SCIREA Journal of Clinical Medicine

ISSN: 2706-8870

http://www.scirea.org/journal/CM

October 7, 2021

Volume 6, Issue 6, December 2021

Long term effects of a standard Mindfulness Based Stress Reduction program in COPD patients.

Saïda Bensliman[1], Vincent Ninane[2] , Naila Bradstreet[1], Christian Mélot[3]

[1]Department of Respiratory Medicine, Hôpitaux Iris Sud – Site Molière-Longchamps, Belgium

[2]Department of Respiratory Medicine, Centre Hospitalier Universitaire Saint-Pierre, Belgium

[3]Department of Emergency, Erasme University Hospital, Université Libre de Bruxelles Brussels, Belgium

Address for correspondence: Dr Saïda Bensliman

Department of Respiratory Medicine, Hôpitaux Iris Sud – Site Molière Longchamps, Rue Marconi, 142, 1190 Brussels, Belgium

Phone: +32473370275

Email: saida.bensliman@yahoo.fr

Abstract

The management of mental health in addition to physical health in patient with chronic obstructive pulmonary disease (COPD) is often overlooked. Many COPD patients report anxiety and depression in relation to their respiratory condition. Mindfulness-based approaches has accrued a robust evidence base in improving mental health outcomes in patients with chronic diseases. We conducted a study to evaluate the effects of the Mindfulness-Based Stress Reduction (MBSR) program in COPD patients who additionally participate to a pulmonary rehabilitation program in comparaison with a control group.

Twenty eight COPD outpatients were enrolled,18 attended the standardized protocol 8-weeks MBSR program and the remaining 10 patients constituted the control group. The primary outcomes of psychological distress were measured with the Hospital Anxiety and Depression Scale (HADS), the State-Trait Anxiety Inventory (STAI-Y2) and the Perceived Stress Scale (PSS) at baseline (T0), 10 weeks (T1), 6 month (T2) and 12 months (T3) follow-up.

A significantly improvement at 12 months were found in the MBSR group compared with the controls for the HADS (1.91 decrease versus 0.7 increase; respectively; 2.61 differential change; p=0.0463) and for the STAI-Y2 with a differential change of - 6.48 between the two groups (p=0.011). There was no statistically significant effect of the intervention versus control in stress level with PSS throughout the 1-year follow-up.

MBSR showed a statistically significant long term effect on the mental health of COPD patients. These results suggest that mindfulness based intervention can be proposed, as a non-pharmacological treatment, in combination with Gold recommended treatment.

Keywords : Mindfulness, MBSR, COPD , mental health

INTRODUCTION

Chronic obstructive pulmonary disease (COPD), which is affecting millions of patients around the world, is one of the main global causes of morbidity and mortality (1). It is expected to become the third cause of death and the seventh cause of disability in 2020 (2). Therefore, prevention and management of COPD represent a major public health challenge. The main guidelines for the standardized management of COPD have been established by the global initiative for chronic obstructive lung disease (GOLD) (3). Despite the availability of these guidelines, the life of people with a chronic disease changes dramatically and leads to significant deterioration in its quality (4). Previous researches have shown that there is a high prevalence of fear, anxiety, panic disorder and depression among COPD patients (5). Psychological distress has a profound impact on how people with COPD experience and manage their disease and is associated with health status impairment and increased mortality. Comorbid depression and anxiety in COPD is often undertreated and increase susceptibility to respiratory tract infections and COPD exacerbations with a disproportionate increase in health care utilization rates and costs (5,6). Therefore, COPD require holistic approach by

health care workers who should take into account not only the medical parameters but also other indicators that influence the overall well-being, that is, mental status.

A recent meta-analysis (n = 2063) of non-pharmacological interventions for symptoms of depression and/or anxiety in adults with COPD concluded that behavioral interventions can reduce symptoms of self-reported depression and anxiety in patients with COPD (7). According to Coventry et al. an efficient cognitive behavioral therapy must be an intervention that promotes an 'accepting mode of response' such as mindfulness and may be appropriate to manage psychological distress in COPD.

Mindfulness is defined as the capacity to intentionally be in the present moment without judgement (8). Through mindfulness training, people learn to recognize and discriminate between components of an experience, including thoughts, feelings, and sensations, and developing a non-reactive awareness to these. Mindfulness-Based Stress Reduction (MBSR) has accrued a robust evidence base in improving mental health outcomes in those with chronic physical health problems (9) such as chronic pain, cancer, chronic fatigue, fibromyalgia, heart disease, asthma, depression, and anxiety (10-14).

The main mindfulness-based approaches include MBSR and Mindfulness-Based Cognitive Therapy (MBCT). Mindfulness reduces perceived stress, anxiety and depression in patients with chronic physical or mental health conditions (15).

So far, the limited amount of researches on meditation in the COPD population demonstrates a relatively limited methodological quality. Mindfulness interventions were based on the standard MBSR program but varied widely in terms of their delivery. The authors did not find any significant statistical improvement in a 6-minute walk, in COPD symptom burden, in quality of life, in respiratory rate nor in emotional function (16-17). The lack of efficacy of meditation interventions in COPD has been associated with poor adherence to mindfulness program (16). More recently, the MBCT program showed a statistically significant and durable effect on psychological distress, indicating that MBCT may be added to pulmonary rehabilitation programs in COPD (18).

The present study was aimed to investigate the effect of the standardized MBSR intervention without any adaptation in a sample of COPD outpatients who additionally participate to a pulmonary rehabilitation program compared with a control group of COPD patients on quality of life, psychological distress and pulmonary function tests.

METHODS

Study design

We conducted a controlled trial to test the efficacy of MBSR on COPD patients. The study was approved by the two ethics committee of Iris Sud Hospital and Saint-Pierre Hospital University. All participants agreed to participate in the study and completed informed consent prior to study.

Subjects

We planned to enroll 40 subjects with COPD from pulmonary care clinics in two hospitals (Iris Sud and Saint Pierre Hospitals). Eighteen patients at Iris Sud Hospital were recruited between June 2015 and September 2015 prior to the start of the 8-week MBSR program and followed up for 12 months. Ten patients recruited between June 2015 and January 2016 at Saint-Pierre University Hospital for the control group and also followed up for 12 months.

Inclusion criteria were: a) presence of airflow obstruction by spirometry (diagnostic criteria for patients with COPD were based on the Global Initiative for Chronic Obstructive Lung Disease (3)), b) participation in a pulmonary rehabilitation program at hospital or at home with a physiotherapist c) ability to read and write French, d) availability of transportation to attend weekly classes. Exclusion criteria were a) severe exacerbation of COPD within 4 weeks prior to enrollment, b) the presence of any active oncology disease.

Intervention

The intervention group attended a standard 8-week mindfulness-based stress reduction program (19-21). The 8-week MBSR program included eight weekly 2h30 group sessions, a day-long retreat between the sixth and the seventh week, and daily home mindfulness meditation practice. Meetings were held in a comfortable quiet room located inside the hospital building. The group sessions consisted of instructor-guided mindfulness body awareness activities, mindfulness meditations, mindful stretching, and group discussions. COPD-specific modifications on meditation included: focus on the body sensations as a mean of attentional stabilization instead of focusing on the breath. The mindfulness meditation intervention used in this study was conducted by qualified MBSR instructor. Home practice was delivered by four compact discs of formal 45-minutes long mindfulness practices and a manual. Participants were asked to practice for 40 to 45 minutes for 6 or 7 d/wk. Participant's

experience of home practice and their developing practices were captured using weekly surveys.

Measurements

The primary end point were psychological (anxiety, depression, stress) outcomes whereas the secondary outcomes were quality of life (QoL), lung function measures and medication adherence. All measures were made at baseline (T0), and at 10 weeks (T1), 6 month (T2) and 12 months (T3) by an evaluator independent of the study.

The primary outcomes measures:

The Hospital Anxiety and Depression Scale (HADS)

HADS screens for clinically significant anxiety and depressive symptoms in medically ill patients. There are 2 sub-scales within this measure: the State Anxiety Scale and the State Depression Scale. Total scores range from 0 to 42 with higher scores representing higher levels of psychological distress (22). An average reduction of 1.5 points on the HADS representing a clinically relevant improvement in patients with COPD (23).

The State-Trait Anxiety Inventory (STAI-Y-2)

The French version of the STAI-Y scale showed psychometric properties similar to the original version and is aimed at detecting and evaluating anxiety symptoms, concerning both state (STAI-Y1) and trait (STAI-Y2) anxiety components (24,25). Trait anxiety (T-Anxiety) was assessed using the sub-scale from the Spielberger State-Trait Anxiety Inventory test (STAI form Y-2), with statements referring to how a person generally feels, and a higher total score reflecting a higher T-Anxiety.

The Perceived Stress Scale (PSS)

The PSS, is a self-report measure of perceived stress, contains 10 items and measures the degree to which situations in life are stressful. Items are designed to evaluate how much one people finds his own life overloaded, unpredictable, and uncontrollable. Each item is scored on a 5-point Likert scale from 0 (Never) to 4 (Very often) (26).

The secondary outcome measures

The Chronic Respiratory Disease Questionnaire (CRQ)

Quality of life was assessed using the chronic respiratory questionnaire: a validated questionnaire that measures the health status of patients with COPD. The CRQ contains 20

items and is composed of four sub-domains: dyspnea, fatigue, mastery (the patient's feeling of control over their disease), and emotional function. Higher scores indicating fewer symptoms. The different domains of CRQ quality of life were assessed: physical function (dyspnea and fatigue) and emotional function (mastery and emotion) (27-29) The minimal clinically important difference accepted for this instrument is 0.5 points (30).

Pulmonary function tests

All patients underwent spirometry by trained staff at the out-patient pulmonary clinic, according to the method described in the American Thoracic Society 1994 update (31). A post-bronchodilator Forced Expiratory Volume in 1 second (FEV1) ≥ 80% (predicted) corresponding to mild COPD, FEV1 50–79% to moderate COPD, FEV1 30–49% to severe COPD, and FEV1 ≤ 29% to very severe COPD, respectively (3).

Six-min walk test (6MWT)

Functional exercise capacity was measured by a 6MWT, according to the ATS statement (32). Patients were instructed to walk as far as possible for 6 min. The distance (6MWD) the patients could walk was recorded. Oxygen saturation was also measured by pulse oximetry at rest 5min prior to the test and immediately after it.

Morisky Medication Adherence Measure (MMAS-8)

The self-reported measure of medication intake was evaluated by the Morisky Medication Adherence Scale (MMAS-8). Advantages include simplicity of the questions and ease of scoring. The current 8-item scale was significantly correlated with the previously validated 4-item self-reported medication-taking scale (33). Scores obtained from this scale range from 0 to 8, where higher scores indicate higher adherence.

Statistical Analysis

Analyses were carried out using R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria). Graphs were built with GraphPad Prism 8.2.1 (GraphPad Software, San Diego, CA). Continuous variables were presented in mean ± SD and compared with unpaired t-tests. Discrete variables were presented in number (with percentage) and compared using the Chi^2 test. A $p<0.05$ was considered significant. Baseline distributions of important patient characteristics were compared by study group based on non-missing data. T-tests compared

Age, BMI, FEV1 (L), FEV1 (% predicted), the 6MWT, the STAI-Y-2, the HADS, the PSS, the CRQ quality of life domains and the MMAS-8.

The primary and secondary outcomes were evaluated on 14 of the 18 participants who completed the standard 8-week mindfulness-based stress reduction program (per protocol analysis), in comparison with the control group (10 patients). The basic analytical strategy was to compare differential trends over time for the intervention versus control group. The main outcomes were derived from a difference-of-difference analysis representing over-time change in the intervention group after accounting for simultaneous change in the comparison group.

Trends over time in HADS, STAI-Y2, PSS, CRQ (physical and emotional functions), FEV1 (in liters and % predicted), 6MWT and MMAS-8 were analyzed using linear mixed models with random intercepts and slopes, with patient as the random effect. Differential change was calculated as the difference in change from baseline for the intervention group versus change from baseline for the control group.

RESULTS

Baseline Characteristics

After assessing for eligibility, 28 subjects were enrolled: 18 of them in the MBSR program group and 10 in the control group. Four (4/18) of the intervention group participants did not complete the study. The Mindfulness group included mostly female persons (10/18), the mean age was 68.1± 7.4. The control group was only comprised of men aged 66.1 ± 9.8 on average. Disease severity did not differ between groups and the post-bronchodilator FEV_1 was 48 ± 16 and 48 ± 18 of the predicted value in the MBSR and control group respectively. In the intervention group, 2 patients used oxygen. Baseline demographic, background information, comorbidities, and COPD outcomes were balanced between groups, as shown in Table 1. There were no difference between groups in age, lung function, exacerbation history, comorbidity burden, QoL

Table 1. Baseline Clinical and Demographic Characteristics

Characteristic	MBSR (n=18)	Control (n=10)	P value
Age years	68.11 ± 7.41	66.10 ± 9.81	0.545
Gender			
Men	8 (44.4%)	10 (100%)	/
Women	10 (55.6%)	0 (0%)	
BMI, kg/m^2	25.73 ± 6.23	25.37 ± 4.85	0.875
Smoking			
Yes	4 (22.2%)	3 (30%)	/
No	14 (77,8%)	7 (70%)	
Marital status			
married/cohabiting	10 (55.5%)	8 (80%)	/
single/widow(er)	8 (44.5%)	2 (20%)	
Occupational status			
full or part time work	3	2	
unemployed	1	1	/
retired	13	6	
sick leave	1	1	
Comorbidity			
history of cancer	1	0	
heart condition	6	4	/
osteoporose	3	2	
depression	2	0	
Hospitalization in past 12 mo	3	4	/
FEV1, L	1.11 ± 0.34	1.50 ± 0.53	0.026
FEV1, %predicted	47.67 ± 15.88	47.6 ± 17.39	0.992
Home oxygen use, n	2	0	/

Characteristic	MBSR (n=18)	Control (n=10)	P value
6MWD, m	525.44 ± 471.92	455.10 ± 74.71	0.646
HADS total	12.78 ± 5.70	13.30 ± 6.06	0.822
STAI-Y2	(n =17) 39.12 ± 10.80	38.5 ± 6.96	0.873
PSS	29.28 ± 5.45	29.10 ± 2.77	0.924
CRQ quality of life domains Physical function Emotional function	 4.57 ± 1.31 4.96 ± 1.09	 4.31± 1.23 4.91 ± 1.39	0.622 0.924
MMAS-8	6.99 ± 1.23	6.53 ± 1.55	0.393

Primary outcomes

All baseline measures, including pre-intervention scores for the HADS, STAI-Y scale, and PSS were similar for the two groups. The results of the psychological outcomes are summarized in Table 2.

Table 2 Primary outcomes: model estimates for baseline, follow-up and change from baseline

	Mean ± SE n				Mean change from baseline to:		
	Baseline	**10 weeks**	**6 months**	**12 months**	**10 weeks**	**6 months**	**12 months**
HADS							
MBSR	13.29 ± 5.44 14	12.00 ± 4.79 14	12.46 ± 6.90 13	11.58 ± 7.74 13	-1.29	-0.83	-1.91
Control	13.30 ± 6.06 10	13.70 ± 7.06 10	12.40 ± 5.36 10	14.00 ± 6.87 8	0.4	-0.9	0.7
Differential change					-1.69	0.07	-2.61
p-value					0.2752	0.9212	0.0463 *
STAI-Y2							
MBSR	40.43 ± 9.56 14	36.79 ± 11.20 14	37.38 ± 9.37 13	37.08 ± 11.60 13	-3.64	-3.05	-3.35
Control	38.5 ± 6.96 10	38.70 ± 10.73 10	38.9 ± 9.28 10	41.63 ± 8.18 8	0.2	0.4	3.13
Differential change					-3.84	-3.45	-6.48
p-value					0.1356	0.1207	0.0107 *
PSS							
MBSR	28.36 ± 5.65 14	27.00 ± 6.37 14	27.46 ± 4.54 13	28.38 ± 6.67 13	-1.36	-0.9	0.02
Control	29.10 ± 2.77 10	29.30 ± 2.98 10	29.00 ± 4.16 10	31.38 ± 4.27 8	0.2	-0.1	2.28
Differential change					-1.56	-0.8	-2.26
p-value					0.24	0.218	0.3144

Differential change was calculated as the difference in change from baseline for the intervention versus change from baseline for the comparison group. The differing numbers of individuals included in each outcome analysis is due to missing data, as not all patients completed these measurements at all time points. HADS: Hospital Anxiety and Depression Scale; STAI-Y2: The State-Trait Anxiety Inventory; PSS: Perceived Stress Scale; * p<0.05

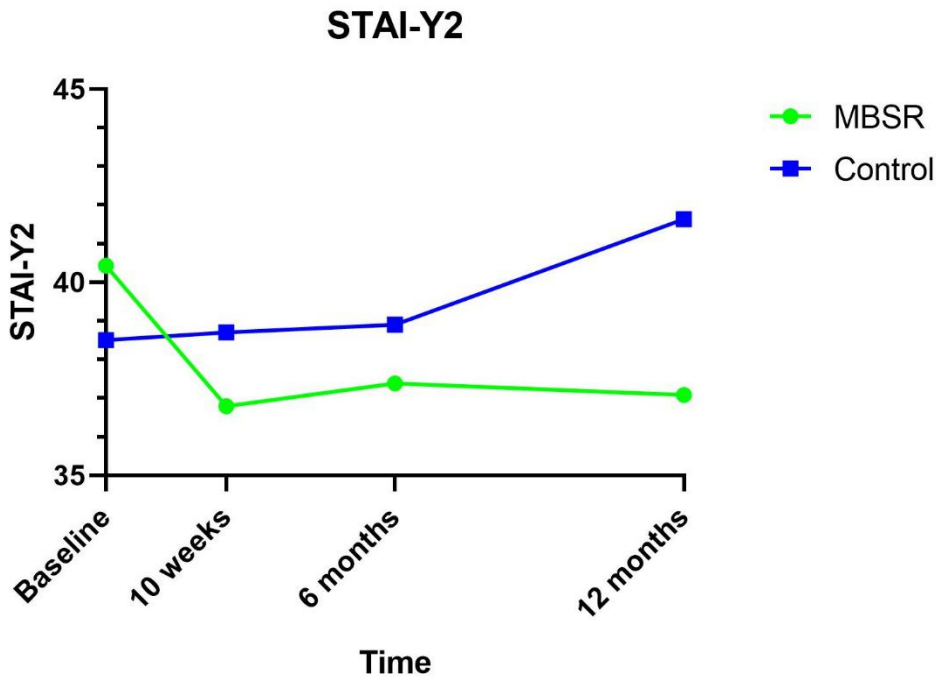
The Hospital Anxiety and Depression Scale

At 12-month follow-up, overall HADS was improved in the MBSR group compared with controls (1.91 decrease versus 0.7 increase; respectively; 2.61 differential change; p=0.0463). Moreover the -1.91 effect of MBSR on overall HADS at 12-month exceeded the -1.50 points reduction that is considered a clinically significant improvement.

The State-Trait Anxiety Inventory (STAI-Y2)

At 12 months STAI-Y2 had significantly improved in the MBSR group compared with the controls. The mindfulness group decreased by -3.35 (from 40.43 ± 9.56 at baseline to 37.08 ± 11.60 at 12 month) whereas the control group increased by 3.13 (from 38.5 ± 6.96 to 41.63 ± 8.18 at 12 month). This differential change of - 6.48 between the two groups was statistically significant (p=0.011) (figure 1).

Figure 1: The State-Trait Anxiety Inventory (STAI-Y2) in both group at baseline, 10 weeks, 6 months, and 12 months. The change between the two groups is statistically significant (p=0.011).



The Perceived Stress Scale (PSS)

There were not significant changes in PSS score between the intervention and the control group at 10 weeks, 6 months and 12 months.

Feasibility and compliance to MBSR program

A review of 8-week mindfulness meditation and stress reduction program revealed that 14 of the 18 (78%) participants completed the standard 8-week mindfulness-based stress reduction program. Among the non-attenders, three of them attended only the first two classes. Reasons for not completing the intervention were painful feeling due to vertebral compaction (n=1), intense back pain (n=1), lack of time to participate in a clinical trial (n = 1), and refusal to complete the program (n = 1). The others were able to participate fully to each weekly 2h30 class and the day-long retreat. Majority of subjects (85%) in the meditation intervention group attended 8 or more meditation classes. The two patients using oxygen completed the 8-weeks. Concerning the daily home mindfulness meditation practice, the participants received each week a self-report questionnaire that they had to fill at home about the number of days meditating per week and they could also note all their observations every day. The mean number of days meditating per week remained significant: 4 day per week (figure 2). During the study, none of the participant was hospitalized due to COPD exacerbation.

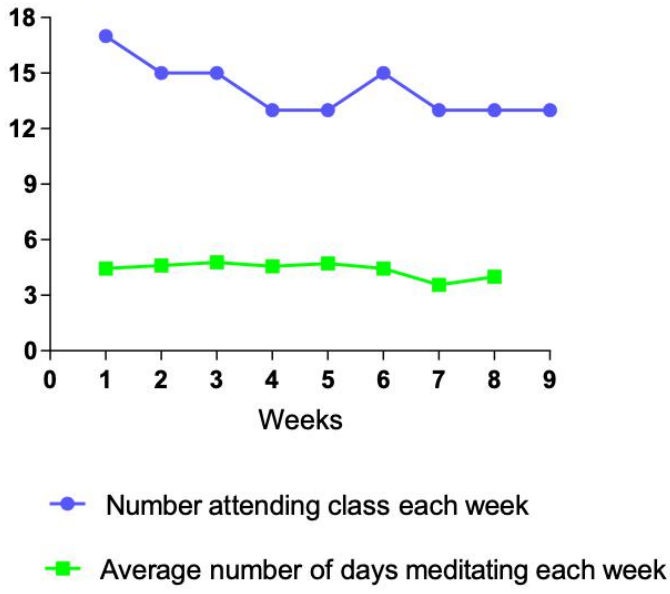


Figure 2: Participation in meditation intervention.

Secondary outcomes

All measures are summarized in Table 3.

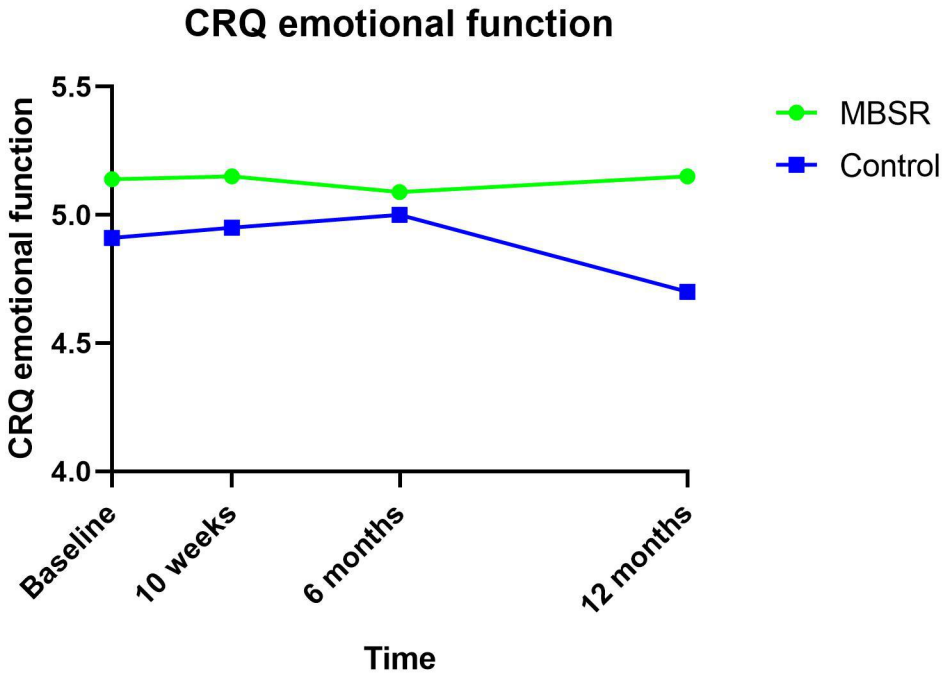
Table 3 Secondary outcomes: model estimates for baseline, follow-up and change from baseline

	Mean ± SE n				Mean change from baseline to:		
	Baseline	**10 weeks**	**6 months**	**12 months**	**10 weeks**	**6 months**	**12 months**
CRQ physical							
MBSR	4.8 ± 1.25 14	4.76 ± 1.41 14	4.72 ± 1.38 13	4.60 ± 1.39 13	-0.04	-0.08	-0.2
Control	4.31 ± 1.23 10	4.23 ± 1.16 10	4.47 ± 1.09 10	4.15 ± 1.25 8	-0.08	0.16	-0.16
Differential change					0.04	-0.24	-0.04
p-value					0.8939	0.2605	0.8122
CRQ emotional							
MBSR	5.14 ± 1.05 14	5.15 ± 1.15 14	5.09 ± 1.23 13	5.15 ± 0.94 13	0.01	-0.05	0.01
Control	4.91 ± 1.39 10	4.95 ± 1.09 10	5.00 ± 0.96 10	4.70 ± 1.22 8	0.04	0.09	-0.21
Differential change					-0.03	-0.14	0.22
p-value					0.9867	0.9172	0.3062
FEV1(litres)							
MBSR	1.14 ± 0.30 14	1.19 ± 0.34 14	1.16 ± 0.28 13	1.15 ± 0.33 13	0.05	0.02	0.01
Control	1.50 ± 0.53 10	1.44 ± 0.58 10	1.45 ± 0.49 10	1.63 ± 0.53 8	-0.06	-0.05	0.13
Differential change					0.11	0.07	-0.12
p-value					0.0911	0.8102	0.9467
FEV1(%)							
MBSR	48.43 ± 16.30 14	50.93 ± 19.37 14	51.92 ± 22.43 13	50.15 ± 21.60 13	2.5	3.49	1.72
Control	47.60 ± 17.39 10	45.30 ± 18.45 10	46.20 ± 16.36 10	52.13 ± 17.52 8	-2.3	-1.4	4.53
Differential change					4.8	4.89	-2.81
p-value					0.0836	0.3563	0.6324
6MWT(m)							
MBSR	454.14 ± 162.48 14	519.29 ± 202.43 14	510.08 ± 109.26 12	422.77 ± 119.49 13	65.15	55.94	-31.37
Control	455.10 ± 74.71 10	469.10 ± 83.60 10	456.56 ± 86.96 9	479.13 ± 72.57 8	14	1.46	24.03
Differential change					51.15	54.48	-55.4
p-value					0.207	0.4984	0.3261
MMAS-8							
MBSR	6.79 ± 1.30 14	7.27 ± 0.74 14	7.08 ± 1.18 13	6.85 ± 1.28 13	0.48	0.29	0.06
Control	6.53 ± 1.55 10	7.25 ± 0.88 10	7.14 ± 1.12 9	7.16 ± 1.32 8	0.72	0.61	0.63
Differential change					-0.24	-0.32	-0.57
p-value					0.5317	0.8306	0.0643

Differential change was calculated as the difference in change from baseline for the intervention versus change from baseline for the comparison group. The differing numbers of individuals included in each outcome analysis is due to missing data, as not all patients completed these measurements at all time points.CRQ :Chronic Respiratory Disease Questionnaire;MBSR: Mindfulness-Based Stress Reduction, FEV1: Forced Expiratory Volume in 1 seconde; 6MWD: 6 min walk distance;MMAS-8: Morisky Medication Adherence Measure; MBSR: Mindfulness-Based Stress Reduction.

The CRQ physical function did not change between groups over time. From baseline to 12 months, the CRQ emotional function in the meditation intervention changed from 5.14 ± 1.05 to 5.15 ± 0.94 at 12-month. For the corresponding values were 4.91 ± 1.39 and 4.70 ± 1.22 and the differential change between the two groups was not significant (p=0.31) (figure 3).

Figure 3: The Chronic Respiratory disease Questionnaire (CQR) - emotional function in both group at baseline, 10 weeks, 6 months, and 12 months. The change between the two groups is not statistically significant (p=0.31).



The lung function measure (FEV1 (litres) did not improve in the MBSR group compared with controls; changes from baseline were 0.01 and 0.13 respectively at 12 month (differential change was not statistically significant). At 10 weeks, the mean increase of 6MWD from baseline in the MBSR group was 65,1m in comparison with 14 m in the control group (differential change 51.1m; p=0.21). At 6 months the MBSR patients also seemed to perform better than the controls patients (mean 6MWD difference of 55.9 m and 1.5 m respectively) but this differential change was also not significant 54.5 m (p=0.5). Analyses showed also no significant differential change between the groups on medication adherence measure.

DISCUSSION

Effect on psychological disorders

The present study demonstrate that participation in the MBSR program as an adjunct to COPD treatment including pulmonary rehabilitation significantly reduces depression and anxiety at 1 year in patients with COPD. The participation to a Mindfulness program in

addition to standard treatment in chronic diseases has the potential to improve management of psychological distress which is frequently experienced by these patients. There is limited literature examining the use of mindfulness among COPD patients. Nonetheless, evidence has only recently emerged in terms of a psychological benefit of Mindfulness based intervention in COPD patient using MBCT (18). This MBCT program derived from MBSR and was initially developed to prevent relapse in previously depressed individuals by enhancing awareness and disengagement from repetitive negative thinking about one's depressive symptoms (35,36). The authors consider therefore that this type of intervention would be more adequate in comparison with MBSR which has shown no beneficial effect on COPD population in previous studies. The mechanisms of change within psychological functioning of meditation-based interventions (MBSR and MBCT) in patients is complex. Some researchers believe that there are potential common mechanisms of action in MBCT/MBSR and this could explain why our results show the same positive effect on HADS as that observed in the MBCT study in patients with COPD (37). Moreover, the finding that the intervention reduced anxiety was also demonstrated by a gradual improvement in STA-Y2 with a significance level at 1 year that was observed in the MBSR group compared to control group. More interestingly, this result indicates that the efficacy of MBSR could be sustained, even after the end of the intervention. This means the MBSR program has the potential to remedy the trait that would affect the onset and continuity of anxiety symptoms. This might represent the particularity of mindfulness, which aims to transform the attitude of COPD patients toward unpleasant events rather than to remove the unpleasant experiences themselves.

There was no statistically significant effect of the intervention versus control in stress level with PSS throughout the 1-year follow-up. Stress has been defined as any uncomfortable emotional experience accompanied by predictable biochemical, psychological and behavioral changes directed towards adaptation to or removal of the stressor. Assessment of stress is very challenging and sensible to the influence of many confounding factors: age, comorbidities and external factors can easily affect the perception of stress. Hence, we would need a properly matched control arm and randomization to determine the real efficacy of the MBSR program on stress.

The feasibility, acceptability of mindfulness intervention

To our knowledge the current study is the first study to demonstrate the good feasibility of a traditional 8-weeks MBSR program which included eight 150 minutes weekly sessions, a

day-long retreat and daily home mindfulness meditation practice in addition to the standard GOLD recommendations for COPD patients. Jon Kabat-Zinn's MBSR program protocol has been meticulously respected considering the fact that COPD patients have the resources to follow it. Indeed as shown in previous studies, Mularski et al (16) proposed a mind–body breathing therapy (MBBT) program with a high drop-out rate, and Chan et al (17) reduced the duration of 8 weekly sessions of MBSR to 60 minutes with a good adhesion. Moreover, these studies used additional techniques (Ujjayi breathing, Qigong style of mindful movement along with mantra-style meditation, …) which could have induced some misinterpretation of the results.

In our study, 78% of the individuals received a complete Mindfulness based-intervention. The dropout rate was quite low (4 of the 18 participants). The majority of patients who entered the study managed to complete the MBSR program, attending an average of eight sessions among the nine scheduled. Mindfulness-Based interventions emphasize the importance of mindfulness practice at home as an integral part of the program. Indeed there is an association between the extent of formal practice and positive intervention outcomes for many participants (34). In this study the mean number of meditative practice at home per week also remained high: about 4 per week. There are several reasons for the good adherence to such a new approach. First, each participant received individual information about the complete structure of the MBSR program. They were aware of the real commitment that the study needs before signing the informed consent and were also motivated to explore a new complementary approach to standard COPD care. Second, the program took place in a large conference room in the same hospital network where the patients were treated. It was therefore a familiar medical environment that could have reinforced a security feeling in this COPD population. All participants suffered from the same known disease and this also could have enhanced belonging feeling.

Effect on quality of life, functional respiratory tests and adherence to therapy

We found no statistically significant effect on disease-specific health-related QoL as measured by CRQ physical function (dyspnea and fatigue domains) and CRQ emotional function (mastery and emotion domains) between the two groups. However, we found that COPD patients in the intervention group in comparison with control group have not deteriorated their emotional function over time based (figure 3). Even if this differential change is not significant, it is an interesting and encouraging finding supposing a potential

effect of the MBSR program in emotional regulation in these patients which is described as one of the mechanisms of mindfulness action by Hölzel (38)

Lung function and the 6-MWT were not significantly affected by the mindfulness intervention over time in comparison with the control group. Our finding support the view that meditative movement in COPD patient compared to no treatment, does not appear to affect respiratory function. However, for the exercise capacity evaluated by the the 6-MWT, our study has documented that a MBSR intervention compared to controls increased the 6MWD by 51.1 m at 10 weeks and 54.4 m at 6 month. It must be pointed out that Redelmeier et al (39) suggested that subjects have to improve their walking distance by at least 54 m after a 6-MWT in order to appreciate this increase as a beneficial clinical effect, whereas Troosters et al (40) reported a mean increase of 52 m in a study of the short- and longer-term benefits of pulmonary rehabilitation delivered over a 6-month period. It is interesting that our data show that a MBSR intervention has allowed to reach the minimal clinical significance limits proposed by these authors. Chronic breathlessness increases anxiety, negative emotions and fear resulting in an unwillingness to participate in activities and further compromises exercise capacity (41-42). The beneficial effects of MBSR intervention on psychological disorder and emotional regulation could explain this encouraging finding by breaking this vicious circle.

Adherence to medications plays a key role in treatment optimization and clinical outcome in patients with chronic disease. Identifying COPD patients who have difficulty in adhering to a therapeutic regimen is then fundamental. A first step is assessing or measuring adherence with a standardized instrument. There are very few published studies focusing on adherence to inhaled medications in COPD patients (43-44). In this study we did not find a significant difference on MMAS-8 between MBSR group and control group after the intervention and throughout the 1-year follow-up. Our result could be explained by the characteristic of our population with a lower number of included patients and a higher proportion of good level of adherence to inhaled therapy in the two groups.

Limitations

The major limitations of the study include a non-random group allocation therefore means As a result, we can not draw definitive conclusions as to the effect of the MBSR program on

COPD patients. Therefore, it is necessary to conduct randomized controlled studies to accurately evaluate its effectiveness in future research.

In addition, the sample size of this controlled pilot study was small and limited the power of analyses and to detect differences in a number of variables. The challenge was to recruit patients over a short period of time to participate in a program that is still little know in the hospital environment in Belgium and this factor explains that the initial sample size was not reached.

Third, the majority of patients in the control group were recruited later in time than the control group and may create confounding factors and bias.

Strengths

The present study has a number of strengths. This is the first study applying rigorously a strict standardized protocol of MBSR in COPD patients and showing some effectiveness. The previous studies have modified the duration of sessions and added different practices to the standard protocol making it difficult to compare results (16,17).

This study also offers a long- term follow-up assessments. Follow-up for the previous studies evaluating MBSR was usually a maximum of 8 weeks (16,17), which may be too short for patients with chronic illnesses, who are likely to have long periods of ill health and fluctuations over time.

Conclusions

In summary, this study represent the first available evidence showing the feasibility for traditional 8-week mindfulness based stress reduction program in patients with moderate to very severe COPD with a good attendance class.

MBSR showed a statistical and clinical improvement with long term effect on anxiety and depression without effect on quality of life, pulmonary function tests and adherence therapy in this population. This research suggests that mindfulness-based intervention can be proposed, as a non-pharmacological treatment to manage psychological distress in COPD, in combination with GOLD recommended treatment.

Funding

This work was supported by a grant of Iris Recherche (htpps://www.iris-hopitaux.be) - Fondation Roi Baudouin (https://www.kbs-frb.be)

Acknowledgements: we thank the nurses and physiotherapists of the Departments of Respiratory Medicine, from Hôpitaux Iris Sud – Site Molière-Longchamps and Centre Hospitalier Universitaire Saint-Pierre and the MBSR teacher.

Authors' contributions: SB, VN, and CM: concept and design. SB and NB: acquisition, and analysis of data. SB: writing of the draft. SB, VN, and CM: interpretation of data, revision of the manuscript, and approbation of the final manuscript.

REFERENCES

[1] Mannino DM, Kiriz VA. Changing the burden of COPD mortality. Int J Chron Obstruct Pulmon Dis. 2006;1(3):219–33.

[2] Rosenberg SR, Kalhan R, Mannino DM. Epidemiology of chronic obstructive pulmonary disease: prevalence, morbidity, mortality, and risk factors. Semin Respir Crit Care Med. 2015;36(4):457–69.

[3] Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187(4): 347–65.

[4] Benzo RP, Abascal-Bolado B, Dulohery MM. Self-management and quality of life in chronic obstructive pulmonary disease (COPD): the mediating effects of positive affect. Patient Educ Couns. 2016;99(4):617–23.

[5] Dalal AA, Shah M, Lunacsek O, Hanania NA. Clinical and economic burden of depression/anxiety in chronic obstructive pulmonary disease patients within a managed care population. COPD. 2011;8(4):293–9.

[6] Laurin C, Moullec G, Bacon SL, Lavoie KL. Impact of anxiety and depression on chronic obstructive pulmonary disease exacerbation risk. Am J Respir Crit Care Med. 2012;185:918–23.

[7] Coventry PA, Bower P, Keyworth C, Kenning C, Knopp J, Garrett C, et al. The effect of

complex interventions on depression and anxiety in chronic obstructive pulmonary disease: systematic review and meta-analysis. PloS One. 2013; Apr 5;8(4):e60532.

[8] Kabat-Zinn J. An outpatient program in behavioral medicine for chronic pain patients based on the practice of mindfulness meditation: theoretical considerations and preliminary results. Gen Hosp Psychiatry. 1982;4:33–47.

[9] Bohlmeijer E, Prenger R, Taal E, Cuijpers P. Meta-analysis on the effectiveness of mindfulness-based stress reduction therapy on mental health of adults with a chronic disease: what should the reader not make of it? J Psychosom Res. 2010;69 614–15.

[10] Parswani MJ, Sharma MP, Iyengar S. Mindfulness-based stress reduction program in coronary heart disease: a randomized control trial. Int. J. Yoga. 2013;6:111–7.

[11] Pbert L, Madison JM, Druker S, Olendzki N, Magner R, Reed G, et al. Effect of mindfulness training on asthma quality of life and lung function: a randomized controlled trial. Thorax. 2012;67:769–76.

[12] Zangi HA, Mowinckel P, Finset A, Eriksson LR, Hoystad TO, Lunde AK, et al. A mindfulness-based group intervention to reduce psychological distress and fatigue in patients with inflammatory rheumatic joint diseases: a randomized controlled trial. Ann Rheum Dis. 2012;71:911–7.

[13] Grossman P, Niemann L, Schmidt S, Walach H. Mindfulness-based stress reduction and health benefits: a meta-analysis. J Psychosom Res. 2004; 57: 35–43.

[14] Chiesa A, Serretti A. Mindfulness-based stress reduction for stress management in healthy people: a review and meta-analysis. J Altern Complement Med. 2009;15: 593-600.

[15] Fjorback LO, Arendt M, Ornbol E, Fink P, Walach H. Mindfulness-based stress reduction and mindfulness-based cognitive therapy: a systematic review of randomized controlled trials. Acta Psychiatr Scand. 2011;124:102–19.

[16] Mularski RA, Munjas BA, Lorenz KA, Sun S, Robertson SJ, Schmelzer W, et al. Randomized controlled trial of mindfulness-based therapy for dyspnea in chronic obstructive lung disease. J Altern Complement Med. 2009;15:1083–90.

[17] Chan RR, Giardino N, Larson JL. A pilot study: mindfulness meditation intervention in COPD. Int J Chronic Obstr Pulm Dis. 2015;10:445–54.

[18] Farver-Vestergaard I, O'Toole MS, O'Connor M, Lokke A, Bendstrup E, Basdeo SA, et al. Mindfulness-based cognitive therapy in COPD: a cluster randomised controlled trial. Eur Respir J. 2018;51:1702082.

[19] Kabat-Zinn J. Full Catastrophe Living. Using the Wisdom of Your Body and Mind to

Face Stress, Pain and Illness. New York: Hachette books. 2013.

[20] Bishop SR. What do we really know about mindfulness-based stress reduction? Psychosom Med. 2002;64:71–83.

[21] Kabat-Zinn J. Mindfulness-based interventions in context: past, present, and future. Clin Psychol Sci Practice. 2003;10:144–56.

[22] Zigmond AS, Snaith RP. The Hospital Anxiety and Depression Scale. Acta Psychiatr Scand. 1983;67:361–70.

[23] Puhan MA, Frey M, Buchi S, Schünemann HJ. The minimal important difference of the hospital anxiety and depression scale in patients with chronic obstructive pulmonary disease. Health Qual Life Outcomes. 2008;6:46.

[24] Spielberger CD, Gorsuch RL, Lushene R, Vagg PR, Jacobs GA. Manual for the State-Trait Anxiety Inventory (form Y). Palo Alto, CA: Consulting Psychologists Press. 1983.

[25] Bruchon-Scweitzer M, Paulhan I. Manuel du STAI forme Y, adaptation française. Paris : Editions du Centre de Psychologie Appliquée (ECPA). 1993.

[26] Cohen S, Kamarck T, Mermelstein R. A global measure of perceived stress. J Health Soc Behav. 1983;24:385-96.

[27] Williams JE, Singh SJ, Sewell L, Guyatt GH, Morgan MD. Development of a self-reported chronic respiratory questionnaire (CRQ-SR). Thorax. 2001;56:954-9.

[28] Singh SJ, Sodergren SC, Hyland ME, Williams J, Morgan MD. A comparison of three disease-specific and two generic health-status measures to evaluate the outcome of pulmonary rehabilitation in COPD. Respir Med. 2001;95:71-7.

[29] Harper R, Brazier JE, Waterhouse JC, Walters SJ, Jones NM, Howard P. Comparison of outcome measures for patients with chronic obstructive pulmonary disease (COPD) in an outpatient setting. Thorax. 1997;52:879-87

[30] Jones PW. Interpreting thresholds for a clinically significant change in health status in asthma and COPD. Eur Respir J. 2002;19:398–404.

[31] Medical Section of the American Lung Association. Standardization of spirometry: 1994 update. Am J Respir Crit Care Med. 1995;152:1107–36.

[32] American Thoracic Society. ATS statement: guidelines for six-minute walk test. Am J Respir Crit Care Med. 2002;166:111–7.

[33] Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. Med Care. 1986;24:67–74.

[34] Parsons CE, Crane C, Parsons LJ, Fjorback LO, Kuyken W. Home practice in mindfulness-based cognitive therapy and mindfulness-based stress reduction: a

systematic review and meta-analysis of participants' mindfulness practice and its association with outcomes. Behav Res Ther. 2017;1:29–41.

[35] Segal ZV, Williams JMG, Teasdale JD. Mindfulness-based cognitive therapy for depression: A new approach to preventing relapse. New York: Guilford. 2002.

[36] Segal ZV, Williams JMG, Teasdale JD, Gemar M. A cognitive science perspective on kindling and episode sensitization in recurrent affective disorder. Psychol Med. 1996;26:371–80.

[37] Alsubaie M, Abbott R, Dunn B, Dickens C, Keil TF, Henley W, Kuyken W. Mechanisms of action in mindfulness-based cognitive therapy (MBCT) and mindfulness-based stress reduction (MBSR) in people with physical and /or psychological conditions: A systematic review. Clin Psychol Rev. 2017; 55:74-91.

[38] Holzel B, Lazar S, Gard T, Schuman-Olivier Z, Vago D, Ott U. How does Mindfulness Meditation work? Proposing mechanisms of action from a conceptual and neural perspective. Perspect Psychol Sci. 2011;6:537-59.

[39] Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: the six-minute walk test in chronic lung disease patients. Am J Respir Crit Care Med. 1997;155:1278-82.

[40] Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. Am J Med. 2000;109:207-12.

[41] Guthrie SJ, Hill KM, Muers, ME. Living with severe COPD. A qualitative exploration of the experience of patients in Leeds. Respir Med. 2001;95:196– 204.

[42] Seamark DA, Blake SD, Seamark CJ, Halpin DM. Living with severe chronic obstructive pulmonary disease (COPD): perceptions of patients and their careers: an interpretative phenomenological analysis, Palliat Med. 2004;18:619–25.

[43] Bourbeau J, Bartlett SJ. Patient adherence in COPD. Thorax. 2008;63:831-8.

[44] Vestbo J, Anderson JA, Calverley PM, Celli B, Ferguson GT, Jenkins C, Knobil K, Willits LR, Yates JC, Joneset PW. Adherence to inhaled therapy, mortality and hospital admission in COPD. Thorax. 2009;64:939-43.