Study Protocol

Cognitive impairment within patients of Schizophrenia and Mood disorder: A Comparative study

Abstract:

Background: Memory dysfunction, deficits in attention and executive functions as well impairment in cognition is found among patient suffering from Schizophrenia and Mood Disorder throughout the course of illness. All these significantly impact various domains of life in them. It also affects the patient's insight of the illness and thus impair therapeutic compliance.

Objectives:

1. To evaluate Cognitive functions in patients of Schizophrenia and Mood Disorder.
2. To compare both groups to see whether cognitive dysfunction varies between them.

Methodology: Study Design: Cross- sectional study which is Hospital based **Study-Setting**: The IPD and OPD of Psychiatry Department, AVBRH, Sawangi (M), Wardha **Sample Size**: 240 (120 patients of Schizophrenia and Mood Disorder each).

Patients clinically diagnosed having Schizophrenia and Mood disorder using ICD-10 criteria of age group 18-55 years, with at least 8 years of schooling will be included in the study after taking written informed consents. After collecting socio-demographic data and screening the patients with Brief Psychiatric Rating Scale, PGI Battery of Brain Dysfunction will be applied on the patients after Ethics Committee clearance.

Results: This study will assess of impairment of Cognitive functions Schizophrenia as well as Mood Disorder patients would tell whether the cognitive impairment is same or different in both groups.

Conclusion: Comparison of impairment in cognitive functions in Schizophrenia as well as Mood Disorder patients would be done. Co-relation of Cognitive impairment with Metabolic syndrome in both the groups can be established.

Keywords: Mood Disorder, Cognitive Impairment, Schizophrenia

Introduction:

In Schizophrenia, there are distortions in thinking and perception. Schizophrenia is a universal phenomenon. Mood disorder is disorder of emotion where Mania and Depression is seen. It occurs in episodes. Prevalence of schizophrenia as well as other psychotic disorders in India is 0.4% and that of Mood disorders is 2.8% [1].

Cognition can be called as information processing in wider sense. It includes thinking, memory, perception, motivation, skilled movements and language. Learning and memory which are important cognitive functions have their neural circuits in Hippocampus. In regards of functioning of mental capacity these denote the perceptual and intellectual aspects. Other functions which are required to evaluate efficacy of cognitive function are orientation, necessary skills learning ability, problem solving, abstraction, reasoning and judgement making, retaining and recalling events ability, arithmetical ability and other forms of symbol manipulation, primitive reactions and behavioural control, language and comprehension, attention, perception and praxis [2].

Cognitive impairment is crucial feature found during the course of illness of various psychiatric disorders such as Schizophrenia and Disorders of Mood. In schizophrenia, cognitive dysfunction is well known and has broader range of deficits across various domains of functioning. There are evidences from studies which have shown that cognitive impairment is crucial factor of schizophrenia. In Mood Disorder patients changes in cognition are seen. However the severity profile of Cognitive impairment differs from that found in Schizophrenia. The overall profile of cognitive impairments appears similar in depression, bipolar disorder and schizophrenia, particularly during symptomatic periods. Nevertheless when compared with healthy controls the severity of cognitive dysfunction found in patients with Severe Depression was of mild to moderate level however the same comparison between healthy controls and Schizophrenia patients was found to be of moderate to severe intensity. When such cognitive impairments were found in Neurological patients they were known as Fronto-striatal. The parameters of cognitive functioning affected included lack in rate of learning new information, however with intactness of delayed recall memory; impaired executive functioning, concentration, and attention; and with slowness of speed of processing. In all it has been evident that the level of cognitive dysfunction is more in Schizophrenia as compared with Bipolar Disorders and Depressive Disorders as found during symptomatic course and throughout the periods of remission [3].

Schizophrenia is characterized by cognitive impairment, distortions in thought process, perception, and abstraction. Of these impairment in cognition is the area which needs more focus.

In patients of Bipolar Disorder, there is impairment of cognition along with and dysfunction of executive function and impairment in memory and attention [4,5]. Executive function impairment exists in beginning of Bipolar Affective Disorder which then gets aggravated during episodes of mania and depression, thus becomes an important marker of the disease [6-8].

Various studies have been still been on-going in these areas for better awareness regarding the underlying etiological mechanisms leading to the formation of cognitive impairment in these Psychiatric disorders. Similarly, development of new psychological tools for assessment of cognitive impairment will help in the diagnosis of these disorders and in future enhance and improvise the treatment outcomes for these disorders. By recognising specific patterns of cognitive deficits for each disorder can pave path for the improvement of current treatment regimens and also for better prognosis in these disorders.

Rationale: Establishment of relation between Cognitive impairment and Metabolic Syndrome in Schizophrenia and Mood disorders can be done. This study will administer psychological tools standardized for Indian Population.

Objectives:

1. For evaluation of Cognitive dysfunctions in Schizophrenia patients and Mood Disorder patients.
2. To compare both groups to see whether cognitive dysfunction varies between them.
3. To establish any co-relation of cognitive dysfunction with metabolic syndrome in both the groups.

Methods:

Design of Study: Cross-sectional study type of study which is hospital based.
Study setting: IPD and OPD pertaining to Psychiatry Department, AVBRH, Sawangi (M), Wardha

Participants:

CRITERIA FOR INCLUSION

1. Patients who have Schizophrenia using ICD-10 criteria.
2. Patients have Mood Disorder using ICD-10 criteria.
3. As the tests will require knowledge of English and Hindi. They should be educated up to 8th standard and above.
4. Patients within 18 to 55 years age, males and females.
5. Either euthymic, remitted patients or patients having stable status for better co-operation in study.
6. Patient should be able to consent.

CRITERIA FOR EXCLUSION

1. Not willing to consent.
2. Acutely ill or uncooperative patients.
3. Patients having major organic brain disease or developmental delay.
4. Patients who have hypertension, diabetes mellitus or dyslipidemia prior to the study.
5. In patients with past history of head injury.
6. Patient who has received recent ECTs in the 6 month period prior to the study.

Sample Size: 240

$$\text{Finite population: } n' = \frac{n}{1+\frac{z^2 \times \hat{p}(1-\hat{p})}{\varepsilon^2 N}}$$

In this, z is z score, ε is margin of error, N is size of population and p̂ is population proportion

Using this formula sample size was calculated was 237 which rounded off to 240 in which there are 120 patients of Schizophrenia and Mood Disorder each.

Methodology: Patients diagnosed clinically with Schizophrenia and Mood Disorder conforming to ICD 10 Criteria would be screened priorly by Brief Psychiatric Rating Scale and then those who are mild to moderately symptommatic will be assessed by application of PGI Brain Dysfunction Battery.

TOOLS FOR ASSESSMENT

1. **Socio-demographic and Clinical Data Sheet:** It will include Name, Age, Gender, Address, time span of illness also treatment duration, History of Psychiatric illness in family and associated co-morbidities.
2. **Brief Psychiatric Rating Scale**: It is a rating instrument consisting of 18 items which assesses variety of symptoms of Psychiatric disorders, in which each symptom is measured from 1 (absent) to 7 (extreme severity) or 0 if the symptom is not assessed [9].

3. **PGI battery of Brain Dysfunction**: It consists 5 different tests of brain functioning -

- Bhatia's Short Battery of Performance Intelligence

- Verbal Adult Intelligence Test

- PGI Memory Scale

- Bender Visual Motor Gestalt Test

- Nahor Benson Test of Perceptual Acuity [10].

Statistical methods: Statistical Product and Service Solutions version 21 with proper methods of statistics.
Expected Outcomes: Cognitive impairment would be assessed among the patients of Schizophrenia and Mood Disorder. Along with the assessment, comparison of cognitive impairment between both the groups would be done. This comparison would tell whether the impairment of cognitive functions in patients having Schizophrenia is more or less than in patients having Mood Disorder.

Discussion:

Paul A. et al did a systemic review in which the cognitive impairment in patient with schizophrenia was more severe than the patients of bipolar affective disorder despite of the fact that patients belonging to both the groups shared similar cognitive impairment profile [11].

Neuropsychological Dysfunction was compared amongst patients with Bipolar Affective Disorder, Schizophrenia and First-Episode Psychosis with Unipolar Depression by S. K. Hill et al in which it was found that dysfunction was present even during early stages in cases of depression as well in cases of bipolar disorder with psychoses but it was less severe than that found amongst patients of first episode schizophrenia. These deficits were of same profile in all the patient groups and were recovered after clinical stabilization in patients with mood disorders and schizophrenia [12].

In a study carried out at University Psychiatry Clinic in Republic of Slovenia, it was found that the impairment in cognition in patients having Acute phase Schizophrenia and Depression were alike. Impairment of learning process and memory were found in both groups [13].

Comparison of Clinical and Neuropsychological characteristics were done in a study at San Diego Medical Centre in University of California between patients of Schizophrenia as well patients of Depression with and without psychosis where it was found that there is impairment in domains of learning, attention, psychomotor speed and motor skills, in cases of Depression with psychosis as compared to cases having Depression without psychosis. The cognitive deficits of patients having Schizophrenia were alike in profile with patients having Depression with psychosis and were found to be trait related [14].

Bora E et al carried out a meta-analysis in which it was found that cognitive impairment was more severe in cases with first episode Schizophrenia as compared to cases with first episode Bipolar disorder [15].

In North India, B K Pradhan et al carried out a study in which cases of Schizophrenia and Bipolar affective disorder aged from 20-60 years were recruited and also normal controls were included. Tests for neuropsychological assessment were applied according to the

following sequence: Wisconsin Card Sorting Test, PGI Memory Scale, Bhatia Battery of Performance

Tests of Intelligence –Short Scale, Bender Visual Motor Gestalt, Trail A and B and the Controlled Word Association Test. Normal controls performed better on these tests as compared to cases having Schizophrenia and Bipolar Affective Disorder. Cases having Schizophrenia did worse as compared to cases of Bipolar Disorder [16].

In a study conducted by Young DA et al among a cluster of Schizophrenia patients with chronic illness, relationship between unawareness of illness and performance on neuropsychological tests was surveyed. For this survey, Scale to Assess Unawareness of Mental Disorder (SUMD) was used along with neuropsychological tests that had the potency to evaluate the performance of Frontal lobe namely the Wisconsin Card Sorting Test, Verbal Fluency Test and Trails A and B. This study led to the finding that the percentage of perseverative response on Wisconsin Card Sorting Test correlated with unawareness of illness as measured by SUMD. Through the two variables of WCST evidently distinguished between patients of high awareness from the patients of low awareness. A linear combination of WCST percent perseverative response and severity of symptoms was given by a univariate function analysis that categorized 84% of aware patients from the unaware patients. All these findings lead to the underpinning of the fact that the presentation of lack of awareness within the patients of Schizophrenia of chronic duration has got an etiology of organic basis which is most probably conciliated by the Frontal lobes [17].

Spitzer M et al conducted a survey of large number of studies with psycholinguistic findings to decipher about the storage of information by human beings. This survey indicated existence of Associative memory which is marked by wide capacity and large duration. Frontal lobe is supposedly to have its anatomical basis and functionally it has been linked with Dopamine release. On the other hand it has been found that Working memory has a restricted capacity, has importance for goal-directed behavior and. The anatomical basis for Working memory has been established in the Frontal cortex and has been linked with dopaminergic pathway involvement. Evidences from experiments by usage of various linguistic tasks that involved decision making and a delayed response task showed some marked features of thinking processes peculiar to Schizophrenia which included loosening of associations, brisk shift of associations, concretization or abstraction of concepts, the deficit of context-sensitivity and intellectual capacity. All these can be explained by a mechanism involving activation or deactivation of associative memory and of an impaired working memory. These findings can be fruitful for further research in cognitive domains of Schizophrenia [18].

In a study carried by Bressi S et al 60 subjects were undertaken in which 30 subjects aged 21-43 years were patients of Schizophrenia and 30 subjects were healthy controls with same age-education profile. In this study, all the subjects were given computerized tracking task which included three concurrent task of Articulatory suppression, Simple Reaction Time to a tone, and Auditory Digit span. The findings suggested that the subjects with Schizophrenia performed worse than the controls. It was found that there was a negative association between tracking performance in concurrent condition with the total scores and in the Andreasen's Scale for Positive Symptoms, however such an association was not found with negative symptoms scores. Thus these findings hypothesized that in patients of Schizophrenia, the capacity to perform concurrent tasks is affected when there is impairment in central executive component of working memory. The results are indicative of the fact that

impairment in working memory of patients of Schizophrenia has a potential role to play in development of positive symptoms [19].

Green et al carried out a study which determined that whether functioning of Schizophrenia patients in outside world have any correlation with the neurocognitive deficits. This study focused on the specific aspects of cognition which are social problem solving, community functioning and predictors of psychosocial skills acquisition. It was found that verbal memory had association with all types of functional outcomes. Skill acquisition and social problem solving were seen to be related with Vigilance. Community functioning was indicated by Card sorting test however same was not seen in case of social problem solving. Relationship between Social problem solving and Negative symptoms was established nevertheless same was not the case with skill acquisition [20].

In a study carried out by Stone M to focus on the working memory and its significance for strategic memory tests in patients of Schizophrenia, inclusion of 18 patients of Schizophrenia and 15 healthy controls all of which were of male gender was done. All the subjects were asked to perform on tests of immediate memory which was assessed by forward digit span; backward digit span, computation and listening was evaluated for assessment of working memory; Recognition memory was evaluated which is marker of nonstrategic memory and long-term strategic memory (free recall, temporal order, and self-ordered pointing) were evaluated. In all the above tests deterioration in performance by Schizophrenia patients was evident. For deficits in working memory, there was no correlation between education, verbal intelligence, and immediate memory capacity in Schizophrenia patients. Among the subjects variance was found in reduced working memory capacity in strategic memory however same was not the case for recognition memory. Thus it can be concluded that there can be probability of impairment in working memory to be marked feature in patients of Schizophrenia. These findings are in accordance with hypothesized frontal lobe dysfunction found in this disease. Further recognition memory deficits can be correlated with the medial-temporal dysfunction [21].

In a longitudinal study carried out by Hughes C et al to probe into changes in psycho-pathology and its relation between cognitive functioning in chronic Schizophrenia, sixty-two subjects were included who were clinically diagnosed with Schizophrenia or Schizoaffective Disorder according to DSM-IV. These patients were subjected to assessment on Positive and Negative Syndrome Scale (PANSS) over a period of 6 months. It also included twenty-five control subjects for the purpose of comparison. Participants were evaluated on both occasions for the cognitive functions of attention, verbal and non-verbal memory, psychomotor processing and executive functioning with the use of full-scale battery of Neuropsychological tasks. Twenty-five control subjects were assessed for comparison purposes. During one occasion, it was found that the poor performance of subjects on IQ, verbal fluency and memory had correlation with the severity of negative symptoms. Nevertheless by using regression analysis, it was found that even with improvements in symptom ratings over time using 2-, 3- or 5-dimesnional models did not prognosticate amelioration in any features of cognitive function assessed, except motor speed. Thus the findings could not establish a causal relationship between the neuropsychological function and symptomatology in patients of chronic schizophrenia [22].

Friedman JI et al assessed cognitive changes in elderly patients of schizophrenia with a history of long-term institutional stay and whether these changes extended to institutionalized younger patients. Comparison was done between the decline rate of cognitive changes with the cognitive changes found in Alzheimer's Disease. 107 patients with schizophrenia belonging to the age group of 20–80 years were followed over 6 years. These patients were evaluated with the help of Clinical Dementia Rating and the Mini-Mental State Examination. Comparison was done between patients of schizophrenia aged 50 and older, 118 patients of Alzheimer's disease aged 50 and older, and 136 healthy comparison subjects. These were assessed in a similar pattern of follow-up. Institutionalized schizophrenic patients showed an age-related pattern of cognitive change which was not found in Alzheimer's disease patients and healthy individuals. Cognitive profile of the patients of Schizophrenia was quite stable until late life which is indicative that cognitive changes might not be occurring in younger patients over an interval as long as 6 years [23]. Other related studies on related aspects of cognitive impairment were reviewed[24-27].

Key results:

Limitations:

Scope of this study which is hospital based is relatively small. For this, similar study on a larger scale for general population and of longitudinal type should be undertaken to know more about the comparison of impairment of cognition amongst patients of Schizophrenia and Mood disorder.

Conclusions:

Through this study, impairment of cognition found in patients of Schizophrenia and Mood Disorder would be assessed. This study will also throw a light on comparative nature of impairment in cognitive functions in both the groups. Co-relation between Cognitive impairment and Metabolic syndrome in both the groups can also be established.

Ethical Implications:

1. Confidentiality will be assured to all participants. Those participating in this study will be giving informed and written consent.
2. The participants will be explained and inclusion would be on voluntary basis.
3. Institutional ethical committee clearance will be obtained.

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