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PATTERN OF ADVERSE DRUG REACTIONS OF ANTIPARKINSONIAN DRUGS IN A TERTIARY CARE INSTITUTE

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ABSTRACT

Aims: To assess the pattern of adverse drug reactions in patients receiving anti-parkinsonian drugs in tertiary care institute. **Materials and Methods:** A prospective, observational study was carried out from March 2018 to May 2019 at Department of Neuromedicine and Department of Pharmacology & Therapeutics, G.S.V.M. Medical College, after getting an approval from institutional ethical committee. Data was collected by analyzing OPD prescription slip, treatment charts and investigation reports. Adverse drug reaction reporting form provided by Indian Pharmacopeia Commission (IPC) was used for data collection. The ADRs were assessed for causality, severity and predictability. Total 45 patients were included in the study, out of which 31 patients came for follow-up. **Result:** During the study period, a total of 31 ADRs reported. Out of them 22(70.96%) were in males and 9(29.03%) were in females. Most of the ADRs were reported due to Levodopa+Carbidopa. Dizziness was most frequent ADR reported. Other ADRs observed were sedation, dry mouth, dyskinesia, drowsiness, blurred vision, discoloration of urine. **Conclusion:** Levodopa+Carbidopa is one of most widely used anti-parkinsonian drug and has a high potential to cause various effects in Parkinson's disease patient. Most of the reactions were of mild severity and were predictable.

KEYWORDS: Levodopa+ Carbidopa, Indian Pharmacopoeia Commission (IPC), Adverse drug reactions (ADRs).

INTRODUCTION

Adverse drug reactions (ADR) are common occurrences in a hospital setting, attributed to the severity and complexity of the disease process, the use of multiple drugs, drug interactions and possible negligence.[1] It is noteworthy that individuals who are diagnosed with neurological diseases are more susceptible to the occurrence of drug related problems, once medications indicated to manage most common conditions have complex dosage regimens, potential for interaction with other drugs and/or are associated with the occurrence of important adverse reactions.[2]

ADRs often go unnoticed due to failed ability of medical teams to recognize ADR or correlate precisely with biochemical, pathological or radiological abnormality.[3]

Adverse drug reactions (ADRs) are a major cause of morbidity and mortality, and leading cause of hospital admission. ADRs negatively affect patient's quality of life and confidence in medications, which consequently leads to worse treatment outcomes. A major limitation in ADR research is that we lack reliable data on the true prevalence and burden of ADRs. This relates to the fact that information about ADRs is traditionally captured through voluntary reporting systems, which vastly under-report the true number of ADRs, and do not capture information about the number of patients at risk, making assessment of the relative frequencies of different ADRs impossible.[4]

Parkinson's disease (PD) is a progressive neurological disorder characterised by a large number of motor and non-motor features that can impact on function to a variable degree. Dopamine concentrations are markedly decreased in the striatum of patients with PD.[5] More recently, genetic mutations, abnormal handling of misfolded proteins by the ubiquitin–proteasome and the autophagy–lysosomal systems, increased oxidative stress, mitochondrial dysfunction, inflammation and other pathogenic mechanisms have been identified as contributing factors in the death of dopaminergic and

non-dopaminergic cells in the brains of patients with PD.[6,7]

MATERIALS AND METHODS

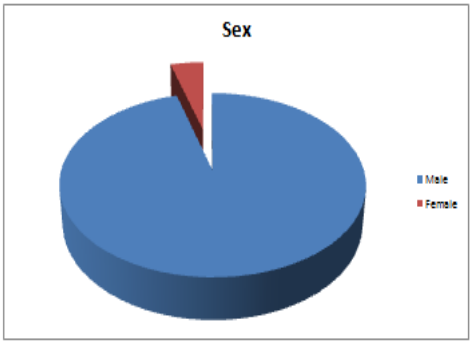
A prospective, observational, spontaneous reporting study approved by the Institutional Ethics Committee (IEC) was conducted from March 2018 to May 2019 among patients admitted in Neuromedicine department, GSVM medical college Kanpur. Patients belonging to either gender and of all ages, who were receiving treatment for Parkinson's disease under any standard regimen, were included for the study. The suspected ADR reporting form recommended by Indian Pharmacopoeia Commission (IPC) was used for collection of all the relevant information regarding the patient. Total 45 patients were included in the study, out of which 31 patients came for follow-up.

After obtaining informed consent from the patients attending Neurology outpatient department, the data regarding age, gender, detailed medical history, age of onset of disease and its duration, clinical signs and symptoms, drugs prescribed for Parkinson disease and other concomitant medications, co-morbid conditions and adverse drug reactions were collected by interacting with the patient and from patient's case record. Information was collected again from the study participants during their routine follow up visits to monitor the symptoms and adverse drug reaction (if any) occurring due to treatment. The patient's subjective response of relief or no relief of symptoms during the follow up visits was recorded. Adverse reactions (ADRs) to antiparkinson drugs and concomitant drugs, if any were noted. Causality assessment was done for them based on Naranjo's probability scale for the causality assessment of suspected ADRs. The data was collected, entered and a master table was prepared using MS excel software. The data was analyzed using appropriate statistical tools like percentage, chi-square test etc and conclusion drawn accordingly.

RESULTS

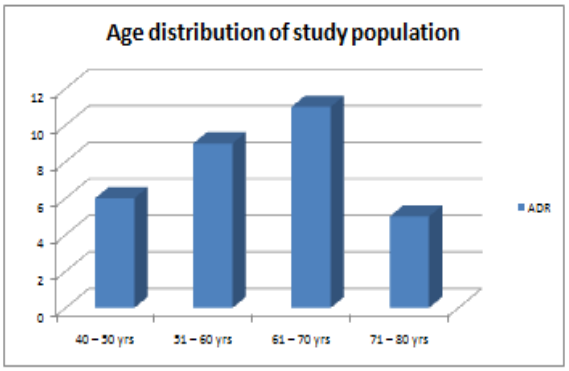
During the study period, a total of 31 ADRs were reported. In our study population, 22(70.96%) were males, 9 (29.03%) were females.

Male	Female
22 (70.96%)	9(29.03%)



All the patients were in the age group 40-80 years. Majority of patients were in the age group of 61 to 70 years 11(35.48%), followed by 9 (29.03%) in the age group of 51 to 60 years (fig2).

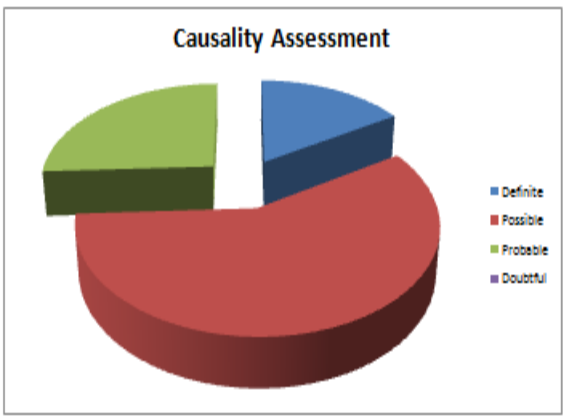
Age group	ADR	Percentage
40 – 50 yrs	6	19.35%
51-60 yrs	9	29.03%
61-70 yrs	11	35.48%
71-80 yrs	5	16.12%



Among the 31 patients who developed ADR, 10(32.25%) patients received levodopa/carbidopa, 8(25.80%) received trihexyphenidyl, 7 (22.58%) received pramipexole, 6(19.35%) received amantadine.

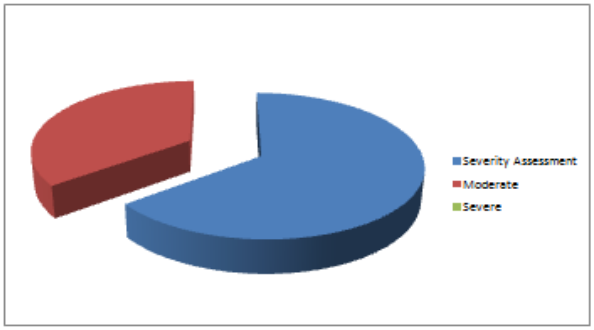
The ADRs observed in the patients were dizziness, sedation, drowsiness, dryness of mouth, dyskinesia, blurred vision, ankle edema, nausea, vomiting, discoloration of urine etc. Dizziness (45.16%) was the most common ADR followed by dryness of mouth (19.35%), sedation (12.90%), dyskinesia (6.45%). Naranjo's probability scale showed that 58.06% of the reactions belong to the category "possible," followed by category "probable," which includes 25.80% of reactions and "definite" category includes 16.12%(Figure 3).

Definite	probable	possible	Doubtful
16.12%	58.06%	25.80%	0



Modified Hartwig's severity scale showed that most of the reactions were of mild category (64.51%) followed by moderate (35.48%) category. No reactions found to be severe.

Mild	Moderate	Severe
64.51%	35.48%	0



Frequency of various ADRs due to Anti-parkinsonian drugs

S. No.	ADRs Observed	No. of ADRs Reported	Percentage %
1.	Dizziness	14	45.16
2.	Dry mouth	06	19.35
3.	Sedation	04	12.90
4.	Dyskinesia	02	6.45
5.	Drowsiness	01	3.22
6.	Blurred vision	01	3.22
7.	Ankle edema	01	3.22
8.	Nausea/vomiting	01	3.22
9.	Discoloration of urine	01	3.22

DISCUSSION

Parkinson disease (PD) generally requires therapy for prolonged periods often with multiple drugs; drug-related adverse effects often add to the existing morbidity. Parkinson's disease has important public health and social implications. In India, with an aging population and increased life expectancy, disease burden due to Parkinson's disease will be enormous.[8] This study was undertaken to analyze the pattern of ADRs among the patients receiving antiparkinsonian drugs in the Neurology department of a tertiary care hospital.

Levodopa is the most commonly used antiparkinsonian drug. In our study numbers of male patients (70.96%) were higher than female patients (29.03%) producing ADRs. Male predominance was also observed in the study by conducted by Shenoy et al. In our study prevalence of ADRs was most common in the age group 61-70 years (35.48%).This finding is similar to study conducted by Jena M et al.[9]

Majority of the ADRs were found to be due to levodopa+carbidopa (32.25%) followed by pramipexole (22.58%).This finding is similar to study conducted by Thaha F et al.[10] The most frequent ADR reported in our study were dizziness (45.16%) followed by dry mouth (19.35%), sedation (12.90%), dyskinesia (6.45%), drowsiness (3.22%) which is similar to study conducted by Thaha F et al. This is in contrast to study conducted by Jena M et al, in which the most common ADR was dyskinesia.

In the present study, causality assessment was done with Naranjo's Causality Assessment scale. Only 16.12% ADRs were definite. In maximum number of cases i.e. 58.06% extent of relationship between the suspected drug and ADR could be assigned as possible. In 25.80% cases drug was probably related to ADR. These findings are similar to study conducted by Thaha F et al in which majority of ADRs recorded belonged to possible category of ADRs.

Among mild ADRs type A ADR cases were 90% and type B ADR cases were 10%. There was no type C case among mild ADRs. Among moderate ADRs type A ADRs were 63.63% and type B ADRs were 36.36%. No severe case reported with anti-parkinsonian drugs. This is similar to study conducted by Thaha F et al.

Almost all ADRs were non- serious (96.77%). Only 3.22% ADRs were serious in nature and of type B.

On maximum occasions ADR cases were predictable 24 v/s not predictable 7.

Limitations

In this study the main limitation is restricted period of monitoring of ADRs, thus long term ADRs were not monitored. The lower frequency of ADRs could perhaps be explained by this fact.

CONCLUSION

The present study found that maximum ADR cases were found between 51-70 years age group. Gender was not found a risk factor for ADRs; however ADRs were more in males (70.96%) than females (29.03%). On severity scale majority of ADRs were of mild severity (64.51%).Moderate cases were 35.48%.No severe case reported. Only 3.22% reactions were serious in nature. Most of the ADRs were reported from Levodopa+Carbidopa (32.25%). Reactions were type A on maximum occasions (80.64%).

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