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CHAPTER 7

Fatigue, quality of life and health status in sarcoidosis

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Although fatigue is a well-known symptom in sarcoidosis, it still seems an underestimated problem in clinical practice. A recent study showed that even physicians experienced in the treatment of sarcoidosis showed poor chance-corrected agreement with patients on the presence of symptoms attributable to sarcoidosis [1]. It was suggested that physicians probably rely more on chest radiographs and lung function and laboratory test results. They may, therefore, underestimate symptoms important to the patient, such as pain, stress, and fatigue, which cannot be assessed using laboratory tests [1]. Previously, only poor relations of objective disease parameters, such as lung function tests and health status [1–3], as well as quality of life (QoL) [4], have been shown in sarcoidosis patients. Presumably, objective clinical parameters do not reflect a patients' perceived well-being.

Sarcoidosis is a young persons disease with a peak at 20–40 yrs [5, 6]. At this age, it may be more difficult to cope with a symptomatic multi-organ disease of unknown origin and unpredictable course than at older age. A chronic disease at a young age may result in working and social problems, especially when the patient looks healthy. When disabling fatigue remains the only symptom, procedures concerning working disability with the employer or the insurance company may be difficult because there is no method of establishing objectively that the patient suffers from serious loss of working capacity.

A number of studies have shown that fatigue is a prominent feature of sarcoidosis and that the health status, as well as QoL, of this patient group is impaired [1, 2, 4, 7]. Different aspects of fatigue, QoL and health status in sarcoidosis are discussed in the present chapter.

Fatigue

Fatigue is a common symptom in a large number of medical conditions. It can be present in autoimmune disorders, such as rheumatoid arthritis, in malignant disease and in viral infections [8]. Recent studies have shown that fatigue is also a prominent problem in sarcoidosis [2, 4, 7, 9]. A substantial number of sarcoidosis patients suffer from persistent fatigue [4, 7]. In a selected group of 1,046 patients (all members of the Dutch Sarcoidosis Society (DSS)), mainly chronic sarcoidosis patients, fatigue was the most frequently reported symptom [7]. In a study among 64 sarcoidosis patients from eight Dutch hospitals [2], 73% of the symptomatic sarcoidosis patients (n=37) reported

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persistent fatigue. In this study, fatigue was by far the most frequent symptom, compared to dyspnoea, cough, arthralgia and thoracic pain. The mean disease duration was 5 yrs. A similar percentage of fatigue was found in another sample of outpatients who had suffered from sarcoidosis for ≤ 2 yrs [10]. In contrast, in a group of 715 newly detected sarcoidosis patients from 19 pulmonary hospitals throughout former West Germany and Switzerland, only 18% reported constitutional symptoms such as fatigue, together with weight loss and night sweats [5]. In the American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and Other Granulomatous Disorders statement on sarcoidosis, constitutional symptoms, such as fever, weight loss, fatigue and malaise, were mentioned as being present in approximately one-third of patients [11].

With regard to sex, results are inconsistent. In a group of patient members of the DSS, females indicated more often that they suffered from fatigue [12]. However, a study among chronic outpatients showed higher scores for fatigue in males [13]. Another study did not find sex differences with respect to fatigue [10].

SHARMA [9] postulated three different types of fatigue in sarcoidosis, *i.e.* early morning fatigue, intermittent fatigue and afternoon fatigue. Patients with early morning fatigue awake unrefreshed. They have difficulty getting out of bed, partly because of joint stiffness and/or muscle pain. Moreover, sleeping disorders (see later) may play a role in this type of fatigue. Patients with intermittent fatigue awake fit, but feel exhausted after a few hours of activity. Rest resolves this type of fatigue and patients can pick-up their activity for a few hours, after which they again become tired. Afternoon fatigue is present in patients who are fit in the morning but completely exhausted in the afternoon. Patients with this type of fatigue may feel as though they have influenza and wish only to go to bed. Although this classification seems plausible, studies examining these different types of fatigue in sarcoidosis are lacking.

Causes of fatigue in sarcoidosis

Some attempts have been made to examine the underlying causes of fatigue in sarcoidosis. The general inflammation and metabolic derangement have been discussed [14]. In a recent study, none of the variables tested, including lung function, metabolic measures, laboratory parameters of inflammation, T-cell activation and granuloma formation, were useful in predicting fatigue in sarcoidosis patients [10]. However, these were cross-sectional studies.

Other factors that may contribute to fatigue in sarcoidosis are myopathy and sleeping disorders, such as obstructive sleep apnoea [15, 16], which is frequent in sarcoidosis, and sleep disturbances associated with periodic leg movements [17]. The prevalence of obstructive sleep apnoea syndrome in the studied sarcoidosis population with clinically significant sarcoidosis was 17%, which was significantly higher than in a control group (3.3%) and the general population (2–4%) [15]. Moreover, patients with lupus pernio were 8.1 times more likely to exhibit sleep apnoea than those without.

In sarcoidosis, pain also appears to be related to fatigue. In a study among a large group of sarcoidosis patients without comorbid conditions, fatigue was associated with the presence of pain and specific types of pain, such as muscle pain, chest pain, arthralgia, abdominal pain and headache [18]. A feeling of general weakness is common in sarcoidosis [7]. It is also possible that lack of exercise contributes to fatigue in sarcoidosis. Fatigue has been examined in relation to psychological factors. In a recent study, a considerable number of sarcoidosis patients were diagnosed with depression, a major symptom of which is fatigue [1, 19]. In a Dutch study, patients appeared to score highly for perceived stress, which was related to fatigue, even after the role of depression was

partialled out [20]. In accordance with this, in a group of USA sarcoidosis patients, a high prevalence of stress was reported [1]. Moreover, the development of fatigue and depressive symptoms might be attributed to involvement of the central nervous system [21].

Recently, it was shown that small fibre neuropathy (SFN) is common among sarcoidosis patients [22, 23]. Since patients with SFN report a range of nonspecific symptoms, such as fatigue, the relationship between SFN and fatigue was examined. Sarcoidosis patients with SFN reported higher fatigue scores (Fatigue Assessment Scale (FAS); see below) than those without SFN [24]. Accordingly, fatigue in sarcoidosis may be caused, at least in part, by autonomic dysfunction. Further studies are needed to examine the pathways between fatigue and SFN.

Assessment

There is no objective parameter for assessing fatigue in sarcoidosis [10]. When features of disease activity, such as the chest radiograph and lung function test results, as well as laboratory test results, have become normal, either spontaneously or after treatment, fatigue may persist [10]. Fatigue is a state that is not necessarily related to the subjective experience of fatigue [25, 26]. A common way of assessing perceived fatigue is by means of questionnaires. In sarcoidosis, fatigue has been assessed using the energy and fatigue facet of the 100-item World Health Organization Quality of Life instrument (WHOQOL-100) [27], the FAS [28] and once with the Multidimensional Fatigue Inventory [29]. The energy and fatigue facet of the WHOQOL-100 physical health domain consists of four questions: "How easily do you get tired?", "How much are you bothered by fatigue?", "Do you have enough energy for everyday life?", and "How satisfied are you with the energy you have?" [4]. In a group of 64 sarcoidosis patients, this facet appeared to differentiate between symptomatic and asymptomatic patients, as well as patients *versus* matched healthy controls [4]. In another study, sarcoidosis patients also reported significantly more fatigue than controls (fig. 1) [18].

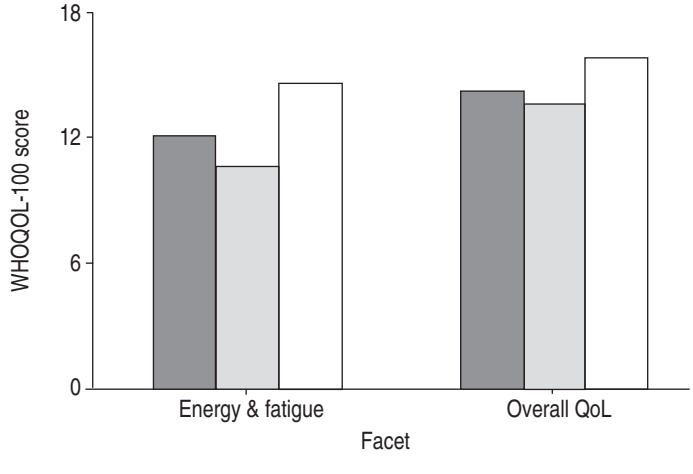

Fig. 1. – Mean 100-item World Health Organization Quality of Life instrument (WHOQOL-100) energy and fatigue facet and overall quality-of-life (QoL) scores in two groups of sarcoidosis patients (■: [4]; ■: [18]) and a control group (□: [18]). Patients reported having significantly less energy ($p<0.05$) than the control group. No differences emerged concerning overall QoL.

The FAS is a promising measure for assessing fatigue in sarcoidosis patients [13]. One study showed that the majority (80%) of a general population sample scored below the cut-off score on the FAS, whereas 80% of sarcoidosis patients scored above that score [13]. Since fatigue has a major impact on QoL in sarcoidosis, establishing the extent of fatigue will provide valuable insight regarding patients' QoL. Thus, in order to find out how the patient feels, measuring fatigue with the FAS would provide such information. Fatigue, measured with a single yes/no question, appears to be related to inflammation, as indicated by an acute phase response [14]. However, single-item measurements are not preferred since the reliability of such instruments is low.

Treatment

As mentioned above, there exists no effective treatment for fatigue in sarcoidosis. In a study examining fatigue in two groups of sarcoidosis patients, it appeared that, in the group of patient members of the DSS, patients using prednisone exhibited higher fatigue scores than patients not using prednisone. In the outpatient group, fatigue was unrelated to prednisone use [10, 13]. Several case reports of sarcoidosis patients treated with anti-tumour necrosis factor (TNF)-α showed a dramatic reduction in fatigue [30–32]. The positive effect of anti-TNF-α on fatigue has also been demonstrated in other diseases, such as Crohn's disease and rheumatoid arthritis [33, 34]. For obvious reasons, however, this kind of drug cannot be given to patients who are suffering exclusively from fatigue without other evidence of disease activity.

When fatigue has a (partly) psychological cause, various treatments are available. Patients with clinical depression can be prescribed antidepressants. Cognitive therapy can be offered to treat coping problems or stress perception. Furthermore, physical training programmes might also improve patients' exercise tolerance. These programmes appear to work in the management of chronic fatigue syndrome [35], and increase exercise tolerance in patients with left ventricular dysfunction [36], who also report severe fatigue.

Quality of life and health status

QoL and health status (often referred to as "health-related quality of life") are increasingly being recognised as important measures of disease impact and therapeutic outcome. Both concepts consist of a physical, psychological and social domain. Since the mid-1980s, QoL and health status have been studied in a considerable number of chronic diseases. Although most of the studies indicate measurement of QoL, it is health status that has been assessed. QoL and health status are two different but complementary concepts. Health status refers to the impact of disease on patients' physical, psychological and social functioning. QoL refers to patients' perception or evaluation of their functioning [37, 38], *i.e.* how satisfied or bothered they are with their functioning [39].

Differences between quality of life and health status

The differences between the types of questions and meanings of the scores from QoL and health status measures are explained below. First, health status may indicate whether or not there are limitations, whereas QoL also reflects to what extent patients experience these limitations as a problem in daily life. Individual expectations regarding health, the ability to cope with limitations and the threshold of tolerance of discomfort modulate

objective health status facts into subjective values, which represent QoL [40]. Consequently, two persons with identical restrictions in functioning (health status) may evaluate these restrictions (QoL) differently. Similarly, a low health status score can coincide with a high score on the corresponding domain of a QoL measure within the same person. Thus using a health status measure to assess QoL can provide misleading conclusions [38]. This can be illustrated using the social domain. Health status measures focus on how often and to what extent physical health and emotional problems have interfered with (unspecified) social activities. Consequently, patients with few social contacts have a low score and are thus expected to have an unsatisfactory social life. A QoL measure enquires about patients' satisfaction with their social contacts. Since this is not related to the size of their social network, few social contacts may reflect a patient's preference.

Secondly, health status and QoL measures differ in their level of differentiation. In general, QoL questionnaires assess more aspects of life than health status measures, in such a way that they provide more detailed information on patients' lives. For example, the psychological domain of health status measures incorporates a wide spectrum of questions, such as the frequency of feeling nervous, down, calm and quiet, depressed, and happy. However, since these questions are aggregated into one score, this does not permit identification of the feelings that are affected. In contrast, a QoL questionnaire assesses a broader range of separate aspects of the domain, *e.g.* negative feelings, positive feelings and self-esteem.

Thirdly, health status measures only aspects that are directly related to health, whereas QoL instruments measure a broader range of aspects of patients' lives. Measuring a wider scope of aspects is important because patients may feel that aspects that are not directly health-related are very relevant to them and determine their QoL [41]. An example is financial resources, which are often influenced by disease, *e.g.* because patients have to reduce their number of working hours. Fourthly, health status measures are characterised by the tendency to assess infirmity or disability, rather than health [39]. Questions focus on the negative consequences of disease and disregard the positive aspects of life, which are part of QoL measures.

The choice of a QoL or health status measure depends on the aim. In general, if information is wanted about what patients can and cannot do (functioning), a health status measure must be used. However, if the interest is in how patients feel about various aspects of their lives, a QoL measure is indicated. Using the right type of questionnaire for achieving the desired aim is of the utmost importance, since QoL and health status measures may provide conflicting results. Using a combination of health status and QoL measures has been suggested by several researchers.

Quality of life and health status measures used in sarcoidosis

To date, only one QoL measure has been employed in sarcoidosis, the WHOQOL-100 [27, 42]. This questionnaire is applicable in chronically ill persons, individuals living under stress and healthy persons. It was originally developed in 15 collaborative centres throughout the world (*e.g.* in the UK, the USA, The Netherlands, France and Russia). The WHOQOL-100 consists of 100 items, assessing 24 facets of QoL within six domains (physical health, psychological health, level of independence, social relationships, environment and spirituality/religion/personal beliefs) and a general evaluative facet of overall quality of life and general health. The response scale is a five-point Likert scale. The psychometric properties, including sensitivity to change, are good [43, 44]. Studies among sarcoidosis patients have shown that the questionnaire is reliable and valid (table 1) [45].

Table 1. – Quality of life (QoL) and health status (HS) questionnaires used or examined in sarcoidosis

	QoL/HS	Items n	Time required min	Quality in sarcoidosis
CRQ	HS	20	20–30	Not good[#]
SF-36	HS	36	10	Good[#]
SGRQ	HS	76	15–20	Good[#]
SHQ	HS	29	10	Good
SIP	HS	136	20–30	Unknown
WHOQOL-100	QoL	100	15–20	Good

CRQ: Chronic Respiratory Disease Questionnaire; SF-36: 36-item Short-Form Health Survey; SGRQ: St George's Respiratory Questionnaire; SHQ: Sarcoidosis Health Questionnaire; SIP: Sickness Impact Profile; WHOQOL-100: 100-item World Health Organization Quality of Life instrument. [#]: validated in interstitial lung disease sample including 10 sarcoidosis patients.

With regard to health status, five different measures have been used in sarcoidosis studies (table 1). The Chronic Respiratory Disease Questionnaire (CRQ) [46] is a respiratory-specific health status measure that was originally developed for chronic obstructive pulmonary disease (COPD) patients. It measures four aspects of health status: dyspnoea, fatigue, emotional function, and mastery. The questionnaire allows patients to rate the severity of dyspnoea associated with individually identified activities. Scores can range 0–100, with higher scores indicating a better health status. Contrary to the other questionnaires used in sarcoidosis, the CRQ is an interviewer-assisted questionnaire. It appears to be a reliable and valid instrument for COPD and asthma patients [46–48]. CHANG *et al.* [49] have used the CRQ in a validation study among patients with interstitial lung disease (ILD), which included 10 sarcoidosis patients (20% of the total ILD group). They concluded that the CRQ was not a good measure for use in ILD.

The 36-item Short-Form Health Survey (SF-36) [50] is a 36-item generic health status measure that assesses health in eight dimensions: physical functioning, social functioning, limitations in usual role activities due to physical problems (role physical), limitations in usual role activities due to emotional problems (role emotional), mental health, vitality, bodily pain, and general health perception. In addition, health changes over the last year may be assessed. Besides scores for each subscale, the testing yields a composite health status score on a scale of 0–100, where a high score indicates good health status. The SF-36 has been widely used and has good psychometric properties [51]. The reliability and validity have been shown to be good in a sample of patients with ILD that included some sarcoidosis patients [49].

The Sarcoidosis Health Questionnaire (SHQ) [3] is a sarcoidosis-specific health status measure that consists of 29 questions covering three domains: daily functioning, physical functioning, and emotional functioning. The response scales range 1 (all of the time)–7 (none of the time). The reliability and validity of this questionnaire appear good [3], but further testing is needed. Unfortunately, fatigue, a major symptom of sarcoidosis, is only represented by one question, which forms part of a domain. Specific information on this symptom cannot be derived from the SHQ. In order to assess fatigue, another specific fatigue measure needs to be used.

The Sickness Impact Profile (SIP) [52] is designed to assess sickness-related behavioural dysfunction in 12 categories: alertness behaviour, ambulation, body care and movement, communication, eating, emotional behaviour, home management, mobility, recreation and pastimes, sleep and rest, social interaction, and employment. It also provides summary scores for physical, psychosocial and overall behavioural dysfunction. The scores are expressed as percentages of the maximal possible score of dysfunction. The scores range 0–100, with higher scores reflecting greater impact of

disease on patients' lives. The SIP has been used in many studies among a wide range of patient populations and its reliability and validity appear to be good [51, 52]. This questionnaire has not been validated for use in sarcoidosis.

The final questionnaire that has been used in sarcoidosis is the St George's Respiratory Questionnaire (SGRQ) [53], a measure developed for COPD patients. It contains 76 items with weighted responses covering three components: symptoms, activity, and impacts. The latter two relate to the patient's current state of health. All component items can be aggregated into a total SGRQ score. Scores can range 0–100, with higher scores indicating poorer health status. The SGRQ appears to have good reliability and validity in COPD and asthma patients [54–56]. Moreover, this final questionnaire was considered a good respiratory-specific measure useful in ILD patients, including 10 sarcoidosis patients [49].

Quality of life in sarcoidosis

QoL research has a short history in sarcoidosis. The first QoL study, using the WHOQOL-100, was published in 1998 [4].

Concerning QoL, nonspecific symptoms, such as fatigue and pain, have an important impact on the QoL of sarcoidosis patients [12, 18, 57]. In one study [4], 64 sarcoidosis patients completed the WHOQOL-100 and a symptom checklist. The patients were divided into two groups: patients with symptoms, such as dyspnoea, cough, chest pain, arthralgia and fatigue, and those who were asymptomatic. The WHOQOL-100 revealed a number of areas in which sarcoidosis patients, especially those with current symptoms, experienced problems. Both patient groups exhibited sleeping problems and impaired general QoL compared with healthy controls. Beside the physical problems mentioned above, patients with current symptoms suffered from impaired QoL, mainly in their level of independence. This area includes problems with mobility, working capacity and activities of daily living. Sarcoidosis has a considerable impact on the QoL of patients, especially in those with current symptoms, but also, to a lesser extent, in patients with a relatively mild respiratory functional impairment [4]. This conclusion was affirmed in three other QoL studies [12, 57, 58].

In one of these studies, the QoL of sarcoidosis patients (n=37) was compared with that of healthy controls and a group of rheumatoid arthritis patients. In comparison to the QoL of the healthy controls, the QoL of both patient groups was impaired. Fatigue, sleep, activities of daily living and working capacity were major problems in sarcoidosis, as well as rheumatoid arthritis, patients. As might be expected, rheumatoid arthritis patients demonstrated more problems related to pain and mobility [57]. In another study, sex differences were examined with regard to QoL and symptoms [12]. Male and female patients with symptoms differed from each other in pain, sleep, positive feelings, appearance, mobility and activities of daily living. Except for positive feelings, female patients exhibited a lower QoL [12]. The patients in this study were all recruited through the DSS. Possible explanations for the sex differences could not be evaluated because relevant medical data about the patients were lacking. A group of outpatients, a group of DSS members matched to the outpatients on the basis of age and sex, and a group of DSS members matched to the outpatients on the basis of age, sex and current symptoms were studied [58]. The outpatient group was, on average, more satisfied with their physical health. They indicated being less bothered by pain and fatigue than the DSS members. Another study showed that patients with SFN had a worse QoL than patients without SFN [24]. No other QoL studies have been conducted in sarcoidosis patients.

Health status in sarcoidosis

Research on health status in sarcoidosis is also relatively recent. The relationship between health status and sarcoidosis was first examined in 1997 [59]. Compared with controls, the sarcoidosis patients scored more highly in the SIP categories alertness behaviour, home management, recreation and pastimes, sleep and rest, social interaction, and employment. In addition, they scored more highly on the summary scores for psychosocial and overall behavioural dysfunction. Correlations were found between respiratory muscle endurance time and the SIP categories mobility and body care and movement. Radiographic stage was related to the SIP categories alertness behaviour, emotional behaviour, home management and social interaction [59].

DRENT *et al.* [2] found an association between SIP scores and depressive symptoms in sarcoidosis patients. With regard to the summary dysfunction scores, patients scored more highly on all three scores, *i.e.* physical, psychosocial and total score. The differences between the sarcoidosis patients and the control group were caused by patients with symptoms. With regard to depressive symptoms, patients with current symptoms also scored more highly in the component cognitive depressive symptoms compared to patients without current symptoms. This latter group experienced more positive effect, whereas no differences were found between the two sarcoidosis subgroups concerning negative effect. Health status, especially the category sleep and rest, was associated with depressive symptoms in general, and depressive cognitions in particular [2].

In two USA studies, the prevalence of depression was high, *i.e.* 60 and 66% [1, 19]. Increased dyspnoea score and number of systems involved were among the risk factors for depression [19]. COX *et al.* [1] found that higher scores for depressive symptoms and perceived stress were related to lower health status scores. In accordance with this study, a Dutch study found that depressive symptoms and perceived stress were substantially related in sarcoidosis patients, and that sarcoidosis patients scored highly for perceived stress [20].

In another sarcoidosis study, the relationship between socioeconomic status and health status was assessed. Patients were asked about activity limitations and social limitations due to physical or emotional disability. Activity limitations due to physical disability were mainly related to insurance status. Patients who reported limitations were more frequently without insurance or had public insurance. Nearly all patients with a high income reported that they were not limited in activity by emotional disability. Furthermore, patients with private health insurance were more likely to report no limitations, while, at the same time, they more often indicated that they were limited in particular kinds of activity. With regard to social limitations, patients with private insurance were again more likely to report no limitations [60]. Thus, in general, patients with a high socioeconomic status reported a better health status. The same conclusion was drawn using data from A Case–Control Etiologic Study of Sarcoidosis (ACCESS) [61].

Health status was also evaluated among lung transplant recipients (n=31), including three sarcoidosis patients [62]. Compared to transplant candidates, the SGRQ and all SF-36 subscale scores, except bodily pain, showed a better score for transplant recipients, indicating a considerable improvement in most dimensions of health status in patients who survived lung transplantation. Finally, a study by BAUGHMAN *et al.* [63] examining the usefulness of fluticasone in patients with acute symptomatic pulmonary sarcoidosis asked patients to complete the SF-36. All patients were on an initial dose of oral corticosteroids prior to enrolment in a randomised double-blind trial of inhaled fluticasone. The results of the SF-36 showed no difference between the fluticasone and the placebo group. However, oral corticosteroids appeared to be associated with significant complaints, whereas inhaled corticosteroids were well tolerated [63].

Clinical implications

Fatigue has a substantial impact on patients' QoL and health status. However, the assessment of QoL and health status in the follow-up of sarcoidosis patients in clinical practice seems not to be feasible. For clinical studies in sarcoidosis patients, however, the use of a health status measure as well as a genuine QoL measure seems essential to be able to evaluate, for example, the effect of an intervention not only on patients' functioning but also on their subjective QoL and well-being.

Although fatigue is not reflected in lung function test results or other clinical parameters, in the follow-up of sarcoidosis patients in daily practice, it is important to take this symptom seriously. One way of assessing fatigue in the clinical setting may be completion of the FAS in regular terms. The FAS is available digitally. When patients complete this questionnaire, a score profile appears on screen. This measure provides the physician with more detailed information about the nature and extent of the patient's fatigue. Although no medication is available for improving this symptom, results from this questionnaire make fatigue a topic of discussion between patient and physician. This may improve patient-physician communication because the patient feels that fatigue is being taken seriously.

Conclusions

In conclusion, fatigue in sarcoidosis is a frequent symptom, although it is still underestimated in clinical practice, especially when lung function test results, chest radiographs and laboratory parameters are normalised. Physicians treating sarcoidosis patients should take fatigue seriously even in the absence of any objective marker of it and when they have no treatment to offer. Absence of evidence does not mean evidence of absence. In particular, QoL is low, especially in symptomatic sarcoidosis patients, with respect to mobility, working capacity and activities of daily living. The health status of sarcoidosis patients is also impaired.

Patients with fatigue may suffer from SFN. Other possible causes are underlying depression or neurosarcoidosis, which should also be taken into consideration. A number of case reports of patients with severe disease treated with anti-TNF-α have indicated a decrease in fatigue in addition to a general improvement in sarcoidosis. However, there is no specific treatment for fatigue in sarcoidosis. Some patients may require help in improving coping and self-management of their disease in general and this symptom in particular. In some cases, cognitive therapy may be indicated. Physiotherapists can advise patients on how to improve their exercise tolerance and physical fitness, taking into consideration their fatigue. Rehabilitation programmes should be developed in order to guide patients properly. Beside physical problems, sarcoidosis has a substantial impact on QoL. It is very important to guide persons involved in the follow-up of patients with sarcoidosis. Moreover, it is important to educate employers and assurance physicians that the absence of objective parameters does not always guarantee that persons are healthy. Since taxability is clearly decreased, activities should be adapted accordingly.

Summary

Fatigue still seems an underestimated problem in sarcoidosis. Objective clinical parameters are not related to fatigue. General inflammation and metabolic derangement, pain, sleeping disorders, small fibre neuropathy and depression have been postulated as possible causes. Since fatigue cannot be assessed using objective measures, validated questionnaires, such as the Fatigue Assessment Scale, are recommended for establishing the extent of fatigue. No effective treatment for fatigue in sarcoidosis is known. Case reports have shown a positive effect of anti-tumour necrosis factor-α on fatigue.

Nonspecific symptoms, such as fatigue, have a negative impact on the quality of life and health status of sarcoidosis patients. Quality of life is particularly impaired with respect to mobility, working capacity and the activities of daily living. As long as there is no effective treatment for fatigue in sarcoidosis, rehabilitation for improvement of physical fitness, coping and self-management should be considered for some patients. Finally, it must be stressed that fatigue should be taken seriously in the management of sarcoidosis patients.

Keywords: Fatigue, Fatigue Assessment Scale, health status, 100-item World Health Organization Quality of Life instrument, quality of life, sarcoidosis.

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