

Management of Mild and Moderate Symptoms of COVID-19 in Infected Subjects using Combi-5 Herbal Supplement: Case Series.

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ABSTRACT

Corona virus Diseases 2019 (COVID-19) has caused significant distortion globally. Concerted efforts are being made to develop treatments including vaccines, however, emerging of new strains of the virus, high cost of available treatments, distortion in global distribution of available vaccines and vaccine hesitancy require that accessible, cheaper and complimentary treatment be explored and developed. This report is aimed to explore the use of Combi-5 herbal supplement in managing subjects with mild and moderate symptoms of COVID-19.

We present case series of two subjects who tested positive for COVID-19 with mild and moderate symptoms, self-managed at home using Combi-5 herbal supplement taken along with vitamin C and Zinc. Both subjects recovered and did not require further medical admission. Phytochemical constituents of herbal supplement were measured using standard methods.

Concomitant use of Combi-5 herbal supplement, zinc and vitamin C could improve prognosis in COVID 19 positive subjects with mild and moderate symptoms. Future studies using Combi-5 should be focused on performing detailed molecular docking, in-vitro SARS-CoV-2 enzyme inhibition experiment and conducting randomized controlled trial to validate the clinical observation.

Key Words: SARS CoV-2, Combi-5, COVID-19, Prognostic outcome, Herbal Supplement, Symptoms

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INTRODUCTION

In late December 2019, China reported to the World Health Organization (WHO) an outbreak of pneumonia-like infection associated with lung failure [1]. The causative agent for the disorder was identified as Severe Acute Respiratory Syndrome – novel Coronavirus 2 (SARS-nCoV-2). The genomic sequence of the virus was identical to viruses which caused Middle East Respiratory Syndrome (MERS) in 2012 and Severe Acute Respiratory Syndrome (SARS) in 2002, but with slight variation [2]. However, the slight difference in the genome observed between MERS and SARS viruses conferred the name SARS-CoV 2 to the virus reported in China [1, 3]. Since the virus was first reported, it has resulted in 262,178,403 infections and 5,215,745 deaths globally [3]. In order to provide lasting curative solution with a view to limiting mortality and morbidity associated with the disease, several treatment solutions are currently being researched and developed. These include vaccines, repurposing of drugs previously used for treating other diseases and exploring the benefits of herbal supplements. However, high cost of available treatments, distortion in global distribution of available vaccines, vaccine hesitancy and emergence of various strains of the virus require that accessible, cheaper and complimentary treatment using alternative and traditional medicine approaches be explored.

Herbal medicine, a form of complementary and alternative medicine has been recognized as component of global health. The Alma Ata declaration of 1978 made provision for developing therapeutic solutions which are

indigenous to the people, universally acceptable and at a cost which the community could afford. [4]. Since the emergence of COVID 19, use of herbal remedies to improve individual's immunity and as possible preventive measures against the disease have increased across different countries [5, 6]. Drug manufacturing companies have made concerted efforts to develop treatments including vaccines. Global agencies such as the World Health Organization (WHO), African Union (AU) and Africa Center for Disease Control (ACDC) aside from commissioning special team to explore the development of traditional medicine for treating COVID 19, have also given strong support to research and develop natural remedies for managing COVID 19 infection, but cautioned that such treatment should be developed following standard protocols [7, 8].

Combi-5 is herbal supplement formulated under well controlled safety condition using five major spices namely: *Zingiber officinale* (Ginger), *Curcuma longa* (Turmeric), *Piper guineense* (black pepper), *Allium sativum* (Garlic) and *Xylopi aethiopica* (Negro pepper). The constituents of Combi-5 are well known and are consumed by individuals from across the globe [2,3,4,6 and 7]. For several years, these natural products have been used as spices for food and as local remedies for different medical conditions including viral and bacterial infections. Study on these spices has shown that they possess different health benefits including immune boosting, antipyretic, antiviral and antibacterial properties among others [6,9].

Constituents of Combi-5 Herbal Supplement



Zingiber officinale - Ginger



Piper guineense-Black pepper



Curcuma longa -Turmeric



Allium sativum -Garlic



Xylo-pia aethiopica, Negro Pepper

Figure1: Herbal Constituents used to formulate Combi-5 Supplement .

Table 1: Phytochemical Constituents of Combi- 5

Phytochemical	Concentration ($\mu\text{g/g}$)
Saponins	389.6
Alkaloids	398.7
Flavonoids	453.7
Tannins	266.9
Phenols	366.9
Reducing Sugar	257.2
Steroids	216.7
Terpernoids	203.7
Cardiac glycosides	328.9

We have earlier, published a case report [10], on the use of Combi-5 herbal supplement to manage a subject with mild to moderate symptoms of COVID-19, but case series using herbal supplement to manage mild and moderate symptoms of COVID-19 has not been published from our environment. We present case series on managing two subjects, who had mild and moderate symptoms of COVID-19 using Combi-5 herbal

supplement taken along with vitamin C and Zinc supplements.

CASE PRESENTATIONS:

Case 1:

Informed consent was obtained from all the subjects before they commenced the herbal supplement. Written informed consent was obtained from all the subjects before

publishing this report. . She was a 46 year old woman. She experienced body weakness, cold, headache and loss of smell on the 6th of July, 2020. She went for COVID-19 test on 7th of July, 2020 using real-time reverse transcription-polymerase chain reaction (rRT-PCR). The result turned out positive on 12th of July, 2020. She commenced treatment with self-administered decoction of pineapple peel, lemon, black seed, ginger and garlic same day. On 13th of July, one of the members of the research team introduced Combi-5 herbal supplement to her and sought her consent to use the supplement. She gave her consent and volunteered to use the supplement to manage her symptoms. After consenting to use the supplement, a pharmacist in the team dispensed to her 60gms of Combi-5 in pulverized form. She commenced Combi 5 on 13th of July at the dose of one tea spoon full (4gms) dissolved in 150 ml warm water taken twice daily. The herbal supplement was taken along with vitamins C, D and Zinc at recommended doses. On 20th of July, she went for a repeat test and her result came positive same day. She continued with Combi-5 at the recommended dose along with other supplements. All symptoms disappeared on 26th of July. She went for another test on 28th of July and the result came out negative on 3rd of August.

Case 2:

He was a 51-year-old man. He experienced general body fatigue, fever, headache and cough on the 6th of July and decided to take the COVID-19 test. He got tested same day using real-time reverse transcription-polymerase chain reaction (rRT-PCR). His result came out positive. He self-managed at home and commenced with Vitamin C and paracetamol at recommended doses. On 13th of July, he went for a repeat test and the result came out Positive.

The next day, one of the members of the research team introduced Combi-5 herbal supplement to him and sought his consent to use the supplement. He gave his consent and volunteered to use the supplement. After consenting to use the supplement, a pharmacist in the team dispensed to him 60gms of Combi-5 in pulverized form at the recommended dose of one tea spoon full (4gms) dissolved in 150 ml warm water taken twice daily. On 20th of July, he went for another COVID-19 test and his result still came out positive. He continued using the dispensed Combi-5 along with vitamins C at the recommended doses. On 30th of July, he reported that all his symptoms were gone and began to feel well. Due to testing logistics, his repeat test was delayed till 7th of August. He was tested on 7th of August and his result came out negative on 10th of August, 2020.

DISCUSSION

Emerging of various strains of COVID-19 pathogenic agent- SARS-CoV 2 has presented a significant challenge to curtailing the spread of the disease, developing effective treatment approaches and limiting its associated mortality and morbidity. Till date five vaccines produced by different companies have been developed and approved for human use following successful clinical trial. However, emergence of different strains of the virus for which available vaccines were not developed using the new emerging strains, logistic in global distribution of vaccines and escalation of infections across countries have posed serious challenges to curtailing viral infection and providing lasting solutions. Based on these, the need to explore the use of herbal supplements for managing COVID-19 symptoms and retarding the progression of the disease to severe stage becomes highly imperative.

Since COVID-19 pandemic, many individuals have resorted to using herbal

supplements to improve their immunity and raise antioxidant status [5, 6, 11]. Reports have shown that some of the herbal supplements regularly consumed are ginger, honey, lemon and garlic. Ginger and garlic are constituents of Combi-5 and they have been well documented as good remedy for managing upper respiratory disorders and inhibit further spreading of respiratory viruses including SARS [5, 11].

In subjects infected with COVID-19, there is upregulation of markers of inflammation such as interleukin 1 (IL-1), IL-6, tumor necrosis factor (TNF) alpha and cytokine IL-10. Upregulation of inflammatory cytokine precipitate disseminated intravascular coagulation (DIC) resulting in failure of major organs of the body [12]. Furthermore, oxidative stress, evidenced by increase in generation of free radicals and reduction in antioxidant biomarkers have also been associated with COVID-19 infection [12]. These metabolic processes if not retarded could result in excessive damage to body organs, increase the requirement for oxygen, resulting in poor prognosis. Herbal supplements are natural sources of antioxidants. Combi-5, comprising different natural spices contains different phytochemicals such as saponins, flavonoids, tannins carotenoids, micronutrients and vitamins [Table 1]. These compounds might have played synergistic roles to limit disease progression in the subjects by reducing excessive generation of free radicals, improving antioxidants biomarkers and preventing upregulation of pro inflammatory cytokines thereby resulting in improved disease outcome. Previous study conducted in China using decoction of named Chinese herbal medicine produced evident based clinical effects [13] which was in consonance with the above hypothesis.

Advanced stage of COVID-19 is expensive to manage especially in resource limited setting such as ours coupled with weak health

systems, limited resources for effective health care and limited manpower. Deploying validated and well researched herbal supplements for managing subjects with COVID-19 could be beneficial in limiting the progression of the disease, put less pressure on available health systems and reduce cost of treatment.

Vitamin C is well known antioxidant through its ability to mop up reactive oxygen species. Supplementation with vitamin C has been reported to improve the body's immune system. Evidence from in vivo experiment has shown that it had effect on certain types of coronaviruses [12, 14].

Zinc has been established to play critical role in immune function as well as limiting viral replications in cells [12, 15]. Deficiency of zinc has been reported to upregulate pro-inflammatory cytokines, such as IL-1, IL-6 and TNF alpha as well as decreasing the body's ability to produce antibodies against diseases [12, 14, 15]. There is a strong probability to suggest that the natural products in combi-5 working synergistically with vitamin C and zinc could be responsible for the good outcome observed in the subjects being reported.

CONCLUSION: Evidence from the cases presented in this report strongly suggest that concomitant use of Combi-5 herbal supplement with zinc and vitamin C could result in good prognosis in COVID-19 positive subjects with mild and moderate symptoms. A randomized controlled trial is needed to validate this assertion; and more studies should be focused on performing detailed molecular docking of the natural products contained in Combi-5 herbal supplements and identifying novel compounds responsible for this observation.

Conflict of interest: Nil

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