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The role of objective and subjective factors in cancer-related fatigue syndrome: a pilot study in advanced cancer patients receiving palliative radiotherapy treatment

Abstract

Background. Cancer-related fatigue is observed in most cancer patients in advanced stage of the disease. It may be caused by both, the disease and treatment — chemotherapy and radiotherapy. During and after palliative radiotherapy treatment, whose objective is to improve patient's quality of life, increase of fatigue might occur. The aims of this study were both to assess the level of fatigue in patients receiving palliative radiotherapy and to determine the role of psychological variables in cancer-related fatigue syndrome e.g. the relation between temperament and cancer-related fatigue, as well as strategies of coping with disease.


Method. 24 patients in advanced or metastatic cancer, undergoing palliative radiotherapy participated in the study. Prior to and after the treatment the patients were asked to complete a series of psychological questionnaires, like temperament questionnaire (FCZ-KT), Mini-MAC, PRE. Physicians, before and after the treatment, completed medical questionnaire, in which objective parameters of chronic fatigue syndrome were monitored (e.g. Haemoglobin level).

Results. Results show correlation between temperament and strategies of coping with disease with the level of fatigue. Psychological features may constitute a predictor for the fatigue level. Because of the group size this study has pilot and explorative character.

Key words: cancer-related fatigue syndrome, temperament, strategies of coping with disease

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Introduction

120,000 people came down with malignant tumours in Poland in 2000. At the same time almost 84,600 people died of cancer [1].

For patients in the IV clinical stage the treatment of choice in most of solid tumours is palliative chemotherapy and/or radiotherapy. As a result of healthy tissues exposure to radiation adverse events may occur, both topical and general (damage to marrow, bad disposition etc.) [2]. Because of fatigue which frequently affects them, many patients suffer from deteriorating quality of life [3, 4]. Weakness is one of the basic and most evident indicators of the chronic fatigue syndrome (CFS — cancer-related fatigue). The etiology or exacerbation of fatigue in patients receiving radiotherapy treatment have not been indisputably determined as yet.

Cancer-related fatigue affects more than 65% of patients receiving radiotherapy [5]. 60% of patients suffering from CFS experience weakness every day; it also affects patients in good general condition [6, 7]. Anticancer treatment results in intensification of anaemia. Anaemia, which plays a critical role in the development of CFS, constitutes a predictive factor for treatment response and significantly lowers the quality of life of cancer patients [5]. Completion of anticancer treatment is not always synonymous with CFS symptoms relief. Almost 2/5 (two fifths) of patients report weakness persisting for a few years following the treatment [8].

Weakness is not the only sign of CFS. Usually, there occur also other ailments of which patients are not always fully aware e.g. chronic tiredness, emaciation, exhaustion, lack of "vigour", quick tiredness, muscle weakness, unwillingness to physical or mental exertion, spontaneous or post-exercise mood disorder, insomnia or chronic sense of sleepiness, disturbed concentration, loss of motivation and reluctance to perform everyday activities, limiting possibilities of 'normal' functioning during the day time. Patients may also suffer from mood disorder. Consequently, these ailments lead to emotional disorders, sense of loneliness and isolation as well as depression. Contrary to weakness affecting healthy people, weakness experienced by cancer patients is not relieved by rest or sleep [9]. CFS symptoms do not impact only the physical sphere of life, but also psychological and social ones. This syndrome leads to limiting daily activity in more than 4/5 (four fifths) of cancer patients [10]. As a result, patients' economic status may deteriorate. Also, basic daily activities such as dressing up, washing, walking up the stairs be-

come a serious problem for them [10], and additionally make their everyday existence more difficult.

Adapting to cancer involves also coping with the awareness of suffering from incurable disease and its consequences, especially direct ones, i.e. pain or bad mood. In the long term one has to handle a plethora of changes profoundly affecting their quality of life [11-13]. The studies carried out in cancer patients, employing the most popular questionnaire (QLQ-C30) developed by European Organisation for Research and Treatment of Cancer (EORTC), revealed that strategies of psychological adaptability to cancer significantly correlate with virtually all quality of life properties connected with this disease [13].

The level of stress one experiences when confronted with cancer depends, to a large extent, on their psychological features such as personality or temperament. Individual differences in people's temperament impact not only their perception of stress, but also the course of stress reaction and ways of coping with stressful situation. In other words, they influence individual's adaptation to the disease, thus shaping an individual's quality of life [11, 12, 14].

To date the relation between temperament and somatic diseases has been examined only in small groups of patients suffering from ischaemic heart disease and in women patients with diagnosed breast cancer. The studies revealed that only emotional reactivity and activity differentiate men suffering from coronary disease from healthy people. However, negative correlation between the disease and emotional reactivity was found in women suffering from breast cancer, which means that emotional reactivity was reported more often in healthy women than in the breast cancer group [14].

Objectives of the study

The aims of the study were:

- assessment of the objective and subjective indicators which characterise CFS in a group examined before and after palliative radiotherapy treatment;
- determination of the psychological variables' role in cancer-related fatigue.

The following research questions were raised:

- what is the level of CFS in metastatic patients before and after palliative radiotherapy?
- is there any correlation between selected factors characteristic for CFS and features of temperament, kinds of cognitive emotion regulation strategies employed and sort of strategies for coping with disease?

- what is the dynamics of CFS indicators in the course of palliative radiotherapy treatment depending on psychological variables?

Methods

Participants

The study was conducted in Radiotherapy Department of the Ministry of Internal Affairs and Administration Hospital and Warmia-Mazury Oncology Centre in Olsztyn. 25 patients with metastatic malignant cancer participated in the study. These patients were treated with palliative radiotherapy (from 5 to 12 days) in the period from January to June 2007. As one person submitted incomplete questionnaire, finally 24 patients were analysed. The agreement to participate in the study as well as to employ the data in the analysis was obtained.

Study outline

Patients whose general condition on the ECOG/WHO scale was not worse than grade 3 were invited to participate in the study. Depending on the cancer type and its stage the patients received palliative radiotherapy treatment lasting 5 or 12 days. On radiotherapy commencement day, prior to irradiation, the physician filled in a medical questionnaire and patient had to complete a battery of questionnaires: FCZ-KT, PRE, Mini-MAC. Additionally, the physician filled in a medical questionnaire on the therapy completion day. After the therapy the patient also filled out a battery of tests, this time without temperament questionnaire.

Materials

In the study document analysis methods based on the medical questionnaire prepared for the sake of the study were employed, as well as questionnaire methods *i.e.* standardised psychological questionnaires:

1. Medical Questionnaire was developed on the basis of standard procedure of cancer patients monitoring, including basic demographic information, medical history and basic parameters of clinical, biochemical and histopathological evaluation. The questionnaire also included 3 questions enabling to determine the level of pain, tiredness and appetite. Patient answered these questions using 0–10 scale, in which 0 means respectively: "I don't feel any pain", "I don't feel tired at all", "I have no appetite" and 10 means respectively: "I feel by far the worst pain ever",

"I feel by far the most tired ever", "I have appetite I have never felt before".

2. Formal Characteristics of Behaviour Questionnaire — Temperament Inventory (FCB-TI) by Zawadzki and Strelau (1997) to measure temperament according to Regulative Temperament Theory by Jan Strelau. This questionnaire measures 6 temperament traits: perseverance, briskness, endurance, emotional reactivity, sensory sensitivity and activity.
3. Cognitive Emotion Regulation Questionnaire (CERQ) by Garnefski, Kraaij and Spinhoven, (2001) in Polish adaptation by Marszał-Wiśniewska and Fajkowska-Stanik (2007), to measure emotion regulation strategies. It measures 9 cognitive emotion regulation strategies: blaming yourself, blaming others, catastrophising, rumination, accepting, concentrating on other positive aspect, concentrating on planning, positive reinterpretation, putting into perspective
4. Mini-Mental Adjustment to Cancer Questionnaire (Mini-MAC) Watson et al. (1988, 1989), in Polish adaptation Juczyński (1997) to measure strategies of coping with disease and its direct consequences. It measures 4 ways of coping with disease in the following scales: helplessness-hopelessness, fighting spirit, anxious preoccupation and positive reinterpretation. Besides, it allows to distinguish two styles: constructive (fighting spirit and positive reinterpretation) and destructive (helplessness-hopelessness and anxious preoccupation).

Statistical methods

In order to answer the research questions basic descriptive statistics (response to research question no.1), factor analysis, correlation analysis and regression analysis (response to questions 2, 3) were applied.

Statistical analysis was performed with the use of SPSS14.0. software.

Variables

In the study the explanatory variables were features of temperament, cognitive emotion regulation strategies, and strategies of coping with disease. The variable to be explained was cancer-related fatigue determined by physiological and biochemical indicators such as: haemoglobin level in blood (HGB, expressed in g/dL) and red blood cells count in blood (RBL, expressed in K/ μ L) as well as subjective indicators, such as: level of pain felt, weakness, appetite level.

Results

The study group consisted of 10 women and 14 men. The subjects were between 33 and 79 years old ($Me = 54$ years; $SD = 11.70$). Most subjects had vocational education (38%). 33% of the subjects had secondary and 21% primary education. Only one patient had higher education (4%). One person did not give his/her education level. 13 patients suffered from cancer with metastases (54%), others were advanced cancer patients. General condition of 12 patients was assessed as grade 2 on ECOG/WHO scale (50%), in 9 patients (38%) — grade 1. One patient commenced the study in general condition at grade 3, and in one case the data was not reported. One patient died during palliative radiotherapy treatment as a result of disease progress.

Comparison of objective and subjective CFS indicators prior to and after palliative radiotherapy treatment reveals that the median of all critical parameters contained in particular indicators is lower after than before the therapy; however, the differences are not statistically significant. Table 1 shows the results.

Prior to proceeding to further analyses, factor analysis was carried out with the use of principal components method and Varimax rotation, thus verifying theoretical assumptions made at the construction of CFS subjective and objective indicators, as well as reducing the number of cognitive emotion regulation strategies (CER scale). Factor analysis confirmed occurrence of two factors: subjective and objective CFS, explaining 65.32% of all variances. Furthermore, the analysis revealed occurrence of three factors of emotion regulation strategies, explaining together 74.71% of variance.

These factors were called respectively: 1) Constructive strategies, such as concentration on planning, concentration on other positive aspect, putting into perspective; 2) Despair i.e. catastrophising, blaming others and lack of acceptance; 3) Persistent sense of guilt, in the form of rumination and blaming yourself.

Further analysis covered the aforementioned factors as well as four manners and two styles of coping with disease determined with Mini-MAC scale.

All analyses were carried out with the control of disrupting variables, i.e. general patient's condition determined with ECOG/WHO scale and the stage of cancer determined with TNM system. Correlation analysis based on measurements taken prior to the therapy revealed that CFS subjective indicator correlates negatively with temperament feature — emotional reactivity.

Additionally, regression analysis ($F(11.4) = 15.98$; $p < 0.05$) showed that for the CFS subjective indicator some temperament variables are particularly significant, i.e. low activity and low sensory sensitivity, and the following coping with disease strategies: high level of constructive strategies and destructive style as well as low level of despair, persistent sense of guilt and constructive style. Table 2 shows detailed data.

We were also interested how subjective and objective indicators will act in dynamic perspective. Dynamics was determined on the grounds of the difference between measurements taken after and prior to the therapy. The dynamics of objective indicator correlates in a statistically significant way with "anxious preoccupation" strategy. The dynamics of subjective indicator correlated in a significant way only with helplessness-hopelessness strategy.

Table 1. Descriptive statistics concerning particular elements of the objective and subjective indicators for cancer-related fatigue

	Measurement taken on the day of qualification for the study					Measurement taken after the completion of palliative radiotherapy treatment				
	RBC [K/uL]	HGB [g/dL]	Pain level	Tiredness level	Apetite level	RBC [K/uL]	HGB [g/dL]	Pain level	Tiredness level	Apetite level
N	24	24	24	24	24	23	23	24	24	24
Data deficiency	0	0	0	0	0	1	1	0	0	0
Mean	3.95	11.70	2.58	3.83	7.50	4.02	11.42	2.42	3.33	6.75
Median	3.95	11.70	3.00	4.50	8.00	3.88	11.40	2.50	3.00	7.00
Standard deviation	0.56	2.01	1.98	2.14	2.41	0.93	1.34	2.10	2.30	2.23
Minimum	2.82	8.10	0.00	0.00	2.00	3.09	9.20	0.00	0.00	3.00
Maximum	5.27	15.9	5.00	8.00	10.00	7.82	14.00	7.00	8.00	10.00

RBC — red blood cells; HGP — haemoglobin

Table 2. Regression coefficients for psychological variables with reference to subjective indicator for cancer-related fatigue syndrome. The table presents only statistically significant variables

	Non-standard coefficients				
	B	Standard error	Beta	t	Significance
Constant	5.786	0.938	–	6.166	0.004
FCZ-KT SENSORY SENSITIVITY	–0.482	0.074	–1.243	–6.533	0.003
FCZ-KT ACTIVITY	–0.086	0.031	–0.322	–2.818	0.048
PRE CONSTRUCTIVE STRATEGIES	1.818	0.224	1.748	8.123	0.001
PRE DESPAIR	–1.525	0.248	–1.499	–6.159	0.004
PRE PERSISTENT SENSE OF GUILT	–0.677	0.183	–0.504	–3.705	0.021
Mini-MAC DESTRUCTIVE STYLE	1.542	0.204	1.555	7.57	0.002
Mini-MAC CONSTRUCTIVE STYLE	–1.396	0.189	–1.112	–7.397	0.002

Table 3. Regression coefficients for psychological variables with reference to the dynamics of objective indicator for cancer-related fatigue syndrome. The table presents only statistically significant variables

	Non-standard coefficients				
	B	Standard error	Beta	t	Significance
Constant	2.121	0.415		5.116	0.036
FCZ-KT PERSEVERANCE	0.093	0.02	0.736	4.671	0.043
FCZ-KT EMOTIONAL REACTIVITY	–0.1	0.021	–1	–4.683	0.043
FCZ-KT ACTIVITY	–0.091	0.013	–0.704	–6.821	0.021
Mini-MAC DESTRUCTIVE STYLE	–0.42	0.091	–0.563	–4.597	0.044

The regression analysis revealed the significance ($F(11.2) = 18.45; p < 0.05$) for the dynamics of CFS objective indicator and perseverance and low “activity” and “emotional reactivity” as well as destructive style (Table 3).

Discussion and conclusions

From the group of all morphological and biochemical parameters monitored during the study we isolated CFS objective indicator, which was composed of blood parameters such as haemoglobin level in blood and red blood cells count. Another factor obtained as a result of this analysis - CFS subjective indicator was made up of patient's subjective evaluation of his/her mood (pain, tiredness, lack of appetite). Isolation of this indicator corresponds with the concepts which assume the role of subjective, individual sense of tiredness by cancer patients in CFS [2–4, 7].

In the study group the parameters making up both subjective and objective CFS coefficient deteriorated (response to the first research question); though it is not a statistically significant change. It may result from short-lived impact of palliative radiotherapy treatment on patient's body.

Potential clinical implications are provided by the response to the second research question. Correlation analysis results showed that high level of emotional reactivity is connected with low level of CFS subjective indicator. Apparently, people who more often tend to experience anxiety, fear, worry, in other words, people highly emotionally reactive feel tiredness, loss of strength or appetite caused by the disease as less severe. This result may seem surprising. However, if we take into account the fact that high emotional reactivity is connected with generally more frequent, independent of disease, suffering from various somatic ailments [15], then we may assume that the presence of the disease itself does not change subjective disposition as much as in the case of people who usually feel well, do not complain of any ailments, experience anxiety or tiredness less intensively and less often. Thus, a hypothesis can be made that for people with low emotional reactivity somatic disease and its consequences may constitute far more difficult an adaptive challenge, because it is a new situation for them. Similar observations were reported in the group of women suffering from breast cancer. Here, low level of emotional reactivity was also connected with higher level of tiredness felt, which constituted an entirely opposite result to

the one obtained in a group of men suffering from coronary disease [14]. Therefore, one cannot rule out, that sex and differences in the level of emotional reactivity affect the level of tiredness during the disease or treatment. Besides, different diseases may differently affect ways of coping with the disease, especially if the disease is characteristic for a particular sex.

No correlation with either temperament features or strategies of coping with the disease was discovered in connection to the objective indicator evaluated prior to the therapy. However, it appeared that the predictors of high subjective cancer-related tiredness occurring prior to the therapy were such temperament features as low sensory sensitivity level, representing a certain kind of cognitive lack of interest in the surrounding environment, and low level of activity. Therefore, patients who are interested in the environment, who pay attention to the changes in the surroundings and get involved in activity, not only physical, do not experience tiredness, pain and loss of appetite so intensely. Similar role of sensory sensitivity was pointed out by Izdebski [16]. The above-mentioned features of temperament can be treated as a kind of psychological 'immunisators' in experiencing somatic ailments. Similarly to the observations obtained in the research carried out to date [14, 17, 18] intensive activity can lead to lack of tiredness experienced in the course of disease. Involvement aids coping with disease symptoms; similar conclusions come from research on positive attitude and mental resistance in coping with disease [19, 20].

Despair and persistent sense of guilt strategies as well as constructive style proved to be the ones which may predispose the patient to subjective feeling of tiredness prior to the therapy commencement. It looks that the more negative the cogitation towards the situation (despair and persistent sense of guilt) the better one feels, but also the more actively, in terms of functioning, one tries to do something with a particular situation, the better they feel. Coping by means of despair strategy and sense of guilt are likely to have similar effect like temperamental high level of emotional reactivity. I am getting used to my bad mood, which in the case of healthy people means applying despair and persistent sense of guilt strategies [21], and disease situation, in this respect, no longer constitutes such a change for me. It improves subjective level of functioning, whereas constructive style, which means active coping, works here similarly to temperamental activity.

The results revealed that the higher the anxiety accompanying the disease, the lower the objective tiredness indicator observed. Therefore, we can speak about higher stability of these physiological parameters during the therapy which determine the objective indicator. Presumably, patient's anxious preoccupation stimulates greater mobilisation of the organism to fight the disease.

In the study, it was also observed that the higher the level of "helplessness-hopelessness" strategy, the more pronounced the difference in the CFS subjective indicator felt by the patient. Thus, people who surrender to disease situation show higher variations of tiredness, strength and appetite level.

The results highlight that psychological variables are particularly significant for the dynamics of objective tiredness indicator. The tendency to think over, look back to past events i.e. high level of perseverance, was connected with higher fluctuations of biochemical indicator parameters. On the other hand, the tendency to experience negative emotions intensively and frequently i.e. emotional reactivity as well as high level of activity related to low level of objective indicator dynamics changes.

As far as coping strategies are concerned the destructive style related to lower scope of objective indicator change. The above-mentioned results are difficult to interpret since the literature lacks data concerning the dynamics of biochemical parameters, such as haemoglobin level and the number of erythrocytes and their relations with psychological variables.

To generalise, firstly, one can state that the temperament feature 'activity' enters into significant correlations with cancer-related fatigue syndrome. It is connected not only with the experienced and observed level of tiredness, but it can act as its predictor as well. Interestingly, particular temperament features and some coping with disease strategies revealed their relationship with subjective indicator prior to the therapy, whereas with CFS objective indicator after the therapy was completed. Presumably, the state of insecurity, which is more frequent in patients commencing the therapy, affects also the level of subjectively experienced tiredness. The situation changes during the therapy, which was also noticed by the authors of the research on changes in the intensity of anxiety induced by the disease and hope of survival during the therapy in the group of patients suffering from cancer, hypertension and with myocardial infarction [22].

The study reveals that psychological properties as well as strategies of coping with disease are significant for CSF subjective and objective indicator.

It would be interesting, in studies covering a bigger group of patients, to verify the above conclusions, as well as carry out assessment of tiredness level and patients' quality of life in the period from 4th to 6th week after palliative radiotherapy treatment completion. Usually, after this time improvement in the quality of life can be observed in most patients, which is the objective of palliative radiotherapy treatment as such.

Practical conclusions that can be drawn from this study show, similarly to other authors [13], that attempts to work with patient through e.g. meeting with a psychologist, especially prior to the therapy, aim at introducing a different way of thinking about the disease. Employing constructive strategies of coping with disease, adaptive strategies or less frequent use of destructive strategies could affect reducing subjective sense of tiredness, which could also translate into objective indicators.

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