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A COMPARATIVE STUDY OF NEUROLEPTIC INDUCED NEUROLOGICAL SIDE EFFECTS IN SCHIZOPHRENIA AND MOOD DISORDERS

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ABSTRACT

Neuroleptic induced neurological side effects were compared over a period of one year (1991-1992) in 45 schizophrenics and age and sex matched 42 mood disorder patients, diagnosed as per DSM-III-R criteria. Prevalence of dystonia was equally common in both groups. Pseudoparkinsonism was significantly high in female mood disorder patients, akathisia in middle aged mood disorder patients and tradive dyskinesia in mood disorder patients. Factors like age of onset, time of onset and mean dose of antipsychotics (chlorpromazine equivalent) did not show any significant difference. The findings are discussed in relation to their practical application and suggestions for future studies are outlined.

Key Words :Neuroleptics, neurological side effects, schizophrenia, mood disorder

The side effects of neuroleptic drugs, both immediate and tardive are commonly encountered in clinical practice and cause concern to the patients and the psychiatrist.They are broadly classified as extrapyramidal syndrome which consists of pseudoparkinsonism, dystonia and akathisia and tradive syndromes of which the commonest is tardive dyskinesia. Despite the ubiquitous nature, estimates of their occurrence vary (Caesey and Keepers, 1988).

Acute dystonia is reported to be the least common with an incidence of 5% which can go up to 50% with more potent neuroleptics. It occurs within hours to several days after initiating the treatment and twice commonly in males. An age predisposition has also been suggested with a preponderance in young, adults and children (Cunningham Owens, 1990).For pseudoparkinsonism an overall prevalence of 25% has been reported. It may begin within several days of starting the treatment and is apparent within 30-50 days of initiating the treatment. Unlike dystonia,pseudoparkinsonism shows a rise in incidence after the age of 40 especially females (Addonizio and Alexopoulose, 1988). Akathisia has a reported rate of 5-50% in routine clinical practice. It usually begins within several days of onset of treatment and 90% occurs within 2-3 months. It is reported that middle aged women are at increased risk for akathisia (Adler et al., 1989). Though a high rate of prevalence (50%) has been reported for TD, clinically significant TD occurs in at least 10-20% of all patients exposed to neuroleptics for more than a year. Older age and female sex appears to be a risk factor for TD (Jeste and Caligiri, 1993 & Dutta et al., 1995).

An interesting finding to emerge in recent years from TD research is that patients with mood disorders may be more vulnerable to the development of TD than patients with schizophrenia (Mukherjee et al., 1986; Caesey, 1988). It is not clear whether a similar difference exists for other side effects. In a retrospective file review study, Nasrallah et al. (1988) found that acute dystonia is more common in mania than schizophrenia. Studies by Remington et al. (1990), Khanna et al. (1992)

and Pandey et al. (1992) do not support this finding. So far no studies have reported a differential side effect profile for other side effects in schizophrenia and mood disorders. Considering these possibilities a study was planned with the following aims:

-to assess the prevalence of dystonia, akathisia, and tardive dyskinesia over a period of 1 year, in schizophrenia and mood disorder patients.,

-to compare the clinical profile of patients who develop these side effects such as age, sex, time of onset and the cumulative dosage of neuroleptics in schizophrenia and mood disorder.

MATERIAL AND METHOD

The study was conducted at the Department of Psychiatry, Christian Medical College, Vellore. The hospital maintains detailed case records of all patients treated either as outpatients or as inpatients. Case records of all patients who received a diagnosis of schizophrenia or bipolar affective disorders as per DSM- III-R criteria (APA, 1987) over a period of 2 years (June 1989 to May 1991) were reviewed and those who had been followed up for a period of 12 months or more were evaluated in detail. The exclusion criteria were :

1) Presence of mental retardation, organic brain involvement or movement disorder by history, examination or investigations.

2) Patients in whom doubts about the initial diagnosis of schizophrenia or mood disorder were entertained later.

3) Patients who had been on neuroleptic treatment prior to the consultation in hospital.

4) Patients in whom there were gaps in follow-up for a period of 3 months or more.

After the exclusion criteria were applied, there were 45 patients with a diagnosis of schizophrenia. They were matched for age and sex with bipolar affective disorder patients of the same period. However, matched bipolar patients could not be obtained for 3 schizophrenic patients, so that the number of bipolar patients were only 42. The records of all 87 patients were evaluated and the following details were documented in a special proforma designed for this study : -

I) Sociodemographic and clinical profile.

II) Information about the side effect such as the presence, type, time of onset and cumulative dose of neuroleptics received (in chlorpromazine equivalent). The data were analysed by

TABLE

NEUROLEPTIC INDUCED NEUROLOGICAL SIDE EFFECTS PROFILE OF PATIENTS WITH SCHIZOPHRENIA AND MOOD DISORDERS

	Schizophrenia (N=45)	Mood disorder (N=42)	Test statistics
Dystonia (total prevalence 17%)			
Prevalence (%)	17.7	16.7	NS
Mean age of onset (yrs)	26	26.6	NS
Gender (% Male)	13.3	7.14	
(% Female)	4.4	9.5	NS
Time of onset (days)	2.02	5.67	NS
Mean chlorpromazine equivalent (gm)	1489	1665	NS
Parkinsonism (total prevalence 54%)			
Prevalence (%)	60	47.6	NS
Mean age of onet (yrs)	27.8	31.1	NS
Gender (% Male)	37.7	19.0	x^2 =5.14
(% Female)	22.2	28.6	(p < 0.05)
Time of onset (days)	17.14	20.90	NS
Mean Chlorpromazine equivalent (gm)	1779	1286	NS
Akathisia (total prevalence 25%)			
Prevalence (%)	28.8	19.0	NS
Mean age of onset (yrs)	25.1	38.7	t = 2.41 (p < 0.05)
Gender (% Male)	24.4	14.3	NS
(% Female)	6.6	4.8	
Time of onset (days)	17.98	10.67	NS
Mean chlorpromazine equivalent (gm)	2266	1164	NS
Tardive dyskinesia (total prevalence 17%)			
Prevalence (%)	6.7	16.7	x^2 = 5.69 (p< 0.05)
Mean age of onset (yrs)	32.6	33.7	NS
Gender (% Male)	11.1	2.4	
(% Female)	4.4	4.8	NS
Time of onset (months)	6.62	7.93	NS
Mean chlorpromazine	1314	1098	NS

SPSS/PC soft ware. The tests done were chi-square test (with Yates correction) and t test for parametric and non-parametric variables respectively.

RESULTS

The prevalence of extrapyramidal side effects including tardive dyskinesia in the total sample was 71%. Comparison of the prevalence of total side effects in schizophrenia (77.8%) and mood disorder (64.3%) was not significant. Comparison of the prevalence of individual side effects, mean age of onset, sex difference, time of onset and mean dose of neuroleptic received (chlorpromazine equivalent) between schizophrenia and mood disorder are given in table.

DISCUSSION

Though literature abounds with studies of neurological side effects of neuroleptic drugs, many questions are left unanswered. In India not many studies have been done on drug induced movement disorders. In our study more than 70% of the patients treated with neuroleptics developed extrapyramidal side effects or tardive dyskinesia. This is in broad agreement with the literature (Glenberg, 1987; Davis et al., 1989). There was no significant difference in the prevalence between schizophrenia and mood disorder patients when all the side effects were considered together. Of the total patients, the individual side effects present were 54% (pseudoparkinsonism), 25% (akathisia), 17% (dystonia) and 17% (tardive dyskinesia). This too is similar to the rates reported previously (Fahn, 1984; Addonizio and Alexopoulose, 1988). Except tardive dyskinesia the prevalence of dystonia,pseudoparki- nsonism and akathisia were equal in 2 groups. Tardive dyskinesia was found to be high in patients with mood disorder. There are plenty of reports showing that the prevalence of tardive dyskinesia is higher in mood disorder than in schizophrenia (Mukherjee et al., 1986; Caesey, 1988 & Dutta et al., 1994). Major depression and bipolar disorder are risk factors for neuroleptic induced tardive dyskinesia. Even among schizophrenic patients a history of mood disorder in first-degree relative may heighten the risk of developing this syndrome (Wegner et al., 1985).

When each side effect was analysed separately for each sex, an interesting factor which emerged was that pseudoparkinsonism was more common in female patients with diagnosis of mood disorder. Previous studies have reported a predilection for pseudoparkinsonism in elderly females (Caesey & Keepers, 1988) but a correlation has not been reported with mood disorder. The gender predisposition of tardive dyskinesia in women and dystonia in men were not borne by this study. Similarly the correlation with age reported for dystonia (in young men), pseudoparkinsonism and tardive dyskinesia (in old age) was not seen in this study. Akathisia was found to be common in middle aged patients in the mood disorder group. There are reports showing that middle aged women are at increased risk for akathisia and its time course is similar to that for drug induced parkinsonism (Adler et al.,1989). Akathisia has been reported with lithium carbonate (Channabasavanna & Goswami, 1984) and tricyclic antidepressant therapy (Krishnan et al., 1984). Since mood disorder patients have received lithium or tricyclic antidepressants in addition to neuroleptics, this may be the reason for the predilection for akathisia in middle aged mood disorder patients.

In this study all side effects except tardive dyskinesia were noted within an average period of less than 3 weeks. Probably this points to the fact that it is during the initial weeks of neuroleptic therapy that we should be vigilant on the search for side effects. If side effects are not promptly treated it may adversely affect the patients' compliance. As a group, schizophrenics received more chlorpromazine equivalent of neuroleptics than mood disorders patients, though it was not statistically significant. Despite receiving less neuroleptics,

tardive dyskinesia was significantly high in mood disorder patients. This again reiterates the fact that neuroleptic dosage and mood disorders are the risk factors for the development of tardive dyskinesia.

Except for tardive dyskinesia the question of differential side effect profile of neuroleptics in schizophrenia and mood disorder has not been addressed to in the literature. There are few reports concerning the prevalence of acute neuroleptic induced dystonia in schizophrenia and mania but there is no uniform consensus in the results as in tardive dyskinesia (Nasrallah et al., 1988; Remington et al., 1990; Khanna et al., 1992; Pandey et al., 1992). Our study has shown three differences between schizophrenia and mood disorders, viz. higher incidence of parkinsonism in female mood disorder patients, higher incidence of akathisia in middle aged mood disorder patients and higher incidence of tardive dyskinesia in mood disorder patients. This generally shows that patients in mood disorder group are more vulnerable to the development of neuroleptic induced neurological side effects. Apparently, the large dose of neuroleptics received by this group in addition to the mood stablising drug could be the reason for the high prevalence of neuroleptic induced neurological side effects in mood disorder patients. We believe that future studies should address this question of differential side effects profile in schizophrenia and mood disorder patients.

Before concluding, the methodological limitations of this study have to be considered. The retrospective chart survey method employed would mean that the prevalence rates obtained may be an underestimation, as the same side effects may have been missed by the clinician who was not especially looking for it. This would be particularly true for akathisia which is often missed by the clinician (Levinson & Simpson, 1987) and for milder forms of tardive dyskinesia. Use of specific rating scales to measure the various side effects and a prospective design would be ideal. The period of follow-up of one year is too short for the study of tardive dyskinesia which requires long term follow-up.

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