CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.1154133

Available online at: http://www.iajps.com Research Article

EFFECT OF *THYMUS VULGARIS* INHALING ON ARTERIAL OXYGEN SATURATION AND HEART RATE IN PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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Abstract:

Background and aim: *Acute exacerbation of chronic obstructive pulmonary disease (AECOPD), due to its debilitating nature, entails irreparable consequences on individual socioeconomic life. Treatment with conventional medicines not only imposes costs on the patient but also is associated with many side effects. Considering the importance of complementary medicine in nursing and the existence of evidence based on the antispasmodic and anti-inflammatory effects reported for thyme and low cost and complications of the plant extract, this study was conducted to determine the effect of T. vulgaris inhaling on arterial oxygen saturation and heart rate in patients with AECOPD.* **Materials and methods:** *The present randomized clinical trial was performed on 60 patients with AECOPD referred to Emergency Department of 22 Bahman Hospital in Gonabad, Iran, in 2016. The patients were selected according to inclusion criteria using convenience sampling and were randomly assigned to two groups of 30 (control and intervention). The intervention group received 1% T. vulgaris inhaling as much as 5 ml for 15 minutes through inhaling treatment mask, and the control group used distilled water inhaling for the same amount and duration with inhaling treatment mask. The arterial oxygen saturation and heart rate of the patients were collected and recorded via a portable finger pulse oximeter before and after the intervention by a researcher who was blind to the intervention. The data were analyzed by SPSS 22 using independent t-test and paired t-test with a significant level of less than 5%.* **Results:** *According to the obtained findings, the two groups had no difference in demographic and clinical variables (P>0.05). After the intervention, the mean arterial oxygen saturation (P = 0.01) and heart rate (P = 0.001) showed statistically significant differences between the two groups.* **Conclusion:** *The results of this study revealed that T. vulgaris inhaling is effective on the levels of arterial oxygen saturation and heart rate in patients with AECOPD. Emergency care nurses can consider these results in the care of patients. However, the use of this approach requires further research.*

Keywords: *Thymus vulgaris inhaling, Arterial Oxygen Saturation, Heart rate, Acute Exacerbation of Chronic Obstructive Pulmonary Disease.*

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Please cite this article in press as Mohammad Mojalli et al., ***Effect of Thymus Vulgaris Inhaling On Arterial Oxygen Saturation and Heart Rate in Patients with Acute Exacerbation of Chronic Obstructive Pulmonary Disease*** *, Indo Am. J. P. Sci, 2018; 05(01).*

INTRODUCTION:

Chronic Obstructive Pulmonary Disease (COPD) is one of the leading causes of mortality in developing and developed countries whose mortality rates are on the rise [1]. At present, 300 million people in the world are suffering from the COPD. Over the last three decades, the prevalence rate, pathogenicity and mortality of this disease have exacerbated. Annually, between 100 and 150,000 deaths are reported due to this disease in the world [2].

The Global Initiative for Chronic Obstructive Lung Disease estimates that the disease will rank from sixth to third leading cause of death worldwide by 2020 [3]. Since the COPD is most prevalent and highly debilitating, there are tremendous costs for the disease directly (costs from health care) or indirectly (costs resulting from absenteeism incurred to the family and community), imposing large socioeconomic burdens on different communities [4]. Economic analysis suggests that more than 70% of the health care costs of these patients are spent on examinations of the emergency department and hospital care that is annually more than $ 10 billion in the United States [5]. No detailed information is available on mortality and morbidity rates of the disease in Iran. Some studies indicate that, on average, 10% of the Iranian population suffers from this disease ranging from 1% to 40% in various communities, depending on the climatic conditions [6]. Others reported a 5.6% prevalence of chronic bronchitis in Iran [7].

There are exacerbation episodes of symptoms in the COPD course, which is called acute exacerbation of the disease. The acute exacerbation of chronic obstructive pulmonary disease (AECOPD) is any change in the natural course of the disease due to alterations in baseline dyspnea, airflow limitation, worsening cough, increased effort of breathing and altered nature or increased sputum happened as acute and out of the ordinary daily changes as well as the enhanced need for daily medication. The acute exacerbation of the disease increases inflammation and spasm of the airways, restricting the airways and worsening the gas exchange process. This leads to inadequate air renewal and ultimately lowering the arterial oxygen saturation level in these patients [8, 9].

The arterial oxygen reductions in patients with AECOPD can lead to various consequences, such as increased pulmonary arterial blood pressure and arrhythmia [10]. Lowering the level of arterial oxygen saturation can also cause damage to various organs of the body, including consequences in the brain such as restlessness of the patient and even damage to some parts of the brain [11].

In the treatment of COPD, there are current various medications, including airway dilators [12], corticosteroids [13], antibiotics and expectorants [14]. New medicine, despite its capabilities and values, is dealing with problems in the treatment of certain diseases, especially chronic diseases [15]. There is no complete recovery in the patients with COPD, despite receiving drug therapies, and only the disease symptoms are attenuated in these individuals. Furthermore, given the huge cost of treatment and the fact that any drug in spite of its beneficial effects has unwanted side effects, it is preferable to select a drug with fewer side effects [16]. Today, the use of complementary and alternative therapies has been considered in nursing and care of patients, which can be helpful in providing better care for patients [17].

Thyme, *Thymus vulgaris*, belongs to the Lamiaceae family. The extract of this plant is a yellowish- or reddish-brown liquid with pleasant, strong and sharp smell [18], consisting of terpene, phenol, thymol, carvacrol, phenolic glycoside, monoterpenoid, thymonin and saponin [19]. Thyme in this plant is a bronchial antispasmodic, expectoric, antimicrobial, antibacterial [20] and antifungal [21] agent, which blocks the L-type calcium channel and hereby reduces heart rate and blood pressure [22]. In lung diseases, the best method of prescribing is inhalation [23]. This treatment, especially in AECOPD, is very effective and worth considering due to the rapid effect of the drug and the prevention of the effect of the drug on other tissues in the body. Lungs are a great absorption site due to the vast surface, abundant blood vessels and alveolar capillary barrier to blood vessels, which facilitate the passage of macromolecular drugs into the blood circulation. Inhalation versus oral routes has no first-pass effects in a liver transplant and enzymatic activity [24]. Moreover, the possibility of drug delivery to the lung through the inhaler can reduce the dose and side effects as well as has no invasive complications of the intravenous method [25].

The use of thyme due to its antispasmodic, anti-inflammatory and blocking effects can have good advantages to improve the oxygenation and hemodynamic status of the patients. To the best of our knowledge, there is no study on the effects of *T. vulgaris* inhaling on arterial oxygen saturation and heart rate in the patients with AECOPD. Hence, the current study was conducted to determine the effect of *T. vulgaris* inhaling on arterial oxygen saturation and heart rate in patients with AECOPD.

MATERIALS AND METHODS:

The present single-blind randomized controlled clinical trial was performed on 60 patients with AECOPD referred to Emergency Department of 22 Bahman Hospital in Gonabad, Iran, in 2016. After obtaining the approval of project by the Ethics Committee of Gonabad University of Medical Sciences (with code of IR.GMU.REC.1395) and registering in the Iranian Registry of Clinical Trials (registration code of IRCT2017020732436N1), the researcher referred to the study environment in order to select the research units. Written and informed consent was obtained after explaining the objectives of the research to the patients or their legal guardian. The patients were selected according to the inclusion criteria using convenience sampling and randomly assigned to two groups of 30 (control and intervention). The inclusion criteria were the absence of anatomic face problem, willingness to participate in the research, completion of the consent form, oriented in time, place and person and understanding the study purposes, age between 50 and 70 years, no hyper sensitivity to perfumes and essential oils, no pregnancy, no other serious illness diagnosed by a specialist, and no nausea and vomiting. Exclusion criteria were unwillingness to continue the study, hypersensitivity to herbal inhaling and intolerance to the inhaling treatment mask.

The sample size was calculated to be 30 subjects in each group based on pilot study on 10 individuals (5 in the intervention group and 5 in the control group) using the formula for comparing the means, 95% confidence interval and test power of 90% and attrition of 10%. The intervention group received 1% *T. vulgaris* inhaling as much as 5 ml for 15 minutes through inhaling treatment mask, and the control group used distilled water inhaling for the same amount and duration with inhaling treatment mask. The arterial oxygen saturation and heart rate of the patients were collected and recorded via a portable finger pulse oximeter before and after the intervention by a researcher who was blind to the intervention.

RESULTS:

According to the results, control group consisted of 53.3% female and 46.7% male. The intervention group had 36.7% female and 63.3% male. The mean age of the research units was 60.96 in the control group and 60.33 in the intervention group. The two groups were homogeneous in terms of other demographic and clinical variables (Tables 1 and 2).
In this study, the samples had no significant difference in the percentage of arterial oxygen saturation in the pre-test stage. In the post-test, the intervention group showed a higher increase in arterial oxygen saturation, and had a significant difference with the control group (Table 3), confirming the effectiveness of the intervention in improving the arterial oxygen saturation in the patients with AECOPD. In addition, the heart rate was decreased in the posttest in the intervention group (Tables 4 and 5).

Table 1- Comparison of research units in two groups based on gender

Gender	Control group		Intervention group		Independent t-test result
	Number	percentage	Number	Percentage	χ^2=1.68 df =1 p =0.15
Female	16	53.3	11	36.7	
Male	14	46.7	19	63.3	
Total	30	100	30	100	

Table 2- Frequency distribution of research units in two groups based on age

Group	Number	(mean ± SD)	Independent t-test result
Control	30	60.96±829	t =0.29 p =0.77 df =58
Intervention	30	60.33±8.25	

Table 3- Comparison of arterial oxygen saturation in control and intervention groups

Phases	Number	Control group (mean ± SD)	Intervention group (mean ± SD)	Independent t-test result
Before inhaling	30	88.8±3.12	89.00±3.73	t =0.33 p =0.73 df = 58
After inhaling	30	89.00±3.31	91.23±3.35	t =2.51 p =0.01 df =58

Table 4- Comparison of mean heart rate of the control group in two phases

Phases	Number	(mean ± SD)	paired t-test result
Before inhaling	30	110.96±9.68	t =1.25 p =0.22 df =29
After inhaling	30	110.13±9.70	

Table 5- Comparison of mean heart rate of the intervention group in two phases

Phases	Number	(mean ± SD)	paired t-test result
Before inhaling	30	101.6±13.87	t =6.92 p =0.001 df =29
After inhaling	30	97.56±13.42	

DISCUSSION:

One of the important consequences of AECOPD is the reduction in arterial oxygen saturation in these patients following increased airway inflammation and spasm. This decrease in arterial oxygen saturation can cause harmful damage to various organs such as the brain and heart. Therefore, it is essential to improve the oxygenation status of these patients by nurses using chemical and herbal medicines for promoting the level of health care.

The results of this study showed that the percentage of arterial oxygen saturation was increased in two groups. This increase was significant in the group receiving *T. vulgaris* inhaling. Given the newness of this study, there was no direct finding confirming our research results. In several studies, some researchers have used the thyme plant with anti-spasmodic properties on smooth muscle and anti-inflammatory and anti-microbial features that are the main components of the treatment of the patients with AECOPD. For example, Boskabady et al. investigated the relaxant effect of thyme on tracheal smooth muscle in pigs and showed that the effect of thyme is comparable to theophylline [26]. Van den Brook argued that flavonoid in the thyme inhibits properly the contractions caused by cellular depolarization and blocks the calcium channel, indicating the antispasmodic properties of thyme [27]. Meister et al., exposed tracheal smooth muscle in pigs to the thyme extract and confirmed the antiprostaglandin and antipsymatic effects of thyme [28]. However, Bayat et al. showed that the thyme drop had no effect on the severity of wheezing in patients with chemical bronchitis [29]. This finding is inconsistent with the results of our study. According to the researcher, this inconsistency cannot be a decisive factor in rejecting bronchodilatorial properties of thyme, but the inability to dilate airways in the patients with bronchitis can be due to possible lung fibrosis in this patient. Hosseinzadeh et al. during in a study on rats found that the thyme extract

had anti-inflammatory (acute and chronic) and analgesic effects [30]. Jafari et al. described the anti-inflammatory effect of thyme, and attributed it to the flavonoid [31]. Beskabadi refers to the anti-inflammatory effect of thyme on the animal model of COPD and suggests that the anti-inflammatory effect of thyme is comparable to dexamethasone and even more potent at high doses [32]. Akbari indicated that thyme has a potential value in inhibiting the in vitro growth of *Candida albicans* [33]. Aymlvan also confirmed significantly thyme antimicrobial activity [34]. Fachini et al. showed that thyme causes inhibition of inflammation and migration of white blood cells [35]. Beskabadi et al. reported that carvacrol in thyme stimulates beta-2 receptor in guinea pig trachea, followed by a reduction in the smooth muscle tone [36]. Jafari et al. demonstrated that thyme affects the β-adrenergic receptor and can therefore reduce smooth muscle tone [37]. In a study of Salmalian, both ibuprofen and thyme reduced the pain severity of dysmenorrheal, probably due to the antispasmodic effect of thyme [38]. Iravani considered the thyme as an effective herbal remedy for the treatment of primary dysmenorrhea, pointed out to the analgesic and antispasmodic properties of thyme, and stated that this drug not only has no gastrointestinal complications unlike non-steroidal and anti-inflammatory drugs, but also is used in digestive disorders such as gastric ulcer, indigestion, constipation and bloating [39]. Babaei et al. revealed that thyme inhibited the contractions of the terminal ileum in guinea pigs, indicating anticholinergic effects of Thyme [40]. Fare Froosh studied in vitro antispasmodic effects of thyme essential oil in Isfahan Faculty of Pharmacy (Iran). They concluded that the essential oil controlled the contractions caused by cellular depolarization, and thus indicating the ability to control contractions with different origin [41]. Roozbahani et al. showed that mefenamic acid and thyme reduced the menstrual pain to a similar extent; they attributed the cause to the anti-prostaglandin and anti-contractile properties of thyme [42].

Our study also found that using *T. vulgaris* inhaling reduces heart rate. Ili et al. also expressed that the thyme because of blocking L-type calcium channel decreases heart rate and blood pressure, which is consistent with our findings [22]. Mihailovic et al. found that the injection of a certain dose of thyme into rats attenuates blood pressure and peripheral vascular resistance [43]. In addition, Aguila et al. observed that thyme lowers blood pressure and heart rate by inhibiting vascular contractions due to renin-angiotensin-aldosterone system and adrenaline [44].

CONCLUSION:

T. vulgaris inhaling through various mechanisms can increase arterial oxygen saturation and decrease heart rate in patients with AECOPD. Therefore, considering that many studies, including the current study, confirm the antispasmodic, anti-inflammatory, antimicrobial and heart rate lowering effects of thyme, the *T. vulgaris* inhaling can be suggested as an option to improve oxygenation and hemodynamic status in the patients with COPD. Inhalation therapy is an appropriate, practical and non-invasive approach without the need for special time and costly equipment, which is applicable to any health center and home though further research is required to comment conclusive in this regard.

ACKNOWLEDGEMENT:

Hereby, the authors would like to thank and appreciate the Graduate Studies Council of Nursing and Midwifery Faculty and the Student Research Committee of Gonabad University of Medical Sciences, colleagues at the Emergency Department of 22 Bahman Hospital, all patients participating in this research and their families.

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