EFFICACY OF PRANAYAMIC BREATHING ON COGNITION AND BALANCE IN PARKINSON’S PATIENTS

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ABSTRACT

Purpose: To investigate the effects of Pranayamic breathing on cognition and balance in Parkinson’s patients.

Introduction: Recent researches have shown that pranayamic breathing shifts autonomic nervous system away from sympathetic dominance. Other physical disorders that are caused by improper mental health have excellent cure through pranayamic breathing exercises.

Materials and Methods: Twenty Parkinson’s patients between 50-80 years of age and stage 3 of Hoehn & Yahr scale were selected purposively and were randomly divided into two groups. Group A received pranayamic breathing with conventional physiotherapy for 4 days a week for 4 weeks. Group B received conventional physiotherapy. Mini Mental State Examination (MMSE), Timed Get Up Go (TUG), Tinetti’s Performance Oriented Mobility Assessment (POMA) were used to assess cognition and balance.

Analysis: To compare values of MMSE, TUG test and POMA at the end of trial in each group, repeated measure ANOVA with Bonferroni test was used. To compare those differences between two groups univariate ANOVA was used. A level of significance was p<0.05.

Results: Comparison of MMSE and POMA score was found to be statistically significant in group A (p<0.05). Comparison of TUG score at the end of trial in each group was found to be statistically insignificant (p>0.05). Comparison of MMSE, TUG and POMA score at the end of week 4 in both group was found to statistically significant (p<0.05).

Conclusion: This study concluded, pranayamic breathing with conventional physiotherapy has shown improvement in cognition and balance in Parkinson’s patients.

Implications: Pranayamic breathing can be used along with conventional physiotherapy to improve cognition and balance in Parkinson’s patients.

KEY WORDS: Pranayama, Parkinson’s disease, Balance, Cognition.

INTRODUCTION

Parkinson’s disease (PD) is a chronic, progressive disease of the nervous system characterized by the cardinal features of rigidity, bradykinesia, tremor, and postural instability [1].

It is one of the commonest neurodegenerative diseases that affect more than 2 percent of population older than 65 years of age and incidence increases with age. The aetiology of Parkinson’s disease remains unknown and the consensus is
that it is multifactorial [2,3].

Sullivan and colleagues [4] suggested that memory deficits were directly related to overall disease severity, with mildly impaired patients showing no decrements in memory performance, while Goldman and colleagues [5] found increasing memory deficit with increasing disease severity, including deficits among those very mildly affected [6]. A brief screen of cognitive function can be obtained using Mini Mental Status Exam (MMSE) [1]. Cognitive impairment in the absence of frank dementia, typically called Mild Cognitive Impairment (MCI), occurs frequently in PD, even among those newly diagnosed [7-11]. Joe Nocera and colleagues gave evidence that motor function, specifically postural control may be negatively influenced by cognitive dysfunction in PD [12].

The upright postures like sitting; standing or walking requires proper functioning of central balancing mechanisms. Afferent impulses of widespread origins, including signals from the periphery, play important role in eliciting and guiding responses, while efferent pathways carry messages to the muscles for the execution of the balancing act. Damage to any one of the central mechanisms or interruption anywhere along the sensory or motor pathway may lead to an inability to maintain body's COG within the base of support, but, no one system direct specifies the position of COG as stated by Brunnstrom (1970) [13].

There are a number of clinical balance tests that examine functional related to balance. The Timed Up and Go Test [14] is particularly valuable instrument for patients with PD because it includes tasks that are typically problematic. Tinetti’s Performance Oriented Mobility Assessment (POMA) [15] includes both static and dynamic balance items, organized into two subsets of balance (nine items) and gait (six items) [1]. Pranayamic breathing, defined as a manipulation of breath movement, has been shown to contribute to a physiologic response characterized by the presence of decreased oxygen consumption, decreased heart rate, and decreased blood pressure, as well as increased theta wave amplitude in EEG recordings, increased parasympathetic activity accompanied by the experience of alertness and reinvigoration [16]. Ravinder Jerath et al gave the hypothesis that voluntary slow deep breathing functionally resets the autonomic nervous system through stretch-induced inhibitory signals and hyperpolarisation currents propagated through both neural and non-neural tissue which synchronizes neural elements in the heart, lings, limbic system and cortex.

Pranayama has been researched mostly for its beneficial applications in treatment of cardiovascular diseases such as hypertension [17-19], pulmonary disease such as asthma [20-22], autonomic nervous system imbalances [23], and psycho logic or stress related disorders [19,24]. Recent studies have shown that motor symptoms are not influenced by dopaminergic stimulation, including postural instability, have been associated with accelerated cognitive decline [25,26]. It is possible that cognition plays a vital role on enhancing balance performance.

Based upon the reported findings, the primary objective of this study is to investigate whether pranayamic breathing will improve the cognition and balance in Parkinson’s. This study will also add to the knowledge of physiotherapy by concentrating on the respiratory aspect to enhance cognition as well along with motor component to improve balance in Parkinson’s patients.

MATERIAL AND METHODS

Participants: A total of 20 subjects clinically diagnosed with Parkinson’s disease participated in this study. Subjects were recruited from Parkinson’s Mitra Mandal Society, Pune. All subjects met the following inclusion criteria: (1) Hoehn and Yahr stage III; (2) Minimum score of 24 on MMSE scale of cognition; (3) Both males and females within the age group of 50-80 years; (4) Subjects with score of 19 and above of POMA scale. Subjects were excluded with following exclusion criteria: (1) Subjects diagnosed with Parkinson’s plus syndrome like Progressive supranuclear palsy, shy dragger syndrome; (2) subjects diagnosed with visual and auditory impairments; (3) History of any other neurological disease, musculoskeletal impairment that will add up to balance impairment like CVA, TIA, Vestibular disorder, joint replacement etc; (4) Subjects with uncontrolled Diabetes mellitus.
subjects were required to sign an written informed consent document approved by the ethical committee at Dr. D. Y. Patil Vidyapeeth, Padmashree Dr. D. Y. Patil College of Physiotherapy, Pimpri, Pune.

**Study Design:** This study was an RCT, taking place during a month period (fig 1). Recruitment began on 20th of September 2012, and the study was on 3rd of November 2012. Twenty subjects were randomly allocated to two groups by the investigator who was involved in data collection, treatment implication, and data analysis. 46 Parkinson subjects were targeted, out of which 20 were included for the study purpose. Subjects in group A (experimental group) received Pranayamic breathing along with conventional physiotherapy treatment. While subjects in group B (control group) received conventional physiotherapy. Both the groups received this protocol for a period of one month, with a frequency of 4 times in a week. Baseline assessments were done after randomization, at the start of the protocol, at the end of week 1, week 2 and week 4. For each subject, all assessment sessions were performed at the same time of day, and all tests were performed in the same order, to control for variations in performance because of medication cycle. All assessments were conducted in the "on" state for those subjects experiencing motor fluctuations. All subjects were required to take their medications at the same time of day for all assessment sessions.

**Fig. 1:** Study design and flow of the participants through each stages of the trial.

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**Assessments:** Mini Mental State Examination (MMSE) [1], Tinetti Performance-Oriented Mobility Assessment (POMA) [14], Timed Get-up and Go Test [15] were the outcome measures taken at baseline, at the end of week 1, week 2 and week 4.

**Rehabilitation Program:** The rehabilitation program consisted of 16 sessions, each 1 hour long, 4 times weekly for 4 weeks. All treatment sessions occurred at the same time of day on the same 4 days of the week throughout the study. Intervention was conducted individually and not in a group format. The physical therapist was involved in performing the intervention as well as conducting the assessments. Pranayamic breathing given to the subjects was of two types, Alternate Nostril Breathing (ANB) and Brahmari Pranayama of which few trial sessions were given before starting the treatment protocol. Subjects were given Jacobson’s relaxation technique to induce relaxation for 5min and commands were given to "let go". Then therapists command were given for alternate nostril breathing, which was continued for a period of 20 minutes. Rest period of few minutes were given to the subjects after every 5 minutes of alternate nostril breathing. Subjects were asked to perform Brahmari Pranayama (10min) in erect sitting posture for a repetition of 3 to 21 times as per their comfort level while keeping their mouth closed. Conventional therapy was incorporated by both the groups as baseline treatment. Conventional therapy (25 min) consisted of gentle rocking movements, gentle range of motion for shoulder joint, thoracic mobilization, dissociated movements, prone on elbows, pelvic bridging, gentle active-assisted movement of knee and ankle, balance exercise in standing with chair support, reaching activities in sitting and standing, gentle perturbations, ground walking. There is evidence in the literature to support each of the components contained in the intervention [27,1].

**Statistical analysis:** Differences in Data were analysed using the SPSS Professional Statistics, version 15.0 software, for Windows. Repeated measures ANOVA was used to compare the improvement of MMSE, TUG and POMA score over 4 weeks period in each group. If a significant effect for cognition and balance was found, the
following post hoc analysis was done using Bonferroni test. One way analysis of variance (ANOVA) with repeated measures was used to compare those differences between two groups at baseline, week 1, week 2 and week 4. An independent t-test was used to compare the age difference between two groups. A level of significance was taken at p<0.05.

RESULTS

In this study 20 Parkinson subjects were taken. In group A, 10 patients were treated with pranayamic breathing and conventional physiotherapy and in group B, 10 patients were treated with conventional therapy. At the end of 1st, 2nd and 4th week, cognition was reassessed by Mini Mental State Examination, balance was reassessed by Time get up and go test and Tinetti’s Performance-Oriented Mobility Assessment. To compare the value of MMSE, TUG test and POMA at the end of trial in each group, repeated measure ANOVA was used. Further post hoc analysis was done using Bonferroni test to see differences between each level in each group. To compare those differences between two groups univariate ANOVA was used. To compare the age between two groups t-test was used. A level of significance was p<0.05. Analysis of within group comparison of MMSE, TUG, POMA score and Post hoc analysis (Bonferroni test) was performed (Table 1a, 1b).

Comparison of MMSE score from baseline to at the end of 4th week was found to be statistically significant in group A (p<0.05). Further post hoc analysis using bonferroni test revealed that there was insignificant difference found between baseline and week 2, week 1 and week 2 (p>0.05). However, there were significant differences noted between baseline and week 4, week 1 and week 4, week 2 and week 4 (p<0.05). Comparison of TUG test from baseline to at the end of 4th week was found to be statistically significant in group B (p<0.05). Comparison of TUG score from baseline to at the end of 4th week was found to be statistically significant in group A (p>0.05). However, there were significant differences noted between week 2 and week 4 (p<0.05). Comparison of TUG score from baseline to at the end of 4th week was found to be statistically insignificant in group B (p>0.05).

In table 2, the baseline, week 1, week 2 and week 4 parameters (MMSE, TUG, POMA) are presented and between group comparisons were done for group A and group B. Comparison of MMSE score at baseline was found to be statistically significant in group B (p<0.05). Further post hoc analysis using bonferroni test revealed that there was insignificant difference found between baseline and week 2,baseline and week 4,week 1 and week 2, week 1 and week 4 (p>0.05). However, there was significant differences noted between week 2 and week 4 (p<0.05). Comparison of TUG score from baseline to at the end of 4th week was found to be statistically insignificant between Group A and Group B (p>0.05). It remained insignificant at the end of week 1 (p>0.05). At the end of week 2 and week 4 it was found to be significant between group A and group B (p<0.05). Comparison of TUG score at baseline, week 1, week 2 and week 4 was found to be statistically significant between Group A and Group B (p<0.05). Comparison of POMA score at baseline was found

Table 1a: Within group comparison of MMSE, TUG, POMA.

<table>
<thead>
<tr>
<th></th>
<th>Baseline Mean ±SD</th>
<th>Week 1 Mean ±SD</th>
<th>Week 2 Mean ±SD</th>
<th>Week 4 Mean ±SD</th>
<th>Repeated Measures ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group A</td>
<td>Group B</td>
<td>Group A</td>
<td>Group B</td>
<td></td>
</tr>
<tr>
<td>MMSE</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>27.90±1.19</td>
<td>27.90±1.19</td>
<td>28.90±1.70</td>
<td>29.90±0.31</td>
<td>F value: 24.75, p value: 0.001</td>
</tr>
<tr>
<td>TUG</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>22.20±0.78</td>
<td>19.60±0.69</td>
<td>22.20±0.78</td>
<td>19.60±0.69</td>
<td></td>
</tr>
<tr>
<td>POMA</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td>n=20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24.75</td>
<td>22.20±0.78</td>
<td>24.75</td>
<td>22.20±0.78</td>
<td></td>
</tr>
</tbody>
</table>

*Significant at ≤ 0.05 with 95% Confidence Interval

Table 1b: Post hoc analysis (Bonferroni test).

<table>
<thead>
<tr>
<th></th>
<th>Baseline v/s Week 2</th>
<th>Baseline v/s Week 4</th>
<th>Week 1 v/s Week 2</th>
<th>Week 1 v/s Week 4</th>
<th>Week 2 v/s Week 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>Group A</td>
<td>0.051</td>
<td>0.001</td>
<td>0.051</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>0.221</td>
<td>1</td>
<td>0.221</td>
<td>0.088</td>
</tr>
<tr>
<td>TUG</td>
<td>Group A</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>POMA</td>
<td>Group A</td>
<td>0.04</td>
<td>0</td>
<td>0.04</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Group B</td>
<td>0.029</td>
<td>1</td>
<td>0.029</td>
<td>0.487</td>
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</tbody>
</table>
to be statistically insignificant between Group A and Group B (P>0.05). It remained insignificant at the end of week 1 (P>0.05). At the end of week 2 and week 4 it was found to be significant between group A and group B (P<0.05).

Table 2: Between group comparison of MMSE, TUG, POMA.

<table>
<thead>
<tr>
<th></th>
<th>Group A Mean ± SD</th>
<th>Group B Mean ± SD</th>
<th>F</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMSE</td>
<td>Baseline 27.90 ±1.19 27.10 ±1.52</td>
<td>1.704</td>
<td>0.208</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 1 27.90 ±1.19 27.10 ±1.52</td>
<td>1.704</td>
<td>0.208</td>
<td></td>
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<tr>
<td></td>
<td>Week 2 28.90 ±0.73 27.20 ±1.47</td>
<td>10.616</td>
<td>0.004</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 4 29.90 ±0.31 27.90 ±1.52</td>
<td>16.514</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td>TUG</td>
<td>Baseline 13.47 ±2.16 20.50 ±3.06</td>
<td>35.116</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 1 13.47 ±2.16 20.50 ±3.06</td>
<td>35.116</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 2 13.58 ±3.73 19.75 ±2.63</td>
<td>18.228</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 4 13.04 ±2.54 19.33 ±3.24</td>
<td>23.19</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>POMA</td>
<td>Baseline 20.10 ±0.59 19.40 ±0.51</td>
<td>3.903</td>
<td>0.064</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 1 20.10 ±0.59 19.40 ±0.51</td>
<td>3.903</td>
<td>0.064</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 2 21.20 ±1.39 19.60 ±0.69</td>
<td>10.473</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Week 4 22.20 ±0.78 19.90 ±1.10</td>
<td>28.855</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Following are the graphs representing distribution of between group comparison of MMSE, TUG, POMA score respectively.

DISCUSSION
Almost all patients with PD suffer from selective cognitive impairments, including difficulties with attention, concentration, problem solving, set-shifting, and memory, which are thought to reflect dysfunction of cortical circuits serving frontal brain regions. These impairments are most frequently reported by patients in terms of the disabilities they cause, such as difficulties in paying attention at work, problems handling more than one project at a time, inability to sequence, plan, and organize tasks at work and home and problems completing tasks that have been started. While dysfunction in the cortico-circuits may underlie cognitive deficits apparent on executive and other frontal tasks, the dopaminergic system is likely not the only neurotransmitter disruption in this disease [6]. The underlying neuropathological disturbance in PD involves selective deterioration of subcortical structures, e.g. dopaminergic neurons in substantia nigra which affects primarily the basal ganglia structures [28].

Cognitive demands associated with balance and locomotion may contribute to the incidence of falling among older adults. The ability to recover a stable posture following an external perturbation is more attentionally demanding for older adults than for younger adults. This would suggest that for some older adults, an increased risk for loss of balance and falls may result if sufficient attentional resources are not allocated to the task of postural recovery [29]. Previous research, demonstrates that as cognitive scores (executive function and working memory) decrease Centre of Pressure (COP) sway area and thus postural instability increases suggesting that cognitive impairment may correlate with motor severity [25]. For example, Levy et al. [30] found that both bradykinesia and axial symptoms were associated with an increased incidence of dementia. This suggests that the training to improve cognition and attention is beneficial. However, few studies have explained that how cognition may play an important role in maintaining balance in older adults. The purpose of this study was to find out whether by giving two types of Pranayamic breathing, does mobility and risks of fall improve by improvement in mild cognitive impairment in
PD. As, studies have also shown, Cognitive impairment in absence of frank dementia, typically called mild cognitive impairment (MCI), occurs frequently in PD [8,9], even among those newly diagnosed [10,11]. And also, Cognitive deficits are common in PD patients with "normal" cognition based on MMSE performance [7].

The findings of present study partially support our main hypothesis in that gains were observed in cognitive function and mobility status of and falls risks related to balance in individuals with PD. Our results reveal significant improvements in Mini Mental State Examination (MMSE), Timed up and go test (TUG), and Tinetti Performance Oriented Mobility Assessment (POMA) score in the experimental group (Pranayamic breathing and conventional physiotherapy), compared with the control group (conventional physiotherapy only). No significant differences between groups were found for MMSE and POMA at the baseline. The within group analysis did not support the between group differences. Significant differences at the end of week 2 and week 4 compared with the baseline were found for the MMSE and POMA in both the groups, along with consistent significance in TUG in both the groups throughout the training period, which indicates that some gains were maintained all the time.

The efficacy of pranayamic breathing on cognition in this study can be explained by changes in the autonomic balance as it has been reported that slow pranayamic breathing generates inhibitory signals and hyperpolarised current within neural and non–neural tissue by mechanically stretching tissues during breath inhalation and retention. It is likely that hyperpolarization current initiates the synchronization of neural elements in the central nervous system, and surrounding tissues ultimately causing shifts in the autonomic balance towards parasympathetic dominance [16]. It has been reported that immediate decrease in all cardiovascular parameters in our patients can be explained by changes in the autonomic balance as it has been previously reported that sympathetic activity is lower during left nostril breathing. It has also been studies that exclusive left nostril breathing repeated four times a day for a month reduced sympathetic activity [32].

As both the groups have shown statistical improvement in MMSE, TUG and POMA post training of pranayamic breathing along with conventional physiotherapy and conventional physiotherapy alone. Study on the relationship between balance and cognition conducted by Joe Nocera et al provided evidence that motor function, specifically postural control may be negatively influenced by cognitive dysfunction in PD. Cognitive impairment is common and has devastating implications on the quality of life for patients in PD [25].

The memory is one of the ability of the brain to store and retrieve information of both verbal and non verbal nature. This retrieval process involves generation of a sequence of entities in the response set which corresponds to the entities of stimulus set. This decides the nature of recall function. For example recall of telephone numbers, etc. The left hemisphere (LH) lobe of cerebral cortex is the seat for recall of numerical, descriptive and analytical data. This involves temporal lobe to register and encode the incoming stimulus information in the parietal lobe for information storage. The display of recall would be a motor output such as the verbal recall involving speech motor pathways. This cortical aspect of retrieval function is also co-related with the regional cerebral circulation [33,34]. Further, few studies reveal the relation between the breathing techniques such as uni-nostril (right and left nostril ) and alternate nostril breathing on enhanced spatial memory performance, etc. An previous research concludes that the right nostril breathing would facilitate better inherent digit backward and digit forward span memory performance of left hemisphere. However, alternate nostril breathing may only refresh the left hemispheric activity during recall function and the associative learning is not affected by any of such interventions [33].

As discussed by Stanley John Winser [36], the result of his experiment provided evidence that, the balance exercises dedicated to stimulate and facilitate the peripheral proprioceptors have beneficial effects in improving balance among individuals suffering from PD. Present study has shown improvement in both the groups, further showing better improvement in the experimental group A. This change might be due to the
added intervention of pranayamic breathing including alternate nostril breathing and bramhary pranayama.

Analysis of present study shows that, when TUG test scores were compared from baseline to at the end of week 4, statistical insignificance was found within the groups A and B, but comparison of TUG test scores at baseline, week 1, week 2 and week 4 had shown statistical significance between groups A and B.

A deterioration of the overall therapeutic effectiveness of L-dopa can be expected over time with a reported increase motor complications of 10 percent per year [1,37]. For many patients the therapeutic window is 5-7 years before optimal benefit wears off. This is thought to result from progressive nigrostriatal degeneration. Wearing-“off” state or end- of- dose deterioration is a worsening of symptoms during the expected time-frame of medication effectiveness. Freezing episodes, or sudden episodes of immobility, may appear. Random fluctuations in motor performance, termed “on-off” phenomenon, occur in about 50 percent of patients treated for more than 2 years and can be very disabling [1]. This may be one of the reason behind no significant improvement in TUG test scores taken, as it assesses the mobility status of and fall risk for individual with PD. Time constraint could also be one of the factor, as training period was of 4 weeks. If the training period had been more, much better results would have been gained as present attained one. The severity of problems, stages of disease, age, phase and setting of rehabilitation, and other factors must all be taken into account in structuring the evaluating data [1].

Additional strategies to promote relaxation included an emphasis on diaphragmatic breathing during exercise, gentle rocking to produce generalized relaxation of excessive muscle tension due to rigidity. During therapy, slow, rhythmic, rotational movements of the extremities and trunk such as range of motion (ROM), stretching, functional training [1,38] Physical therapy also included, hook lying, lower trunk rotation, side lying rolling, upper and lower trunk segmental rotation, PNF techniques of rhythmic initiation (RI) were designed to promote relaxation and to help overcome the effects of rigidity in PD. Stress management techniques are an important adjunct to relaxation training [1]. In present study, Patients were also benefitted from pranayamic breathing, conscious recognition and release of muscle tension (Progressive Relaxation Technique/ Jacobson’s Relaxation) [39].

In a multidisciplinary rehabilitation program for people with PD, Wade et al [40] showed short term gains in mobility, with worsening disability at 6 months. Heterogeneity between groups related to medication adjustments and activity level may contribute to the lack of significant findings across outcome measures between the training period assessment. It is worthy to consider, however, that perhaps people with a long term chronic degenerative disease need intervention to occur over a longer time period [41]. Instead of receiving a bout of exercise and Pranayamic breathing for a shorter period, they may need to continue the program for several months or more to maintain gains shown early on.

CONCLUSION

The finding of this study supports our main hypothesis that Pranayamic breathing along with conventional therapy is more effective on cognition and balance in Parkinson’s patients. Subjects with clinically diagnosed PD within stage three of Hoehn and Yahr grade benefit in short term with regards to cognition and balance.

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Conflicts of interest: None

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