Symptom reduction in palliative care from single session mindful breathing: a randomised controlled trial

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**ABSTRACT**

**Context** There has been increasing evidence of the role of mindfulness-based interventions in improving various health conditions. However, the evidence for the use of mindfulness in the palliative care setting is still lacking.

**Objectives** The objective of our study was to determine the efficacy of a single session of 20 min mindful breathing in alleviating multiple symptoms in palliative care.

**Methods** Adult palliative care in patients with at least one symptom scoring ≥5/10 based on the Edmonton Symptom Assessment Scale (ESAS) were recruited from September 2018 to December 2018. Recruited patients were randomly assigned to either 20 min mindful breathing and standard care or standard care alone.

**Results** Forty patients were randomly assigned to standard care plus a 20 min mindful breathing session (n=20) or standard care alone (n=20). There was statistically significant reduction of total ESAS score in the mindful breathing group compared with the control group at minute 20 (U=98, n₁ = n₂ = 20, mean rank ₁ = 15.4, mean rank ₂ = 25.6, median reduction ₁ = 6.5, median reduction ₂ = 1.5, z=−2.763, r=0.3, p=0.005).

**Conclusion** Our results provided evidence that a single session of 20 min mindful breathing was effective in reducing multiple symptoms rapidly for palliative care patients.

**INTRODUCTION**

The concept of mindfulness has been described as a fundamental activity of our consciousness, involving attention or awareness. In particular, it requires a receptive attention to one’s surroundings and a clear awareness of both one’s inner and outer world. A two-component operational definition of mindfulness involves self-regulation of attention to one’s immediate experience, followed by adopting a curious, open and accepting orientation towards it in the present moment. In short, mindfulness is a natural ability of our mind to pay full attention to an object or experience as it is without trying to form any judgement, conceptualisation or reactions.

There has been increasing evidence of the role of mindfulness-based interventions in improving various health conditions. The body of evidence to date included both clinical trials as well as observational and qualitative studies showing evidence of benefit. One of the earliest documentations of therapeutic use of mindfulness was in the form of mindfulness-based stress reduction (MBSR) programme in chronic pain, where it was shown to effectively reduce pain indices for various pain conditions ranging from facial pain to angina pectoris. This was back in the 1980s. At recent years, mindfulness-based interventions have further documented benefit in alleviating suffering and distress, as well as improving psychological well-being. Besides these patient-reported outcomes, more objective outcome measures looking at physiological changes in response to mindfulness-based interventions have also been documented. The scope of study participants were wide, with involvement ranging from healthy volunteers to palliative care patients, as well as family caregivers.

Focussing on the palliative care setting, the evidence for mindfulness-based interventions was still lacking. A systematic
review in 2017 found only four studies examining the use of this modality among the palliative care population, with only two deemed suitable for analysis. Hence, this study aimed to address and reduce this gap in current evidences. More specifically, the objective of our study was to determine the efficacy of a single session of 20 min mindful breathing in alleviating multiple symptoms in palliative care.

**METHODOLOGY**

The study was conducted in adherence with the Declaration of Helsinki and Good Clinical Practice guidelines. With approval from the Medical Ethics Committee, we conducted a parallel-group, open-label, randomised controlled study in University of Malaya Medical Centre, Malaysia. It was conducted from September 2018 to December 2018. The patient and public were not involved in the design of this study. The inclusion criteria were (1) adult palliative care patients aged 18 years and above and (2) at least one symptom scoring ≥5/10 based on the Edmonton Symptom Assessment Scale (ESAS). Patients who were confused based on the Confusion Assessment Method or non-communicative were excluded. Those who fulfilled the criteria were recruited into the study and written consent was obtained.

Patients’ demographic and clinical data, including age, sex, ethnicity, diagnosis and functional status were recorded at recruitment. ESAS, which is a validated scale, was used to assess 10 symptoms commonly experienced by patients, which are; pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, anorexia, other symptoms and feelings of well-being. The severity of each symptom was rated on a numeric scale of 0 to 10 (0, no symptoms; 10, worst possible severity). A baseline score was obtained at recruitment. ESAS, which is a validated scale, was used to assess 10 symptoms commonly experienced by patients, which are; pain, fatigue, nausea, depression, anxiety, drowsiness, shortness of breath, anorexia, other symptoms and feelings of well-being. The severity of each symptom was rated on a numeric scale of 0 to 10 (0, no symptoms; 10, worst possible severity). Written informed consent was obtained.

Patients were randomised on a 1:1 ratio and assigned to either 20 min mindful breathing and standard care or standard care alone. This was done using a computer-generated random number list with separation of allocations into single sheets that were opened only on patient recruitment to allow allocation concealment. Patients allocated to the mindful breathing group were informed that they would undergo the 20 min mindful breathing exercise, followed by a repeat ESAS immediately at the end of the 20 min. They then received the 20 min mindful breathing session which consisted of four 5 min breathing exercises done consecutively, guided by the investigator, with instructions to relax their body, focus their attention on their breathing and redirect their attention back to their breathing if distracted. The four exercises are presented in box 1. After completion of this 20 min of mindful breathing, ESAS was repeated to document any change in symptoms. Patients randomised to the control group were told that the investigator would converse with them for a baseline score was obtained at recruitment.

**Box 1 20 min mindful breathing exercise**

**Step 1 (5 minutes): Identifying the in-breath and out-breath**
Make yourself comfortable. Relax your body. Close your eyes gently. Take two deep breaths slowly. Then, breathe naturally. Notice the flow of air through your nose. Rest your attention gently on the breath. Breathing in, you know you are breathing in. Breathing out, you know you are breathing out. In – out, in – out, in – out. If you are distracted by any sounds, body sensations, thoughts or feelings, gently come back to your breath. Be aware of your in-breath and out-breath for the next few minutes.

**Step 2 (5 minutes): Following the entire length of the breath**
Continue to relax your body with your eyes closed. Continue to pay attention to your breath. Follow the entire length of your breath. Follow the beginning, the middle and the end of your in-breath, and the beginning, middle and the end of your out-breath. If you are breathing in a long breath, you know you are breathing in a long breath. If you are breathing in a short breath, you know you are breathing in a short breath. If you are breathing out a long breath, you know you are breathing out a long breath. If you are breathing out a short breath, you know you are breathing out a short breath. Do not force yourself to take a long or short breath. Just breathe naturally. Be aware of the entire length of the breath. In – in – in, out – out – out, in – in – in, out – out – out. If you are distracted by any sounds, body sensations, thoughts or feelings, gently come back to your breath. Follow the entire length of your breath for the next few minutes.

**Step 3 (5 minutes): Bringing the mind back to the body**
As you follow the entire length of your breath, bring your mind back to your body. Instead of thinking about the past or future, bring your mind back to now. Bring your mind and body together as one. As you breathe in, feel your whole body moving with your breathing in. As you breathe out, feel your whole body moving with your breathing out. Breathing in, you are aware of your whole body as you are breathing in. Breathing out, you are aware of your whole body as you are breathing out. Feel the different parts of your body as you breathe in and out. Then, feel the body as a whole, fully united with your mind. Feel the wholeness of yourself with each breath for the next few minutes.

**Step 4 (5 minutes): Relaxing the body**
Once your breathing is harmonious, your body will relax naturally. Feel whether there is any tension in your body. Breathe and relax the tension one by one, from the top to the bottom. Relax your head, face, neck, arms, forearms, hands, chest, abdomen, legs, feet..Then relax your whole body all at once. Breathing in, you calm your body when you are breathing in. Breathing out, you smile. Again, breathing in, you calm your body when you are breathing in. Breathing out, you smile. In – out – calm – smile, in – out – calm – smile, in – out – calm – smile. Feel your breath flowing through your body and calming your body. Feel your breath leaving your body and smile. Continue to relax your whole body for the next few minutes.
20 min followed by a reassessment of their symptoms with the ESAS. During these 20 min, the investigator stayed by the patient’s bedside and engaged in social conversation with the patient. ESAS for the control group was repeated after 20 min have elapsed from the time of completing the baseline ESAS. All patients for both groups remained in their bed throughout the 20 min between baseline ESAS and the repeat ESAS.

Both groups were already receiving standard care prior to being approached for the study. Standard care included both pharmacological management of various symptoms with drugs, as well as non-pharmacological management such as provision of medical information, physiotherapy, psychosocial support and so on depending on the specific symptom. It was also noted that during the 20 min between assessment of baseline ESAS and ESAS at 20 min, no other pharmacological or non-pharmacological interventions were given to patients in both groups, as they were accompanied by study investigator.

Primary outcome analysed was the reduction in ESAS score at minute 20 compared with baseline, where a reduction in score suggested symptom improvement. Secondary outcome was the reduction in individual ESAS score at minute 20 compared with baseline. For a power of 80% and type 1 error of 0.05, taking a minimal significant difference of 5 and with possible dropouts, a sample size of 40 (20 in each arm) was determined. Statistical analyses were performed using SPSS (V.21). Within-group differences in ESAS score at minute 20 from baseline were analysed using Wilcoxon signed-rank test, while the between-group differences in ESAS scores were analysed using Mann-Whitney U test. Non-parametric tests were used because the data were not normally distributed.

RESULTS

Fifty-one palliative care patients were screened for the study. Seven declined to participate, with the the most common reason being too tired and four were excluded due to their low symptom burden. Forty patients were randomly assigned to either 20 min mindful breathing and standard care (n = 20) or standard care alone (n = 20). All 40 were included in the analysis. Figure 1 outlines the CONSORT (Consolidated Standards of Reporting Trials) diagram while table 1 shows the demographic characteristics and baseline ESAS of the patients. There was no significant difference in baseline characteristics between the two groups. For baseline ESAS, there was no statistically significant difference between the groups except for depression and the total ESAS score, based on Mann-Whitney U test.

For within-group differences, a Wilcoxon signed-rank test indicated that the median post-test ranks for total ESAS score, median_{\text{post}}=28.3, were statistically significantly lower than the median pre-test ranks, median_{\text{pre}}=38.3, in the intervention group (z=-4.3, r=0.5, p<0.001). There was no significant improvement in these paired scores for the control group of standard care alone (median_{\text{post}}=29.0, median_{\text{pre}}=28.7, z=0.145, r=0.02, p=0.886). For individual symptoms, the Wilcoxon signed-rank test
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For between-group differences, a Mann-Whitney U test indicated that there was significant reduction of the total ESAS score in the intervention group compared with the control group at minute 20 (U=98, n₁ = n₂ = 20, mean rank₁ = 15.4, mean rank₂ = 25.6, median reduction₁ = 6.5, median reduction₂ = 1.5, z = -2.763, r=0.3, p=0.005). For individual symptoms, a significant reduction was seen for depression (U=121.5, mean rank₁ = 16.6, mean rank₂ = 24.4, median reduction₁ = 1.5, median reduction₂ = 0, z = -2.203, r=0.2, p=0.033) and anxiety (U=115.0, mean rank₁ = 16.3, mean rank₂ = 24.8, median reduction₁ = 2.0, median reduction₂ = 0, z = -2.439, r=0.3, p=0.021) in the intervention group compared with the control group. No statistical significance was seen for the other symptoms based on the ESAS score. These results are shown in table 3.

We conducted a one-way analysis of covariance to compare the changes in ESAS after 20 min, using baseline ESAS as covariate, after removing outlier to normalise the data. After adjusting for baseline ESAS, there was still a significant difference between the two groups. F (1, 36)=11.3, p=0.002, partial eta squared=0.2.

Table 1 Demographic characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>20 min mindful breathing (n=20)</td>
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<tr>
<td>Mean age±SD</td>
<td>66.75±3.22</td>
</tr>
<tr>
<td>Gender, n (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11 (55)</td>
</tr>
<tr>
<td>Female</td>
<td>9 (45)</td>
</tr>
<tr>
<td>Diagnosis, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hepatobiliary and gastrointestinal malignancy</td>
<td>8 (40)</td>
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<tr>
<td>Lung malignancy</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Urological malignancy</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Breast malignancy</td>
<td>1 (5)</td>
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<tr>
<td>Gynaecological malignancy</td>
<td>3 (15)</td>
</tr>
<tr>
<td>Endocrine malignancy</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Musculoskeletal malignancy</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Non-malignant diagnosis</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Eastern Cooperative Oncology Group (ECOG) performance status, n (%)</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>1 (5)</td>
</tr>
<tr>
<td>2</td>
<td>6 (30)</td>
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<td>3</td>
<td>6 (30)</td>
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<tr>
<td>4</td>
<td>7 (35)</td>
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Table 2 Comparison of the change in ESAS scores at Minute 0 and Minute 20 within the control group and 20 min mindful breathing group (Wilcoxon signed-rank test)

<table>
<thead>
<tr>
<th>Control group (n =20)</th>
<th>Median (IQR)</th>
<th>T0</th>
<th>T20</th>
<th>Z</th>
<th>P value</th>
</tr>
</thead>
</table>
| Pain                  | 1.0 (5)      | 2.0 (5) | -1.433 | 0.152
| Tiredness             | 5.0 (4)      | 5.0 (4) | -0.474 | 0.635
| Drowsiness            | 4.0 (4)      | 5.0 (4) | -0.656 | 0.512
| Nausea                | 0.0 (1)      | 0.0 (1) | -0.213 | 0.832
| Lack of appetite      | 4.0 (6)      | 3.5 (7) | -0.916 | 0.36
| Shortness of breath   | 0.0 (5)      | 0.5 (4) | -0.75  | 0.453
| Depression            | 3.0 (5)      | 2.0 (5) | -1.905 | 0.057
| Anxiety               | 3.0 (4)      | 3.0 (5) | 0     | 0.999
| Well-being            | 5.0 (5)      | 4.5 (6) | -0.314 | 0.754
| Total score           | 28.7 (7.2)   | 29.0 (12.3) | 0.145 | 0.886

ESAS, Edmonton Symptom Assessment Scale.

Table 3 Comparison of the change in ESAS scores at Minute 0 and Minute 20 within the control group and 20 min mindful breathing group (Wilcoxon signed-rank test)

<table>
<thead>
<tr>
<th>20 min mindful breathing (n =20)</th>
<th>Median (IQR)</th>
<th>T0</th>
<th>T20</th>
<th>Z</th>
<th>P value</th>
</tr>
</thead>
</table>
| Pain                             | 3.0 (4)      | 2.5 (6) | -0.725 | 0.468
| Tiredness                        | 5.0 (4)      | 4.0 (6) | -1.63  | 0.103
| Drowsiness                       | 5.0 (4)      | 3.0 (4) | -2.087 | 0.037
| Nausea                           | 0.0 (1)      | 0.0 (0) | -1.826 | 0.068
| Lack of appetite                 | 6.0 (2)      | 4.5 (4) | -2.39  | 0.017
| Shortness of breath              | 2.5 (7)      | 3.0 (6) | -0.473 | 0.636
| Depression                       | 5.5 (5)      | 3.0 (5) | -2.91  | 0.004
| Anxiety                          | 5.0 (7)      | 3.0 (5) | -2.32  | 0.02
| Well-being                       | 5.0 (3)      | 5.0 (4) | -2.972 | 0.003
| Total score                      | 38.3 (12.9)  | 28.3 (15.5) | -4.312 | < 0.001

* Student’s t-test.
† χ² test.
‡ Fisher’s exact test.
§ Mann-Whitney U test.

ECOG, Eastern Cooperative Oncology Group; ESAS, Edmonton Symptom Assessment Scale.

indicated that there were significant improvement in the following individual symptom in the intervention group: drowsiness (z = -2.1, r=0.2, p=0.037), lack of appetite (z = -2.4, r=0.3, p=0.017), depression (z = -2.9, r=0.3, p=0.004), anxiety (z = -2.3, r=0.3, p=0.002) and general well-being (z = -3.0, r=0.3, p=0.003). These results are shown in table 2.
Figure 2 shows the change in total ESAS for all 40 patients in a waterfall plot. The Minimal Clinically Important Difference (MCID) for total ESAS was \(-1\). Hence, 20 min mindful breathing, caused a statistically and clinically significant reduction in total ESAS for 85% of patients in the intervention group compared with the control group (\(\chi^2 = 4.286, df=1, p=0.038\)).

DISCUSSION
This was the first study to show the rapid reduction of multiple symptoms with a single session of 20 min mindful breathing in the palliative care setting using the ESAS score. The results contributed to the body of evidence on the use of mindfulness as an adjunct to standard care for symptom control in the palliative care population. Previous publications on the use of single session of mindful breathing in palliative care were limited to alleviating suffering and distress in general but not specific symptoms. Compared with other mindfulness-based interventions that usually need 6 to 8 weeks of commitment, the results offered evidence that a brief, simple 20 min session of mindful breathing was effective as an add-on in palliating multiple symptoms in palliative care.

Comparing the ESAS score at 0 min and 20 min, we can see that 20 min mindful breathing helps patients tremendously in their overall symptom burden (r=0.5, large effect size) with significant reduction in the total score from a median of 38.3 at 0 min to 28.3 at 20 min. This showed the rapid effect of mindful breathing on multiple symptoms, which would be useful when a quick relief is needed, even if a sustained effect is yet to be proven.

The improvement in drowsiness suggested that going through 20 min of mindful breathing activity was not too demanding for palliative care patients who might have limited reserves. Such improvement was much welcomed as a non-pharmacological option to improve fatigue, a common yet difficult to manage symptom in the palliative care setting. The significant positive effect on appetite was also a valuable benefit as it was another inherently difficult symptom to address with limited effective interventions available. The improvement in psychological symptoms of depression and anxiety, as well as patient’s perception of their well-being, was in keeping with previous studies that has demonstrated improvement in these parameters.

Examining the difference between the intervention and control group, the clinically and statistically significant reduction in total ESAS score when 20 min mindful breathing was added to standard care suggested it was useful to improve patient’s overall symptom burden. While breaking down the scores to individual symptoms, the effect was significant for the psychological component, depression and anxiety. However, looking at the mean ranks, there was a notable trend towards a lower score for all the symptoms listed, in the 20 min mindful breathing group. This trend was most notable for tiredness, drowsiness and general well-being, followed by pain, lack of appetite and nausea. A larger sample size may be necessary to show statistical significance.

The positive outcome of this study suggested that 20 min of mindful breathing activity was a useful and feasible non-pharmacological intervention for quick relieve of multiple and specific symptoms in the palliative care population, including drowsiness, lack of appetite, depression and anxiety. It also improves patient’s overall perception of general well-being and total symptom burden, leading to improvement in...
quality of life. However, mindfulness-based activities did require patient participation, including their time and attention. As such, we recommend offering 20 min mindful breathing to patients who are interested and willing to engage in this activity, while ongoing standard care.

There are several limitations. The study has a small sample size and was conducted in a single tertiary centre. It might not be powered sufficiently to show statistical significance for all the items on the ESAS score. The baseline ESAS was higher in the intervention group compared with the control group, indicating a greater room for symptom improvement. However, after controlling for this difference in baseline ESAS, there was still a statistically significant difference between the two groups. The information on the pharmacological and non-pharmacological treatment that each patient was on prior to our recruitment was not collected. Another limitation was the lack of blinding as patient’s active participation was required. This might lead to reporting bias as the outcome measure was subjective. In terms of duration of follow-up, we only explored the immediate effect at one time point (T20), with no further follow-up evaluation for the sustained effect of 20 min mindful breathing.

Future research can be conducted to study the effect of mindful breathing with a larger sample size through involvement of multiple centres, with consideration of outcome measures over a longer duration and at multiple time points, as well as with inclusion of the specifics of the pharmacological and non-pharmacological treatment that the patients were already receiving. Establishing a known level of palliation prior to administration of intervention could ensure a comparable baseline for both groups. Adding a standardised placebo activity in the control arm would be useful to reduce bias. This will further substantiate and confirm the immediate as well as sustained effect of this activity on patient reported symptom burden. Previous studies have also used different mindfulness-based intervention protocols. Future research comparing these different approaches will also be useful to determine the optimal protocol to be implemented in the palliative care setting.

In conclusion, this study provided evidence that 20 min mindful breathing plus standard care was effective in the rapid relief of multiple symptoms based on ESAS, when compared with standard care alone in palliative care patients. As pharmacological control of symptoms are still lacking in efficacy and fraught with adverse effects, developing evidence in support of the salutary effect of mindful breathing as a promising addition to the non-pharmacological arsenal of symptom control paraphernalia is a priority.

Contributors The contributions of the authors are outlined below. Study design: MLL, SBT, LYL, ECL and CLL. Recruitment: MLL and LYL. Statistical analyses: MLL, SBT, LLH, CGN, HAY, DLCN and CSC. Manuscript preparation: MLL, SBT, LLH, CGN, HAY, LYL, DLCN, CSC, ECL and CLL.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Approval obtained from the Medical Ethics Committee of University of Malaya Medical Centre (MREC no: 2018936641).

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. Data are kept as hardcopy and softcopy by the authors.

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