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Prevalence of Extrapyramidal Side Effects in Patients on Antipsychotics Drugs at a Tertiary Care Center5

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Abstract

Background: Antipsychotic drugs are associated with adverse effects that can lead to poor medication adherence, stigma, distress and impaired quality of life. Among the various side effects of anti-psychotics extra pyramidal symptoms constitute one of the important side effects interfering with the compliance of the patients towards medication.

Objective: Evaluation of extrapyramidal side effects by AIMS in patients who are on antipsychotics.

Results: The extrapyramidal symptoms were more commonly seen in males (62.85%), the age of incidence of maximum in the age group of 34.28, Maximum was seen among the patients on the Risperidone (45.7%), Involvement of the extremities was common (42.85%) and 64.28% of individuals had moderate severity and 54.28% of individuals were aware of the extrapyramidal symptoms which provided mild distress.

Conclusion: Extrapyramidal symptoms are one of the commonest side effect of the antipsychotics interfering with compliance of the patients towards adherence to medications, thereby decreasing the efficacy.

Keywords: Extrapyramidal symptoms; Compliance; Antipsychotics; AIMS.

Introduction

Psychosis is the most severe psychiatric disorder, in which there is marked impairment of behavior, serious inability to think coherently, comprehend and lack of insight. Positive symptoms include hallucinations, delusions and experiences that are not characteristic of normal mental life. Negative symptoms represent deficits in normal functions such as blunted affect, asocial behavior and diminished motivation. Symptoms of impaired cognition include deficits in working memory, processing speed and social norms [1].

The mesolimbic pathway being associated with the positive symptoms and mesocortical pathway associated with negative and cognitive symptoms [2]. Dopamine role in the causation of psychosis is complex. The positive symptoms are due to over activity in the mesolimbic dopaminergic pathway activating D_2 receptors whereas negative symptoms may result from decreased activity in the mesocortical dopaminergic pathway where D_1 receptors dominate [3]. Glutamate also has a role in the etiology of psychosis; NMDA antagonist such as phencyclidine, dizocilpine can produce both positive and negative symptoms in contrast to amphetamine which produces only positive symptoms. Glutaminergic and GABAergic neurons play a complex role in controlling the neuronal activity in the mesolimbic and mesocortical pathway.

NMDA receptors hypofunction will reduce the level of activity in the mesocortical dopaminergic neurons which results in the negative symptoms. This enhances the dopamiergic activity in the mesolimbic pathway. In this pathway NMDA receptors are located on the GABAnergic neurons. Thus it results in reduced GABAnergic inhibition of the mesolimbic neurons and result in the enhanced dopamine release in the limbic area resulting in the production of positive symptoms [4].The term neuroleptics refers to typical antipsychotics [5]. The first antipsychotic chlorpromazine was introduced in 1952 [6]. They act through D_2 receptor blockade. These typical antipsychotics chlorpromazine, haloperidol or fluphenazine are effective in relieving positive symptom of the psychosis but have some serious limitations such as lack of efficacy against negative symptoms and adverse effects like extrapyramidal symptoms [7]. The inhibitory effects of dopaminergic neurons are normally balanced by the excitatory actions of cholinergic neurons in the striatum. Blocking dopamine receptors alters this balance, causing a relative excess of cholinergic influence, which results in extrapyramidal motor effects. The appearance of the movement disorders is generally time and dose dependent [8].

Advances in the treatment have emerged from discovery of newer antipsychotics also called as second generation antipsychotics potentially antagonize the $5HT_2$ receptor, block the D_2 receptor less potently than typical antipsychotics.The development of these atypical antipsychotics such as clozapine, risperidone, olanzapine, quetipine in 1990's fulfilled great expectations in treatment of psychosis by reducing the extrapyramidal symptoms [9].

Antipsychotics induced extra pyramidal symptoms include a variety of movement disorders Acute extrapyramidal symptoms are like acute dystonia, akathisia and parkinsonism develop within hours or weeks after initiating or increasing doses of antipsychotics. Tardive dyskinesia and tardive dystonia are delayed onset syndromes and usually develop after a prolonged use of antipsychotics [10].

The term "neuroleptic" meaning "to fix or hold a neuron" was used to describe the neurological adverse effect of conventional antipsychotics rather than their therapeutic effects [11]. Antagonism of dopamine (D_2) receptors is involved not only in antipsychotic effects,

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but also in causing extra pyramidal symptoms. Studies with positron emission tomography showed antagonism of 60-70% of dopamine (D_2) receptors is required for antipsychotics to be effective and 75-80% of dopamine(D_2) receptor blockade leads to the occurrence of acute extra pyramidal symptoms [12]. The use of second generation antipsychotics clozapine is associated with a lower risk of movement disorders when compared to the use of first generation antipsychotics. Goldstein pointed out that long standing use of clozapine was not associated with increased occurrence of extra pyramidal symptoms [13]. There are few comparable data available for assessing the risks carried by atypical antipsychotics for the induction of extra pyramidal symptoms. The order causing extra pyramidal symptoms according to Tarsy is clozapine< quetiapine <olanzapine [14].

Dystonia are characterized by intermittent or sustained muscle action. Movements vary from fleeting disturbance to maintained abnormal postures [15]. It may occur in 25% to 40% of patients receiving typical antipsychotics. Younger adults and children are more commonly affected. Dystonia occurs after years of use of antipsychotics, but may also occur after a significantly shorter exposure to antipsychotic therapy. Dystonia is typically focal, but it can also affect several muscle groups. It manifests in the cranial, pharyngeal, cervical and axial muscles leading to oculogyric crisis, stiff jaw, tongue protrusion, torticollis, laryngeal, pharyngeal spasm, dysarthria, dysphagia, and sometimes difficulties in breathing, cyanosis, opisthotonus [16]. Dystonia is a very unpleasant experience for patients and sometimes even painful. About 50% of the acute dystonia cases reported occur within the first two days of use of antipsychotics, and 90% in the first four days. Risk factors for development of dystonia include primarily the duration of use and high dose of antipsychotics, younger age, male gender, and mental retardation, positive family history of dystonia, previous dystonic reaction, a recent cocaine and alcohol abuse [17]. When diagnosing antipsychotic induced dystonia it is important to exclude neurological disorders that can also be the cause.

Akathisia is a frequent and serious adverse effect of treatment with antipsychotic drugs. It includes 50% of extrapyramidal symptoms and is considered one of the most common movement disorders caused by antipsychotics [18]. Akathisia may also be caused by antiemetics, serotonergic agents, serotonin reuptake inhibitors and cocaine [19]. The patients suffer from the feeling of restlessness and an irresistible urge to move. They describe a very upsetting experience of pressure, nervousness, tension, increased motor activity consisting of complex, often meaningless stereotyped and repetitive movements [20]. The prevalence of akathisia varies from 5 to 36.8% among extra pyramidal side effects. Akathisia occurs in 10% to 20% of patients treated with atypical antipsychotics, which is less than 20% to 52% with typical antipsychotics [21]. Akathisia may persist for the duration of antipsychotic therapy and usually ceases after the discontinuation of antipsychotics [22].

Drug induced Parkinsonism is the most common especially in elderly patients. The duration between the start of the antipsychotic drugs and onset of the symptoms are variable which may range from few days to few months. It is characterized by the triad of bradykinesia, muscle rigidity and tremor. Postural tremor is more common than resting tremor. Tremor of the lips and perioral muscles can be observed, which is called as "rabbit syndrome". In patients who have used antipsychotics, the prevalence is about 15%. Parkinsonism is considered as a reversible condition usually lasts up to 4 months. In some cases it may lastup to 6-18 months. 15% antipsychotics induced Parkinsonism is said to be persistent [23].

Tardive dyskinesia is manifested by involuntary choreoathetoid movements of the orofacial region, extremities, trunk and respiratory muscles. The movements are more pronounced with excitement, and disappear during sleep. Sometimes the patients set up their mind to decrease the intensity of the involuntary movements and succeed in doing but only short time [24]. Significant number of patients does not notice these involuntary movements or are not bothered by them. Tardive dyskinesia can occur in all patients treated with antipsychotics. It develops after months or years of continuous use of antipsychotics. Tardive dyskinesia can also persist after the discontinuation of antipsychotics or may even be irreversible. The incidence of tardive dyskinesia associated with typical antipsychotics therapy in long-term studies is 5% per year in adults and cumulative annually 25-30% in the elderly. With atypical antipsychotics treatment, the incidence of tardive dyskinesia is significantly lower. Risk factors for occurrence of tardive dyskinesia include elderly patients as well as female patients with brain damage, dementia, mood disorders, increased duration of antipsychotic therapy, and use of anticholinergic drugs, antiparkinsonism drugs and previous occurrence of extra pyramidal symptoms [25].

Abnormal involuntary movement scale is used by physicians for detecting and monitoring abnormal movements associated with tardive dyskinesia which occurs on treating the patients on antipsychotic medications. It rates the severity of abnormal movements from 0 to 4. It is a valuable tool for clinicians who are monitoring the effects of long term treatment with neuroleptic medications and also for researchers studying the effects of these drugs. The abnormal involuntary movement scale test is given every three to six months to monitor the patient for the development of tardive dyskinesia. Usually tardive dyskinesia develops three months after the initiation of antipsychotic drugs, but in elderly it can occur early within one month after the initiation of the treatment [26].

The neuroleptic malignant syndrome is one of the life threatening disorders occurring in patients who are extremely sensitive to the extrapyramidal side effects of antipsychotics. The initial symptom is marked rigidity, fever, changes in the mental status and the autonomic dysfunction [27].

Materials and Methods

The present study was conducted in a tertiary care Mc Gann district hospital teaching hospital, Shivamogga Institute of Medical Sciences, among the patients attending the psychiatry outpatient department. The study was conducted for duration of one year. The study involved the assessment of the extrapyramidal symptoms caused by the antipsychotic medications. "Abnormal involuntary movement scale "AIMS, was used to assess the extrapyramidal symptoms. The different types of the extrapyramidal symptoms, there severity and the awareness of these symptoms by the patient was assessed.

Inclusion criteria

1. Patients diagnosed with psychosis and being treated.
2. Patients diagnosed with depressive psychosis and being treated.
3. Patients diagnosed with bipolar disorder and being treated.

Exclusion criteria

1. Newly diagnosed psychiatric patients.
2. Psychotic patients not compliance with the medication.

3. Patients not diagnosed with psychosis.

Ethical considerations

1. The study is approved by Institutional Ethical Committee.

2. Informed consent by the patient are their caregiver was procured before administering AIMS.

Results and Discussion

The present study involved total number of seventy patients on antipsychotics was diagnosed with the extrapyramidal symptoms.

The present study was conducted among the patients on antipsychotics diagnosed with the extrapyramidal symptoms. The study involved total number of seventy patients among which 44(62.85%) of patients were male and 26 (37.14%) of patients were female. In a similar study conducted by Ayehu et al. males were 67.21% and the females were 32.8%.

The extrapyramidal symptoms were seen more common in the individuals of the age group 30-39 years with 34.28% followed by 40-49 years with 25.71%, 20-29 years with 18.57% and in patients above 50 years with 20%.The extrapyramidal symptoms were seen least in the age group of 10-19 years. Similarly in the study conducted by the Ayehu et al. the extrapyramidal symptoms were seen most commonly in the age group of 18-29 years followed by the age group above 35 years with 35.9% and in the age group 25-34% with 20.3%.

In the present study 72.85% of patients were diagnosed with the psychosis, 15.715 with the maniac depression and 11.42% with the bipolar depression.

Tab. Resperidone was most commonly prescribed among 45.71% of patients, followed by the combination of the Tab. Resperidone with Tab. Fluphenazine in 25.71% patients, Tab. Aripiprazole in 17.14%, Tab. Lithium in 12.85%, Tab. Resperidone with Tab. Chlorpromazine with 5.7% and Tab. Trifluphenazine and Tab. Chlorpromazine had the equal incidence of the extrapyramidal symptoms with 4.28%.

Among the extrapyramidal symptoms the involvement of the extremities were the most common in 42.5% individuals, followed by the Trunk in 35.7% and facial and the oral involvement in 21.42%.

The severity of the extrapyramidal symptoms was moderate in the 45% individuals, mild in the 25.71% individuals and severe in the 10% individuals.

In the present study 54.28% of the patients were aware of the extra pyramidal symptoms which produced mild distress, followed by the 41.42% patients in whom the symptoms were aware and it produced moderate distress, awareness with no distress was seen in the 2.85% individuals and awareness with severe distress was seen in the 1.42% individuals.

Further studies are required to delineate the influence of the dose of antipsychotics in the occurrence of EPS (Tables 1-7 and Figures 1-7).

Sex	Number
Male	44(62.85%)
Female	26(37.14%)
Total	70

Table 1: Sex distribution among the patients with extrapyramidal symptoms.

Age(Years)	Number
10-19	1(1.42%)
20-29	13(18.57%)
30-39	24(34.28%)
40-49	18(25.71%)
50-59	7(10.00%)
>60	7(10.00%)

Table 2: Age distribution in the study population.

Diagnosis	Number
Psychosis	51(72.85%)
Maniac depression	11(15.71%)
Bipolar disorder	8(11.42%)

Table 3: Diagnosis of the patient in the study population.

Antipsychotics	Number
Tab.Resperidone	32(45.71%)
Tab.Aripiprazole	12(17.14%)
Tab.Trifluphenzine	3(4.28%)
Tab.Chlorpromazine	3(4.28%)
Tab.Lithium	9(12.85%)
Tab.Resperidone+Tab. Trifluphenzine	18(25.7%)
Tab.Resperidone+ Tab.Chlorpromazine	4(5.7%)

Table 4: Antipsychotics used in the study population.

Extrapyramidal symptoms	Number
Facial and oral	15(21.42%)
Trunk	25(35.7%)
Extremities	30(42.85%)

Table 5: Extrapyramidal symptoms involving different parts.

Extrapyramidal symptoms severity	Number
Minimal	0
Mild	18(25.71%)
Moderate	45(64.28%)
Severe	7(10.00%)

Table 6: Severity of the extrapyramidal symptoms.

Awareness of extrapyramidal symptoms	Number
No awareness	0
Aware, no distress	2(2.85%)
Aware, mild distress	38(54.28%)
Aware, moderate distress	29(41.42%)
Aware, severe distress	1(1.42%)

Table 7: Patient's awareness of the extrapyramidal symptoms.

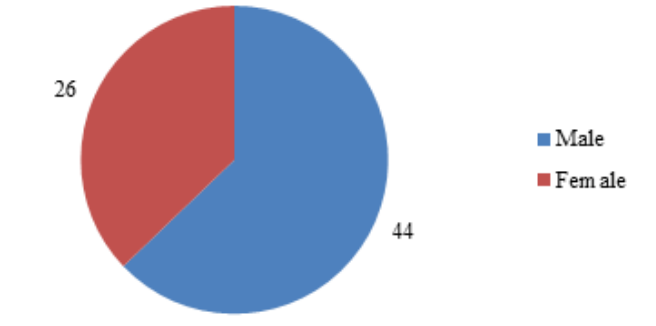

Figure 1: Pie chart representing the sex distribution in the study population.

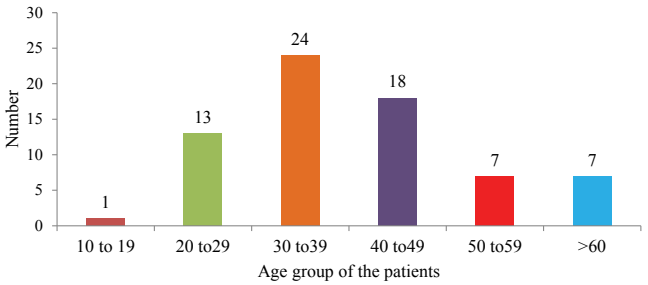

Figure 2: Bar graph representing the age group of patients in the study population.

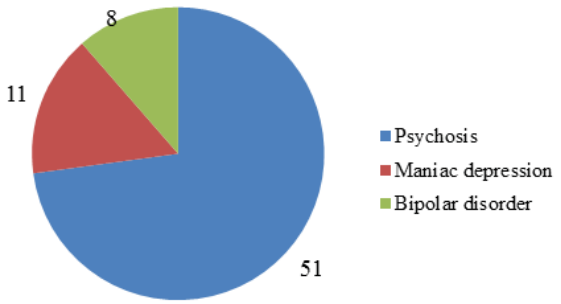

Figure 3: Pie chart representing the diagnosis of the patients in the study population.

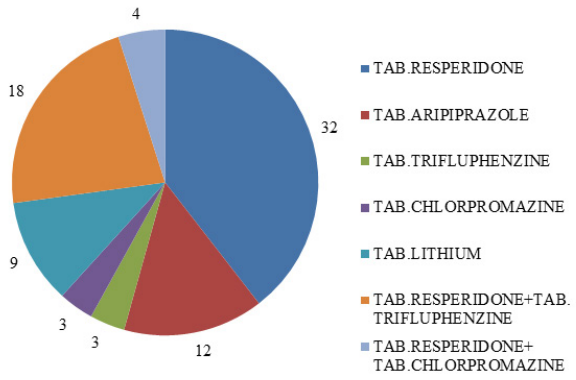

Figure 4: Pie chart representing the antipsychotics used in the study population.

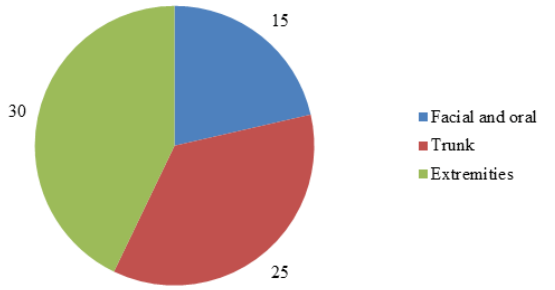

Figure 5: Pie hart representing the extrapyramidal symptoms involving various parts.

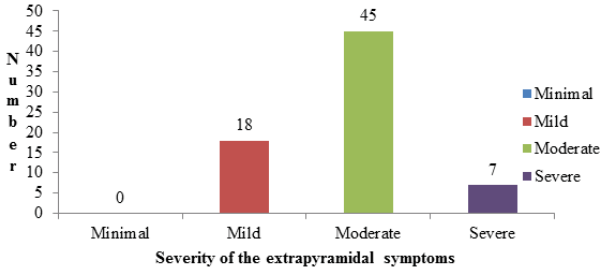

Figure 6: Bar graph representing the severity of the extrapyramidal symptoms.

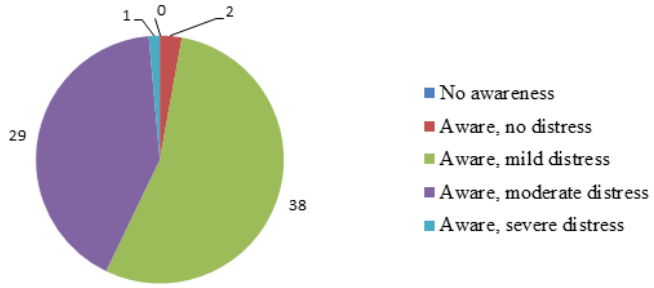

Figure 7: Pie chart representing the awareness of extrapyramidal symptoms among the patients.

Conclusion

Extrapyramidal motor symptoms are one of the major side effects of the antipsychotic medications. It has a great influence on the compliance of the patients towards the antipsychotic medications leading to failure of the treatment .Hence the extrapyramidal side effects to be properly diagnosed and appropriately treated so that there is increased compliance and efficacy of the medications.

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