioning
- Physical role limitations
- Emotional role limitations
- Mental health energy validity
- Bodily pain and general health perceptions.

Except for a few items, the assessment uses Likert-type scoring and considers the patients experiences over the last 4 weeks. The subscales are scored between 0 and 100 with 0 reflecting a poor health condition, and 100 a superiors one.

OBSERVATIONS AND RESULTS

- Here the totals of 154 patients were included in our Study and total subjects were randomly assigned to two groups. Where 77 patients who were treated with typical Antipsychotic Haloperidol of 2-4 mg/day and patient using this medication for more than 6months in treatment of Schizophrenia. And 77 patients using Atypical antipsychotic Olanzapine of 10-20mg /day for more than 6months in treatment of Schizophrenia.
- Before taking the data, we assessed for the medication Adherence, where we collected the complete follow up records of patients and by taking the complete medication adherence questions we came to know that all Patients have good medication adherence .Some of them are saying that there is difficulty in remembering to take their medications, but with the help of care taker they were taking medication daily without missing. And they were coming to hospital monthly for medications. Finally we came to know that in both groups they have good medication adherence .
- Of the 154 included in the study, 60 were male and 94 were female. The mean age of patients using typical antipsychotics was 34.94 ± 7.79 years, and that of the patients using atypical antipsychotic was 34.73 ± 8.29 years. No statistically significant difference was found between the two groups in terms of Sociodemographic characteristics including age, Gender, Education, Occupation, Marital Status ($P > 0.05$) . Here we selected the patients who were diagnosed with schizophrenia and using the treatment of typical and atypical antipsychotics for more than 6 months. Because, the drug takes minimum of 3-4 months to show their action.
- The Sociodemographic characteristics of Participants are shown in table 1.

DEMOGRAPHICS OF PATIENTS WITH SCHIZOPHRENIA IN STUDY COMPARING NEUROCOGNITIVE EFFECTS OF TYPICAL AND ATYPICAL ANTIPSYCHOTICS

Table 1: Sociodemographic Characteristics of Patients of Schizophrenia.

Characteristic	Typical antipsychotic Group (N=77)	Atypical antipsychotic Group (N=77)	Analysis (P)
Age , Mean \pm SD	34.94 \pm 7.79	34.73 \pm 8.29	0.295*
Sex ,n (%)	28 (36 %)	32 (42 %)	
Male	49 (64 %)	45 (58 %)	0.621 ⁺
Female			
Educational Status			
0 -5	39 (51 %)	30 (39 %)	
6 -10	22 (29 %)	16 (21 %)	
Inter	5 (06 %)	10 (13 %)	0.130 ⁺
Degree	10 (13 %)	20 (26 %)	
PG	1 (01 %)	1 (01 %)	
Marietal Status			
➤ Single	11 (14 %)	13 (17 %)	
➤ Married	63 (82 %)	63 (82 %)	0.558 ⁺
➤ Widowed	3 (04 %)	1 (01 %)	

*Student T test+ Chi Square Test.

MMSE:-

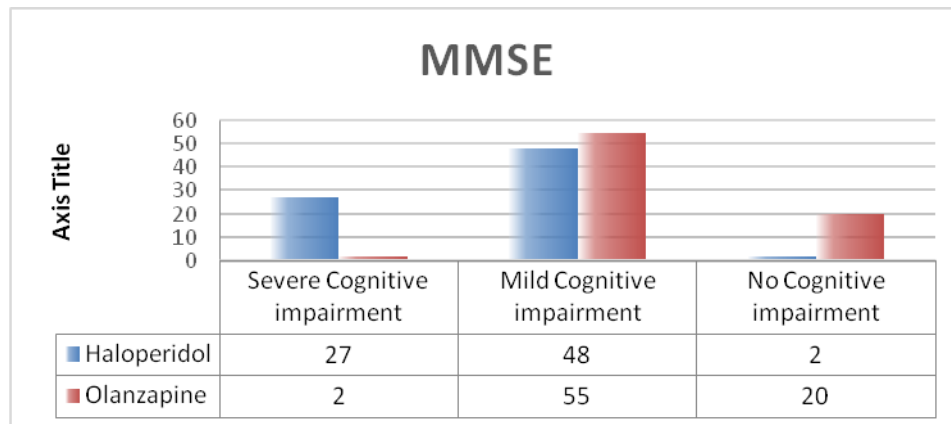


Fig 1 :- describes the Comparison of MMSE among patients taking treatment with typical and atypical antipsychotics.

Attention and concentration:-

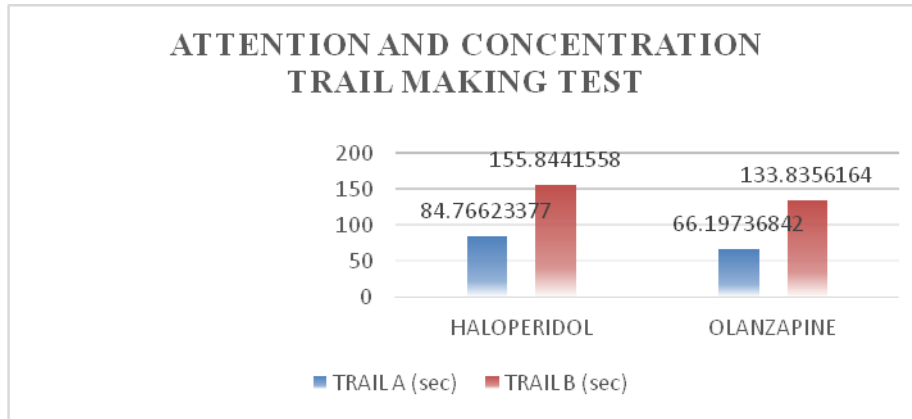


Fig 2 :- describes the Comparison of attention and concentration among patients taking treatment with typical and atypical antipsychotics.

DIGIT SPAN TEST

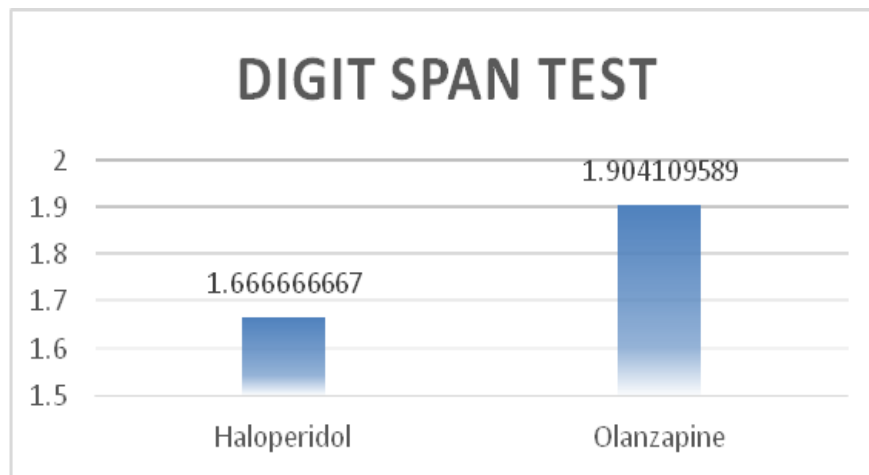


Fig 3 :- describes the comparison of digit span test results for the patients in treatment with typical and atypical antipsychotics.

MEMORY

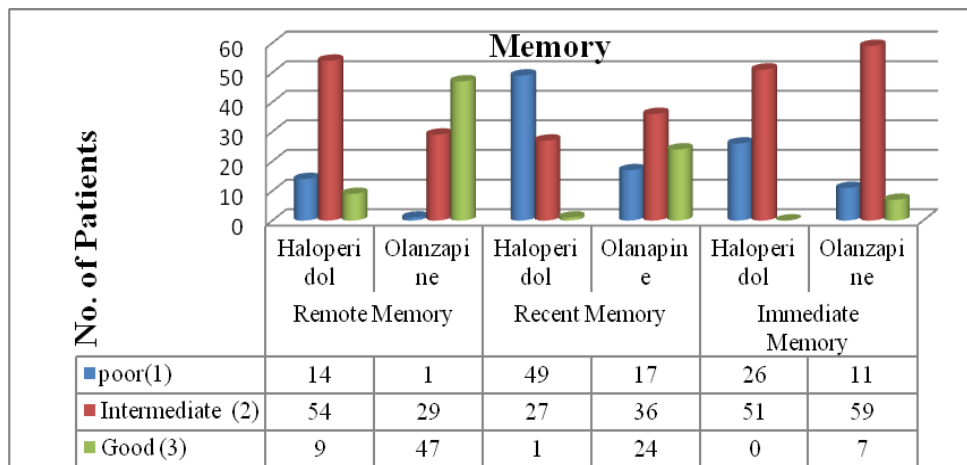


Fig 4:- Comparison of memory levels of the patients in treatment with typical and atypical antipsychotics.

INTELLIGENCE

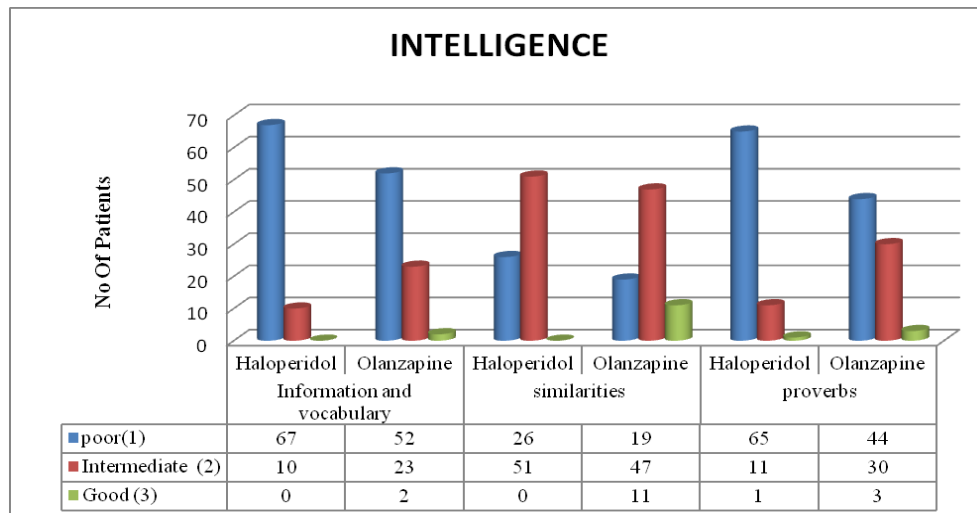


Fig 5 :- Comparison of intelligence levels of the patients in treatment with typical and atypical antipsychotics.

SF 36 FOR QUALITY OF LIFE

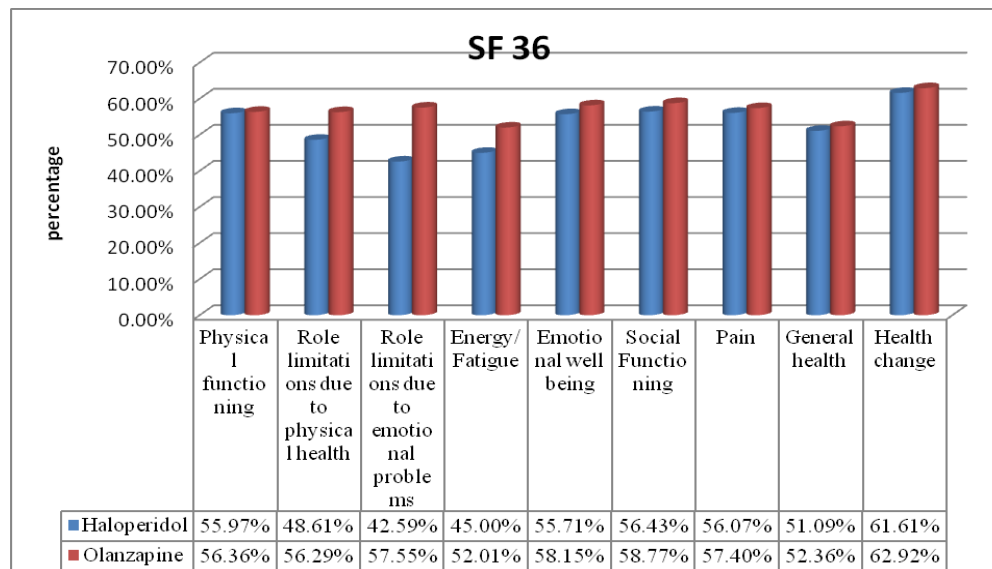


Fig 6 :-Comparison of Quality of Life.

When the patients using Haloperidol and Olanzapine were compared in terms of MMSE to assess the cognitive function, there was a statistically significantly higher cognitive improvement among with atypical antipsychotic compared with typical antipsychotic (p < 0.0001).

And in our study we are assessing Neurocognition mostly Attention, Memory and Intelligence. To assess Attention we used trail making test and digit span test. When Attention was compared ,there was a statistically significantly higher improvement among Olanzapine than haloperidol which is typical antipsychotic (p 0.042) which is of p<0.05.

When we comparing Memory levels we assessed by questions of Recent memory, remote memory and immediate memory, we found there exists statistical difference which is higher improvement among Olanzapine than Haloperidol (P = <0.001)

To Assess Intelligence levels we used Questions of information &Vocabulary, Similarities and Proverbs .We found there was a statistically significantly higher Intelligence levels among with atypical antipsychotic compared with typical antipsychotic (p < 0.05).

In terms of SF 36 Subscales, we found that overall QOL is statistically significantly higher among Atypical antipsychotics compared with typical Antipsychotics (P 0.047 which is <0.05).

Comparison of MMSE, Neurocognition and QOL Of Participants are shown in table 2

COMPARISION OF MMAS, MMSE, NEUROCOGNITION AND SF-36 VALUES

Table 2 : Treatment comparision in case of MMAS, MMSE, Neurocognition and SF-36

Characteristic	Typical (N=77)	Antipsychotic Group	Atypical (N=77)	Antipsychotic Group	P Value		
MMAS							
Low Adherence	2 (2.59%)		1 (1.30%)		0.5 ⁺		
High Adherence	75 (97.40%)		76 (98.70%)				
MMSE							
• Severe cognitive impairment	27 (35.06%)		2 (2.59%)		<0.0001 ^λ		
• Mild cognitive impairment	48 (62.33%)		55 (71.42%)				
• No cognitive impairment	2 (2.59%)		20 (25.97%)				
Attention & Concentration (Sec) Mean	84.76623 155.8442		66.19737 133.8356		0.042 [*]		
Memory	Poor	IM	Good	Poor	IM	Good	
Recent memory	14	54	9	1	29	47	< 0.0001 ^λ
Remote memory	49	27	1	17	36	24	
Immediate memory	26	51	0	11	59	7	<0.0001 ^λ 0.003 ^λ
Intelligence	Poor	IM	Good	Poor	IM	Good	
Information and Vocabulary Similarities	67	10	0	52	23	2	<0.001 ^λ
Proverbs	26	51	2	19	47	11	0.004 ^λ
	65	11	1	44	30	3	0.003 ^λ
SF-36	55.97%			56.36%			0.74
Physical functioning	48.61%			56.29%			0.032
Role limitations due to physical health							
Role limitations due to emotional problems	42.59%			57.55%			0.0002
Energy/Fatigue	45.00%			52.01%			0.00024
Emotional well being	55.71%			58.15%			0.043
Social functioning							
Pain	56.43%			58.77%			0.208
General health	56.07%			57.40%			0.308
Health change	51.09%			52.36%			0.62
Overall Quality of life	61.61%			62.92%			0.78 0.047^λ

+: Chi Square test

λ: Kruskal Wallis test

*: T test

DISCUSSION

In this study, we are aiming to compare the Typical antipsychotics and atypical antipsychotic drug therapy in terms of Neurocognition and Quality of life in Schizophrenia Patients, because in Schizophrenia there is Cognitive impairment along with positive and negative symptoms. Hereby comparing the both groups we observed that Atypical antipsychotic therapy was more effective than Typical antipsychotic therapy.

During this 6months study, 150 Subjects were Randomly selected whereas 77patients of Schizophrenics who were taking typical antipsychotics and 77 patients of patients taking atypical drugs were taken as study subjects and subjects were recruited based on criteria that were set in the protocol there is no difference in case of Sociodemographics and all patients having good medication adherence. Based on follow up records we came to know that these patients were coming regularly for medicines and using without fail.

Unlike Keefe, Bilder, et al. (2007)^[27], Richard SE Keefe et al (2006)^[28] who included only patients with chronic schizophrenia, the present study also comprised all schizophrenic patients who are on antipsychotics, as in the study conducted by Lisa Hartling(2012) the most frequent comparisons involved are haloperidol and risperidone or Olanzapine however the number of studies available for each comparison and outcome was often limited.

Here we compared Olanzapine and haloperidol. There were several methodological differences as it is a randomized controlled trail and this is a cross sectional comparative study. Comparing with this study our study is also having a same limitation of short term study.

The result of the comparison between the typical and atypical antipsychotics reveals more favourable results for the atypical antipsychotics. In this study we mostly focused on the cognitive domains like attention and concentration, memory and intelligence whereas the study conducted by Georgina **Guilera** focused on automaticity, verbal comprehension, memory and visual learning. Limitation of this study they had mentioned is the inclusion criteria they included patients aged between 16 and 65.they mentioned that in further studies in this area should avoid the inclusion of patients over the age of 55. Here we overcome the limitation by taking the inclusion criteria of patients considering only below 55 years.

However, previous studies reported that side effects of antipsychotic drugs (eg, akathisia, sexual dysfunction, weight gain) frequently result in non adherence to medication and drug rejection in patients with schizophrenia, Kane et al⁽⁴⁾ and this non adherence leads to relapse of disease so in our study we assessed the medication adherence and we excluded those patients who are non adherent to medication.

In the present study, general health perception, which is among the quality of life subscales, which was statistically significantly higher in patients using Atypical antipsychotics than in those using typical antipsychotics. In addition to the nature and severe psychopath psychology of schizophrenia, the drugs used to treat this disease also effect the Quality of life of patients with Schizophrenia.

Limitations of the study:

Our study has some limitations, First that large group could not be formed, because of small sample size ,it was not possible to perform any subgroup analysis. So any potential differences between subgroups were not recognized. Another limitation was Study duration due to this we can't able to get more subjects and not able to conduct the follow up so we performed cross-sectional assessment of patients and this cross-sectional assessment may be another limitation of the study. Hope for further studies it should be

CONCLUSION

Our study concluded that Patients of Schizophrenia who are taking atypical antipsychotics showed positive results than typical antipsychotics in terms of Neurocognition (Attention, Memory and Intelligence) and Overall patients Quality of Life(QOL). Both in typical and atypical antipsychotics general health and physical health improment is same in patients with schizophrenia. As we already know that Neurocognitive dysfunction is a core feature of schizophrenia and it is related to the functional outcome of the illness. And majorly patients may experience relapses where in case of poor adherence, here we found that all patients have good medication adherence. Atypical antipsychotic drugs, as opposed to conventional antipsychotics, improve cognitive function in patients with schizophrenia.

Declaration of interest

There are no conflicts of interest.

ACKNOWLEDGEMENTS

We would like to bring to light those who have helped us in the completion of our research work without which this work would not have reached its destination.

First and foremost, all praise to the ALMIGHTY, without whose blessings, we would not have been able to submit this research.

We would like to express our gratitude to *Dr. S.RAJU NAIDU, MD., RT*, Superintendent, Govt. General Hospital, Guntur for providing us all the facilities for our postgraduate studies and dissertation work.

We extend our grateful thanks to *Prof. RAMA RAO NADENDLA M. Pharm., PhD., F.I.C Chalapathi Institute of pharmaceutical Sciences*, Principal, for his support and help.

We would like to acknowledge with deep sense of gratitude to *Dr. N.MURALI KRISHNA, MD., Professor & HOD*, Department of Psychiatry, Government General Hospital, Guntur, for his invaluable guidance and constant encouragement.

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