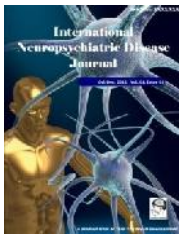

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Pharmacotherapy in Patients with Drug-induced Parkinsonism: A Case Series

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Short Research Article

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ABSTRACT

Drug-induced Parkinsonism develops in a number of patients with schizophrenia or schizo-affective disorders. Conventionally, anti-parkinsonism drugs, such as levodopa and dopamine agonists have been avoided due to their potential to result in an increase in psychotic symptoms, hallucinations and behavioral disturbance.

We present ten cases series of drug-induced Parkinsonism in whom a trial of anti-parkinsonism medications administered commenced with good effect. In particular, there was no deterioration in psychotic symptoms. A number of cases had asymmetrical signs, suggesting that these patients had a component of idiopathic Parkinson's disease in addition to long standing drug-induced Parkinsonism.

The diagnosis of idiopathic Parkinson's disease on clinical grounds is often difficult in patients who have been on or are currently on an anti-psychotic drug. A trial of levodopa or a dopamine agonist is worth considering, albeit cautiously. In our series of cases a relapse or exacerbation of psychotic symptoms did not occur after commencing levodopa and dopamine agonists.

Keywords: Drug-induced parkinsonism; anti-psychotic medication.

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1. INTRODUCTION

Drug induced Parkinsonism is the second most common cause of Parkinsonism in older people after idiopathic Parkinson's disease (PD) [1]. Risk factors for developing drug-induced Parkinsonism include older age, female gender, dose and duration of treatment and the type of agent used [2]. In most patients, Parkinsonism is reversible upon stopping the offending drug, though it may take several months to resolve fully, but in some patients it may persist [2]. If symptoms persist or are disabling, conventional teaching is to use beztropine (Cogentin) to treat symptoms.

Specific parkinsonism drugs, such as levodopa and dopamine agonists have been generally avoided due to their potential to result in an increase in psychotic symptoms, hallucinations and behavioral disturbance.

Antipsychotics have been used for many years to treat psychiatric and neurological disorders. Their effectiveness is often associated with a high incidence of side effects, especially neuroleptic-induced movement disorders or extra pyramidal side effects (EPS) resulting in drug-induced Parkinsonism [3].

EPS can be categorised as acute (dystonia, akathisia and parkinsonism) and tardive (tardive dyskinesia and tardive dystonia) syndromes. They are thought to have a significant impact on subjective tolerability and adherence with antipsychotic therapy in addition to impacting function. Unlike conventional antipsychotic medications, atypical antipsychotics have a significantly diminished risk of inducing acute EPS at recommended dose ranges. Nevertheless, EPS with these drugs can occur, particularly when prescribed at high doses [4].

2. PRESENTATION OF CASES

We present ten cases of presumed drug- induced Parkinsonism from patients that were referred to the author working who works in both a regional rehabilitation unit and a dedicated Parkinson’s disease clinic.

Two illustrative cases are discussed below, with all cases being summarised in Table 1.

2.1 Case 1

Mr RC, a seventy year old man was admitted to a rehabilitation ward after a surgical admission for bowel perforation due to splenic flexure cancer. He had a history of schizoaffective disorder for over forty years and had been on a number of anti-psychotic agents, including Risperidone and Haloperidol. He ceased these about two years and since then has been Olanzapine 7.5mg daily.

During his rehabilitation admission, he was noted to be Parkinsonian with a short shuffling gait, bradykinesia of fine finger movements, upper limb rigidity and a marked resting tremor which was interfering with his function. Prior to his admission, it was thought that these symptoms were extrapyramidal side effects of long standing anti-psychotic medications, as he had had them for more than 5 years.

Table 1. Summary of cases

Patient	Age	Sex	Diagnosis	Years since Diagnosis	Years of Parkinsonism	Medication implicated	Anti-PD Rx	Parkinsonian signs	Response
RC	70	M	Schizo-affective disorder	40	0.5	Risperidone, Haloperidol previously; currently olanzapine	Madopar 100/25 tds	Bilateral tremor, cogwheel rigidity, bradykinesia	Tremor resolved, improved bradykinesia and tone
KR	62	F	Schizo-affective	30	1	Quetiapine, Flupenthixol, Apipiprazole	Pramipexole 125 µg tds	Tremor, cogwheel rigidity, slow gait,10MWT 14sec	Tremor resolved, 10MWT 11sec
BT	79	F	Depression with psychosis	20	2	Olanzapine, Venlafaxine	Sinemet 100/25 tds then Cabergoline 2mg nocte	Left sided tremor, bradykinesia, rigidity	No response to sinemet, but decrease tremor and tone with cabergoline
CA	95	F	Meniere's Disease	5	0.5	Prochlorperazine	Sinemet 100/25 tds (plus cessation stemetil)	Bilateral hand tremor, rigidity, bradykinesia, slow gait	Improved hand tremor, decreased tone
PMc	61	F	Depression with psychosis	10	1	Chlorpromazine	Madopar 100/25 tds	Right hand tremor, bradykinesia, 10MWT 26 sec;	10MWT 18 sec, bradykinesia no change
DN	56	F	Depression	5	3	Haloperidol	Sinemet 250/25 tds	Tremor both hands, rigidity, slow gait	Improved gait, tone and tremor. Ongoing bradykinesia
KJ	73	M	Paranoid schizophrenia	2	1.5	Olanzapine	Sinemet 100/25 tds	Bradykinesia, slow and shuffling gait; increased tone	Tone decreased, reduced shuffling
ES	57	F	Depression with psychosis	5	2	Quetiapine	Madopar 200/50 tds	Increased tone, cogwheel rigidity and bradykinesia	Tone normal, no evidence of bradykinesia
AC	76	M	Depression with psychosis	2	0.5	Olanzapine	Sinemet 100/25 tds	Tremor, rigidity. 10MWT 11secs	Tremor improved 10MWT 9 secs
MD	77	F	Psychosis	15	1	Risperidone, on-going	Madopar 200/50tds	Tremor, bradykinesia, shuffling gait, cogwheel rigidity	Improved tremor and gait

He however had some asymmetry of signs and he was commenced on trial of levodopa in the form of Madopar 100/25 half a tablet twice a day, which was increased over a 2 week period to 1 tablet 3 times per day. This resulted in a marked improvement in his mobility and tremor. This medication did not result in an exacerbation of his psychotic symptoms. He was subsequently discharged home, being independent with all his activities of daily living and mobilising independently without aids.

On review 2 weeks later, he had reduced facial expression but loud speech. His gait was wide based but steady with reduced arm swing bilaterally. His 10 metre walk test was good taking only 10 seconds. Glabellar tap was positive. He still had tremor of both hands at rest, but this was not as prominent as before and bradykinesia of fine finger movements.

Given Mr RC's good response to a low dose of Madopar, it is likely he had idiopathic Parkinson's disease with long standing drug-induced Parkinsonism.

2.2 Case 2

Mrs KR, a sixty two year old lady with a thirty year history of a chronic schizo-affective disorder. She had been on Quetiapine and Flupenthixol and recently had been commenced on Aripiprazole. She presented with a twelve month history of right sided rest tremor, deterioration in her walking, frequent falls and soft speech.

On examination, she had reduced facial expression and blink rate. Glabellar tap was positive. Her speech was soft and monotonous. She had rest tremor of her right hand, which increased on concentration. Her tone was increased in the upper limbs, with cog-wheeling on reinforcement. She had bradykinesia of gross and fine finger movements, worse on the right. Her gait was slow and shuffling with a slightly forward flexed postured and reduced arm swing bilaterally. She had marked retropulsion. Her 10 metre walk test was slow taking 14 seconds and her Timed Get up and Go Test took 19 seconds.

In the past, she was given a trial of levodopa, but this resulted in an increase in psychosis. Given this, Pramipexole at a low dose of 125 micrograms at night was commenced. This results in a marked improvement in her Parkinsonism symptoms. The dose was increased to 125 micrograms three times a day with resolution of tremor and an improvement in her walking. Her Timed Get up and Go Test improved from 19 to 16 seconds and her 10 mete walk test from 14 to 11 seconds.

Given her good response to a low dose of Pramipexole and unilaterally of signs, it is likely she has idiopathic Parkinson's disease with underlying long standing drug-induced Parkinsonism.

3. DISCUSSION

The number of patients with schizophrenia who develop idiopathic PD is difficult to determine due to the fact that all neuroleptics cause parkinsonism, so that the diagnosis of idiopathic PD on clinical grounds is often difficult in a patient who has been on or is currently on an anti-psychotic drug [5].

It is a widely-held concept that the best option for management of drug-induced Parkinsonism is cessation of the offending drug. This is not always possible, and certainly

not always effective. Dopaminergic drugs are associated with a greater incidence of side effects, such as hallucinations in patients who have not had a documented psychotic disorder but there are very limited data on levodopa's role in drug-induced Parkinsonism management.

In 1985, a single subject experimental trial of levodopa in a patient with neuroleptic-nonresponsive schizophrenia with a longstanding negative syndrome showed an improvement in attention, abstract thinking, passive withdrawal, psychomotor retardation, and a cluster of seven negative parameters, while positive symptoms were unaffected [6].

There is no other data to suggest that levodopa is implicated in worsening psychosis in patients with an established history of psychotic disorder.

4. CONCLUSION

In this case series, we have shown some positive outcomes after commencing levodopa and dopamine agonists in patients with drug induced Parkinsonism, without any relapses or exacerbations of psychotic symptoms. Most of our patients had been on anti-psychotic medications for a number of years, up to forty years, with symptoms of Parkinsonism developing 6-24 months prior to presentation.

Asymmetrical signs suggest the development of idiopathic Parkinson’s disease in addition to long standing drug-induced Parkinsonism.

CONSENT

All authors declare that written informed consent was obtained from the patients for publication of their case reports.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

There are no competing interests that need to be declared. The authors do not have any financial and personal relationships with people or organizations that could inappropriately influence (bias) their work.

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