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EFFICACIOUS PSYCHOLOGICAL TREATMENTS FOR REDUCING FATIGUE IN CANCER SURVIVORS: THE STATE OF THE QUESTION AND FUTURE PROSPECTS

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El cáncer sigue siendo un grave problema de salud en todo el mundo. Sin embargo, debido a la eficacia de los tratamientos y a la mejora de los sistemas de sanidad el número de supervivientes al cáncer ha aumentado significativamente a lo largo de los años. La fatiga es una de las consecuencias del cáncer que aparecen con una mayor frecuencia causando importantes alteraciones en la vida de los supervivientes. Diferentes tratamientos psicológicos han sido utilizados para reducir la fatiga en este grupo de pacientes. Las terapias de tipo cognitivo-conductual y el mindfulness son las que aportan mayores datos que avalan su eficacia, por delante de las intervenciones de tipo psico-educativo. Sin embargo, la mayoría de los estudios se han llevado a cabo con supervivientes al cáncer de mama, por lo que sería deseable probar la eficacia de estas técnicas en una mayor variedad de tipos de cáncer.
Palabras clave: *Cáncer, Oncología, Supervivientes, Fatiga, Tratamientos psicológicos.*

Cancer remains a major health problem worldwide. Due to the efficacy of the treatments and the improvements in healthcare systems, however, the number of cancer survivors has increased significantly over the years. Fatigue is one of the consequences of cancer that appears most frequently, causing significant changes in the lives of survivors. Different psychological treatments have been used to reduce fatigue in this patient group. Cognitive-behavioural techniques and mindfulness therapies are the ones that have the most data supporting their effectiveness, ahead of psycho-educational type interventions. The majority of studies, however, have been conducted with breast cancer survivors, and it would be desirable to test the effectiveness of these techniques with a greater variability of cancer types.
Keywords: *Cancer, Oncology, Survivors, Fatigue, Psychological treatments.*

THE IMPORTANCE OF CANCER WORLDWIDE

Cancer continues to be a health problem throughout the world. According to data collected by the International Agency for Research on Cancer (IARC), in 2012 there were 14.1 million new cases of cancer diagnosed worldwide, with a mortality of 8.2 million. Comparing these data with those obtained by the same organisation in 2008, an upward trend can be observed; the number of new cancer cases was 12.7 million in 2008, with a mortality of 7.6 million. Of the different types of cancer, lung cancer presents the highest incidence globally (13% of the total), followed by breast cancer (11.9%), and colorectal cancer (9.7%). The highest mortality is also observed in lung cancer (19.4%), followed by cancer of the liver (9.1%) and the stomach (8.8%) (Ferlay et al., 2013).

In the year 2012, there were 215,534 new cases of cancer diagnosed in Spain, of which two thirds were patients over the age of 65, with a rate of 215.5 cases for every 100,000 inhabitants. The prediction for 2015 shows an increase in new cases of cancer, reaching 227,076, which is explained by the progressive aging of the population. The most common types of cancer in men are prostate, lung and colorectal, whereas breast cancer is the most common form in women, ahead of colorectal and uterine cancer. In terms of mortality, the number of cancer deaths in Spain was 102,762, one third of which were in patients over 65 years of age. Predictions for 2015 indicate an increase in mortality, with about 108,390 deaths expected due to cancer. In men, the highest mortality was observed in lung cancer (27.4%), followed by colorectal cancer (13.7%) and prostate cancer (8.6%). In women, the highest mortality was observed in breast cancer (15.5%), followed by colorectal cancer (15.2%) and then lung cancer (9.4%) (Sociedad Española de Oncología Médica [Spanish Society of Medical Oncology], 2014).

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THE HISTORY AND DEFINITION OF SURVIVAL

Despite the increased number of cases and deaths due to cancer observed in the statistics worldwide, thanks to the improvements in treatment and health care the number of patients who survive the disease has also increased significantly over the years. If we take as a reference the creation of the National Cancer Act in the US in 1971, the number of cancer patients who survived the disease was 3 million, rising to 12 million survivors in the year 2010 in the United States (Valdivieso, Kujawa, Jones & Baker, 2012). Currently, the cancer survival rate in Spain is within the European average. Looking at the survival statistics by type of cancer in Spain, we find that the highest survival rate is observed in melanoma (84.6%), followed by prostate cancer (84.7%), breast cancer (82.8%) ahead of non-Hodgkin type lymphoma (60.4%), kidney (57.8%), colon (57.1%), rectal (56.4%), ovarian (36.8%), stomach (25.6%) and finally lung cancer with a 10.7% associated survival rate (De Angelis et al., 2014). As discussed above, an important milestone in the study of survival was the creation in 1971 of the National Cancer Act in the United States, a federal law that aimed to increase research into the causes of cancer and the development of effective treatments (Valdivieso et al., 2012). Following this line of action, the survival movement in the United States is often associated with two important events. Firstly, there was the publication in 1985 of an article written by Dr. Fitzhugh Mullan, in which he describes his personal experience with cancer. In this article, Mullan proposed the first classification of cancer survival divided into three phases (acute, extended and permanent) from a psychosocial perspective, integrating people's adjustment responses over time (Mullan, 1985). The other important event was the creation in 1986 of the National Coalition for Cancer Survivorship (NCCS). At its first meeting, the coalition established a new definition in which a person could be considered a cancer survivor from the moment of diagnosis. Members of the coalition argued that this new definition offered a space for hope in addition to providing appropriate support for decision-making regarding the choice of treatment. Recently, the National Cancer Institute (2014), has suggested that survival begins once the treatment has ended, and continues until the end of the patient's life. This definition includes the physical, psychological and economic aspects of cancer in addition to the long-term effects of treatments, the appearance of a second cancer, and the overall quality of life for patients that have survived cancer as well as their family members and carers.

FATIGUE

Fatigue is one of the most frequently occurring changes in cancer survivors. It is observed in a high percentage of survivors affecting between 4 and 91%. Its severity increases with the progression of the disease, since it is the most common symptom after the treatment ends, and high levels can be observed up to ten years later (Escalante & Manzullo, 2009; Garabelli Cavalli Kluthcovsky et al. 2012; Harrington, Hansen, Moskowitz, Todd & Feuerstein, 2010; Lawrence, Kupelnick, Miller, Devine & Lau, 2004; Pachman, Barton, Swetz & Loprinzi, 2012; Sadja & Mills, 2013). Fatigue in cancer survivors is defined as an exceptional feeling of tiredness that is accompanied by high levels of discomfort, which is disproportionate to the activity undertaken by the patient and, furthermore, it is not relieved by rest or sleep (Weis, 2011). Within the definition of fatigue as well as tiredness, we also find other symptoms such as apathy, weakness and exhaustion (Cancer Symptoms, 2013). Fatigue can occur in patients for as long as the treatment is active, and some authors suggest it may be caused by the inflammation of tissues due to the effects of different therapies, although there is no complete consensus about the causes of the existence of fatigue in this patient group (Bower, 2014). Fatigue is related to different aspects of the wellbeing of patients, such as a lower quality of life, the presence of depression, anxiety, sleep disturbances, a lack of adequate social support, pain and, moreover, fatigue is associated with a poorer prognosis for survival (Berger, Gerber & Mayer, 2012; Bower, 2014; Kuhnt et al., 2009). There are certain factors that act as predictors of fatigue after treatment. For example, in breast cancer survivors it is observed that younger age, pain, dyspnea, insomnia, nausea and vomiting and the presence of intrusive thoughts predict the occurrence of fatigue in this patient group (Dupont, Bower, Stanton & Ganz, 2014; Garabelli Cavalli Kluthcovsky et al., 2012).

THE EVALUATION OF FATIGUE

A variety of scales have been developed to assess fatigue in cancer patients. Thus we find the BFI (Brief Fatigue Inventory) that has adequate psychometric properties and has been validated in cancer patients. This

scale allows us to differentiate between three categories of fatigue: mild, moderate and severe. Another widely used scale is the POMS-F (Profile of Mood States-Fatigue). This scale assesses the severity of fatigue based on the answers to 7 items and obtains adequate psychometric indices (= 0.90). We also have the EORTC QLQ C30 scale (European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30); although it was developed to assess the quality of life in cancer patients, this scale includes an assessment of the severity of fatigue using 3 items independently. The psychometric properties are adequate, although weaker than other scales that include a larger number of items related to fatigue (Bower et al., 2014) Among the scales that have been validated to assess fatigue in cancer survivors we find the Revised Piper Fatigue Scale, which has robust psychometric properties in breast cancer survivors and has 22 items distributed in different scales and which has recently been adapted to Spanish by Cantarero-Villanueva et al (2014) in addition to the CIS (Checklist Individual Strength) which includes 8 items that specifically assess fatigue and whose psychometric properties are adequate (Vercoulen, Alberts & Bleijenberg, 1999).

EXERCISE AND PHARMACOLOGICAL TREATMENT

Before beginning to describe the psychological interventions, we should mention another type of intervention that is usually recommended in the healthcare field. Firstly, increasing evidence supports the application of physical exercise to relieve the symptoms of fatigue in cancer survivors, with more positive effects for programs of moderate intensity that include endurance exercise (Battaglini et al., 2014; Brown et al, 2011). In addition, these programs have a high adherence among patients (Blaney, Lowe-Strong, Rankin-Watt, Campbell & Gracey, 2013). On the other hand, there are data that support the use of some psychostimulants such as methylphenidate to alleviate fatigue in cancer patients with active treatment or advanced disease, however, the evidence for the use of psychostimulants to achieve this goal in cancer survivors is limited (Bower et al., 2014).

THE SELECTION OF ARTICLES

The information search was conducted using the key words: cancer, survivors, fatigue, treatment or cancer, survivors, fatigue, intervention. The information included was from complete articles and abstracts published in the databases Pubmed/Medline, PsycINFO and Web of Knowledge (WOK) in the last 10 years. The inclusion criteria for the articles were as follows: the participants in the studies had to be over 18, have been diagnosed with cancer and have completed active treatment. Regarding the type of study, priority was given especially to the inclusion of randomised controlled trials, although other types of tests with a lower level of control were also taken into account. The interventions selected were those of a psychological nature. The results are shown in Table 1.

CONCLUSIONS AND FUTURE PERSPECTIVES

Cancer remains one of the main concerns of healthcare systems worldwide. Although the data indicate that in the coming years the figures regarding cancer incidence and mortality will continue to grow, fortunately the number of people who survive the disease also continues to rise. This increase in cancer survival is associated with the greater efficacy of treatments and the access that exists in the healthcare systems of developed countries. But overcoming the disease represents a new challenge for patients since they have to face different consequences in many areas: physical, psychological and social. Within these consequences of the illness, fatigue is one of the most frequent among survivors, as it occurs in a large percentage of patients and its effects may persist over time. Therefore, the implementation of interventions that can help alleviate these symptoms in survivors is of paramount importance. In this sense, the efficacy of physical exercise in reducing fatigue in this patient group has high empirical support which backs its use ahead of pharmacological treatments, the efficacy of which is yet to be determined among survivors (Battaglini et al., 2014; Blaney, Lowe-Strong, Rankin-Watt, Campbell & Gracey, 2013; Brown et al., 2011; Bower et al., 2014).

As for the psychological techniques, treatments that follow a cognitive behavioural conception have been shown to effectively relieve these symptoms. These results have been observed in several types of cancer and, moreover, the effects are maintained over time, which suggests adequate efficacy and supports their use in this group of patients. Although it is important to note that when CBT is presented together with physical exercise, CBT does not improve the results obtained by exercise alone, which further underscores the positive influence of

TABLE 1
CHARACTERISTICS AND RESULTS OF THE STUDIES INCLUDED

Authors/year	Number of Patients	Type of test	Type of cancer	Instruments	G. Treatment Intervention	G. Control Intervention	Results	Follow-up
Prinsen et al., 2013	37	Randomised and controlled	Various types of cancer	N.A.	Cognitive-behavioural therapy	Wait list	Significant reduction in fatigue and increase in physical activity	6 months: The results were maintained
Glielissen, Verhagen & Bleijenberg, 2007	68	Randomised and controlled	Various types of cancer	Checklist Individual Strength (CIS)	Cognitive-behavioural therapy	Wait list	Significant reductions in fatigue	Between 1 and 4 years: the results were maintained
Glielissen, Verhagen, Witjes & Bleijenberg, 2006	112	Randomised and controlled	Various types of cancer	Checklist Individual Strength (CIS)	Cognitive-behavioural therapy	Wait list	Significant reductions in fatigue	6 months: The results were maintained
Van Weert et al., 2010	209	Randomised, controlled and multicentre	Various types of cancer	Multidimen-sional Fatigue Inventory (MFI)	Two groups: a)CBT + exercise b)Exercise	Wait list	Significant reductions in fatigue in both treatment groups	No follow-up
Matthews et al., 2014	56	Randomised and controlled	Breast	N.A.	CBT for insomnia	Placebo treatment	Better efficiency and reduced sleep latency. No effect on fatigue.	6 months: The results were maintained
Dirksen & Epstein, 2008	72	Randomised	Breast	N.A.	CBT for insomnia	Education and sleep hygiene	Significant reductions in fatigue	No follow-up
Espie et al., 2008	150	Randomised and controlled	Various types of cancer	N.A.	CBT for insomnia	Usual treatment	Significant reductions in night-time wakefulness and fatigue	6 months: The results were maintained
Reif, De Vries, Peter-mann & Görres, 2013	261	Randomised, controlled and multicentre	Various types of cancer	N.A.	Educational program to reduce fatigue	Usual treatment	Significant reductions in fatigue, and significant improvements in quality of life, self-efficacy, physical activity, anxiety and depression	N.A.
Yun et al., 2012	273	Randomised and controlled	Various types of cancer	Brief Fatigue Inventory (BFI) y Fatigue Severity Scale (FSS)	Educational program via the Internet based on the guidelines of the National Comprehensive Cancer Network and the trans-theoretical model	Usual treatment	Significant reductions in fatigue.	No follow-up
Johnston et al., 2011	12	Randomised and controlled (pilot)	Breast	Brief Fatigue Inventory (BFI)	Educational program (exercise, nutrition, stress management) + acupuncture	Usual treatment	Significant reductions in fatigue	No follow-up
Fillion et al., 2008	87	Randomised and controlled	Breast	N.A.	Educational program (stress management) + exercise	Usual treatment	Significant improvements in fatigue, energy levels, quality of life and emotional distress	3 months: The results were maintained
Bower et al., 2014	71	Randomised and controlled	Breast	N.A.	Mindfulness	Wait list	Significant reductions in fatigue, stress, depression and sleep alterations	3 months: The results were not maintained
Johns et al., 2014	35	Randomised and controlled (pilot)	Various types of cancer	N.A.	Mindfulness	Wait list	Significant reductions in fatigue, vitality, depression and sleep disturbances	1 and 6 months: The results were maintained.
Van der Lee & Garssen, 2012	100	Randomised	Various types of cancer	Checklist Individual Strength (CIS)	Mindfulness	Wait list	Significant reductions in fatigue	6 months: The results were maintained.
Hoffman et al., 2012	229	Randomised and controlled	Breast	Profile of Mood State (POMS).	Mindfulness	Wait list	Significant reductions in fatigue	3 months: The results were maintained.
Lengacher et al., 2012	N. D	Randomised	Breast	M.D. Anderson Symptom Inventory	Mindfulness	Usual treatment	Significant reductions in fatigue	No follow-up

N.A. (Not available)

exercise on fatigue in survivors (Glielissen, Verhagen, Witjes & Bleijenberg, 2006; Glielissen, Verhagen & Bleijenberg, 2007; Prinsen et al, 2013; Van Weert et al, 2010). Within this category, positive effects of CBT are also observed for insomnia, resulting in improvements in the fatigue of survivors, although in this case, the results are contradictory so they should be considered with caution (Dirksen & Epstein, 2008; Espie et al. 2008; Matthews et al, 2014). Some educational programs have also been shown to be effective in reducing fatigue and other relevant aspects for the survivors, such as quality of life, anxiety or depression, although in this case, the heterogeneity of these programs makes it difficult to interpret the results. It should be noted, however, that in some of these programs exercise is included as a technique, again showing beneficial effects on fatigue in these patients (Fillion et al. 2008; Johnston et al, 2011; Reif, De Vries, Petermann & Görres, 2013; Yun et al, 2012). Despite these problems, these data should be considered for future research in this line of action. Finally mindfulness has shown high efficacy in reducing the symptoms of fatigue in cancer survivors in tests with varying degrees of control and with different types of cancer, the positive results being maintained over time (Bower et al., 2014; Hoffman et al., 2012; Johns et al., 2014; Lengacher et al., 2012; Van der Lee & Garssen, 2012).

In summary, out of the psychological treatments, the greatest efficacy in reducing the symptoms of fatigue in cancer survivors is observed in patients who receive cognitive-behavioural and mindfulness therapy, ahead of educational programs. However, it is necessary to point out some issues for the future. For example, the majority of the studies were conducted with groups of limited size comprising breast cancer survivors. It would be desirable to include a greater variety of types of cancer to evaluate the efficacy of the interventions. Moreover, the variability in the scales used in the studies to measure fatigue suggests that efforts should be made towards achieving greater agreement with regards to the use of scales for assessing fatigue in survivors.

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