Evaluation the Effect of Sublingual Glutathione on the Quality of Life in COPD Patient by Using Saint George respiratory questionnaire

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Abstract:

Background: Chronic obstructive pulmonary disease (COPD) is a chronic inflammatory disorder of the airways associated with airway narrowing with airflow obstruction leading to difficulty in breathing impair daily activity and cause poor quality of life. Patients and **methods:** Fifty patients whom diagnosed with COPD are divided into two groups, 1st control group includes 25 patients assigned to receive conventional therapy of Formoterol fumarate 12 microgram inhaler twice daily, and 2nd interventional group also includes 25 patients assigned to receive conventional therapy with (300 mg/ 2 times daily) sublingual glutathione for two months. Saint George respiratory questionnaire (SGRQ) were measured before and after first and second months after treatment in both study groups. Aim of the **study:** This study was object to assess the changes in quality of life by using SGRQ following sublingual glutathione supplements therapy in COPD patients. Results and **conclusion:** After two months treatment, the mean values of SGRQ showed a significant increase compared to pre-treatment levels in both groups ($P<0.01$). There was highly significant improvement in SGRQ in both COPD patients' groups after 2 months of treatment with much significant improvement in intervention group which may indicate the beneficial effects of adding glutathione sublingually administered supplements in COPD patient's conventional therapeutic regiment.

Key words: Chronic obstructive pulmonary disease, Sublingual, Glutathione, Saint George respiratory questionnaire.

تقييم تأثير الجلوتاثيون تحت اللسان على نوعية الحياة لدى مرضى الانسداد الرئوي المزمن باستخدام استبيان سانت جورج التنفسي

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الخلاصة:

مرض الانسداد الرئوي المزمن هو اضطراب التهابي مزمن في الشعب الهوائية مرتبط بتضييق مجرى الهواء مع انسداد تدفق الهواء مما يؤدي إلى صعوبة في التنفس ويضعف النشاط اليومي ويسبب سوء نوعية الحياة. المرضى والطرق: تم تقسيم خمسين مريضا تم تشخيص إصابتهم بمرض الانسداد الرئوي المزمن إلى مجموعتين ، تضم المجموعة الضابطة الأولى ٢٥ مريضا مخصصا لتلقي العلاج التقليدي المكون من فورموتيرول فومارات ١٢ ميكروغرام مرتين يوميا، وتشمل المجموعة التداخلية الثانية أيضا ٢٥ مريضا مخصصا لتلقي العلاج التقليدي مع الجلوتاثيون تحت اللسان (٣٠٠ مجم/ ٢ مرات يوميا) لمدة شهرين. تم قياس استبيان سانت جورج التنفسي قبل وبعد الشهرين الأول والثاني بعد العلاج في كلتا مجموعتي الدراسة. الهدف من الدراسة: كانت هذه الدراسة تهدف إلى تقييم التغيرات في نوعية الحياة باستخدام استبيان

سانت جورج بعد العلاج بمكملات الجلوتاثيون تحت اللسان في مرضى الانسداد الرئوي المزمن. النتائج والاستنتاج: بعد شهرين من العلاج ، أظهر متوسط قيم الاستبيان زيادة معنوية مقارنة بمستويات ما قبل العلاج في كلا المجموعتين (P<0.01). كان هناك تحسن كبير للغاية في معلمات الاستبيان في كل من مجموعات مرضى الانسداد الرئوي المزمن بعد ٢ أشهر من العلاج مع تحسن كبير في مجموعة التدخل والتي قد تشير إلى الآثار المفيدة لإضافة مكملات الجلوتاثيون تحت اللسان في مرضى الانسداد الرئوي المزمن مع الطرق العلاجية التقليدية.

الكلمات المفتاحية: الانسداد الرئوي المزمن – تحت اللسان -جلوتاثايون - استبيان سانت جورج التنفسي

Introduction

The global initiative for chronic obstructive pulmonary disease (COPD) define COPD as a common curable condition with severe airflow restriction result from excessive exposure to unpleasant particles and gases causes changes in the airway and alveoli.[1] One of the most prevalent lung diseases is COPD, affecting around 251 million people worldwide and affects 10% of adults in affluent countries.[2] The most frequent causes of COPD are toxic gases, such as cigarette smoke, and are followed by various forms of air pollution, fumes, dust, and chemical agents. Despite the fact that smoking is thought to be the main risk factor for COPD, only 25% of those who have been diagnosed with the disease have ever smoked, and the majority of smokers do not report developing COPD.[3] As a result, aging, hereditary factors, and environmental interactions all contribute to the development of COPD. The symptoms of COPD are remarkably similar to those of aging lungs; hence it is sometimes referred to as a disease of progressive pulmonary aging. COPD typically develops in people over the age of 40. [4,5]
Almost often patients with COPD have other coexisted diseases and thereby they are on multiple drug therapy or polypharmacy; such as, using statins, [6-8] antidiabetic therapy, [9-12] allopurinol, [13-15] proton-pump inhibitors for associated gastric problems to reduce stomach problems of polypharmacy. [16-18]
Glutathione is a plentiful chemical agent found in plethoric quantities in all tissues both in the intra and in extracellular part of cells. Glutathione consists of 3 peptides bind by ɤ- peptide linkage: glutamate, cysteine and glycine amino acids, and a typical peptide connects the carboxylgroup to the glycine portion.[19] Unfortunately, the glutamyl transferase enzyme breaks down glutathione into its constituent basic protein amino acid bases after ingestion, resulting in a poor oral absorption of less than 10%. The innovative sublingual formulation of glutathione performed significantly better than the orally consumed counterpart in terms of absorption qualities, antioxidation & stress protective properties.

Patients and Methods

Fifty-five patients with COPD who are diagnosed during their visit to Alsadir teaching hospital in Maysan governorate. The patients are supervised by a pulmonologist and are treated based on the clinical medical guideline of COPD disease.

Inclusive criteria

- COPD patients irrespective to gender and age ≥20 years.
- Patient are able to read and write in Arabic.
- COPD patients are diagnosed depending on the global initiative for COPD (GOLD) guideline.[1]

Exclusive criteria

- Patients diagnosed with DM, CVD, arthritis, asthma, or other respiratory disease except for COPD.
- Patients who are unable to perform acceptable spirometry.
- Patient on vitamin, antioxidant supplement and current administration of corticosteroid therapy for other disease.

- Pregnant & breast-feeding patients
- A validated COPD-specific quality-of-life assessment tool, the SGRQ Quality of life pulmonary Questionnaire for COPD Patients (SGRQ-C) is utilized for both COPD and asthma.[20] A self-administered quality of life evaluation called the SGRQ comprises 50 items and 76 weighted responses broken down into three categories: symptoms, activities, and consequences. The complaints section contains details about the severity of symptoms, such as coughing frequency, sputum production, wheezing, and the duration and frequency of dyspnea or wheezing. Exercises that cause or are impeded by breathlessness were the focus of the Activity component. In the Effects section, issues like job, managing one's health, anxiety, social stigma, the need for medication and its side effects, health outlooks, and general quality of life deterioration are covered. In addition to the cumulative scores that total the responses to all of the questions, each component is given a score between 0-100.The SGRQ-C has 2 parts: [21-23]
- While Part II also generates the Activity and Impact values in addition to the total score, Part I only generates the Symptomatology scores. The SGRQ-C is a reduced version of a survey that was created following in-depth data analysis from significant meta-analysis studies and is only used for COPD [21-23]

- Each patient completed 40 questions, with scores ranging from 0-100 for each item and a total score reflecting the patient's response to all questions. both at the start and after 2 months. A score of 100 (the highest perceived distress) indicates a worsening of quality of life, while a score of zero indicates no impairment. Accordingly, the questionnaire is ideal for use in situations where there is a high level of perceived anguish. [21-23]

Result

At the pre-treatment evaluation, health assessment scores using the SGRQ between the control and intervention groups with regard to symptoms, activity, impact subscales and total sum scores are: (P = 0.9, 0.07, 0.05, 0.05 respectively). As a result, there are no significant differences between the intervention and control groups prior to treatment (table 1).

At 2-month SGRQ assessment: control (Control) treated group show no significant improvement with regard to symptoms, activity, impact sub-score, p value =0.09,0.2,0.1 respectively. Although total SGRQ Scores show significant improvement (p-value =0.01). While interventional (glutathione) treated group reveal a significant improvement in sense of total and symptoms, activity, impact subscales (p-value= 0.0001).

The differences between control and intervention groups at 2 months are significant in regard to symptoms, impact, total scores (p-value = 0.01, 0.0002, 0.0008). The glutathione-treated group outperformed the Control -treated control group. In terms of physical activity, however, there are no significant variations between the two groups (p-value=0.3).

Table (1): Presented the following results for SGRQ

Variable	Study groups		
SGRQ total scores	**Control**	**Intervention**	***P- value***
Pretreatment	40 ± 5.5	43.8 ± 5.9	0.05
After 2 months	36 ± 5.26	30.76 ± 5.59	*0.0008**
P- value	*0.01**	*0.0001**	

(P<0.05) is regarded Significant difference

Paired t-test is statistically utilized to assess the difference between Pretreatment& 2 months post treatment results in same group.

Two-sample (unpaired) t-test is used to compare preor 2 months post treatment between control & intervention treated patients.

Table (2): SGRQ total scores and sub-scores of controls and interventional groups

SGRQ	Control group Mean (95%CI)	Intervention group Mean(95%CI)	*P-value Unpaired t-test*
Baseline			
Symptoms	53.3 (48.5, 58)	53.59 (47.84,59.3)	0.9
Activity	37 (32.9,41.2)	42 (38.2,45.9)	0.07
Impact	37.4 (34.2,40.6)	42.7 (38.2,47.21)	0.05
Total	40.5 (38.19,42.82)	43.8 (41.3, 46.27)	0.05
2 months assessment			
Symptoms	47.2 (41.6, 52.8)	39.2 (36 ,42.4)	0.01
Activity	34 (30.5, 37.6)	31.4(28.06, 34.94)	0.28
Impact	33.7 (30.5, 36, 8)	26 (23.6, 28,45)	0.0002*
Total	36.232 (34.06,38.4)	30.76 (28.45,33.07)	0.0008*

Mean (with 95% Confidence interval)

Discussion

In this study reveal that at 2-month assessment the SGRQ for: control group show no significant improvement with regard to symptoms, activity, impact sub-score (p- value =0.09, 0.2, 0.1) respectively. Although total SGRQ Scores show significant improvement (p-value =0.01), While the interventional group reveal a significant improvement in sense of total and symptoms, activity, impact subscales (p-value= 0.0001).

The differences between control and intervention groups at 2 months are remarkable regarding to symptoms, impact, total scores (p-value = 0.01, 0.0002, 0.0008) as the Intervention group outperformed the control group. However, in term of physical activity, there is no significant variation between the two groups (p-value=0.3). These results reflect a possible beneficial role for glutathione therapy in mitigating COPD symptoms and progression.

In a study performed by Panahi et al (2016), who used curcuminoids/piperine to indirectly increase glutathione in patient with chronic pulmonary disease found that Serum levels of GSH were increased by the end of the study there were significant improvements in the total as well as subscales (symptoms, activity and impact) of SGRQ compared to placebo ($p < 0.001$) with the elevation of GSH.[24]

Using the St. George questionnaire, Moussa et al. (2016) [25] searched for incapacity and impairment in the quality of life of smokers with COPD and those who did not have it. When the glutathione and protein sulfhydryl levels in blood samples were

analyzed, it was discovered that the COPD group had significantly lower physical activity scores with a markedly reduced quality of life and glutathione levels. One explanation for the inability and disabil ity seen in the COPD group could be because of oxidative damage causing exhaustion and depletion of pulmonary glutathione system.[26] Moreover, antioxidant effects provided by glutathione could be directly responsible about stabilization of subcellular receptors,[27] which could be attained by other antioxidant agents including Q10 providing lung protection.[28]

Failure to achieve good response could be due to localized inflammatory reaction due to release of immunomodulatory cytokines by cells, [29,30] and tissue oxygen levels modulate cellular response, [31,32] due to hypoxia of COPD itself. These released cytokines further destruct the tissues and eventually participate in the course of COPD pathogenesis. [33,34]

Conclusion

There was highly significant improvement in St. George Score in both COPD patients' groups after 2 months of treatment with much significant improvement in intervention group which may indicate the beneficial effects of adding glutathione sublingually administered supplements in COPD patient's conventional therapeutic regiment.

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