‘Best supportive care’ has had its day

Michael Cullen

The term ‘best supportive care’ has been used since 1988 to describe the control arm in trials evaluating chemotherapy in advanced cancers. There are problems with this term. First, it implies that we more strenuously optimise these components of care in trials than in routine oncology practise, when there is no evidence that we do. Secondly, the name implies that it is effective, when usually it is not. Finally, ‘best’ suggests that we have reached a clear landmark of progress in non-chemotherapeutic palliation, when clearly we have not. ‘Best supportive care’ is an unhelpful and misleading term which should be avoided. In future trials, it should be replaced by ‘standard palliative care ’ with the type and frequency of key palliative interventions documented

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Perhaps the single most important stage in the evaluation of chemotherapy in malignant disease is the phase III trial in which chemotherapeutic intervention (Figure 1) is compared with standard treatment but no chemotherapy. In the setting of widespread disease, this standard treatment is referred to in various ways in trial protocols and reports. In the first report (published in the *European Journal of Cancer* in 1988) of an Italian randomised trial that assessed chemotherapy in 92 patients with advanced non-small-cell lung cancer (NSCLC), the control group was described in the title as being assigned ‘no treatment’.[1] By the time a further 36 patients had been accrued, this same trial group had become one receiving ‘best supportive care’ in the title of the final report (published in the *Journal of Clinical Oncology* in 1991).[2] How the authors defined ‘best supportive care’ was not given, although only eight of 26 patients with stage III M0 disease received radiotherapy. One would have expected a higher proportion of patients to have symptoms that might have benefited from radiotherapy.

During the interval between the two reports of that trial, the very influential Canadian three-arm trial (National Cancer Institute of Canada) was published; this evaluated cisplatin plus vindesine versus cisplatin, doxorubicin, and cyclophosphamide versus no chemotherapy.[3] The term ‘best supportive care’ was used to describe the approach used in the control group, probably for the first time. Since then, this term has slipped into regular use in chemotherapy trials in lung and other cancers.[4]

There are two serious problems with the term ‘best supportive care’. First, it implies something different from standard non-chemotherapeutic palliation and second, it implies efficacy. Both implications are inaccurate.

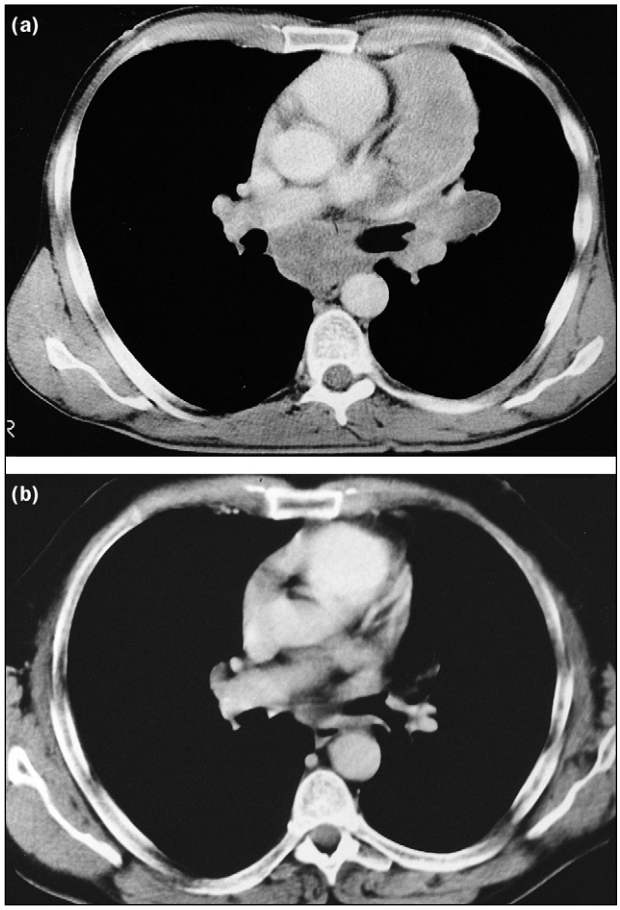

Figure 1. (a) Mid-thoracic CT scan image showing large left para-mediastinal mass, left hilar and carinal lymphadenopathy in a patient with squamous carcinoma in the left main bronchus. (b) Identical slice in the same patient following four cycles of MIC (mitomycin, ifosfamide and cisplatin) chemotherapy.

In the National Cancer Institute of Canada trial, patients in the group labelled ‘best supportive care’ were given “palliative radiotherapy as required for SVCO, hemoptysis, painful osseous metastases, brain metastases, or bronchial obstruction. Antibiotics were used to control infections. Corticosteroids were used to treat hypercalcaemia or increased intracranial pressure.” Unless further information is given to the contrary, many would assume this description

MC is at the Cancer Centre, Queen Elizabeth Hospital, University Hospital Birmingham, B15 2TH, UK. Tel: +121 627 2444. Fax: +121 697 8433. Email: michael.cullen@university-b.wmids.nhs.uk

was simply standard palliative care. The frequency with which these interventions were required was not given. In particular, the proportion of patients in this study group who needed palliative radiotherapy was not reported. This is a simple endpoint to record, and it gives at least an indication of the intensity of non-chemotherapeutic palliation.

Palliative care vs MIC plus palliative care

The randomised trial we carried out in the UK, comparing palliative care alone with mitomycin, ifosfamide, and cisplatin plus palliative care in advanced NSCLC, included 351 patients.[5] The non-chemotherapeutic interventions available for palliation (in both study groups) were identical to those used in the National Cancer Institute of Canada trial and were deployed "without restriction according to the standard practice of the collaborating centres". The proportion of patients in the group assigned palliative care alone who needed radiotherapy was 68%, compared with only 40% in the combined treatment group. The chest was the target in 82% and 73% of these patients, respectively. The median thoracic dose of 30 Gy and the interquartile range of 20–35 Gy were identical in the two study groups, which implies a similar 'intensity' of palliation in the patients in both groups who needed radiotherapy, but less need for this treatment in the patients gaining some relief from chemotherapy. This interpretation is supported by the data on quality of life collected in an unselected cohort. Using the change in quality-of-life score from baseline to week 6, we found that there was a significant deterioration in 42 patients randomly assigned palliative care alone, whereas those assigned chemotherapy plus palliative care experienced improvement. We also used an area under the curve method to compare quality of life over a 15-week treatment phase. A patient surviving the 15 weeks completely free of symptoms of disease or toxicity would achieve 15 quality-adjusted life weeks (QALWs). Patients who had palliative care alone had 9.4 QALWs, compared with 12.0 for those in the chemotherapy group (p=0.004). Clearly, an active palliative approach, which appears identical to that described by others as best supportive care (and which was similar to that adopted in the intervention group in the same trial), fails to counteract the negative effect of an untreated advanced malignant disease on quality of life, even in the early weeks after diagnosis.

Trials with newer chemotherapy drugs

Similar conclusions emerge from trials of newer agents in NSCLC. In a recent example involving gemcitabine, best supportive care was defined as any palliative treatment excluding chemotherapy.[6] As with our trial, fewer chemotherapy-group patients required palliative radiotherapy (49% compared with 79% of controls), and there was overall improvement in mean quality-of-life score over 2 months in that group, but deterioration in the controls. In contrast to our study of mitomycin, ifosfamide, and cisplatin, there was no survival benefit from gemcitabine. Again, best supportive care did not improve quality of life in the early weeks after the diagnosis of advanced NSCLC. Very recently, Shepherd and colleagues have reported a trial comparing docetaxel versus best supportive care in patients previously treated with cisplatin-based chemotherapy.[7] There was an overall deterioration in performance status in both treatment groups, but the greatest deterioration was in the patients assigned best supportive care.

Similar findings have been reported in advanced colorectal cancer. In a trial of irinotecan as second-line chemotherapy versus a control group assigned best supportive care, half of all patients in the control group who were pain-free at the time of randomisation had developed pain within 2 months, even though a higher proportion of this group received opioid analgesics.[4]

Nursing intervention vs best supportive care

This issue is not restricted to trials designed, run, and reported by oncologists evaluating chemotherapy. Bredin and co-workers[8] reported a randomised controlled trial of nursing intervention versus best supportive care for breathlessness in patients with lung cancer or mesothelioma. The trial group were treated by a range of strategies combining breathing control, activity pacing, relaxation techniques, and psychosocial support. Best supportive care was defined as the standard management and treatment for breathlessness available to patients within each centre. The authors gave no details of what this involved. The change between baseline and 8 weeks was one of universal deterioration in all 11 items assessed in the group assigned best supportive care. In the intervention group, there was deterioration in seven of the 11 items and no change in four. There was wide variation among patients, with some improving and others deteriorating substantially in both groups. Overall, there was less deterioration in the intervention group, which was significant for five of the seven assessed items. Breathlessness is a notoriously difficult symptom to palliate, and it is not surprising that best supportive care was ineffective, or that specific intervention simply limited the deterioration. Indeed, the general downward trends in quality of life in groups assigned best supportive care almost certainly disguise worthwhile palliation for some symptoms in some patients, which would emerge only with evaluation of robust multidimensional outcomes.

The evidence supporting a role for chemotherapy in advanced NSCLC with the aim of extending life, at least in patients with good performance status,[9] is now overwhelming, and evidence of improved quality of life is accruing. There is no place in this disorder for further first-line chemotherapy trials with a 'no chemotherapy' control group, however it is described. Nevertheless, attempts at palliation with radiotherapy, analgesics, corticosteroids, oxygen, antibiotics, and so on will remain important in advanced lung cancer alongside palliative chemotherapy and in patients unsuitable for, or declining, chemotherapy. There is no doubt that individual symptoms can be relieved in these ways. However, the data reviewed here show that when many variables are monitored in advanced lung cancer and other cancers, the overall trend in quality of life, even in the early stages after diagnosis, is one of deterioration. The reason could be that we are not proficient enough in our delivery of these palliative measures, or that they are simply

not effective enough to counter the systemic toxicity of advanced cancers. Clearly, we must continue to work on the former, but also accept the likelihood of the latter. We must also continue our attempts to refine the instruments used for measuring and analysing quality-of-life data,[10] as well as considering what approaches constitute the key recordable components of standard palliative care. I have already referred to palliative radiotherapy. At the other extreme, it is unrealistic for most trialists to document every dose of every oral medication that might be relevant. However, patients or their representatives might well be able to record the frequency and type of physician's assessments (oncologist, palliative care specialist, general practitioner, and so on), specialist nurse's assessments (chemotherapy nurse, tumour-site-specific support nurse, palliative care nurse), and hospital/hospice attendances and admissions.

The term 'best supportive care' carries the strong implication that we have reached the limits of progress in non-chemotherapeutic palliation (because the best cannot be improved upon), and that in trials adopting this label we optimise these components of care more strenuously than in routine oncology practice. I feel sure we have not and suspect that we do not.

In conclusion, there is now increasing evidence to support the use of chemotherapy for palliation in many patients with advanced cancers, including NSCLC. Nevertheless, palliation is still required in patients unsuitable for chemotherapy, in those who fail to respond to or decline it, and for use after chemotherapy. 'Best supportive care' is an unhelpful, misleading term, which should be avoided. In future trials with a non-chemotherapy control group, this term should be replaced by 'standard palliative care', with the type and frequency of key palliative interventions documented. Further research is needed to improve the efficacy of standard palliative care, which, at present, seems relatively ineffective in countering the inevitable subjective decline associated with an untreated, advanced malignant disease.

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