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Association of L-DOPA with recovery following *Ayurveda* medication in Parkinson's disease

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Abstract

Ayurveda, the Indian system of traditional medicine, uses a concoction of several spices, herbs and minerals for the treatment of diseases. In a clinical prospective study we have evaluated the efficacy of *Ayurveda* treatment (a concoction in cow's milk of powdered *Mucuna pruriens* and *Hyoscyamus reticulatus* seeds and *Withania somnifera* and *Sida cordifolia* roots) in 18 clinically diagnosed (with a mean Hoen and Yahr value of 2.22) parkinsonian patients. As per *Ayurveda* principles, 13 patients underwent both cleansing (for 28 days) and palliative therapy (56 days), 5 patients underwent palliative therapy alone (84 days). Only the former group showed significant improvement in activities of daily living (ADL) and on motor examination as per UPDRS rating. Symptomatically, they exhibited better response in tremor, bradykinesia, stiffness and cramps as compared to the latter group. Excessive salivation worsened in both the groups. Analyses of powdered samples in milk, as administered in patients, revealed about 200 mg of L-DOPA per dose. The study establishes the necessity of cleansing therapy in *Ayurveda* medication prior to palliative therapy. It also reveals contribution of L-DOPA in the recovery as observed in Parkinson' disease following *Ayurveda* medication.

Keywords: Parkinson's disease; Herbal medicine; *Mucuna pruriens*; *Withania somnifera*; Efficacy of *Ayurveda* treatment; *Sida cordifolia*; *Hyoscyamus reticulatus*

1. Introduction

The ancient medical science being practised in India from the *Vedic* times (1500–1000 BC), ''*Ayurveda*'' ('knowledge concerning longevity'), uses plant tissues as medicine [1]. Based on *Ayurveda* principles given in ''*Charakasamhitha*'', the classical text in *Ayurveda*, a concoction in cow's milk of powdered *Mucuna pruriens* and *Hyoscyamus reticulatus* seeds and *Withania somnifera* and *Sida cordifolia* roots is prescribed for treating Parkinson's disease [2]. *M. pruriens* is reported to contain L-DOPA as one of its constituents [3]. *H. reticulatus, W. somnifera* and *S. cordifolia* contain a number of neuroactive constituents like hyoscyamine, somniferin, ephedrine, etc. [2,3]. Commercial preparations (HP-200; Zandu Pharmaceuticals, Bombay) of *M. pruriens* are available in India for the treatment of Parkinson's disease. In this clinical prospective study, we have evaluated the effects of *Ayur-*

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veda medication on the symptoms and signs in 18 patients of Parkinson' disease. The study also compared the effects, if any, of cleansing and palliative therapy as prescribed in ancient text books as compared to that of palliative therapy alone. Contents of L-DOPA were also analysed in the seeds and roots of the plants used as medicine.

2. Materials and methods

Clinically diagnosed [4] Parkinson's disease in-patients of the Govt. *Ayurveda* hospital were recruited to the study after obtaining informed consent. The institutes' respective Ethical committees approved the study. The mean age of the patients was 59.8±5.8 (S.D.), disease duration was 3±2.6 years, male to female ratio was 5:4, and their mean Hoen and Yahr score in ''off'' condition was 2.22±0.73. All medications, including herbal preparations, were discontinued 15 days prior to the initiation of the study. We evaluated symptoms and signs such as stiffness, tremor, bradykinesia, cramps, blinking of eyes, staring look, expressionless face, dysphonia and monotonous speech, dysarthria, wasting, cogwheel rigidity, primitive reflexes like Glabellar tap, shuffling gait, contractures, loss of associated movements, postural fixation and excessive salivation, and conducted objective tests (walking, sitting-up as well as, left/right finger–nose tests) to assess the motor function before the administration of the *Ayurveda* treatments (baseline), and every 4 weeks for the next 3 months. These data were converted to UPDRS for better representation and interpretation. In the study, a positive response was determined when more than 50% of the patients showed improvements in stiffness, tremor, bradykinesia and cramp-like pain in lower limbs and in the objective tests. Five patients underwent only palliative therapy for 84 days. Thirteen patients were subjected to a cleansing or eliminative therapy (''*panchakarma*'') [5] for 28 days prior to 56 days of palliative therapy. The eliminative therapy included oleation, sudation, purgation, enema and errhines by administering prescribed *Ayurveda* drugs. Palliative treatment consisted per-oral administration in milk of the dried seeds and roots of four plants obtained through Govt. *Ayurveda* College Pharmacy. Powdered samples each (in gms) of *M. pruriens* (4.5) *H. reticulatus* (0.75), *W. somnifera* (14.5) and *S. cordifolia* (14.5) were suspended in 200 ml luke warm milk, and administered twice daily an hour prior to any meals. Separate samples of powdered material were deproteinized and acidified in perchloric acid (0.4 N), and the content of L-DOPA was estimated employing high-pressure liquid chromatography coupled with electrochemical detector [6]. Samples suspended in milk were also deproteinized and extracted in to perchloric acid and estimated for L-DOPA content. Duplicate samples were analysed. Results are presented as mg/g of dried tissue.

3. Results

Tremor and bradykinesia were present in 100%, and stiffness and cramp-like pain respectively in 15.4% and 61.6% patients who underwent cleansing and palliative therapy. These symptoms were improved in 61.5, 69.2, 100 and 75% patients following *Ayurveda* treatment. The patients, who underwent palliative therapy alone had stiffness (60%), tremor (80%), bradykinesia (100%) and cramps (40%); and 33.3, 50, 40 and 100% of these patients revealed improvement. Other symptoms like loss of blinking of eyes, staring look, expressionless face, dysphonia and monotonous speech, dysarthria, wasting, cogwheel rigidity, primitive reflexes like Glabellar tap, shuffling gait, contractures, loss of associated movements and postural fixation showed no improvements in any of the 18 patients. Excessive salivation worsened in both the groups. Mentation, behaviour and mood were not affected in 72% of patients studied (Fig. 1). Activities of daily living (ADL) and motor examination (rating) were improved in patients who underwent both the therapies (Fig. 1; sample numbers 1–13). In patients, who underwent only palliative therapy, there appeared no improvements in ADL and motor examination rating (Fig. 1; sample numbers 14–18). This was evident in total UPDRS, as shown in Fig. 1 (last panel). A single dose of the medication as administered in milk contained a total of 200±5 mg of L-DOPA. Powdered samples of *M. pruriens*, *H. reticulatus and W. somnifera* respectively contained 29.8±1.2, 0.012±0.002 and 0.19±0.003 mg of L-DOPA/g of dried tissue. *S. cordifolia* did not contain L-DOPA. The sensitivity of the method employed for measuring L-DOPA was in the range of ng level.

4. Discussion

The UPDRS show improvement in the condition of the patients who underwent proper *Ayurveda* treatment. Our results show improvement in symptoms like stiffness, tremor, bradykinesia and cramp-like pain in lower limbs as well as in objective tests in patients who underwent both eliminative (''*panchakarma*'') and palliative therapy indicating the effectiveness of proper *Ayurveda* treatment in Parkinson's disease. The cleansing therapy administered in patients such as purgation and enema could have rejuvenated the gastrointestinal tracts for better absorption of the *Ayurveda* drugs administered for palliative therapy. These results indicate that such 'preparations' of patients prior to palliative therapy may be beneficial in other disorders too need to be explored, since it is recommended in the classical text of *Ayurveda* (*Charakasanhita*). Our clinical findings confirm that *Ayurveda* treatment could be helpful in improving the symptoms and signs, at the least, in a sub-population of Parkinsonian patients. L-DOPA contained in the herbal medication may explain the improve-

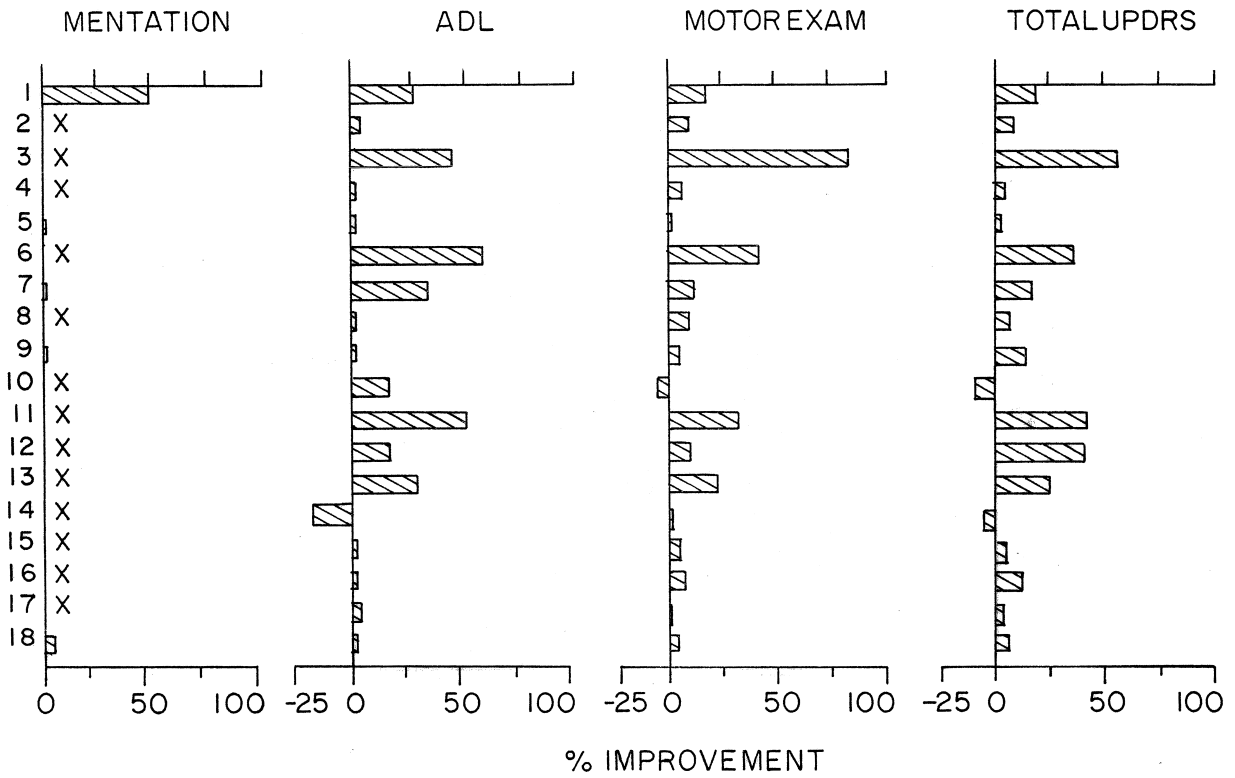

Fig. 1. Effects of *Ayurveda* medication on Parkinson's disease patients (UPDRS). Eighteen parkinsonian patients with an average Hoen and Yahr score of 2.22±0.73 underwent an *Ayurveda* system of treatment. Thirteen patients (sample nos. 1–13) received both eliminative and palliative therapy and the rest five (sample nos. 14–18) endured palliative therapy alone. In most of the patients higher mental functions were unaffected ('X'). In all the patients ADL and motor functions were affected. Both ADL and mental functions showed improvement (shaded bars) in patients, who underwent both eliminative and palliative therapy. Percentage improvement is calculated as % decrease in individual scores from the baseline score (prior to *Ayurveda* treatment). Total UPDRS (Mean score 59±12) also showed significant ($P \leq 0.05$, Student *t*-test) improvement in 62% of these patients (sample nos. 1, 3, 6, 7, 9, 11–13). Patients who underwent only palliative therapy, the improvement was not marked. Two patients (from either group) showed deterioration in symptoms (samples 10 and 14).

ment observed in the present study. Other factors also could have contributed, since in a recent study in an animal model of Parkinsonism, *M. pruriens* has been shown to be more effective than L-DOPA alone [7]. However, any other factor(s), which might have contributed to the effectiveness of *Ayurveda* treatment, could not be deduced from the present study. While *M. pruriens* with its high content of L-DOPA could provide relief, *W. somnifera* is known to up-regulate cholinergic receptor functions in the brain [8]. This will adversely affect some of the Parkinsonian syndromes, and may explain the worsening of excessive salivation as observed in the present study.

The holistic approach of *Ayurveda* takes advantage of the unknown active biochemical ingredients of the plant tissue. The obvious disadvantage is the bulkiness of the preparation and the difficulty in its administration. Thus, extracts of such medicinal preparations, with out loosing the active ingredients for easy use by patients, need to be made available. This study establishes the importance of eliminative therapy followed by palliative therapy in (*Ayurveda*) treatment of Parkinson's disease. This study also emphasises the need for a complete biochemical characterisation of medicinal plants as well as the need to assess whether *Ayurveda* treatment can be more beneficial or can improve upon L-DOPA therapy in Parkinson's disease.

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