Multicentre randomised controlled trial of nursing intervention for breathlessness in patients with lung cancer

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Abstract

Objective To evaluate the effectiveness of nursing intervention for breathlessness in patients with lung cancer.

Design Patients diagnosed with lung cancer participated in a multicentre randomised controlled trial where they either attended a nursing clinic offering intervention for their breathlessness or received best supportive care. The intervention consisted of a range of strategies combining breathing control, activity pacing, relaxation techniques, and psychosocial support. Best supportive care involved receiving standard management and treatment available for breathlessness, and breathing assessments. Participants completed a range of self assessment questionnaires at baseline, 4 weeks, and 8 weeks.

Setting Nursing clinics within 6 hospital settings in the United Kingdom.

Participants 119 patients diagnosed with small cell or non-small cell lung cancer or with mesothelioma who had completed first line treatment for their disease and reported breathlessness.

Outcome measures Visual analogue scales measuring distress due to breathlessness, breathlessness at best and worst, WHO performance status scale, hospital anxiety and depression scale, and Rotterdam symptom checklist.

Results The intervention group improved significantly at 8 weeks in 5 of the 11 items assessed: breathlessness at best, WHO performance status, levels of depression, and two Rotterdam symptom checklist measures (physical symptom distress and breathlessness) and showed slight improvement in 3 of the remaining 6 items.

Conclusion Most patients who completed the study had a poor prognosis, and breathlessness was typically a symptom of their deteriorating condition. Patients who attended nursing clinics and received the breathlessness intervention experienced improvements in breathlessness, performance status, and physical and emotional states relative to control patients.

Introduction

Breathlessness is increasingly recognised as not simply a symptom of disordered breathing but also a complex interplay of physical, psychological, emotional, and functional factors.[1] Between 10% and 15% of patients with lung cancer have breathlessness at diagnosis, and 65% will have the symptom at some point during their illness.[2] Alongside cough, it is the symptom most frequently reported by patients with lung cancer.[3] The subjective experience of breathlessness may not be directly related to the extent of the disease. Factors such as anxiety can play an important part in exacerbating the symptom, and this is particularly evident in the context of an imminently life threatening illness such as lung cancer.[4]

Pharmacological and non-pharmacological interventions for breathlessness have not been evaluated. Although recognised palliative interventions are used, breathlessness remains unrelieved.[5]

Corner and colleagues set out to identify and evaluate nursing strategies for managing breathlessness and adopted an integrated approach that emphasised the importance of not separating psychological and physical aspects of the symptom.[4] They developed a therapeutic intervention that aimed to increase fitness and tolerance of restricted lung function and reduce functional disability while acknowledging the meaning of breathlessness in the context of life threatening illness. In a small randomised controlled study, distress caused by breathlessness was reduced and functional ability and ability to perform activities of daily living increased.[6] A larger multicentre study was organised to evaluate the effect of the intervention on a larger, more diverse sample and to establish the feasibility of integrating the new approach in a range of treatment centres.

Methods

Study design

This multicentre study was coordinated from the Macmillan Practice Development Unit at the Centre for Cancer and Palliative Care Studies, Institute of Cancer Research, London. Patients diagnosed with small cell lung cancer, non-small cell lung cancer, or mesothelioma who had completed treatment and reported breathlessness were invited to take part in the study. Entry criteria for the study defined shortness of breath as a reported change in breathing or a degree of breathlessness as perceived by the patient and reported as a problem that caused distress.

In each of the participating centres, once a patient from one of the participating centres had consented to take part in the trial, a telephone call was made to the Institute of Cancer Research's clinical trials office, which was responsible for independent randomisation to either intervention or control groups. The trials office informed the participating centre which group the patient had been assigned to. The patient was then asked to confirm whether he or she remained happy to participate in the study. Patients in the control group were given standard care and also had their breathlessness and its effects on life monitored; patients in the intervention group attended a nursing clinic. In the nursing clinics, patients received a package of interventions tailored to individual patients (box) aimed at helping them to cope with breathlessness and maximise their existing lung function. Many of these strategies are commonly used in settings for patients with chronic lung diseases but are not routinely used with lung cancer patients. Best supportive care was defined as the standard management and treatment for breathlessness available to patients within each

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Intervention carried out by specialist nurses

- Detailed assessment of breathlessness and factors that ameliorate or exacerbate it
- Advice and support for patients and their families on ways of managing breathlessness
- Exploration of the meaning of breathlessness, their disease, and feelings about the future
- Training in breathing control techniques, progressive muscle relaxation, and distraction exercises
- Goal setting to complement breathing and relaxation techniques, to help in the management of functional and social activities, and to support the development and adoption of coping strategies
- Early recognition of problems warranting pharmacological or medical intervention

centre. This included pharmacological and palliative treatments and treatment of associated problems such as anxiety and depression. All patients taking part had access to all routinely available supportive care.

Patients in the intervention group were invited to attend the nursing clinic once a week for up to eight weeks (and for not less than three weeks). Data were collected from both groups at weeks 1, 4, and 8. An independent data monitoring committee was set up to advise on the conduct of the study.

Recruitment of centres

Six hospital centres from around the United Kingdom volunteered to join the study. Each centre was granted ethical approval from its local research ethics committee. Informed written consent was obtained from patients, who were also aware of their ability to withdraw from the study at any time. All nurses taking part were taught the intervention in the same way, using a practice guideline, and the correct delivery of the intervention was monitored.

Outcome measures

Several self completed outcome measures were used to assess the effects of the intervention. Patients' subjective experience of breathlessness was assessed with visual analogue scales measuring breathlessness at worst and at best and distress due to breathlessness. The primary outcome measure was distress due to breathlessness. Other measures included the WHO performance status scale,[7] the hospital anxiety and depression scale,[8] and the Rotterdam symptom checklist.[9]

Statistical methods

Data from the research interviews and assessment instruments were entered onto EXCEL and SPSS–PC. As the data were not normally distributed, descriptive statistics and the non-parametric Mann-Whitney test were used in the analysis. The intended accrual was 150 patients to detect a difference in the proportion of patients who showed an improvement over 8 weeks, corresponding to 10% showing an improvement in one group and 30% in the other, or 25% in one group and 50% in the other (approximate 90% power, 5% two sided significance level). In the final sample of 100 patients the power would be 70-75%.

At the outset of the study the principal time point chosen for analysis was from baseline to 8 weeks; we assumed that this was when the intervention would show its maximum impact.[6] Patients who withdrew from the study for any reason other than that they reported being too well to continue were given a change score that was one more (that is, worse) than the maximum of the patients who did not withdraw. Similarly, any patient who withdrew because he or she reported being too well to continue was given a score which was one less than the minimum score of the patients who did not withdraw. This method of treating withdrawals is recommended by Gould,[10] who ranked patients who withdraw for reasons other than an improvement in their condition below patients who did not withdraw, and ranked those who withdrew because they improved above those who did not withdraw.

Results

A total of 119 patients were recruited to the study. One centre failed to adhere to the trial protocol, and data for its 16 patients were excluded on the advice of the data monitoring committee (an audit of data indicated that control patients from the centre also received strategies identified as being part of the intervention). At baseline the intervention group (51 patients) and the control group (52 patients) were similar in terms of age, sex, diagnosis, and metastatic disease and the outcome measurements for the groups did not differ significantly (table 1).

Sixteen patients died during the course of the study and 28 patients withdrew. Of the 27 patients who withdrew but did not report an improvement in their breathlessness, 16 withdrew because of a deterioration in their condition (13 control, 3 intervention, exact $P = 0.01$) and four were unhappy with the arm to which they had been allocated (3 control, 1 intervention). This left seven patients who withdrew for other reasons (2 control, 5 intervention). The major difference in the number of withdrawals between the groups therefore occurred where the patient's condition deteriorated. This was also reflected by the fact that the survival of the patients who withdrew from the control arm was significantly worse than the survival of patients withdrawing from the intervention arm (hazard ratio 2.5, $P < 0.05$, excluding the intervention patient who withdrew because he felt better). Survival of all withdrawals versus non-withdrawals was also significantly worse (hazard ratio 2.0, $P < 0.01$). All withdrawing patients or those who died were assumed to have a poor outcome relative to all the patients for whom an eight week assessment was available.

As overall survival of the two groups of patients did not differ significantly, it cannot be concluded that the intervention improved survival. However, the pattern of mortality showed that the intervention patients may have had improved survival over the first 6 months, but this was not maintained. No appreciable differences in medication between the two groups were found. The proportion of patients taking opioids in intervention group patients at baseline was 22%, and at 8 weeks 27%, the corresponding figures for the control group were 23% and 33% (the respective percentages for other medications were: steroids—intervention 31%

and 45%, control 27% and 30%; bronchodilators—intervention 27% and 27%, control 31% and 44%; non-opioid analgesics—intervention 51% and 33%, control 44% and 55%; antibiotics—intervention 5% and 15%, control 2% and 11%; and psychotropics—intervention 14% and 18%, control 17% and 22%).

At baseline both groups reported high levels of distress due to breathlessness and associated functional impairment (table 2). At 8 weeks, the intervention group showed significant improvement for breathlessness at best, WHO performance status, levels of depression, and physical symptom distress. Levels of anxiety and distress due to breathlessness improved slightly. Activity levels did not differ (P = 0.10). The groups were similar in breathlessness at worst, psychological distress, and overall global quality of life.

Table 1 Baseline data for intervention and control groups

Questionnaire	Intervention group: No of patients	Intervention group: Median (range)	Control group: No of patients	Control group: Median (range)
Visual analogue scale:				
Distress caused by breathlessness	47	6 (0-10)	49	5 (0-10)
Breathlessness at worst	47	7.5 (0-10)	49	7.9 (0-10)
Breathlessness at best	47	4 (0-9.1)	49	3.5 (0-8.9)
WHO performance status	49	2 (0-3)	51	1 (0-3)
Hospital anxiety and depression scale:				
Anxiety	48	7 (0-17)	49	6 (0-17)
Depression	48	6 (0-16)	49	5 (2-14)
Rotterdam symptom checklist:				
Psychological symptoms	48	14 (7-27)	49	14 (7-26)
Physical symptoms	48	50 (34-77)	49	49 (30-77)
Activity (total items 38-44)	45	12 (7-26)	49	12 (7-27)
Activity (subitems R41, R43, R44)	45	6 (3-12)	49	5 (3-12)
Quality of life	45	3 (1-6)	49	3 (1-6)

Scores of patients who died were not included in this analysis. In several cases data were missing because patients did not complete individual questions on the questionnaires.

Table 2 Change between baseline and 8 weeks in intervention and control groups in scores

Questionnaire	Intervention group: No of patients	Intervention group: Median (range) change	Control group: No of patients	Control group: Median (range) change	P value
Visual analogue scales:					
Distress caused by breathlessness	49	0 (–9-11)	51	10 (–7-11)	0.09
Breathlessness at worst	50	1 (–7.2-8.5)	52	4.8 (–6.2-8.5)	0.14
Breathlessness at best	50	1.3 (–7.1-8)	52	7.0 (–3.3-8)	0.03
WHO performance status	51	0 (–3-3)	52	2 (–1-3)	0.02
Hospital anxiety and depression:					
Anxiety	50	0 (–7-11)	52	9.5 (–6-11)	0.08
Depression	50	0.5 (–10-7)	52	6 (–7-7)	0.02
Rotterdam symptom checklist:					
Psychological symptoms	50	1 (–9-13)	52	9 (–8-13)	0.21
Physical symptoms	50	2.5 (–24-16)	52	14 (–11-16)	0.04
Activity:					
Items 38-44	47	2 (–12-15)	52	8.5 (–4-15)	0.1
Subitems R41, R43, R44	47	0 (–6-9)	52	5.5 (–3-9)	0.05
Quality of life (1 item)	47	1 (–4-4)	52	2 (–2-4)	0.25

Negative scores show improvement.

Discussion

Breathlessness in advanced lung cancer is an unpleasant and intractable problem that directly interferes with all aspects of daily living and can provoke intense anxiety.[6] Patients may also receive little or no help or advice on how to cope during attacks of breathlessness.[11] This is the first multicentre randomised controlled study that set out to evaluate nursing strategies for managing breathlessness in various treatment centres in the United Kingdom. The findings show that patients attending nursing clinics for breathlessness experienced improvements in breathlessness, performance status, and physical and emotional states.

Precisely how the intervention affects depression and anxiety is unclear. Changes from baseline to eight weeks in scores on the hospital anxiety and depression scale suggest a general improvement in mood for the intervention group. Two particular elements of the intervention might be responsible for the improvements: the emphasis on teaching more effective ways of coping with breathlessness and the opportunity to talk about difficult feelings and concerns.

Possible criticisms

The analysis rested on the assumption that patients who withdrew from the study had a poor outcome; clearly, it would have been preferable if their outcomes had actually been assessed. The method of analysis also assumed that all patients were able to show a change in either direction on the rating scales, but patients whose baseline measurements were at the extremes of a scale would be able to show change in only one direction. As the groups were similar at baseline, however, both groups should have been affected equally by this problem. Though the analysis of such a large number of outcomes would imply that one or two might be significant by chance even if the intervention had no effect, 5 out of 11 outcomes reached conventional levels of significance and all outcomes favoured the intervention group. Though the differences between the two groups were significant, the magnitude of the effect of intervention is more difficult to assess, and data need to be interpreted with caution. Not all patients benefited, but performance status gives an idea of the degree of benefit some patients experienced. The median change for the intervention group was 0: this group maintained the ability to carry out activities. For the control group there was a median deterioration of two points, so that for patients at baseline whose score was 2 (that is, up and about for 50% of waking hours, and capable of self care) typically deteriorated to grade 4 at eight weeks (that is, confined to bed or chair, no self care, completely disabled).

Conclusion

This study set out to evaluate a nursing intervention for breathlessness in patients with lung cancer and to replicate a previous study.[6] Most patients who managed to complete the study had a poor prognosis, and breathlessness was typically a symptom of their deteriorating condition. Considering the difficulties of randomising very ill patients to an eight week intervention study, the completion and results of this study are an achievement in the field of palliative care. The results confirm the findings from the earlier study and show that intervention based on psychosocial support, breathing control, and coping strategies can help patients deal with their breathlessness.

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Key messages

- In lung cancer, high levels of distress, anxiety, and functional impairment are associated with the symptom of breathlessness
- Evidence on the use of many treatments for this common and frightening symptom is lacking
- Interventions based on psychosocial support, breathing control, and learning coping strategies can help patients to cope with the symptom of breathlessness and reduce physical and emotional distress

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Contributors: JC had the original idea; initiated the study; developed the intervention; participated in establishing the study and supervising and supporting researchers and nurses; and helped to interpret data. HP developed the intervention and participated in establishing the study and supervising and supporting researchers and nurses. CB developed the study protocol, intitated the study and training of nurses in each centre, and coordinated the study for the first half of data collection. MB coordinated the second half of the study and supported nurses in study sites; was responsible for data management, checking, and entry; and carried out data analysis. RA'H was statistical adviser to the project and helped with analysis and presentation of data. MK helped initiate the study, support researchers and nurses, and manage and check data. The Macmillan and specialist nurses listed above collected the data. MB, JC, and RA'H wrote the paper. All authors read and commented on the draft paper. JC and BM are guarantors.

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Effect of screening on incidence of and mortality from cancer of cervix in England: evaluation based on routinely collected statistics

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Abstract

Objective To assess the impact of screening on the incidence of and mortality from cervical cancer.
Design Comparison of age specific incidence and mortality before and after the introduction of the national call and recall system in 1988.
Setting England.
Subjects Women aged over 19 years.
Results From the mid-1960s, the number of smears taken rose continuously to 4.5 million at the end of the 1980s. Between 1988 and 1994, coverage of the target group doubled to around 85%. Registrations of in situ disease increased broadly in parallel with the numbers of smears taken. The overall incidence of invasive disease remained stable up to the end of the 1980s, although there were strong cohort effects; from 1990 incidence fell continuously and in 1995 was 35% lower than in the 1980s. The fall in overall mortality since 1950 accelerated at the end of the 1980s; there were strong cohort effects. Mortality in women under 55 was much lower in the 1990s than would have been expected.
Conclusions The national call and recall system and incentive payments to general practitioners increased coverage to around 85%. This resulted in falls in incidence of invasive disease in all regions of England and in all age groups from 30 to 74. The falls in mortality in older women were largely unrelated to screening, but without screening there might have been 800 more deaths from cervical cancer in women under 55 in 1997.

Introduction

Invasive cervical cancer is the second most common cancer in women worldwide, but 80% of cases occur in developing countries. The incidence of the disease has been falling in many western countries, but not in Great Britain, over the past 40 years. The cervical smear test was developed over 50 years ago, and screening began in Great Britain, some Nordic countries, and parts of North America in the 1960s.

Although cervical screening in England started in 1964, for over 20 years it failed to achieve sufficient coverage of women or follow up of all women with