Original article

Effect of Trihexiphenidyl and Procyclidine for the management of resting tremor

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Abstract

Parkinson's disease is the main etiology of resting tremor but may also rarely occur in Essential Tremor, Multiple System Atrophy & Progressive Suprneuclear Palsy. Levodopa improves bradykinesia, rigidity and other commonly associated symptoms. When resting tremor is the predominant presenting symptom of Parkinson's disease or when tremor persists despite adequate control of other parkinsonian symptoms with low dosages of levodopa, an anticholinergic agent such as trihexyphenidyl or Procyclidine may be the treatment of choice. This prospective interventional study was carried out in the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka from March, 2014 to June, 2014 with the intention to outline effectiveness, similarities and differences between Trihexyphenidyl and Procyclidine in alleviating resting tremor. For Parkinson's disease, patients presenting with predominant tremor but minimal bradykinesia and rigidity were purposively selected for the study. Resting tremor was assessed by unified parkinson's disease rating scale (UPDRS). A total of 30 consecutive patients, both male and female, having resting tremor due to different etiology & attending both indoor and outpatient department of Neurology, BSMMU were randomized to receive either Trihexyphenidyl or Procyclidine for two weeks. For most of the patients (93%) resting tremor were due to Parkinson's disease and only 7% were due to Essential tremor. In case of Trihexiphenidyl, constancy and amplitude of resting tremor were improved in 60% and 80% respectively. In case of Procyclidine, constancy and amplitude of resting tremor were imoroved 87% and 67% respectively. The difference of improvement between Trihexiphenidyl group and Procyclidine group was not statistically significant.

Key words: Resting tremor, Parkinson's disease, Trihexyphenidyl, Procyclidine

Introduction

Tremor is the involuntary, rhythmic oscillation of reciprocally innervated, antagonistic muscle groups, causing movement of a body part about a fixed plane in space.[1,2] Tremor is primarily classified on the basis of when it occurs, either with a certain posture, at rest or during action. A resting tremor occurs when the patient is attempting to maintain the position of a body part at rest (e.g., when the patient's hands exhibit a tremor as they are resting in the patient's lap). Postural tremor is observed when the patient tries to maintain a posture against gravity, such as holding the arms out in front of the body. An action tremor (kinetic or intention tremor) occurs during movement of the affected body part from one point to another. A task-specific tremor occurs only when the patient begins to perform a highly skilled activity, such as writing or speaking.[2]

The tremor in Parkinson's Disease (PD) occurs at rest and is characterized by a frequency of 4 to 6 Hz and medium amplitude. It is classically referred to as a "pill rolling" tremor of the hands but can also affect the head, trunk, jaw and lips.[2,3]

Resting tremor mainly occurs in Parkinson's Disease. It may also occur in multiple system atrophy (MSA), progressive supranuclear palsy (PSP) and essential tremor. These disorders are mostly age related excepting essential tremor, which occur anywhere between the second and sixth decades of life, occur sporadically or can be inherited.[4] The few incidence studies that have been published have shown that the rate of Parkinson's disease rises sharply after the fifth decade, although whether there is a progressive rise in late life or a decline in incidence remains controversial.[5]

The etiology of isolated resting tremor is still obscure. Some patients initially have a parkinsonian resting tremor without overt signs of rigidity or bradykinesia.[6,7] This so-called "monosymptomatic resting tremor" (mRT) was

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defined by the Consensus Statement of the Movement Disorder Society on Tremor[8] with the following criteria: (i) pure or predominant resting tremor; (ii) no signs of bradykinesia, rigidity, or problems with stance-stability sufficient to diagnose PD; and (iii) tremor duration of minimum 2 years.[9]

Dopamine replacement therapy by means of levodopa clearly revolutionized the treatment of Parkinson's disease.[4] In addition to modulating the tremor associated with Parkinson's disease, levodopa improves bradykinesia, rigidity and other commonly associated symptoms. When tremor (resting) is the predominant presenting symptom of Parkinson's disease or when tremor persists despite adequate control of other parkinsonian symptoms with low dosages of levodopa, an anticholinergic agent such as trihexyphenidyl[4] or Procyclidine may be the treatment of choice.

The anticholinergic drugs used in the treatment of parkinson's disease, despite their adjunct role, are nevertheless important agents as they provide an alternate mechanism of action which may alleviate some of the troublesome symptoms of the disease, in particular the involuntary resting tremor.[10]

Anticholinergic agents can be divided into those occurring in nature and those that are synthetically derived. Before an understanding of the pharmacology of parkinson's disease, all naturally occurring "medications" were tested in patients with parkinsonism, but only those agents containing the belladonna alkaloids were effective. Atropine and scopolamine, both naturally occurring belladonna alkaloids, had their effect by central atropine-acetylcholine antagonism. Before the 1950s atropine and scopolamine (the natural belladonna alkaloids.) were primarily used in Parkinson's disease. In the 1950s synthetic anticholinergic agents were introduced which included Benztropine, Trihexyphenidyl, Procyclidine , Biperiden and Ethopropazine.[11]

The aim of this study was to outline effectiveness, similarities and differences between Trihexyphenidyl and Procyclidine to alleviate resting tremor.

Methods

This was a prospective interventional study. This study was carried out in the department of Neurology, Bangabandhu Sheikh Mujib Medical University, Dhaka. The study period was from March, 2014 to June, 2014. A total of 30 consecutive patients, both male and female, having resting tremor due to different etiology attending the outpatient department of Neurology, BSMMU were included in the study.

For Parkinson's disease, patient presenting with predominant tremor, but minimal bradykinesia and rigidity were purposively selected for the study.

A resting tremor was defined as 'coarse, rhythmic tremor usually confined to hands and forearms, occurring when the patient is attempting to maintain the position of a body part at rest with relaxed limbs and disappears with active limb movements.[1]

Thirty patients with resting tremor were randomly divided in to two groups with 15 patients in each group. One group received Procyclidine, 5 mg, twice daily for two weeks and the other group received Trihexiphenidyl 2 mg thrice daily for two weeks. Among 30 patients suffering from resting tremor, the underlying diagnosis was Parkinson's disease in 28 patients. Two patients were suffering from essential tremor.

For the rest two patients, the underlying diagnosis was essential tremor. They had previously been treated with beta blocker but with no improvement.

Resting tremor was assessed by unified parkinson's disease rating scale (UPDRS).[12] Tremor along with activity of daily living were assessed at the onset during inclusion of the patients in the study & noted in a structured data sheet. After completion of two weeks of treatment either with Procyclidine or Trihexiphenidyl resting tremor was again assessed by unified parkinson's disease rating scale. Improvement was assessed in both the groups & noted in a structured data sheet.

Patients were enquired about occurrence of any adverse effect, either with Procyclidine or Trihexiphenidyl, during the study period was also noticed.

Informed consent from each patient was obtained prior to the study. Ethical issues were dealt with appropriately. Statistical analyses of the results were done by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-17). Comparison between the groups was done by two sample proportion test. Overall improvement was assessed by chi-square test.

Results

Total 30 patients having resting tremor were included in this study. Mean age was 53.8 years and all patients were within 25 to 88 years age range. Male patients were 22 in number and 7 patients were female. (Table-I)

Table -I: Age distribution

Age	Number of patient
21 -30	2
31 -40	4
41 -50	8
51 -60	4
61 -70	10
71 -80	1
>80	1
Total	30

Duration of illness was less than 2 years in 16 patients and more than 2 years in 14 patients. For most of the patients (93%) resting tremor were due to Parkinson's disease and only 7% were due to Essential tremor (Table-II).

Table-II: Causes of resting tremor

Cause of resting tremor	Number of patient
Parkinson's disease	28
Essential tremor	2
Total	30

About 30% patients were facing problem in performing daily activities due to resting tremor (Table-III)

Table-III: Problem in performing daily activities

Problem in performing daily activities	Number of patient
Yes	9 (30%)
No	21 (70%)
Total	30 (100%)

Among 30 patients, 15 patients were treated with Trihexiphenidyl and 15 patients were treated with Procyclidine. In case of Trihexiphenidyl constancy and amplitude of resting tremor were improved in 60% and 80% respectively. In case of Procyclidine constancy and amplitude of resting tremor were imoroved 87% and 67% respectively. The difference of improvement between Trihexiphenidyl group and Procyclidine group was not statistically significant ($p > .05$). (Table - IV & Table – V).

Table-IV: Improvement of constancy of resting tremor

Name of drug	Number of patient	Improvement
Trihexiphenidyl	15	9 (60%)
Procyclidine	15	13 (87%)
Total	30	22 (73%)

Table-V: Improvement of amplitude of resting tremor after treatment

Name of drug	Number of patient treated with drug	Improvement after treatment
Trihexiphenidyl	5	12 (80%)
Procyclidine	15	10 (67%)
Total	30	22 (73%)

Discussion

Thirty consecutive patients of resting tremor with a mean age of 53.8 years, having 15 patients in each group, were treated either with Procyclidine or Trihexiphenidyl for two weeks.

Cause of resting tremor is Parkinson's disease in most of the cases. Essential tremor and other causes are rare.[1,13] In this study, although total number of patients was small, Parkinson's disease came out to be the etiology of resting tremor in 90% cases.

Tremor, rigidity and bradykinesia are the common manifestations of Parkinson's disease.[1,3] Trihexiphenidyl and Procyclidine can improve tremor in Parkinson's disease, but is ineffective in controlling the other cardinal motor features i.e. rigidity and bradykinesia of PD.[13] Parkinson's disease patients presenting predominantly with tremor, but with minimal/no bradykinesia and rigidity were purposively selected for the study & randomized to receive either Trihexiphenidyl or Procyclidine.

All of the patients had troublesome resting tremor and among them 70% had problems in performing daily activities. After two weeks treatment with either Trihexiphenidyl or Procyclidine, there was significant improvement in 73% of the study subjects in both the groups as revealed by improvement of unified parkinson's disease rating scale (UPDRS).[12]

For the constancy of resting tremor, 87% in Procyclidine group in comparison to 60% in Trihexiphenidyl group. But the difference of improvement between the groups was not statistically significant ($p > .05$).

Regarding the amplitude of resting tremor, 80% patients showed improvement in Trihexiphenidyl group in comparison to 67% in Procyclidine group. Again the difference of improvement between the groups was not statistically significant ($p > .05$).

Sedation is the main side effect in addition to anticholinergic symptoms such as blurred vision, dry mouth and urinary retention, and is usually the limiting factor in the use of this agent.[13] But no significant adverse effect was observed in any of the patients during the study period.

It was evident from the study that, anti-muscarinic medications i.e. Trihexyphenidyl & Procyclidine have a role in the management of resting tremor in Parkinson's disease, particularly for those presenting predominantly with tremor with minimal/no bradykinesia and rigidity. Further large scale studies are required to evaluate the role of Trihexyphenidyl & Procyclidine in Parkinson's patients with tremor, rigidity and bradykinesia who are intolerant to dopaminergic drugs or in whom these drugs have failed to control their tremor.

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