Treatment of the terminal stages of breast cancer

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Abstract

To assess the intensity of and changes in diagnostic investigations and treatment in the terminal stages of breast cancer 555 patients in the area of Tampere University Central Hospital in whom breast cancer had been diagnosed from 1977 to 1980 were followed up for five years. The case notes for the last visit of 519 patients were analysed. The amount of diagnostic activity was similar for those who died and for the survivors. A higher proportion of women who died than of women who survived received treatment at the last follow up visit, and 2-6 times as many of those dying within one week of the last visit were given chemotherapy as were survivors with recurrent disease.

Resources devoted to diagnostic investigations and treatment of cancer in terminally ill patients could be better used for care of the patients. This would be more likely to improve the patients' quality of life and conserve resources.

Introduction

Most studies of cancer treatment concentrate on remission and survival. Yet many patients with cancer ultimately die of their disease, and a recent consensus meeting concentrated on overtreatment of patients with cancer.¹ We conducted a retrospective study of case notes to determine the extent of investigations and

treatment in patients with breast cancer who were near to death and compared this with such activity in patients with breast cancer who were not close to death.

Methods

The Finnish cancer registry identified 555 women resident in the district served by Tampere University Central Hospital who had been diagnosed during 1977-80 as having breast cancer. We studied the 519 for whom follow up had been organised within the district, looking at the case notes of either the patient's last visit before death (or before admission to hospital and subsequent death) or the visit before the routine check after five years. We looked at which radiological examinations (including chest radiography, bone radiography, ultrasonography, and computed tomography) and laboratory tests (including a full blood count and measurement of calcium alkaline phosphatase or alanine aminotransferase activity) had been undertaken and which treatments for cancer (including chemotherapy, hormone treatment, operation, and radiotherapy) or for symptoms of cancer (including pain killing and psychoactive drugs) had been prescribed.

Results

Of the 555 patients with breast cancer identified in the resident population, four were followed up outside the central hospital district, nine died before their first visit (or the diagnosis was made at necropsy), five were denied follow up by the official health services, and 18 were found by the doctor carrying out the first course of treatment not to need follow up. During the first five years of follow up 195 of the remaining 519 patients died (163 from breast cancer and 32 from other causes). Those who died made on average a similar number of visits (17 per person; total 3299) as those who survived (15 per person; total 4949) but attended more frequently (8.2 v 3.1 visits a year).

Altogether 218 patients were alive with no recurrence. Table I shows the response to treatment of the patients who survived but had recurrent disease, who died a week or more after the last visit, and who died within a week of the last visit. Although most (52%) of the patients alive with recurrent disease had responded to treatment, the disease was assessed as progressing in 85% of the 104 patients who died less than a week after the follow up visit.

Table II shows that patients who died had a similar number of investigations to those who survived. Three quarters of those who died less than a week after attending hospital had had radiological investigations, and over 90% had had laboratory tests. Three of the 54 terminally ill patients might have benefited from the diagnostic activities (one was found to have anaemia and two to have hypercalcaemia). The results were

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TABLE I—Response to treatment of patients with breast cancer followed up for five years after diagnosis. * Values are numbers (percentages)

Response to treatment	Alive with recurrent breast cancer (n=104)†	Died ≤7 days after visit (n=104)‡	Died >7 days after visit (n=52)†
Complete or partial	54 (52)	6 (6)	
No change	32 (31)	10 (10)	1 (2)
Progressive disease	18 (17)	88 (85)	51 (98)

*In addition 218 patients were alive with no recurrence of breast cancer.

†Response of two patients was not known.

‡Response of five patients was not known.

TABLE II—Investigation and treatment at last follow up visit of patients with breast cancer

	Alive with no recurrence (n=218)	Alive with recurrence (n=106)	Died >7 days after visit (n=109)	Died ≤7 days after visit (n=54)
No (%) investigated with:				
x Rays	182 (83)	89 (84)	69 (63)	40 (74)
Clinical tests	187 (86)	98 (92)	87 (80)	50 (93)
Isotopes	8 (4)	8 (8)	5 (5)	2 (4)
Other	14 (6)	4 (4)	8 (7)	
No (%) given treatment for cancer:				
Chemotherapy	2 (1)	13 (12)	28 (26)	17 (31)
Hormone treatment	10 (5)	61 (58)	76 (70)	43 (80)
Operation	3 (1)	1 (1)	6 (6)	
Radiotherapy		3 (3)	12 (11)	1 (2)
Other	8 (4)	1 (1)	15 (14)	9 (17)
No of treatments/patient	0.1	0.7	1.2	1.3
No (%) given other treatment:				
Pain killing drugs	21 (10)	25 (24)	69 (63)	40 (74)
Psychoactive drugs	6 (3)	14 (13)	45 (41)	22 (41)
Other	16 (7)	5 (5)	15 (14)	10 (19)
No of drugs/patient	0.2	0.4	1.2	1.3

similar for the 109 patients who died more than a week after the last visit and were discovered to have treatable conditions.

Those who died received more treatment than did survivors (table II). Seventeen (31%) of those who died within a week were receiving chemotherapy and 43 (80%) hormone treatment, and the findings in those who died after more than a week were similar. The prevalence of chemotherapy among those who died within a week was 2.6 times that among those alive with recurrent disease (31% *v* 12%). Generally, the intensity of treatment for cancer increased the closer the patients were to death. In addition, of all those who died, two thirds were receiving analgesics and two fifths were receiving psychoactive drugs.

Discussion

Patients in the terminal stages of breast cancer were being intensively treated for both their disease and their symptoms. Indeed, they were being more intensively treated for their disease than those patients who were not in the terminal stages but may have had recurrent disease. Many of the patients in the terminal stages were also being investigated for other conditions but only three of 54 would have been likely to benefit.

It is difficult to predict when a patient is in the terminal stages of a disease, but our analysis of the notes suggested that death had been adequately predicted. The case notes showed that 53 of the 54 terminally ill patients had been assessed to have

progressive disease that responded poorly to treatment. Treatment may have been intensified in the hope of extending the patient's life. It is well established, however, that treatment does not extend the average survival at this stage,^{2,5} so that if some patients are having their lives extended others must be having their lives shortened. Sometimes treatment may be given for palliation. This is especially true of radiotherapy, but in our study a higher proportion of women who died than survived were being given chemotherapy, which often has side effects even when drugs are taken to ameliorate those effects. Such palliation might be more easily and less expensively achieved with pain killing or psychoactive drugs.

Our findings suggest that more attention was being paid to the cancer than to the patient. More emphasis on the care and comfort of patients in the terminal stages of cancer than on continuing diagnostic activity and treatment of the cancer would increase the patient's quality of life and conserve hospital resources.

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The polymerase chain reaction: a new epidemiological tool for investigating cervical human papillomavirus infection

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Abstract

The polymerase chain reaction is an *in vitro* method for primer directed enzymatic amplification of specific target DNA sequences. The technique was used to detect human papillomavirus types 11 and 16 simultaneously in cellular DNA recovered from cervical smears in 38 women referred for colposcopy to evaluate cytological abnormality and 10 women with no history of cytological abnormality. The polymerase chain reaction was shown to be both specific and sensitive in detecting human papillomavirus DNA such that a single human papillomavirus molecule was detected in 10⁵ cells. Of the 38 women with cytological abnormality, all were positive for human papillomavirus on testing with the polymerase chain reaction; 36 were infected with human papillomavirus type 16 and 22 dually infected with human papillomavirus types 11 and 16. Seven of the 10 women with no cytological abnormality were also infected with human papillomavirus type 11 or 16.

The use of the polymerase chain reaction will facilitate epidemiological investigation of the aetiological role of human papillomavirus in cervical neoplasia. This preliminary analysis suggests that the prevalence of human papillomavirus infection is greater than previously reported.

Introduction

Though the precise aetiology of cervical neoplasia is unknown, the epidemiological profile of the disease

makes it almost certain that oncogenesis is the result of sexual transmission of an infectious agent.^{1,2} Cytological, histological, and immunohistochemical studies have shown an association between human papillomavirus infection and cervical neoplasia.^{3,5} This has been confirmed by the cloning of various human papillomavirus genotypes from genital lesions (human papillomavirus types 6, 11, 16, 18, 31, 33, and 35) and the subsequent detection of these virus types in intra-epithelial and invasive cervical lesions.⁶⁻¹⁴ Human papillomavirus types 6 and 11 are associated predominantly with benign lesions (condylomas) or low grade dysplasias whereas types 16 and 18 occur in most invasive cervical carcinomas¹⁴; human papillomavirus types 31, 33, and 35 have been less commonly found in carcinomatous tissue.¹¹⁻¹⁴

Recent reports have cast doubt on the role of human papillomavirus in cervical cancer; human papillomavirus type 16 DNA has been detected in normal cervical tissue,¹⁵⁻²¹ and the results of one study have suggested that the apparent association between this virus type and cervical neoplasia disappears after adjustment for age.¹⁹ One of the main factors contributing to the difficulties in obtaining clear epidemiological evidence of the role of human papillomavirus in cervical neoplasia is the lack of an appropriate method for assessing type specific human papillomavirus infection. The techniques of Southern, dot-blot, and "filter in situ" hybridisation have problems of sensitivity and specificity, particularly when DNA extracted from cervical smears is examined.²² Thus

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