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Research Article

Herbal Supplements (CovETS) in Treating Covid 19 Related Pneumonia

Edessy M*, Tawfik R and Alyamani A

Professors at Obstetrics and Gynecology Department, Al Azhar University Medical School, Egypt

***Corresponding Author:** Edessy M, Professors at Obstetrics and Gynecology Department, Al Azhar University Medical School, Egypt.

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Abstract

Background: Coronavirus disease 2019 (COVID-19) acquired pneumonia is the leading cause of death worldwide. Hospital mortality among patients with COVID-19 infection is still high. Medicinal plant has been used for thousands of years for treating respiratory infections. Nowadays many complementary therapies are offered for patients with covid-19 pneumonia, it is not very clear whether herbal supplements are suitable therapy for this type of pneumonia.

Aim: Evaluation of the efficacy of the herbal supplementary mixture of volatile oils of *Rhus coriaria*, thyme and star anise (CovETS) in cases of COVID-19 acquired pneumonia.

Subjects and Methods: A prospective controlled clinical study during the period of 3 months from 20 march to 20 June 2020, conducted on 88 patients assigned to one of two groups, the control (Non-CovETS) group (43 patients) received conventional WHO anti Covid-19 protocol alone and the study (CovETS) group (45 patients) received a combination of the same conventional WHO protocol and the covets.

Results: A statistically significant improvement of the CovETS group (patients who received both who protocol and herbal supplements), regarding time of clinical stability (p = 0.001), hospital stay (p = 0.001), mechanical ventilation (p = 0.045), post covid syndrome (p = 0.037) and hospital mortality (p = 0.029) of the COVID 19 pneumonic patients.

A highly statistically significant improvement in the success and mortality rates among the CovETS than the non-CovETS groups of the pneumonic high-risk patients.

Conclusion: CovETS improved the clinical profile and mortality rates of the covid-19 pneumonia patients.

Keywords: *COVID-19 Related Pneumonia; Herbs; CovETS*

Introduction

Covid-19, caused by the severe acute respiratory syndrome coronavirus SARS-COV-2. While COVID-19 is primarily a respiratory illness, it can affect multiple organ systems including gastrointestinal tract (GIT), hepatic, cardiac, neurological, and renal systems [1].

In addition to vaccination, synthetic virucidal and antiviral substances are the backbone of efficient antiviral control interest worldwide [1]. Against this background, phyto-antiviral compounds have also come into the focus of research. Recently, increased efforts have been made to identify new antiviral and virucidal substances that can prevent or at least mitigate a SARS -COV-2 infection. In this context numerous extracts and isolated individual from medical plants have been investigated *in vitro* for their potential antiviral properties [2].

Sumac (*Rhus coriaria*) is an herbal product, commonly consumed as a spice, it contains tannins, polyphenols, flavonoids, organic acids and essential oils. Recent study demonstrated that sumac has a protective effect against liver damage, anti-hemolytic, leukopenia and anti-fibrinogenic effects, along with its antiviral, antimicrobial, anti-inflammatory and antioxidant properties [3].

There are numerous scientific *in vitro* and *in vivo* studies that investigated the antiviral effects of sumac against several viruses. In previous studies, sumac showed inhibitory activities against respiratory viruses, influenza a, influenza b and measles. Also, herpes viruses (HSV 1, HSV 2) and varicella zoster virus which are all enveloped viruses, contain dense lipids in their envelops. It is worth mentioning that coronaviruses share the same common features of this group [4]. Sumac is likely to affect the lipid layer in these viruses envelop including coronaviruses, disrupting the adsorption to the host cell, and preventing virus from penetration the host cell, positively contributing to the infection [5].

Thyme (*Thymus vulgaris*) which its essential oils (EOS) and plant extract were found to have antimicrobial and antioxidant properties. Ocana and Reglero [6] reported that thyme extracts significantly reduced production and gene expression of the pro inflammatory mediators TNF-α, il-1β and il-6. Their results suggest that thyme extract could have anti-inflammatory effects. Furthermore, extracts from thyme have been used in traditional medicine for treatment of several respiratory diseases as asthma and bronchitis. These extracts have antiseptic, antispasmodic, antitussive, antimicrobial, antioxidant and antiviral properties [7].

The spice star anise belongs to illicium family. It possesses a variety of pharmacological properties such as anti-bacterial, antiviral, anthelmintic and gastro protective. The extract of star anise exerted inhibitory effects on key inflammatory biomarkers. Park., *et al*. [8], reported similar findings when TNF-α stimulated HASMC cells were treated with anise extract.

The biological activity of medicinal plants strongly depends on their composition. Aqueous extracts of a combination like *Rhus coriaria*, thyme and star anise could be potential drug candidates against covid-19.

Previous study of Edessy and Tawfik on CovETS effects showed highly significant improvement of the medically disordered covid-19 patients and highly significant reduction of mortality of all covid- 19 patients [9].

COVID-19 pandemic has posed a great threat to healthcare across the globe. Many phyto-antiviral compounds have come into the focus of research. *In vitro* experimental studies revealed that several essential oils (EOS) and essential oils compounds (EOCS) from different medicinal and aromatic plants are potent antiviral and virucidal agents that inhibit viral replication cycle, focusing on important enveloped viruses that cause endemic and/pandemic diseases such as sars-cov-2 and others [10].

There are many *in vitro* and *in vivo* studies that investigate the antiviral effects of sumac against several viruses, Parsania., *et al*. [11], evaluated the antiviral effect of sumac (*Rhus coriaria*) fruit extract on acyclovir resistant herpes simplex virus type 1 (hsv-1) before and after the infection of Hela cell line at different concentrations of the extract. Gharabolagh., *et al*. [12], evaluated the inhibitory effect of *Rhus coriaria* (sumac) aqueous extract on hepatitis b virus replication and HBs Ag secretion. this study represents the inhibitory effect of sumac on multiplication of HBV and its antigen secretion.

Shereif., *et al*. [13] in their study explored the effects of sumac active polyphenolic constituent against the sars-cov-2 main protease enzyme m pro. They found 6 phenolic compounds of sumac are proposed for synthesis as potential inhibitors against Mpro of corona virus and have potential for treatment of covid-19.

In vivo study done by IM., *et al*. [14] indicated that sumac extract could prevent the coagulation of human peripheral blood cells as the extract had antiplatlets and antiobesity activities.

Lagunas-antiangle and Chavez-Valencia [15] reported that inflammatory effects of sumac were demonstrated *in vitro* and *in vivo* studies. As sars-cov-2 viral infection results in varying degrees of inflammation severity, over production of pro inflammatory storm (cytokine storm) observed in patients of severe covid-19 infection might be associated with acute respiratory distress syndrome which was associated with increased mortality.

In another study Xiong., *et al*. [16] added that there was a significant positive correlation between the severity of pneumonia and c reactive protein (CRP), erythrocyte sedimentation rate (ESR) and lactate dehydrogenase (LDH). Therefore, sumac could be useful in COVID-19 infection due to its anti-inflammatory effects.

The second component of the CovETS, the thyme, Oliviera., *et al*. [17] studied the effects of a standardized hydroalcoholic extract of thyme on primary human airway (bronchial/tracheal) epithelial cell lines. They found significant anti-inflammatory cytokine IL-1β and IL-8A and mucus secretion in human bronchial and tracheal epithelial cells. They concluded that thyme extract might be an effective treatment of chronic diseases based on inflammatory responses when hypersecretion of mucus overwhelms the ciliary clearance and obstructs airway causing morbidity and mortality. These results substantiated the traditional uses of thyme in the treatment of respiratory diseases.

Star anise is the third component of the CovETS. Anthenol is one of anise compounds responsible for the aroma and flavor. It exerts a potent anti-inflammatory effect by inhibiting the activation of NF-kb in lipopolysaccharide induced acute lung injury in mice, also reduced the pro-inflammatory mediators' levels of TNF-α and IL-6 [18]. Trans-anethole another major constituent found in star anise. It attenuated the elevated levels of cytokines such as il-4, il-5 and il-13 in the asthmatic *in vivo* model [19].

Zhan., *et al*. [20] stated in his review that antiviral effect of *Rhus coriaria* (Sumac) has been demonstrated in clinical laboratory studies which support that sumac may be effective on COVID-19 virus.

Aim of the Study

Evaluation of efficacy of covets in treating of covid-19 acquired pneumonia.

Subjects and Methods

During the period of 3 months from 20 march to 20 June 2020, this prospective controlled clinical study compared the efficacy of two regimens of treatment for patients suffering from covid 19 pneumonia. It was conducted at 4 quarantine hospitals in Cairo on 88 patients with covid 19 related pneumonia. They were randomly assigned to one of two groups, the control group (43 patients) received conventional WHO protocol and the study group (45 patients) received a combination of the same conventional who protocol and covets.

All patients were followed up for one month. The primary outcomes were improvement of one or more of respiratory symptoms as fever, cough, and respiratory distress, while the secondary outcomes were clinical stability or in-hospital mortality.

A written consent was obtained from each patient after clarification of the study.

Preparation: The plants were collected, sieved, grinded prepared as powder form stored until use. The powder component added to distilled water. The plants materials were hydro-distilled for using stainless steel condensed steam container. Condensation occurs, so

liquid and oil were mixed again, boiled, then it was left for cooling down, then it was filtered. The final extract of with aromatic oils was packed in 250 ml sterile bottles and stored.

Data were analyzed using the statistical package for social sciences, version 23.0 (SPSS inc., Chicago, Illinois, USA), p-value is significant at < 0.05. The qualitative variables were presented as number and percentages.

Results

Demographic Data	Control Group (N = 43)	Study Group (N = 45)	Test Value	P-Value
Age (Years)				
< 30	15 (34.9%)	11 (24.4%)	1.152	0.283
30 - < 40	14 (32.6%)	11 (24.4%)	0.719	0.397
40 - < 50	6 (14.0%)	6 (13.3%)	0.009	0.924
50 - < 60	3 (7.0%)	8 (17.8%)	2.315	0.128
≥ 60	5 (11.6%)	9 (20.0%)	1.147	0.284
Sex				
Male	19 (44.2%)	17 (37.8%)	0.368	0.544
Female	24 (55.8%)	28 (62.2%)		
Outcome				
Pregnancy	10/24 (41.7%)	12/28 (42.9%)	0.488	0.485
Non-Pregnancy	14/24 (58.3%)	16/28 (57.1%)		

Table 1: *Comparison between control group and study group according to demographic data.*

Using: Chi-Square Test; P-Value > 0.05 NS.

This table shows statistically nonsignificant difference between groups according to demographic data regarding age, sex, and outcome, with p-value > 0.05.

Variable	Category	Control Group (N = 43)	Study Group (N = 45)	Test Value	P-Value
Time of Clinical Stability (Days)	1 - 6	0 (0.0%)	25 (55.6%)	33.026	< 0.001**
	7 - 10	8 (18.6%)	12 (26.7%)	0.812	0.368
	> 10	35 (81.4%)	8 (17.8%)	35.191	< 0.001**
Hospital Stays (Days)	3 - 10	16 (37.2%)	40 (88.9%)	25.110	< 0.001**
	11 - 15	17 (39.5%)	4 (8.9%)	11.207	< 0.001**
	> 15	10 (23.3%)	1 (2.2%)	8.843	0.003*
Mechanical Ventilation		11 (25.6%)	4 (8.9%)	4.038	0.045*
Post COVID Syndrome		4 (9.3%)	0 (0.0%)	4.334	0.037*
Hospital Mortality		10 (23.3%)	3 (6.7%)	4.748	0.029*

Table 2: *Comparison between control group and study group according to clinical profile.*

This table shows highly statistically significant improvement among the covets group regarding time of clinical stability (days), hospital stay (days), mechanical ventilation, post covid syndrome and hospital mortality.

Variable	Control Group (N = 43)	Study Group (N = 45)	Test Value	P-Value
No. of High-Risk Patients	22/43 (51.2%)	34/45 (75.6%)	5.596	0.018*
DM	8/22 (36.4%)	8/34 (23.5%)	1.070	0.301
Hypertension	12/22 (54.5%)	23/34 (67.6%)	0.960	0.327
Cardiac	2/22 (9.1%)	2/34 (5.9%)	0.202	0.653
Smoking	0/22 (0.0%)	1/34 (2.9%)	0.638	0.425
Success	6/22 (27.3%)	21/34 (61.8%)	6.253	0.012*
Mortality	10/22 (45.5%)	3/34 (8.8%)	9.911	0.002*

Table 3: *Comparison between control group and study group according to success in high-risk cases and hospital mortality.*

This table shows highly statistically significant improvement in the success and mortality rates among the covets than the non-CovETS groups of the pneumonic high-risk patients.

Discussion

In pneumonic patients of the present study, the hospital mortality rates were significantly higher among the non-CovETS than the CovETS group. Also, the mortality rates were significantly higher among the non-CovETS than the CovETS group.

In Egypt, from 3 January 2020 to 10:36 pm CEST, 18 April 2021, there have been 231,803 confirmed cases of COVID-19 with 13,591 deaths, reported to WHO, 5.9% [21], which is non significantly different from that (6.7%) of the second group of another study [9] and highly significantly different from that (1.3%) of the Covets group.

According to https://www.worldometers.info/coronavirus/ 18th may, 2021 [22], the death rate among the COVID 19 patients was found to be 2.01% and the overall deaths in another study [9] was 2.8%, while in the Covets group was found to be 1.04%.

Regarding the hospital stay and according to the present study, 88.9% of the CovETS group and 37.2% of the non-CovETS group, were discharged within 10 days, also, the hospital mortality was found to be 6.7%, and 23.3% among the CovETS and the non-CovETS groups respectively. In another study, Coronavirus SARS-CoV-2 and Diabetes outcomes was evaluated in 2796 diabetic patients. Within 28 days, 1404 (50.2%) were discharged from hospital with a median duration of hospital stay of 9 (5 - 14) days, while 577 participants died (20.6%) [23].

Regarding to the improvement rates, In the pneumonic high-risk patients of the present study there was a highly significant increase in the success rates of the CovETS than the non-CovETS group. Also, according to Edessy and Tawfik [9], among the high risk Covid 19 patients, there was significant increase in the number of improved cases in the CovETS group (97.1%) compared to the non-CovETS group (46.2%).

In the evaluation of the COVID 19 patients with hypertension, the death rate was found to be 20.7% [24], while according to Edessy and Tawfik [9], there was no deaths among the Covets group.

In the study about the short-term outpatient follow up COVID 19 patients [25], out of Eighty-one cardiac patients, 34 (41%) had been admitted to the ICU. According to Edessy and Tawfik [9], the improvement rate among the cardiac patients was found to be 50% in the non-CovETS group and 100% in the Covets group.

Conclusion

1. CovETS improved the clinical profile, hospital stay, the need for mechanical ventilation, Post COVID 19 syndrome and the hospital mortality rates among COVID 19 pneumonic patients.

2. CovETS improved the high-risk pneumonic patients' clinical profile and decreased their mortality rates.

Recommendation

Another study is needed to use covets as a sole treatment of Covid 19.

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