

HYPNOSIS AND CANCER: HOST DEFENCES, QUALITY OF LIFE AND SURVIVAL

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Abstract

In recent years it has become increasingly clear that the diagnosis and treatment of cancer are stressful experiences. Not surprisingly, therefore, high levels of psychiatric morbidity and psychological distress have been reported (Derogatis et al., 1983). There is now evidence, however, from prospective, randomized, controlled trials, that psychological interventions can enhance the quality of life of patients with cancer (see Meyer and Mark, 1995 for a meta-analysis). In addition, psychological interventions, including hypnosis, can modulate the immune response in a way that might be relevant to the progression of malignant disease (Walker and Eremin, 1995).

Key words: relaxation, cancer, survival, quality of life

Development of interventions for nausea and vomiting

Our interest in psychosocial aspects of cancer began in 1982. A 25-year-old female patient with Hodgkin's disease was referred for help. The previous week, she had come for the fifth cycle of chemotherapy in a course of six cycles. However, she had refused chemotherapy because of the effect that it was having on her quality of life – nausea, vomiting and anxiety related to treatment. The patient fully understood the need to continue with chemotherapy and she had been asked to come back a week later for chemotherapy. Despite the implications for her prognosis, she had again indicated that she did not wish further treatment. The haematologist added that she would like the problem resolved within a week. The patient duly attended and we devised a psychological intervention consisting of training in progressive muscular relaxation and cue controlled relaxation, direct hypnotic suggestion and a new procedure called nausea management training. Whilst hypnotized, nausea is elicited (for example, by asking the patient to remember a previous experience of feeling sick or, in this case, to smell an alcohol swab that reliably elicited conditioned nausea). The patient is then asked to eliminate the nausea by abdominal self-massage, diaphragmatic breathing and the application of cue controlled relaxation. To our surprise, after several sessions, she was willing to receive chemotherapy on schedule the following week. The patient completed her prescribed course without any further nausea, vomiting or significant distress (Walker, 1985).

Encouraged by this, the haematologist referred a series of 18 patients (Walker et al., 1988; Walker, 1992). They all had severe chemotherapy side effects despite judicious use of antiemetic medication. Patients were given between two and six sessions of the treatment described above. All patients, including two who were refusing to

have further chemotherapy, went on to complete their prescribed course of chemotherapy. Early onset nausea (that is nausea occurring before or within 20 minutes of the start of the infusion) was eliminated or improved in 88% of the patients and early onset vomiting was improved in 75%. Nausea and vomiting occurring later was also improved (in 55% and 63% of cases respectively). These results are striking: the patients had been selected because of the severity of the chemotherapy side effects despite appropriate antiemetic medication.

In order to evaluate the treatment further, a randomized, prospective, controlled trial was carried out. The main aim was to try to identify the helpful components of the package. Sixty-nine patients were recruited at the time of first diagnosis of Hodgkin's disease, non-Hodgkin's lymphoma or testicular teratoma. All patients received antiemetics during the six cycles of chemotherapy. They were randomized to one of three interventions:

1. antiemetic medication with relaxation training,
2. antiemetic medication with relaxation training, nausea management training and hypnotherapy,
3. detailed discussion of side effects with a review of antiemetic medication (to control for attention).

These interventions occurred following the third cycle. Contrary to our expectation based on local experience, and published results from other centres, a high proportion of the patients were more or less free from side effects at the third cycle of chemotherapy. For many patients, therefore, the prospect of a psychological intervention was prophylactic. We did not encourage patients to persist unless they particularly wished. Despite this the patients randomized to hypnotherapy had significantly less anxiety at the final cycle: patients randomized to relaxation therapy had less late onset nausea (Walker et al., 1991; Walker, 1992). One interpretation of these findings is that the initial detailed briefing about side effects, and our interest in ameliorating these, may have had considerable prophylactic value.

Doctor-patient interaction and adjustment to cancer

These findings led us to study the possible importance of doctor-patient communication in determining patient satisfaction and subsequent adjustment to cancer (Paraskevidis et al., 1993). One hundred and seventeen women were followed up at a gynaecological oncology clinic. They completed a 72-item *ad hoc* questionnaire as well as several psychological tests including the Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983).

Women who were anxious or depressed at follow-up were more critical of the amount of information they had received (usually, they considered it too little). Also, although satisfaction with the doctor-patient relationship was high, the women who were depressed at follow-up were significantly more dissatisfied than those who were not depressed, thereby emphasizing the importance of doctor-patient relationships in determining adjustment following the diagnosis.

Psychological factors and survival

Five years after we had completed the prospective, randomized, controlled study of side effects, we followed up the patients to examine possible prognostic factors for

survival (Ratcliffe et al., 1995). Data were analysed by means of the Log Rank test and Cox's proportional hazards regression. As expected, univariate analysis revealed that survival was related to age, stage of disease at presentation and performance status. However, two psychosocial factors also achieved statistical significance, namely depression scores at diagnosis: Hospital Anxiety and Depression scale (Zigmond and Snaith, 1983) and L scores, Eysenck Personality Questionnaire-Revised version (Eysenck and Eysenck, 1991). The L scale was originally developed to measure the tendency of some subjects to 'fake good'. In addition, however, it also measures a stable personality factor thought to denote social naiveté or conformity (Eysenck and Eysenck, 1991). It may measure, therefore, one aspect of the so-called Type C ('cancer prone') personality (Ratcliffe et al., 1995). When the data were stratified for L scores, the analysis indicated that patients who received the psychological intervention had lived significantly longer (Log Rank = 5.82, $p = 0.02$). Figure 1 shows the Kaplan-Meier survival curves for the control and intervention groups by L scores. For example, of the 13 patients who had an L score of seven or above, all four in the

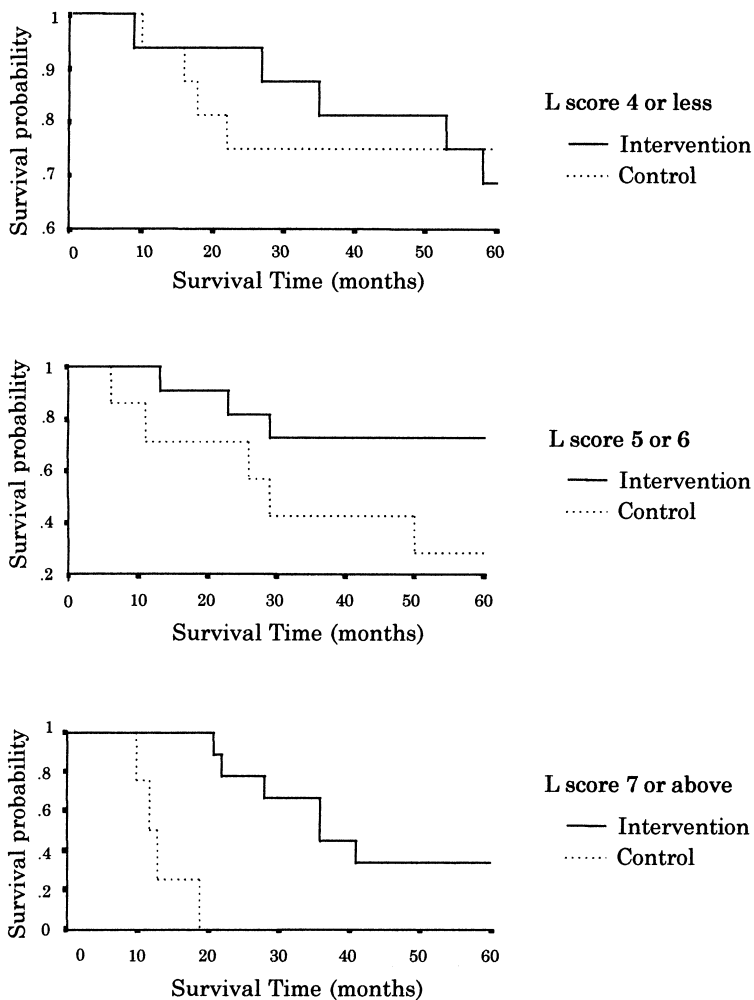


Figure 1. Effect of intervention (relaxation with, or without, hypnotherapy) and L scores.

control group were dead in 19 months whereas three of the nine randomized to one of the psychological interventions were still alive at five years.

Because univariate predictors may intercorrelate, the data were subjected to multivariate analysis using the Cox's proportional hazards model. This method identifies statistically independent prognostic factors. Stage, depression scores, L scores and the psychological intervention all emerged as significant independent prognostic factors for survival (Ratcliffe et al., 1995). These data suggest that psychosocial factors may be important determinants of survival in the lymphomas.

The enhanced survival in patients receiving relaxation therapy, with or without hypnotherapy, is in keeping with the results reported by Spiegel et al. (1989) (breast cancer), Grossarth-Maticek and Eysenck (1989) (breast cancer) and Fawzy et al. (1993) (malignant melanoma), who also found enhanced survival following a psychosocial intervention. It is important to emphasize that all of these studies are small and the findings must be considered provisional. Additional work is required to confirm the findings in the lymphomas and in other cancers.

If psychological interventions can modify disease progression, however, the obvious question is 'How might this be achieved?'. One hypothesis is that the effect is mediated by psychoneuroimmunological mechanisms (Ader et al., 1991; Lewis et al., 1994; Walker and Eremin, 1995).

Modulation of host defences by hypnosis and relaxation

Several years ago, we carried out a prospective, randomized trial to investigate the immunological effects of relaxation training for three weeks and the extent to which previous relaxation training together with direct hypnotic suggestion could modulate the immune response to an experimental stressor (Johnson et al., 1996). Twenty-four healthy volunteers were recruited. Daily relaxation for three weeks improved mental state as measured by a number of tests and it was also associated with a reduction in lymphocyte responsiveness and secretion of the key cytokine interleukin-1 (IL-1). On exposure to the experimental stressor (a doctor-patient role play recorded on video and fed back to the volunteers), however, previous relaxation training and pre-exposure hypnotic suggestion led to enhanced lymphocyte responsiveness and IL-1 secretion. Interestingly, some of the changes were modulated by hypnotic susceptibility. Changes in IgA in blood during the three weeks of relaxation practice were positively correlated with scores on the Creative Imagination Scale (Wilson and Barber, 1978). Moreover, enhancement of IL-1 following exposure to the stressor was positively correlated with Creative Imagination Scale scores in the experimental group and negatively in the control group. Other studies have also suggested that relaxation and hypnosis can modify immune status (Walker et al., 1993).

Of course, the demonstration of changes in immunological parameters in healthy volunteers does not necessarily have any clinical relevance to understanding the aetiology and progression of cancers. Fawzy et al. (1993) found that their group psychosocial intervention prolonged survival in patients with malignant melanoma. However, although the intervention improved natural killer cell activity, these immunological changes did not predict survival.

We have recently completed a prospective, randomized study of the psychoneuroimmunological effects of relaxation training and guided imagery (visualizing host defences destroying cancer cells) in women with large, or locally advanced, breast cancers. The women received six cycles of primary chemotherapy at intervals of three

weeks followed by surgery (mastectomy or breast conservation), hormone therapy and 20 fractions of radiotherapy. They were followed up at four and 12 weeks after radiotherapy.

During chemotherapy, women assigned to relaxation and imagery had better quality of life than women in the control group. More specifically, patients in the experimental group were more relaxed and more easy going. The intervention also reduced emotional suppression (Courtauld Emotional Control Scale; Watson and Greer, 1983) (Walker et al., 1996a).

Immunologically, women assigned to relaxation and imagery had higher absolute numbers and higher percentages of activated T cells (CD 25), lower levels of tumour necrosis factor-alpha and higher lymphokine activated killer cell cytotoxicity. Interestingly, changes in natural killer cell cytotoxicity during the 37-week study period were correlated with self-rated imagery intensity and the frequency of relaxation practice (Walker et al., 1996b). It is important to note, however, that the clinical or pathological responses to primary chemotherapy did not differ in the two groups.

The results to date indicate clearly that relaxation and guided imagery can enhance quality of life and modulate host defences. The biological significance of these effects, however, is not yet clear. We plan to follow up the patients to find out if the intervention affects recurrence and survival.

Conclusions

Several prospective, randomized studies have found that psychological interventions prolong survival in patients with cancer. However, these studies are relatively small and further work is required to substantiate the findings. Various interventions, including relaxation and hypnosis, can alter host defences and this could be relevant to the biology of some types of malignant disease. With technological advances in immunology, the prospects for psychosomatic and psychosocial medicine have never been more exciting. In the meantime, however, a great deal can be done to help patients cope with the diagnosis of cancer and the side effects of treatment (Meyer and Mark, 1995).

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