Journal of Cardiovascular Disease Research
ISSN:0975-3583,0976-2833 VOL14,ISSUE04,2023

ORIGINAL RESEARCH

Assessment Of Adverse Drug Reaction To Antiparkinson Agents In Idiopathic Parkinson Disease

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Received: 16 February, 2023 Accepted: 24 March, 2023

Abstract
Background: Parkinson's disease (PD) is characterized by both motor and non-motor manifestations. Symptoms correlate with the site of affection of susceptible nerve cells and spread of pathological process in the brain. The present study was conducted to assess adverse drug reaction to antiparkinson agents in idiopathic Parkinson disease.
Materials & Methods: 140 cases of adverse drug reaction to antiparkinson agents in idiopathic Parkinson disease of both genders were classified into certain, probable, possible, unlikely, unclassified and unclassifiable.
Results: Out of 140 subjects, males were 80 and females were 60. There were 65 patients with ADRs with Levodopa /Carbidopa, 17 with Amantadine, 40 with Pramipexole, 10 with Entacapone and 22 with Trihexyphenidyl. ADRs per drug was 1.5, 1.2, 1.1, 2.3 and 1.6 respectively. There were 63 cases of possible and 2 cases of unlikely ADRs with Levodopa /Carbidopa, 16 possible and 1 unlikely ADRs with Amantadine, 37 possible and 3 unlikely with Pramipexole, 9 possible and 1 unlikely with Entacapone and 20 possible and 2 unlikely ADRs with Trihexyphenidyl respectively. The difference was significant ($P< 0.05$).
Conclusion: Maximum incidence of ADRs was observed with levodopa+carbidopa followed by Pramipexole and Trihexyphenidyl hydrochloride.
Key words: Adverse drug reactions, Parkinson's disease, Carbidopa

Introduction

Parkinson's disease (PD) is characterized by both motor and non-motor manifestations. Symptoms correlate with the site of affection of susceptible nerve cells and spread of pathological process in the brain.[1]
There are several medications used to treat PD, including levodopa, dopamine agonists, MAO-B inhibitors, and COMT inhibitors. While these medications can be effective in managing PD symptoms, they can also cause adverse drug reactions (ADRs).[2] Some common ADRs associated with PD medications include dyskinesias: involuntary, uncontrolled movements of the face, arms, and legs, nausea and vomiting are side effects are most commonly associated with levodopa, hallucinations and delusions particularly with dopamine agonists, orthostatic hypotension, sleep disturbances including insomnia and daytime sleepiness, cognitive impairment: particularly with long-term use of anticholinergic drugs and behavioral changes including impulse control disorders such as pathological gambling, hyper sexuality, and binge eating.[3]
It is important for individuals with PD and their caregivers to be aware of these potential ADRs and to work closely with their healthcare providers to monitor and manage any side effects.[4] In some cases, adjustments to medication dosages or switching to alternative medications may be necessary to minimize the risk of ADRs.[5]
The choice of drug depends on whether it is tremor dominant or a kineto-rigid parkinsonism, age of onset and presence of comorbidities. Levodopa is considered the standard therapy for PD due to its ability to control motor symptoms.[6] The present study was conducted to assess adverse drug reaction to antiparkinson agents in idiopathic Parkinson disease.

Materials & Methods

The present study consisted of 140 cases of adverse drug reaction to antiparkinson agents in idiopathic Parkinson disease of both genders. The study was conducted in the Hind Institute of Medical Sciences,

Barabanki (U.P) after taking Institutional Ethical Committee approval. All gave their written consent to participate in the study.
Data such as name, age, gender etc. was recorded. ADRs were classified into certain, probable, possible, unlikely, unclassified and unclassifiable. Schumock and Thornton scale classified ADRs as definitely preventable, probably preventable and not preventable based on a set of questions for each level. Using modified Hartwig and Siegel scale, ADR was classified as mild, moderate or severe with various levels according to factors like requirement for change in treatment, duration of hospital stay and disability produced by adverse reactions. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I: Distribution of patients

Total- 140		
Gender	**Male**	**Female**
Number	80	60

Table I shows that out of 140 subjects, males were 80 and females were 60.

Table II: Incidence of ADRs on antiparkinsonian drugs

Drug	Number	ADRs per drug
Levodopa /Carbidopa	65	1.5
Amantadine	17	1.2
Pramipexole	40	1.1
Entacapone	10	2.3
Trihexyphenidyl	22	1.6

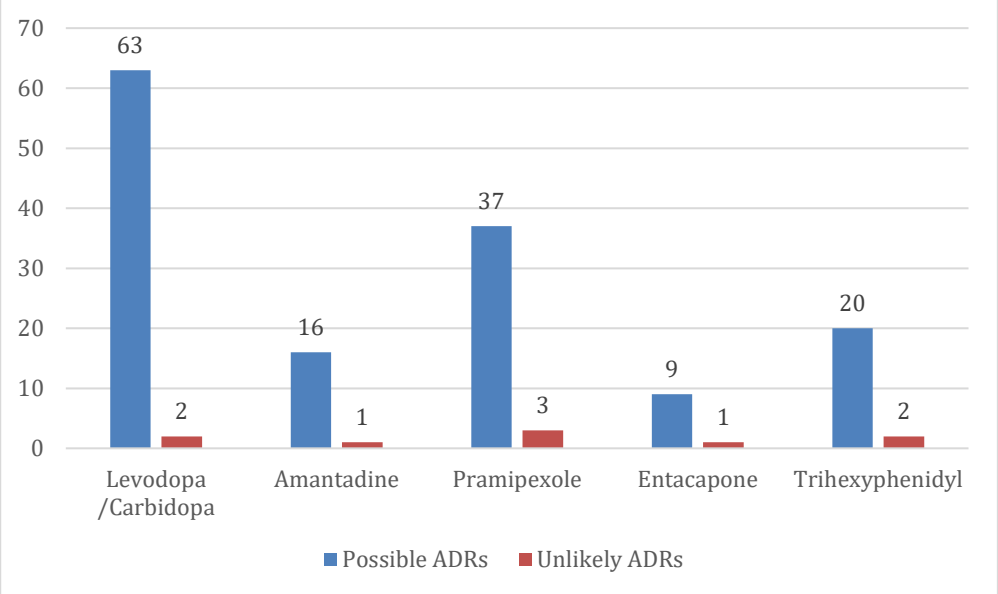
Table II shows that there were 65 patients with ADRs with Levodopa /Carbidopa, 17 with Amantadine, 40 with Pramipexole, 10 with Entacapone and 22 with Trihexyphenidyl. ADRs per drug was 1.5, 1.2, 1.1, 2.3 and 1.6 respectively.

Table III: Causality assessment

Drugs	Possible ADRs	Unlikely ADRs	P value
Levodopa /Carbidopa	63	2	0.05
Amantadine	16	1	
Pramipexole	37	3	
Entacapone	9	1	
Trihexyphenidyl	20	2	

Table III, graph I shows that there were 63 cases of possible and 2 cases of unlikely ADRs with Levodopa /Carbidopa, 16 possible and 2 unlikely ADRs with Amantadine, 37 possible and 3 unlikely with Pramipexole, 9 possible and 1 unlikely with Entacapone and 20 possible and 2 unlikely ADRs with Trihexyphenidyl respectively. The difference was significant (P< 0.05).

Graph I: **Causality assessment**



Discussion

Parkinson's disease (PD) is a chronic, progressive neurodegenerative disorder that affects the central nervous system, causing tremors, rigidity, bradykinesia, and postural instability.[7,8] Several medications are used to manage the symptoms of PD, including levodopa, dopamine agonists, MAO-B inhibitors, and COMT inhibitors.[9] However, these medications can also cause adverse drug reactions (ADRs), some of which are specific to PD.[10] It is important for PD patients and their caregivers to be aware of these potential ADRs and to report any unusual symptoms to their healthcare provider. A careful balance must be struck between managing the symptoms of PD and minimizing the risk of ADRs.[11] The present study was conducted to assess adverse drug reaction to antiparkinson agents in idiopathic Parkinson disease.

We found that out of 140 subjects, males were 80 and females were 60. Thaha et al[12] in their study found that ADRs were experienced in 87 patients (82.1%) out of 106 patients and most of these patients were on combination therapy (66%). No gender difference in distribution of ADRs was observed. The most common reactions were sedation, dizziness, dry mouth and fatigue. The drug usage was in the order of Pramipexole (58.4%), levodopa+carbidopa (55.7%), Trihexyphenidyl (28.3%), Entacapone (5.7%) and amantadine (7.5%). Majority of the ADRs were mild level 1 (71.1%). ADR was maximum with Entacapone. Majority of ADRs belonged to the causality possible ADR category. All the ADRs came under the definitely or probably preventable category.

We found that there were 65 patients with ADRs with Levodopa /Carbidopa, 17 with Amantadine, 40 with Pramipexole, 10 with Entacapone and 22 with Trihexyphenidyl. ADRs per drug was 1.5, 1.2, 1.1, 2.3 and 1.6 respectively. We found that there were 63 cases of possible and 2 cases of unlikely ADRs with Levodopa /Carbidopa, 16 possible and 2 unlikely ADRs with Amantadine, 37 possible and 3 unlikely with Pramipexole, 9 possible and 1 unlikely with Entacapone and 20 possible and 2 unlikely ADRs with Trihexyphenidyl respectively. Pinter et al[13] in their study seventy- eight patients of either sex with advanced Parkinson's disease and treatment complications such as motor fluctuations were enrolled and assigned to add on treatment with Pramipexole (n=34) versus placebo (n=44) to a previously stabilised antiparkinsonian medication (7 weeks dose titration interval, 4 weeks maintenance period). The primary end point of efficacy was the change from baseline in the total score of the unified Parkinson's disease rating scale (UPDRS) in the on "period" (2 hours after intake of study medication). Safety and tolerability were assessed on the basis of adverse events, vital signs, laboratory measurements, and ECG recordings. There was a significant improvement of the Pramipexole group in UPDRS total scores, sub scores part II, III (activities of daily living and motor examination), and IV (complications of therapy). Mean UPDRS total score decreased by 37.3% under Pramipexole compared with 12.2% under placebo ($p<0.001$). Patients under Pramipexole reported an overall reduction in "off" periods of 12%--resulting in 1.7 more hours "on" time a day--compared with an increase in "off" periods of 2% under placebo. There were no unexpected safety results. The adverse event profile disclosed a high tolerability. The most important adverse events under Pramipexole were fatigue, dyskinesia, and vivid dreams.

The limitation the study is small sample size.

Conclusion

Authors found that maximum incidence of ADRs was observed with levodopa+ carbidopa followed by Pramipexole and Trihexyphenidyl hydrochloride.

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