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EFFECT OF CHANGE OF ANTIPSYCHOTIC DRUG THERAPY IN PATIENTS EXPERIENCING EXTRAPYRAMIDAL SIDE EFFECTS

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ABSTRACT

Extra-pyramidal side effects are commonly seen with anti-psychotic drugs and are a major cause of non-compliance. In an effort to reduce the severity of these EPS, either an additional anticholinergic drug is prescribed, the dose of the offending drug is altered or the class of the antipsychotic drug is changed. To understand the effect of these changes, the alterations in the prescriptions of 100 patients with extra-pyramidal side effects due to anti-psychotic drugs were analyzed. Only, 83 prescriptions underwent alterations; 53 as dose reduction. An antipsychotic drug was removed, added or substituted in 9, 8 and 13 cases, respectively, while 17 remained unchanged. 73 of these 100 prescriptions already had an anticholinergic drug since initiation. The severity of the EPS was measured before and after change in anti-psychotic drug therapy. The difference in the mean score for tremors (1.14, 95% CI 0.99-1.28), akathisia (2.79, 95% CI 2.02-3.57) and acute muscle dystonia (3.43, 95% CI 1.84-5.02) at the end of 30 days was statistically significant (p: <0.0001, <0.0001 and 0.0019 respectively).

KEYWORDS: Tremors, Parkinsonism, Akathisia, AMD, dose reduction, dose titration.

INTRODUCTION

The use of drugs can result in unintended, unwelcomed, and potentially adverse consequences for the patient.[1] These adverse consequences affect the quality of life, not only of the patients but also of their caretakers.[2] Secondly, if a drug causes a discomforting effect, there is a possibility that the patient may avoid taking the drug altogether which leads to failure of compliance that can have its own implications. Similarly, a long acting parenteral preparation may be preferred by some over daily oral tablets.[3,4] Adverse effects may make it difficult for the individual to attend to his offices leading to a loss of wages, which further complicates adherence to treatment. Therefore, one has to be careful while prescribing medicines with the sole aim that the drug should provide the desired therapeutic outcome while minimizing adverse side effects and cost to the patient.

Although the patient is the cornerstone of a treatment strategy, adverse effects also have an impact on the healthcare costs. In the United States, it was observed that preventable adverse effects constituted between 43.3% and 80% of all adverse outcomes leading to emergency visits and hospital admissions. In the year 2000, the cost of problems due to drug use in an ambulatory setting was more than $US177 billion.[5] For the betterment of the society and the reduction in the healthcare burden, trying to curb adverse effects as much as possible is a must.

Antipsychotic drugs form the cornerstone of psychosis management. However, they are known to cause extrapyramidal side effects (EPS) including Parkinsonism, Akathisia, Acute Muscle Dystonia (AMD) and Tardive Dyskinesia besides other metabolic and endocrine side effects.[6] A few strategies can be employed to reduce the severity of the EPS. Dose titration forms the first and foremost method while switching from a typical antipsychotic to an atypical one is as frequently practiced.[7] The present study was planned to determine the effect of change in antipsychotic drug therapy on the severity of EPS.

MATERIAL AND METHODS

The study was conducted after obtaining permission from the institutional ethics committee at a tertiary care teaching hospital in India between June 2015 and May 2016. Prescriptions of 100 patients who experienced EPS with antipsychotic drugs were analyzed. The sample size of 100 was reached in accordance with the number of patients with EPS due to antipsychotic drugs visiting the psychiatry department (out-patient and in-patient) over a period of one year. Details of the EPS and change in the therapy were noted in the case record form. Each patient was followed up for a period of 1 month (30 days) to assess the effect of change in therapy on the severity of the EPS. Only those adults who developed EPS due to antipsychotic drugs and were willing to give written informed consent were included in the study. Written informed consent was obtained from the legally

acceptable representative (LAR), wherever applicable. Simpson Angus scale (SAS), Barnes Akathisia Rating Scale (BARS), Global Dystonia Scale (GDS) and Abnormal Involuntary Movement Scale (AIMS) were used to characterize Tremors (Parkinsonism), Akathisia, Acute Muscle Dystonia and Tardive Dyskinesia, respectively. Paired t test was employed to compare the scores at Day 0 and Day 30.

RESULTS AND DISCUSSION

In the present study, prescriptions were altered in the form of dose reduction (53 prescriptions), removal of the antipsychotic drug (9), addition of an antipsychotic drug (8), substitution of the antipsychotic drug (13). 17 prescriptions, however, remained unchanged as referenced in Table 1. Administration of an antipsychotic drug at the regular dose and a lower dose on alternate days helps reduce the severity of EPS.[8] However, this kind of alteration in the prescription was not observed in the present study.

Recovery from EPS was observed in 86 of 100 patients at the end of 30 days, which was statistically significant ($p < 0.05$). However, 9 patients experiencing akathisia and 5 patients experiencing tremors did not show any change in their EPS symptoms at the end of one month. Tables 2 and 3 summarize the changes in the EPS at 30 days following changes in the antipsychotic drug prescription.

In likeness with the current study, multiple case reports demonstrate an improvement in the severity of EPS following alteration in the antipsychotic drug therapy. An improvement in the EPS symptoms was reported in a series of 10 cases wherein the offending antipsychotic drug was withdrawn in 9 and the dose was reduced in 1 patient, with or without discontinuation of concomitant medications, along with addition of an anticholinergic drugs.[9] Similarly, switching from one antipsychotic drug to another helped abate dysphagia in a schizophrenic individual.[10] Though tardive dyskinesia was not observed in the current study, replacing the offending antipsychotic drug with another and addition of an anticholinergic drug helped curtail the EPS.[11] On the contrary, in a patient with auditory musical hallucinations it was not possible to change the antipsychotic drug or its dose, EPS was then managed with an anticholinergic drug.[12]

Despite not being observed in the present study, multiple incidences of EPS may be reported in the same individual. Akathisia, Parkinsonism and Akathisia with Parkinsonism was reported in a patient with different antipsychotic drugs and was handled with either dose reduction and/or addition of an anticholinergic drug.[13] Similarly, a patient with a history of neuroleptic malignant syndrome with a combination of antipsychotic drugs developed akathisia with another drug. In the prior condition, the offending drugs were discontinued while in the latter, dose of the drug was reduced; improvement was reported both times.[14]

Table 1: Change in Antipsychotic Therapy (Prescription).

Change / EPS	Dose Reduction	Drug Removal	Drug Addition	Drug Substitution	No change	Total
Tremors	25	5	6	8	15	59
Akathisia	22	4	2	4	2	34
AMD	6	0	0	1	0	7
Total	53	9	8	13	17	100

Values represent numbers, n=100

Table 2: Changes in EPS at Day 30.

Improvement / Extrapyramidal side effect	Yes	No	Total
Tremors	54	5	59
Akathisia	25	9	34
AMD	7	0	7
Total	86	14	100

Values represent numbers, n=100

Table 1: Severity of EPS after modification of antipsychotic drug therapy.

n=100	Score at Day 0 (mean ± SD)	Score at Day 30 (mean ± SD)	Mean Difference ± SE of mean	p value
Tremors, 59	1.49 ± 0.53	0.35 ± 0.51	1.14 ± 0.07	<0.0001
Akathisia, 34	6.32 ± 1.75	3.52 ± 1.76	2.79 ± 0.37	<0.0001
AMD, 7	3.85 ± 1.51	0.42 ± 0.37	3.43 ± 0.64	0.0019

Scales for Scoring: SAS for Tremors, BARS for Akathisia, GDS for AMD

CONCLUSION

A modification in the prescription definitely leads to the diminution in the severity of the side effects; care has to be taken that such a revision of the prescription does not negatively affect the severity of the disease. An appropriate measure of risks and benefits must thus be taken into account so as to maximize the health benefit to the patient and the society.

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