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The effect of stress management incorporating progressive muscle relaxation and biofeedback-assisted relaxation breathing on patients with asthma: a randomised controlled trial

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ABSTRACT

Background: Previous evidence indicates a negative influence of elevated stress on asthma symptoms and asthma-related quality of life.
Objective To investigate the effects of stress management (SM; progressive muscle relaxation accompanied by biofeedback-assisted relaxation breathing),on stress levels, asthma control, asthma-related quality of life and physical exercise in patients with intermittent and mild chronic asthma.
Methods: This is a phase 2, two-armed, parallel randomized controlled trial using an intervention SM group (N=23) and a usual care (UC) control group (N=19). The measurements included the Perceived Stress Scale (PSS), the Asthma Control Test (ACT), the Mini Asthma Quality of Life Questionnaire (MAQLQ) and one Likert-type question measuring frequency of weekly exercise. The assessments were carried out at baseline and after 8 weeks.
Results: Most patients had experienced zero or one asthma exacerbation during the previous year, while the mean duration of the disease was about 14 years for both groups. No differences were noted between the two groups at baseline. Patients in the SM group showed significant less perceived stress ($p<0.0001$), better asthma-related quality of life (regarding symptoms, daily activity/limitations and emotional function) and asthma control ($p <0.0001$) and higher frequency of physical exercise ($p=0.001$) than patients in the UC group at the end of the follow-up.
Conclusions: This study provides more evidence in favor of the role of SM in the treatment of asthma. Future studies should replicate and expand these results.

1. Introduction

Asthma is defined as the reversible airway obstruction that presents with a constellation of physical symptoms like wheezing, dyspnea, airway hyperresponsiveness, cough, and mucus hypersecretion [1]. Asthma is the most prevalent chronic respiratory disease worldwide. Data from the 2015 Global Burden of Disease study indicate that its incidence increased by 12.6% from 1990 to 2015 [2].

Notably, failure to effectively control the symptoms of asthma causes stress which has an aggravating effect on the patients' quality of life [3]. On the other hand, patients' physical and mental health (e.g. low levels of physical activity, increased asthma-related distress) may, on their turn, adversely affect the manifestations of the disease [4,5].

In the context of the reciprocal relationship between stress and asthma, many asthmatic patients resort to Complementary and Alternative Medicine (CAM) therapies. Yet, according to the 2010 Behavioral Risk Factor Surveillance System survey and the 2010 Asthma Callback Survey, those patients practicing CAM therapies have worse mental and physical health compared to those not practicing them [6]. This paradoxical finding leads to the conclusion that either CAM therapies have a harmful effect on asthmatic patients, or that asthmatic patients experiencing many physical and mental health problems are more inclined to opt forCAM therapies than those with less problems.

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Progressive muscle relaxation (PMR) is a CAM intervention that includes repetitive cycles of tensiion and relaxation of successive major muscle groups, frequently accompanied bydeep diaphragmatic breathing exercises [7,8]. Importantly, this technique is considered efficient to decrease stress levels in the general population [9]. To date, several studies have been carried out regarding the effect of PMR on the mental and physical health of other populations with chronic illnesses. Several systematic reviews support that this technique helps to manage the pain of osteoarthritis [10], to decrease elevated blood pressure [11], to improve the mental state and subjective well-being of patients with schizophrenia [12] and to decrease anxiety and chemotherapy-related toxicity in cancer patients [13].

Regarding asthma, few independent interventional studies have provided support on the beneficial efficacy of PMR asthma symptoms and patients' quality of life [14–20]. Yet, there is no evidence for the effect of PMR on patients' stress levels, which would provide a proof of concept for the stress-asthma reationship Furthermore, to our knowledge, there is no study examining the role of relaxation breathing (RB) along with PMR in chronic asthma, although there is evidence that RB alone can improve asthma-related quality of life In this context, the aim of the specific study was to replicate and strengthen the previous evidence regarding the effect of PMR accompanied with biofeedback-assisted relaxation breathing (altogether called stress management-SM- in this study) on asthmatic patients' stress, asthma symptoms-control and quality of life. Based on pertinent studies in clinical populations, we assume that SM through simple techniques can lead to beneficial changes in the aforementioned outcomes [14–21].

2. Methods

2.1. Study design

This is a phase II, non-blind, superiority, randomized, usual care-controlled, parallel group (1:1 allocation ratio) trial. Participants were randomized into either the SM group or the usual care (UC) control group. After trial commencement no important changes were made.

2.2. Procedures

The study was conducted at the "Sotiria" Chest Diseases Hospital (Athens, Greece), a major reference hospital for lung diseases treating patients from the whole country. Prior to the beginning of the study, an approval was gained from the hospital's bioethical committee (number 2783), as the study was in line with the Declaration of Helsinki. All participants had intermittent to mild chronic asthma based on asthma symptoms and forced expiratory volume (i.e. FEV1 $\geq$80% predicted). All patients were on short acting b2 agonists when necessary. The participants were informed of the study purpose by their treating physician, who assessed them for study eligibility. The inclusion criteria were the following: a) Having received a diagnosis of asthma based on the Global Initiative for Asthma 1995 guidelines [22] 2) Being 18 years old or over 3) Living in Athens, Greece. The exclusion criteria were the following: a) Having a change in asthma medication during the previous one month 2) current use of psychotropic medication 3) current use of another stress-management technique (e.g. autogenic training) 4) Experiencing asthma symptoms due to non-respiratory causes (e.g. left ventricular failure) 5) Having diseases or syndromes with symptoms similar to asthma such as hyperventilation syndrome, panic disorder, upper airway obstruction, vocal cord dysfunction, chronic obstructive pulmonary disease, non-obstructive lung diseases (e.g. diffuse parenchymal lung disease) etc. 6) inability to communicate verbally or in written in Greek. Recruitment lasted six months, at a frequency of once per week (the same day each week).

In case patients were interested to participate they were further informed of the study purpose by the principal investigator (the first author, GG), who was an external researcher. Using an external researcher to include the patients in the study was considered as more ethical, in order to avoid the barriers of using the treating physician or any other person of the medical staff having a dependent relationship in patient recruitment [31]. Subsequently, all eligible patients were enrolled in the study after providing informed consent and were randomized in the two study groups. All patients were initially provided with the study measures, which should had been returned during the next 2–3 days. At first encounter, all the participants received printed and verbal information regarding the relationship between stress, healthy lifestyle behaviours and the exacerbation of asthma. After 8 weeks, the study measures were re-administrated to both groups.

2.3. Intervention

In the intervention group, training and explanation of the stress management program took place during three extra visits, once per week, for the next three weeks after the enrollment in the study. Each of these sessions included teaching of biofeedback-assisted RB and PMR. [32]. RB consistes of nasal inspirations (except in the cases of nasal obstruction) followed by slow prolonged expirations. Galvanic skin response (GSR), respiratory (RSP) and heart rate variability (HRV) animated biofeedback was used to achieve the appropriate relaxation response during RB [32–34]. PMR comprises of successive contractions and relaxations of different large muscle groups in a down-top orientation, as previously described by Jacobson [7]. In each step, patients were encouraged to focus on the difference between tension and relaxation, thus gradually sharpening the perception of the relaxation response. The patients were instructed to omit any step causing them harm or discomfort. Relaxation breathing and PMR techniques were also administered in the form of an audio CD, consisting of 10 min of RB and 15 min of PMR, in order to be easier for the participants to practice at home. All participants were instructed to practice the guided RB-PMR CD twice a day for 8 weeks (for a maximum of 112 sessions), preferably after waking up and before going to sleep. After the third week, the participants were contacted by telephone once each week until the administration of the endpoint assessments in order to enhance their compliance in the program and to solve practical problems (e.g. replacing a lost CD).

2.4. Measurements

2.4.1. Socio-demographic and disease-related variables

These variables included age, gender, marital status (married/unmarried), employment status (working/not working), smoking status (current/ex-smoker/no), frequency of asthma exacerbations in the previous year (0–1/$\geq$ 2) and time since asthma diagnosis.

2.4.2. Mini asthma quality of life questionnaire

The Mini Asthma Quality of Life Questionnaire (MAQLQ) is a short and simple questionnaire comprised of 15 items in four domains ("symptoms", "activity limitations", "emotional function", "environmental stimuli") with a two-week recall period. The overall MAQLQ score is the sum of the scores for each item, divided by 15 (the number of items). Scores range from 0 to 7 with higher scores indicating better quality of life [23,24]. The internal consistency, measured by Chronbach's α [25], was acceptable (i.e. >0.7) for all domains except for environmental stimuli at baseline (i.e. 0.56), thus it was omitted.

2.4.3. Asthma control test

The Asthma Control Test (ACT) consists of five items regarding (a) activity limitations in work or school, (b) night awakenings due to asthma symptoms, (c) perceived breathlessness, (d) consumption of rescue medication, and (e) perceived asthma control. It evaluates asthma control during the past 4 weeks. The total score is obtained by summing the scores for each item and ranges from 5 (poor control of asthma) to 25 (complete control of asthma) [26]. The version used in the present study was developed through a previous validation of the ACT in the Greek population [27]. Cronbach's α was 0.87 & 0.89 at the baseline and endpoint assessment, respectively.

2.4.4. The perceived stress scale

The Perceived Stress Scale (PSS) is a 14-item questionnaire measuring a responder's level of perceived stress [28]. Each item is rated on a five point Likert-type scale (0 = never to 4 = very often). Half of these items are stated positively and half negatively. Higher scores reflect higher stress. The Greek version of the PSS used in this study is considered as a valid standardized version of the original PSS questionnaire [29]. The Cronbach's *a* was 0.86 at the baseline and 0.94 at the endpoint assessment.

2.4.5. Frequency of weekly exercise

The frequency of weekly exercise (FWE) was measured using the question: "How often do you exercise in a week?" The participants entered a numeric value between 0 (never exercise) and 7 (daily exercise) in a Likert-type scale.

2.5. Sample size

The study sample was determined only by the length of the recruitment period (i.e. 6months) and the recruitment frequency (once per week).

2.6. Randomization

A computerized random number generator was used to allocate patients in the treatment group in blocks of 4 patients to assure 1:1 allocation ratio. There was a randomization concealment for the recruiting physicians who made only eligibility assessments. Group allocation was made by a member of the research team (GG) not blind of the allocation sequence.

2.7. Blinding

Researchers, patients and statisticians were not blind for the treatment assignment.

2.8. Statistical analysis

All statistical calculations were performed using the SPSS for Windows (version 21) statistical software (SPSS INC., Chicago, IL). Baseline group characteristics are presented as means, standard deviations, absolute and proportion values. Differences between the baseline assessments of the two groups were estimated by the use of Pearson's Chi-square and Fisher's exact test in case of nominal variables and by Mann-Whitney U in case of scale variables. The outcome analysis involved group comparisons of the mean difference (follow-up minus baseline score) for each group using the non-parametric Mann-Whitney U test, due to small sample size. The level of significance was set at 0.05 for all the analyses.

3. Results

Fifty patients were found eligible for this study (25 in the SM group and 25 in the UC group). Finally, twenty-three patients were included in the intervention and 19 in the control group. Two patients in the SM group discontinued for personal reasons (death of a relative or disliked the program). Six patients in the UC group discontinued (i.e. 2 for personal familial reasons, 4 for unknown reasons).

The sample consisted mainly of middle-aged women, mostly unmarried and no smoking. Most patients had experienced zero or one asthma exacerbation during the previous year, while the mean duration of the disease was about 14 years for both groups. As indicated by Table 1, there were no statistically significant differences between the two groups at baseline.

According to Table 2, significant beneficial changes were recorded for all study outcomes, meaning that patients in the SM group showed less stress ($p < 0.0001$), better asthma related quality of life (symptoms $p = 0.003$; activity limitations $p < 0.0001$; emotional function $p = 0.001$) and asthma control ($p < 0.0001$) and more physical exercise ($p = 0.001$) than patients in the UC group. No side effects were reported during communication with the research staff.

4. Discussion

This study supports that SM (i.e. PMR accompanied by biofeedback-assisted RB) may be an effective intervention for reducing stress and improving asthma control, asthma-related quality of life and physical exercise in asthmatic patients with intermittent to mild chronic asthma. These results replicate previous PMR studies on the matter [14–20].

Apart from recording the changes occurring after the practice of simple SM techniques like PMR assisted with RB in this study, it is important to identify a pathway between stress management and the associated benefits. A potential mechanism of the effects on

Table 1
The differences between the intervention and the control group at baseline.

	Intervention group (N = 23)	Control group (N = 19)	P^1
Age, mean (SD)	49.43 (13.08)	49.05 (13.27)	0.91
Gender (%)			1.00
Men	7 (30.4)	5 (26.3)	
Women	16 (69.6)	14 (73.7)	
Marital status (%)			1.00
Married	9 (39.1)	7 (36.8)	
Unmarried	14 (60.9)	12 (63.2)	
Employment status (%)			0.95
Yes	12 (52.2)	11 (57.9)	
No	11 (47.8)	8 (42.1)	
Smoking (%)			0.43
Current smokers	4 (17.4)	1 (5.3)	
No-smokers	8 (34.8)	9 (47.4)	
Ex-smokers	11 (47.8)	9 (47.4)	
Frequency of asthma exacerbations (%)			1.00
0-1 previous year	19 (82.6)	16 (84.2)	
$\geq$ 2 previous year	4 (17.4)	3 (15.8)	
Duration of asthma, mean (SD)	14.48 (9.62)	14.47 (7.38)	0.78
PSS, mean (SD)	31.30 (6.37)	30.21 (7.46)	0.57
ACT, mean (SD)	22.10 (2.92)	21.58 (2.91)	0.47
MAQLQ symptoms' domain, mean (SD)	6.12 (0.96)	5.93 (0.89)	0.33
MAQLQ activity limitations, mean (SD)	6.23 (0.61)	6.11 (0.57)	0.35
MAQLQ emotional function, mean (SD)	5.39 (1.21)	5.33 (0.95)	0.59
FWE, mean (SD)	1.39 (2.08)	1.32 (2.34)	0.71

Abbreviations: ACT, Asthma Control Test; FWE, Frequency of Weekly Exercise; MAQLQ, Mini Asthma Quality of Life Questionnaire; PSS, Perceived Stress Scale; SD, Standard Deviation.

[1] Mann-Whitney U or chi-square test for numerical and categorical variables, respectively.

Table 2
Differences between the two groups after the intervention[1].

	Intervention group (n = 23)	Control group (n = 19)	P[2]
ΔPSS ± SD	−13.83 ± 4.30	−0.84 ± 2.61	<0.0001
ΔACT ± SD	0.91 ± 0.79	0.05 ± 0.52	<0.0001
ΔMAQLQ symptoms' domain ± SD	0.104 ± 0.16	−0.01 ± 0.46	0.003
ΔMAQLQ activity limitations ± SD	0.17 ± 0.16	0.01 ± 0.06	<0.0001
ΔMAQLQ emotional function ± SD	0.78 ± 0.49	0.02 ± 0.14	0.001
ΔFWE ± SD	2.70 ± 2.42	0.21 ± 1.32	0.001

Abbreviations: ACT, Asthma Control Test; FWE, Frequency of Weekly Exercise; MAQLQ, Mini Asthma Quality of Life Questionnaire; PSS, Perceived Stress Scale; SD, Standard Deviation.
[1] Values represent score differences (follow-up minus baseline) ± standard deviations.
[2] Mann-Whitney U test.

stress reduction is the disengagement from unnecessary goal-directed and analytic activity, occurring through the technique [34], which, in our case, could be over-thinking of the asthmatic symptoms. It also could be supported that the improvement of stress is a result of the decrease in levels of stress-related hormones, such as cortisol, which has been reported after practicing PMR [35,36]. It is also possible that the effect of SM on the asthmatic symptoms is mediated through the decrease of stress hormones, due to the well-known pathway between the neuroendocrine and autonomic nervous system responses and lung function [4]. The improvement of quality of life could also be an additional effect of stress management, based on the strong inverse association between psychological distress and asthmatic patients' quality of life [37]. Nonetheless, there is a variety of limitations concerning the internal validity of the study. First, the study sample was small, a barrier that makes trial results prone to type I error [40]. Another limitation is that there were no measures of compliance to the intervention content in order to reveal a potential relationship with the benefits recorded. In addition, the reporting of asthmatic symptoms was recorded by the use of self-reports, which is a less reliable method for data collection in medical research compared to biomarkers, since they are subject to the Hawthorne bias [41]. Furthermore, the follow up was carried out after a short time. Therefore, the sustainability of the benefits recorded is yet unknown. It is also possible that the intervention and the control group participants, treated at the same hospital unit, shared part of the interventional content between them, a limitation that is common for all studies applying non-pharmacological interventions recruiting intervention and control group participants from the same environment [42]. Last, there was no sham arm in order to minimize the placebo-effect of the intervention, although there is evidence that in asthmatic patients the effectiveness of CAM interventions is limited when compared to sham study arms [43].

In this context, the aim of future trials should be to establish the effect of PMR on similar study outcomes compared to placebo-controlled groups, a major challenge for all CAM interventions [44]. Sham sessions of similar time frame could be developed by teaching participants to inhale and exhale at a usual pace and continuously repeating an exercise, such as tensing the same muscle or making any other body part move, instead of tensing all muscle groups in a specific order. This type of pseudo-session resembles the fake placebo needles used to equalize the placebo effect between different study arms in acupuncture research [45] and could result to patient blinding.

Apart from including larger samples of patients and biomarkers, which is necessary to increase the methodological quality, future studies should also expand the range of the measurements applied. More specifically, it would be interesting to measure the cost of health care utilization of asthmatic patients receiving PMR. It has been previously reported that CAM can decrease the cost of health care provision and have cost-effective benefits for the health systems due to lower morbidity for those practicing [46,47]. Hence, since as supported by this study there is a reduction in the symptoms of asthma through the practice of PMR, it would be interesting to investigate cost-effective benefits from this intervention.

It is also necessary for this technique to draw the attention of clinicians involved in asthma care. Apart from the use of biofeedback, which is not accessible to all, the interventional content of this study is quite simple and it is possible that PMR could be a feasible intervention for the vast majority of asthmatic patients. In addition, the resources demanded for the integration of this technique in clinical care are low, both in funds and human resources required, since this technique can be applied at home by the use of a CD, without the constant need of a health professional. Health professionals not able to use biofeedback may focus on constructing appealing digital material that will ensure the successful practice of RB and PMR by patients. Therefore, PMR might be an easily administrated technique in order to alleviate the mental and physical burden of the disease and to promote a patient's healthy lifestyle.

5. Conclusions

This study supports that stress management techniques such as progressive muscle relaxation and biofeedback-assisted relaxation breathing may have a beneficial role in asthma patients. Yet, a variety of limitations downgrade the trustworthiness of the findings. Future research regarding should replicate and expand the results of this study.

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Conflict of interest

The authors declare that they have no conflict of interest.

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