Prevalence and Severity of Adverse Drug Reactions (ADRs) in patients subjected to different Anti-psychotic drugs in an Out-Patient Department of a Psychiatry Hospital in Kashmir; a prospective observational study

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ABSTRACT

Background: Adverse effects are usually dose dependent and can be influenced by patient characteristics including age and gender and these confounding factors should be considered in clinical practice and in the interpretation of research data. Selection of an antipsychotic drug should be on an individual patient basis. Patients should be involved in prescribing decisions and this should involve discussion about adverse drug reactions and their severity. **Objective:** Current study was carried out with the aim to look into the severity with which the adverse drug reactions were associated with various antipsychotics used in our day to day practice. **Materials and Methods:** It was a prospective observational study conducted over a period of one year in the Outpatient Department of Institute of Mental Health and Neurosciences (IMHNS), Government Medical College Srinagar. An assessment of severity was done using modified Hartwig and Siegel scale. **Results:** A total of 100 ADRs of different types were observed in 77 patients out of total 177 patients included in our study, with an overall prevalence of about 43.5%. Most (83.0%) of the ADRs were mild in severity while ADRs moderate in severity were found in only 17 (17.0%) according to modified Hartwig and Siegel scale. None of the reported ADRs belonged to 'severe' or 'lethal' category. There was no statistically significant relationship between development of ADRs with age ($p=0.8$) or sex ($p=0.6$) of the patients included in the study. **Conclusion:** Although with the utilization of antipsychotics, the prevalence of ADRs in our study was as high 43.5%, most of them (83%) were mild in nature and only 17% of them were of moderate severity and none of our patients showed the development of any severe ADR which would lead them to discontinue the therapy.

Key words: Antipsychotics and ADRs, Modified Hartwig and Siegel scale, ADR reporting, ADR prevalence, ADR severity due to Antipsychotics.

Citation: Afkat A, Arshad H, Samina F, Shagufta P, Vineeta S, Zubair A. Prevalence and Severity of Adverse Drug Reactions (ADRs) in patients subjected to different Anti-psychotic drugs in an Out-Patient Department of a Psychiatry Hospital in Kashmir; a prospective observational study. Int J Pharmacol and Clin Sci. 2016;5(1):12-16.

INTRODUCTION

The antipsychotic drugs are chemically diverse but posses the common property of alleviating the symptoms of both functional and organic psychosis.[1] These drugs can be of great benefit in a range of psychiatric disorders including bipolar affective disorders and schizophrenia and their use is increasing day by day, but all are capable of causing a wide range of potential adverse reactions that can lead to non compliance, can impair quality of life, cause stigma, cause physical morbidity leading to discontinuation of medication and in extreme cases be fatal.[2]

Received : 16-12-2015 **Revised :** 20-03-2016
Accepted : 22-03-2016
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Conflict of interest: Nil ; **Source of support :** Nil
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DOI : 10.5530/ijpcs.5.1.3

Adverse effects are usually dose dependent and can be influenced by patient characteristics including age and gender. These confounding factors should be considered in clinical practice and in the interpretation of research data. Selection of an antipsychotic drug should be on an individual patient basis. Patients should be involved in prescribing decisions and this should involve discussion about adverse drug reactions.[2]

Although the antipsychotic drugs have had a revolutionary and beneficial impact on medical and psychiatric practice, their liabilities especially the adverse effects of the older typical or neuroleptic agents must be emphasized. Newer antipsychotics are atypical in having less risk of extrapyramidal side effects but these agents present their own spectrum of adverse effects.[3]

Antipsychotic drugs have a high therapeutic index and are generally safe agents. Adverse effects often are extensions of many pharmacological actions of these drugs. The most important are those on the cardiovascular, central, autonomic nervous system and endocrine systems.[2,4-6] Knowledge of how the prevalence and severity of adverse effects vary for different antipsychotics allows the clinicians to choose the safer therapy for his patients and reduce the occurrence of these effects.[7] The present study was aimed to assess the severity of various adverse drug reactions (ADRs) associated with the utilization of various antipsychotics used in our patient suffering from different psychiatric disorders.

MATERIALS AND METHODS

It was a prospective observational study conducted by the Department of Pharmacology in collaboration with the Department of Institute of Mental Health and Neurosciences (IHMNS), Government Medical College Srinagar for a period of one year. All the diagnosed patients (old and new) of various psychiatric disorders who were receiving different antipsychotics were included in our study. The ADRs were reported either spontaneously by the treating consultant or by patients being treated or their guardians. A questionnaire was also used to ask the patient specific questions related to likely ADRs and patient's responses were recorded in the Case Record Form. An assessment of severity was done using modified Hartwig and Siegel scale.

Statistical analysis

Data was entered in Microsoft Excel. Continuous data was summarized as mean (±) standard deviation. Categorical variables were summarized as percentages. Chi-square test was used to test for independence of two categorical variables. An exact p-value (two-sided) was reported when chi-square was not valid (as per Chochran Criteria).[8]

Table 1: Distribution of study population according to age and ADR

Age (years) Present (N, %)		ADR Absent		Total
≤10	Count	1 (33.3)	2	3
	%	33.3%	66.7	100.0%
11-20	Count	14	17	31
	%	45.2%	54.8%	100.0%
21-30	Count	25	31	56
	%	44.6%	55.4%	100.0%
31-40	Count	24	24	48
	%	50.0%	50.0%	100.0%
41-50	Count	8	17	25
	%	32.0%	68.0%	100.0%
51-60	Count	3	4	7
	%	42.9%	57.1%	100.0%
61-70	Count	2	5	7
	%	28.6%	71.4%	100.0%
Total	**Count**	**77**	**100**	**177**
	%	**43.5%**	**56.5%**	**100.0%**

p= 0.825, chi square test (Exact p).

Table 2: Distribution of study population according to sex and ADR

SEX Present		ADR Present	ADR Absent	Total
Female	Count	37	44	81
	%	45.7%	54.3%	100.0%
Male	Count	40	56	96
	%	41.7%	58.3%	100.0%
Total	**Count**	**77**	**100**	**177**
	%	**43.5%**	**56.5%**	**100.0%**

P=0.649, chi-square test.

Table 3: ADR status in patients according to drugs used

Drugs used	ADR Present N (%)	ADR Absent N (%)	Total
Olanzapine	26 (43.3)	34 (56.7)	60
Risperidone	13 (32.5)	27 (67.5)	40
Quetiapine	12 (38.7)	19 (61.3)	31
Aripiporazole	3 (30.0)	7 (70.0)	10
Haloperidol	6 (85.7)	1 (14.3)	7
Amisulpride	2 (28.6)	5 (71.4)	7
Olanzapine+Amisulpride	3 (42.9)	4 (57.1)	7
Trifluoperazine	4 (66.7)	2 (33.3)	6
Clozapine	3 (100.0)	0 (0.0)	3
Flupenthixol	0 (0.0)	1 (100.0)	1
Amisulpride+Aripiprazole	1 (100.0)	0 (0.0)	1
Aripiprazole+Flupenthixol	1 (100.0)	0 (0.0)	1
Quetiapine+Fluphenazine	1 (100.0)	0 (0)	1
Risperidone+Amisulpride	1 (100.0)	0 (0)	1
Trifluperazine+Olanzapine	1 (100.0)	0 (0)	1
Total	**77 (43.5)**	**100 (56.5)**	**177**

Table 4: Frequency of ADRs according to organ system involved

System involved	Frequency	Percentage
Neurological	44	44.0
Metabolic/Endocrine	25	25.0
Gastrointestinal	14	14.0
Autonomic	6	6.0
Psychiatric/Behavioural	3	3.0
Sexual	3	3.0
Others	5	5.0
Total	**100**	**100.0**

Table 5: Severity of ADR in the study population according to the modified Hartwig and Siegel scale

Severity of ADR	Frequency	Percent
Mild	83	83.0
Moderate	17	17.0
Severe	0	0.0
Lethal	0	0.0
Total	**100**	**100.0**

RESULTS

Out of total 177 patients enrolled for the study, 54.2% was constituted by males and 45.8% of the study population were females with the average age of patients being 32.9 years ± SD of 13.42 years. Out of the total study population, 77 patients reported at least one or more ADRs out of which 37 were females and 40 were males. However there was no statistically significant relationship of ADRs with age (p=0.83) or gender (0.65) of the study population (Table 1 & 2). Most frequently prescribed drugs were olanzapine, risperidone and quetiapine in decreasing order of their frequency of 33.9%, 22.6% and 17.5% respectively and the other drugs used included either clozapine alone or the combination of various antipsychotics. Though the number of patients put on clozapine and other combinations (Table 3) was less and thus the overall number of patients showing ADRs was also less but whatever was the number, all of them had one or more ADRs giving the percentage as 100% while as among the patients receiving other frequently prescribed drugs, though the number was more but there were still some patients who did not show any ADRs and thus the percentage was less than that seen with clozapine and certain combinations.

The overall prevalence of ADRs in the study population was found to be 43.5%. (Table 1 & 2) and the most frequently involved organ system in the decreasing order of their frequency were neurological, endocrine giving rise to various metabolic disturbances, gastrointestinal and autonomic (Table 4). When the percentage of individual ADRs was taken into consideration, the most common

Table 6: Severity of ADR according to drug used

Drug	Mild	Moderate	Total
Amisulpride	4	0	4
Aripiprazole	1	2	3
Aripiprazole+Amisulpride	0	1	1
Clozapine	4	0	4
Flupenthixol+Aripiprazole	1	0	1
Haloperidol	1	9	10
Olanzapine	34	0	34
Olanzapine+Amisulpride	2	1	3
Quetiapine	13	0	13
Quetiapine+Fluphenazine	1	0	1
Risperidone	17	2	19
Risperidone+Amisulpride	1	0	1
Trifluoperazine	4	0	4
Trifluoperazine+Olanzapine	0	2	2
Total	**83**	**17**	**100**

ADR was increase in weight (10.7%) followed by increased appetite (6.8%), sedation (5.6%), and akathesia (5.1%).

As per modified Hartwig and Siegel scale[9] for assessing the severity of ADRs, 83 (83.0%) ADRs were mild in severity and only 17(17.0%) ARDs were moderate in severity. None of the reported ADRs belonged to the 'severe' or 'lethal' category (Table 5). On the basis of the severity of adverse reactions, when the drugs used in our study population were compared, most of them showed mild adverse effects and those showing moderate adverse effects included mostly the combinations and only few individual drugs like haloperidol and aripiprazole (Table 6).

DISCUSSION

Atypical antipsychotics are now considered as first line agents based on treatment efficacy, better tolerability and reduced risk of extra-pyramidal symptoms.[3] Knowledge about the association of various ADRs with various antipsychotics can prevent their frequency as well as the severity when various factors influencing the same are taken into consideration. So the present study was conducted and the results were compared with the studies conducted earlier and we also tried to determine their relationship with age and sex of the patients. In the present study, the participants were in the young and middle age groups and the male female ratio was 1.2 and the results were similar to those reported by Haddad PM *et al*[2] and Wallace M *et al*.[5] However there was no significant relationship of ADR with age (p=0.83) or sex (p=0.65) of the enrolled patients. The proportion of patients with at least one ADR was found to be 43.5% and most of them (83.0%) being mild in severity. Though the number of females showing adverse drug reactions was less as compared to the males but the prevalence of the same was more in them as the number of female patients under study was less (81) compared to males which was 96 and thus the percentage of females showing the ADRs is 45.7% (37/81) and in males, the same is 41.75% (40/96). It is a well reported fact that the prevalence of ADRs is more in case of females than the males.[6,10]

Increase in weight, increased appetite, sedation, and akathesia were the most common ADRs observed in our study population in decreasing order of their occurrence. When compared to other studies[5,1] conducted earlier, weight gain was reported as the most common ADR while as others like Prajapati HK *et al*[11] had observed that tremor was the most common ADR followed by weight gain. This difference may be attributed to a different patient population group used by Sengupta G *et al*[12] and Prajapati HK *et al*.[13] It is also worth to mention that these studies reported ADRs in a population of patients on psychotropic drugs whereas in our study, the patients were receiving only antipsychotics among psychotropic drugs. Since the most frequently drugs prescribed in the present study were olanzapine, resiperidone and quietapine and as such more patients showing adverse effects related to them were seen while as the percentage of patients showing adverse effects to clozapine and the combination of various antipsychotics was 100% but the number of patients receiving such medication was very less and thus needs evaluation through further research.

In our study, most (83.0%) of the ADRs were mild in severity and only 17% of patients showed ADRs of moderate severity. This may be because of the fact that the present study was an OPD based study even though efforts were made to obtain information about all ADRs a patient might have experienced. Same has been reported by Lucca JM *et al*[6] where the majority of the ADRs in the outpatient settings were mild and self limiting. The findings of the present study confirm the results reported by others.[1,11,14-16] All these studies have reported that most of the ADRs are mild to moderate in severity. In our study none of the ADRs was reported to belong to 'severe 'or 'lethal' in category.

CONCLUSION

The prevalence of ADRs associated with the use of various antipsychotics in our study population was as high 43.5%

and most of them (83%) were mild in nature and only 17% of them were of moderate severity and none of our patients showed the development of any severe ADR which would lead them to discontinue the therapy. The present study adds to the existing information on the prevalence and severity of ADRs following antipsychotic medication from the other centers where such studies have already been conducted and also create awareness among our own health care professionals about the importance of carrying out active surveillance studies regarding severity of ADRs with various antipsychotic drugs. Psychiatrists and other health care professionals treating psychiatric patients should have a good knowledge about the possible ADRs and their severity following antipsychotic medication and thus keep an active vigil to prevent, treat and alleviate the adverse health effects due to ADRs. The establishment of an active Pharmacovigilance programme is hence an essential requirement to any health institution. This will pave way to improve the quality of patient care by ensuring safer use of drugs.

ACKNOWLEDGEMENT

The authors would like to thank Prof. M. Maqbool Dar, Head; Department of Institute of Mental Health and Neurosciences (IHMNS), Government Medical College Srinagar for allowing the present study to be conducted and Dr Inam ul Haq, Assistant professor; Department of PSM for his timely help in making statistical calculations and also giving suggestions from time to time.

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