Short Communication

A prospective clinical study of an Ayurveda regimen in COVID 19 patients

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1. Introduction

It has been 6 months since the novel coronavirus disease (COVID 19) was declared as a pandemic by WHO [1]. To contain the pandemic, many countries including India, underwent a series of lockdowns. The strategies recommended for containing the disease included sanitization measures, social distancing, regular use of mask, testing and quarantine for suspected carriers [2]. A variety of therapeutic measures have also been deployed to prevent and treat the infection; however, formal trials of known Ayurvedic formulations have not been done. In fact, the ministry of health, Govt. of India has not included Ayurvedic formulations in their recommendations for clinical management of COVID 19 [3]. The Indian Council of Medical Research (ICMR) had identified key areas of research to generate critical intelligence for prevention and control efforts.[4] The Ministry of AYUSH (Ayurveda, Yoga, Unani, Siddha & Homeopathy) has come up with recommendations for the prevention, (through boosting immunity) and symptomatic treatment of the disease [5].

Epidemiological studies conducted by Ministry of Health & Family Welfare (MoHFW), Government of India (GoI) have produced results parallel to those obtained elsewhere [6]. The Centre for Disease Control (CDC) observed that among hospitalized COVID patients, 81% cases fell in moderately symptomatic category [7]. It had been demonstrated that upper and lower respiratory tracts were the major targets of the novel coronavirus [8]. The Ayurvedic system of medicine, recommends a variety of herbal formulations for the treatment of diseases affecting the respiratory tract; it was therefore postulated that a regime containing Dasamoolkaduthrayam Kashaya and Guluchyadi Kwatham considered among the best for treatment of respiratory diseases could be useful for COVID 19 patients. The current study was conducted to test this hypothesis. The objectives of the study were to determine the efficacy of an Ayurveda regime containing Dasamoolkaduthrayam Kashaya and Guluchyadi Kwatham in patients of COVID 19 infections, with mild and moderate symptoms and to determine the rate of resolution of symptoms in patients with the Ayurvedic formulation as an add-on to Standard of Care (SoC) compared to SoC alone.
2. Methodology

Patients tested as COVID 19 positive using RT-PCR and admitted in a tertiary care hospital were screened for this prospective, open-label interventional clinical trial.

Inclusion criteria were:

1. Patients of either sex between 18 and 65 years of age.
2. Those suffering from mild to moderate symptoms included patients of either sex, suffering from mild to moderate symptoms as per MoHFW – GoI guidelines [6].

Exclusion criteria were:

1. Pregnant/Lactating mothers
2. Patients with co-morbidities like Chronic Obstructive Pulmonary disease (COPD), Ischemic Heart Disease (IHD), Chronic Kidney Disease (CKD), coagulopathy and cancer
3. Patients with significant morbididity after oral surgery and unable to swallow.
4. Patients who were on immuno-suppressant, oral steroids or chemotherapy
5. Patients k/c/o Diabetes Mellitus (DM) taking insulin
6. Patients with Sr. Creatinine > 1.6 mg/dl, Sr. Sodium < 128 mEq/L, Hemoglobin (HB) < 7.0 gm% SPO2 < 90%.

The patients were randomly allotted from the daily admission list by physicians who were not part of this study into treatment and control groups. Patients of both the groups received the SoC as per the ICMR guidelines (Supplementary Table S1). The SoC and oxygen supplementation was decided by the treating physicians.

The treatment group received the Ayurveda regimen that was a combination of two tablets (Tab.) viz., Tab. Dasamoolkaduthrayadi Kashaya + Tab. Galuchyadi Kwatham. These tablets were manufactured by GMP certified units. These formulations are in the market for more than two decades. Detailed formulation of the Ayurvedic products is given in Supplementary Tables S2, S3. Two tablets of each were administered 12 hourly after meals. The duration of treatment as recommended by guidelines is 7 days [9].

Table 2

3. Results

Total 112 patients were screened as per inclusion criteria, 11 failed the screening, and 101 patients recruited in the trial. Two patients complained about difficulty in swallowing the tablets and were discontinued on Day 3. Finally, 99 patients completed the study were analyzed. Out of 99 patients, 60 patients received Ayurveda regime as an add-on, while 39 patients received only SoC (Fig. 1).

The treatment and control groups had similar demographic distribution. The biochemical and hematological parameters at baseline are shown in Table 1.

The median day of admission from the onset of symptoms was 6th (range 1st to 12th) in treatment group; while it was 5th day (range 1st to 16th) in control group. Patients with co-morbidities like diabetes and hypertension were 90.04%. Asthma and hypothyroidism were observed as other co-morbidities among the rest.

Fever, breathlessness, cough, ageusia, headache were the symptoms that were observed throughout the study. Table 2 shows the number of patients suffering from each of these on day 1,3 and 7 of treatment. The most common symptom was fever, while headache was experienced by the least number of patients. The percentage of patients suffering from breathlessness fell from 53% to 16% to 1.6% on day 1,3 and 7 in the treatment group while in the control group the percentage fell from 46% to 38% to 28% respectively. Ageusia is considered a significant symptom of COVID 19; the percentage of patients suffer from the same reduced from 75% to 25% to 3.3% in the treatment group while in the control group it fell from 46% to 36% to 26% on day 1,3 and 7 respectively. In both groups, there was a similar fall in the percentage suffering from fever. Reductions in breathlessness and ageusia were statistically significant (p < 0.001 Chi squared) at day 3 and day 7, while reduction in fever was not.

Fever, oxygen requirement (p = 0.2 Mann–Whitney test), body-ache & fatigue (p = 0.5 Chi squared), had similar response rate in both the groups [Table 2]. Hiccups were reported by 2 patients on day 4 and 5 of the treatment, which was self-limiting. Salty taste (Lavanasyata) and polydipsia (Talushoosha) was reported on day 3 and day 5 respectively, by 2 different patients in study group.

Chest digital roentgenograms (X-ray) were compared in few patients. The patchy opacities were reduced without anti-viral drugs in study group on follow-up chest X-ray by day 4. The observed changes were clinically significant; though statistically not analysed [Fig. 2A and B].

Median hospital stay for COVID pharyngitis patients in the study group was 5 days as compared to 7 days in the control group. The patients with COVID pneumonia had the median hospital stay of 7 days in study group as compared to 8 days in control group.

One patient in the study arm was asymptomatic from day 3 to day 7; but, had symptoms on Day 7. The patient was further treated with the same add-on regime, till the patient turned asymptomatic on day 15th. The disease progression was observed in 1 patient in control group who later required intensive care unit had prolonged stay of 23 days.

The percentage of co-morbidities was more in the study group; despite that, 1 of 60 patients in the study group required Remdesivir while 2 of 36 patients required it in the control group. 1 of 60 patients in study group required Remdesivir as well as Tocilizumab during hospital stay while 2 of 36 patients required the same in control group.

4. Discussion

This study was conducted after 4 months of COVID 19 pandemic alert; no specific antiviral treatment/vaccine had been recommended or made available by then [10]. This study was intended to explore the potential from Ayurveda with evidence over just experience. This study was initiated after extensive discussions among the physicians from the departments of infectious disease, intensive care and Ayurveda of this institute. COVID 19 patients were presented with low grade fever, dry cough, muscle pain, or malaise. In some patients sore throat and headache were observed. Cough and shortness of breath were present without signs of severe pneumonia at presentation. Ageusia was observed predominantly [11,12]; anosmia in few. An European study mentioned that in mild to moderate COVID 19 category, 88% patient had the gustatory dysfunction [13,14]. It was observed that dry cough was often associated with difficulty in breathing. Chest X-ray showed bilateral multifocal alveolar opacities. The radiological improvement was observed on 4th and 5th day. Majority patients had elevated levels of C-reactive protein; few had elevated levels of d-dimer [15]. Ayurveda medicines used were indicated in Ayurveda texts [16,17]; scientific publications suggested analgesic, anti-pyretic, anti-platelet aggregation, anti-viral activity for Dasmoolkaduthraya [18–20] and Galuchyadi Kwatham [21,22]. The significant recovery in breathlessness and ageusia in the add-on arm reduced hospital stay for the patients. The early discharge from hospital was important in view of scarcity of oxygen equipped beds. In India, only 3.2 hospital beds were available per 10,000
population and in Maharashtra, this number was 2 per 10,000 population [23]. The majority number of beds were mainly concentrated in urban India, than rural [24]. The reduced hospital stay could be directly proportional to availability of hospital beds for accommodating more needy patients. All over the world COVID 19, has shown a variable natural course, though a lot of effort has gone into attempts to identifying factors associated with higher morbidity or mortality, consensus is still awaited. Given these uncertainties, obtaining statistical significance in a series as small as this is difficult.
4.1. Notable strengths and limitations of this study

4.1.1. Strengths
Cost effective: The present add-on Ayurveda regimen was the low risk & highly cost effective as it reduced hospital stay. Adverse effects: No adverse effects observed in study group.

4.1.2. Limitations
A systematically randomized large sample study would be better with tighter controls would be preferred. However, the public response to the pandemic makes it difficult to strictly adhere to trial protocols. Comparison of hematological & biochemical parameters will be desirable, once the global standards are evolved for COVID 19. A comparative radiology imaging is also recommended for future studies.

5. Conclusion
Early clinical improvement in breathlessness was observed with the present add-on Ayurveda regimen. Ageusia reduced early with add-on Ayurveda regimen. The median duration of hospital stay was reduced; this factor is of importance in view of shortage of hospital beds in India. The learning from this study is the potential of Ayurvedic therapy in treating COVID 19.

Ethics approval
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CTRI registration
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Conflict of interest
None.

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Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.jaim.2020.10.008.

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Fig. 2. A) Chest digital roentgenograms (X-ray) at day 1. B) Chest digital roentgenograms (X Ray) at Day 4.
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