

Fatigue in Systemic Lupus Erythematosus

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Abstract

Fatigue is reported by up to 90% of people with Systemic Lupus Erythematosus (SLE). The exact cause of this symptom is as yet unknown however some of the causes considered are (i) that it is an independent symptom of SLE, (ii) that it occurs as a result of increased disease activity and (iii) that fatigue is as a result of the psychosocial impact of managing the daily impact of SLE. Regardless of the underlying causative mechanism of this symptom, fatigue is identified as the most difficult and troublesome aspect of the disease. Despite its high prevalence, people with SLE report that little attention is given to fatigue during hospital or clinic visits. This oversight is thought to arise from inadequate understanding and recognition of the symptom by health professionals and a lack of medical interventions to alleviate the symptom. This chapter presents the debate on the causes of fatigue in SLE and factors that increase fatigue. It then focuses on the impact of fatigue for the person with SLE and presents research on how people with SLE describe their fatigue and its impact on daily activities with a particular emphasis on work. The final section of the chapter provides an overview on measuring fatigue and provides simple fatigue management strategies that health professionals can recommend to people with fatigue.

Keywords: Fatigue, causes, impact on daily activities, measurement, fatigue management.

Introduction

Fatigue in SLE is described as a feeling of tiredness, a lack of energy and endurance, or extreme exhaustion (Ahn and Ramsey-Goldman, 2012). It is experienced as a sensation beyond ordinary tiredness and something that rest does not always improve (Schmeiding and Schneider, 2013). As a symptom, it is non-specific and very subjective. It is reported as having serious consequences in terms of health-care expense and impact on work ability (Norheim et al, 2011).

Fatigue is present in many chronic conditions such as chronic inflammatory, neurological, psychiatric diseases and cancer. However it is particularly prevalent in rheumatic diseases. Norheim et al., (2011) provided fatigue rates for Rheumatoid Arthritis, primary Sjögrens Syndrome and Fibromyalgia as 42-80%, 60-67% and 49-70% respectively. However they reported that fatigue is more prominent in SLE with up to 90% of people reporting fatigue. Finlayson et al (2012) identified two types of fatigue: primary and secondary fatigue. Primary fatigue is caused by disease-related inflammation, while secondary fatigue is believed to be as a result of non-disease specific factors such as de-conditioning,

medication side effects, sleep problems, poor nutrition or overly demanding personal routines and habits. Both types of fatigue are believed to impact considerably on functional capacity.

Causes of fatigue in SLE

Many factors are believed to contribute to fatigue in SLE. Norheim et al., (2011) investigated biological mechanisms of fatigue across a range of chronic autoimmune and inflammatory diseases. They presented explanatory models for the biological origins of fatigue which outlined how biological agents such as pro-inflammatory cytokines interfere with the immune system; that mitochondrial dysfunction causes fatigue; and explained the role of oxidative stress and genetic susceptibility as a cause of fatigue. Morris et al (2015) also proposed that fatigue is driven by peripheral immune activation and systemic inflammation inducing mitochondrial damage which accounts for intractable fatigue in autoimmune diseases. However, none of this has been confirmed and therefore drug trials acting on the biological agents of fatigue have to date provided inconclusive results.

Hewlitt et al., (2011) presented a multidimensional model of fatigue. This model proposed three categories for examining a multifactorial aetiology of fatigue. The three categories are: (i) disease factors which include disease activity, pain and co-morbidities; (ii) cognitive-behavioural factors which include depression, anxiety and sleep disruption and (iii) personal factors such as reduced levels of fitness, physical activity and social supports. Although this model is intended for RA, given the similarity in symptoms, and the similar debate between the disease process of RA and fatigue, this model will be applied here to discuss causes of fatigue in SLE.

Impact of disease activity, pain and co-morbidities on fatigue

Disease activity

The relationship between disease activity and fatigue is constantly researched and debated in the literature. Krupp et al., (1989) were one of the earliest researchers to examine this relationship when developing the Fatigue Severity Scale, a fatigue measure specifically for SLE. Since then many studies have been carried out to identify the cause of fatigue in SLE and have arrived at conflicting conclusions regarding the impact of disease activity on fatigue. For example, Tesch et al., (2000), studied 120 women with a recent diagnosis of SLE and reported a weak association between disease activity and fatigue scores. Although their study found that fatigue scores were significantly higher for those with active disease than those with quiescent disease, they also reported significant levels of fatigue in the non-active disease group. They therefore concluded that other factors besides disease activity contribute to fatigue. They contended that the relationship between fatigue and disease activity is neither strong nor linear and that a number of other variables contribute to fatigue especially in periods of non-active disease.

In contrast to this, Tayer et al., (2001), reported a significant association between disease activity and fatigue in a longitudinal study of 81 individuals with SLE.

This study measured disease activity with the physician rated Systemic Lupus Activity Measure (SLAM). Study participants were also required to complete self-report measures of mood, feelings of helplessness and fatigue. In contrast to Tesch et al., (2000), Tayer et al., (ibid) reported that disease activity predicted fatigue independently of psychosocial variables of mood and feelings of helplessness.

In a later study, Jump et al., (2005), reported no significant association between physician rated disease activity and self-reported fatigue in their study of 127 women with SLE. As medication-use, has also been proposed as a cause of fatigue, Jump et al (ibid) examined the use of corticosteroid medication and fatigue and reported no significant differences in levels of fatigue between steroid users and non-users. There was however a significant difference in fatigue between users of non-steroidal anti-inflammatories and non-users, before controlling for pain, thus demonstrating a relationship between pain and fatigue.

These contradictory findings have remained in subsequent studies. A recent systematic review reported continued inconsistencies in research investigating the impact of disease activity on fatigue (Ahn and Ramsey-Goldman, 2012). However, despite the debate on which precedes the other, and which causes the other, it appears that fatigue is present even in times of disease remission and is reported as a constant and troublesome symptom.

Qualitative studies have also reported the constant nature of fatigue with a fluctuating pattern. Connolly et al., (2014), interviewed individuals on their experiences of fatigue in SLE. The participants, mainly female, ranged in age from 22 to 62 years with an average time since diagnosis of 14 years. Participants' occupations included full and part-time employment, working within the home full-time, full time student, and volunteering. Although experiencing fatigue to varying levels, all study participants identified fatigue as their worse symptom. For some of the participants, fatigue was constantly present while for others it fluctuated daily, weekly and monthly. Study participants also identified an unpredictable nature to the onset of fatigue in SLE which made it difficult to manage fatigue and its impact on their daily activities.

Pain

Joint pain is often one of the first symptoms experienced by people with SLE. Up to 95% of people report pain, with the small joints of the hands and feet being the most effected (Wallace, 2014). Pain is caused by inflammation of the synovial membrane in the joints and is increased in times of flares. Muscle pain is also common in SLE with up to 70% of people identifying this as a source of pain (Wallace, 2014). Muscle pain is also believed to be caused by the inflammatory process. There appears to be a symbiotic relationship between pain and fatigue as reported in many studies which have examined the causes of fatigue in SLE and other (non)inflammatory diseases. Those who experience chronic and enduring pain reported greater difficulty completing routine daily tasks and this difficulty resulted in higher levels of fatigue (Petri et al., 2013).

In a study from Southern California, Moldovan et al., (2013), examined the impact of pain on fatigue and vitality in a cohort of 125 adult Caucasian and Hispanic individuals with SLE. Study participants were required to complete questionnaires on disease activity, fatigue, vitality, pain and general health. Physician rated disease activity was also measured. In this study ethnicity was associated with fatigue in that Caucasian participants had higher levels of fatigue and Hispanic participants had higher levels of vitality. Using hierarchical multiple regression analysis, pain and depression were the two most significant factors in predicting fatigue. In contrast, none of the socio-demographic and disease activity-related measures were associated with fatigue. This study therefore demonstrates that pain and fatigue are strongly linked however it does not distinguish between which precedes the other: pain or fatigue.

Many studies have examined the pain-fatigue nexus in an effort to identify a cause and effect relationship. The questions often posed include: does pain, and the difficulties it causes in everyday activities, result in fatigue? Do people who experience greater levels of pain also have higher levels of fatigue? Or is it the reverse in that, do people that are tired have less resources to manage their pain, and therefore experience higher pain levels?

The temporal nature of pain and fatigue was explored in a study of people with Rheumatoid Arthritis (RA). Although RA is a different rheumatic disease from SLE, many of the symptoms are similar including pain and fatigue. van Dartel et al., (2013) conducted a longitudinal study collecting monthly data on fatigue and pain levels in a cohort of 228 people with RA. Their study found a significant positive relationship between pain and fatigue. However they were unable to determine if pain preceded fatigue or vice versa. Their study reported monthly fluctuations in pain and fatigue that were synchronous but was unable to show that pain preceded fatigue or that fatigue preceded pain. In a qualitative study on impact of fatigue on work ability, study participants were unable to identify a pain and fatigue relationship stating they viewed the two symptoms separately (Connolly et al., 2015). The implications of these findings is that both symptoms must be addressed independently and that an assumption cannot be made that an improvement in one symptom will automatically result in improvements in the other.

In summary, these studies indicate that pain and fatigue are strongly related in SLE but that a cause and effect relationship has not yet been determined. It appears that other disease-related factors may be contributing to fatigue. Moldovan et al (2013) contends that neither fatigue nor energy levels are a direct result of disease activity. Therefore based on the weight of evidence to date it appears that a reduction in disease activity alone will not lead to improvements in fatigue or energy levels. Therefore a range of treatment and management approaches are indicated.

Comorbidity

Fatigue is a common symptom associated with a wide range of chronic diseases including cardiac, respiratory, cancer, hepatitis, multiple sclerosis and many others (Whitehead, 2009). Wallace (2014) reported that 20% of people with one

autoimmune disease often have a second autoimmune disease. Iaboni et al. (2006) reported that between 11% and 22% of people with SLE also have fibromyalgia. As already outlined, Norheim et al., (2011), identified high prevalence rates for fatigue across a range of autoimmune diseases including up to 70% for people with fibromyalgia. This therefore indicates that the co-existence of a chronic disease for people with SLE could be a contributing and compounding factor to their fatigue.

On examining the impact of fatigue in work, with 234 people with rheumatic diseases, almost 40% reported the presence of another chronic disease (Connolly et al., 2016). In this observational study, participants were required to complete self-report questionnaires on disease activity, fatigue severity, the impact of arthritis on their work, ability to meet work-related demands, mood and health-related quality of life. Those with co-morbidity had significantly higher levels of fatigue in all domains of the Multidimensional Fatigue Inventory (MFI), their arthritis impacted significantly higher on their work, they had significantly more difficulties meeting the demands of their work and they had significantly lower quality of life than those with no co-morbidity. This indicates the additional difficulties that people with comorbidity experience with fatigue and that the presence of comorbidity should be a trigger for clinicians to provide early interventions for fatigue management with the aim to minimize the impact of fatigue on work ability at an early stage in the disease trajectory.

Cognitive-behavioural factors (depression, anxiety and sleep patterns) and fatigue

Mood

Fatigue is a core feature of depression and is used as a symptom in the diagnostic criteria for depression (Jump et al., 2005). A person with SLE may experience reduced mood or depression associated with managing the chronic and progressive nature of SLE alongside other life demands. Prevalence rates of depression in SLE have been examined over the past three decades. In 1991, Giang, reported prevalence rates for depression for people with SLE at 31-52%. Tench et al. (2000) on examining the association between fatigue and anxiety, reported that over a third of the cohort had clinical levels of anxiety and depression, but that only 13% of these individuals were on antidepressants. Given the enduring nature of SLE, and the organ involvement for some individuals, it is perhaps not surprising to identify such high levels of mood disturbance.

In a more recent systematic review of fatigue in SLE, Ahn and Ramsey-Goldman (2012) reported prevalence rates of 28% for anxiety and 24% for depression in people with SLE. In a qualitative study of fatigue in SLE, participants identified an interdependent relationship between anxiety and fatigue in that participants stated that when they experienced stress that this increased their fatigue and that when they were fatigued that they had more difficulty dealing with stressful events in their daily lives (Connolly et al., 2014). In a study of mixed rheumatic diseases, including SLE, Connolly et al., (2016) reported a 43% prevalence rate of

depression as measured on the mood domain of the EuroQoL utility index (EQ-5D-3D) for people in employment.

In a mixed methods study investigating the impact of fatigue on work ability the impact of fatigue on mood was a frequent issue discussed within the qualitative component of the study (Connolly et al., 2015). Participants described how when they are tired, they then become frustrated with themselves and irritable with their colleagues. This then resulted in feelings of guilt, which impacted on their mood and ultimately increased their fatigue. Low mood was also caused by difficulty meeting deadlines for work tasks, fear of losing their jobs, and difficulty fulfilling roles outside of work.

However there may be other disease-related factors influencing the fatigue-depression relationship. Jump et al., (2005), reported that depression was a unique contributor to fatigue but that pain was also positively associated with depression. They stated that the potential for a depression-fatigue-pain triad to be present in people with SLE was significant. This therefore appears to be an area that needs to be assessed during clinic visits with referrals made to relevant members of a multidisciplinary team to equip people with SLE with self-management strategies for fatigue, anxiety and pain.

Sleep quality

Patients with SLE report poor sleep quality, frequent awakenings over the course of the night and restlessness. Iaboni et al. (2006) compared sleep patterns in a group of 35 individuals with SLE with 17 healthy controls. This study showed that in comparison to healthy controls, the SLE group had lighter sleep and poorer sleep continuity. More recent research has identified that 56-91% of individuals with SLE report disturbances to their sleep patterns (Schmeding & Schneider, 2013; Ahn and Ramsey-Goldman, 2012). It appears therefore that people with SLE do not feel refreshed when they awake in the morning and therefore may not have adequate energy levels to meet the demands of their daily activities which further compounds their fatigue.

The symptom of pain can lead to disturbed sleep as does anxiety and stress. People with rheumatic diseases often report finding it hard to get comfortable in bed due to muscle and joint pain and that this impacts on the quality of their sleep. The ability to stay sleeping through the night is reduced by pain and stiffness. This results in un-restorative sleep which results in higher fatigue levels (Iaboni et al., 2006).

Impact of personal factors of fitness levels, physical activity, and social supports on fatigue

Physical activity and aerobic exercise has been found to improve fatigue in chronic diseases including rheumatic diseases (Mancusco et al, 2011). In non-rheumatic diseases, factors such as physical inactivity, low fitness rates, obesity and reduced muscle strength are all linked to fatigue. On assessing physical fitness, women with SLE had lower fitness levels than matched controls (Ahn and Ramsey-Goldman, 2012). Physical activity is recommended for a range of

chronic diseases and is considered a protective factor for development of chronic diseases as well as a management strategy. This will be discussed further under fatigue management strategies.

Social supports

Social supports are considered a protective factor for the impact of living with, and managing a, chronic disease such as SLE (Mazzoni and Cicognani, 2016). Seawell and Danoff-Burg (2004) identified that family and friends are the most important aspect of the lives of people with SLE but that individuals with SLE are often dissatisfied with the level of support they receive. The authors reported that this dissatisfaction is also related to a perceived lack of understanding or support from healthcare professionals.

In contrast to the benefits of social supports, Mazzoni and Cicognani (ibid) also discussed problematic social supports. This involves unhelpful behaviours from family and friends which can negatively impact on physical and psychological health and ultimately increase fatigue. Despite this finding however, the authors suggested that social support is a modifiable factor that could improve functioning. This was confirmed by Backman (2006) who reported that negative spousal support was significantly associated with pain severity however support from family members was a positive contributor to performance in work and household activities.

People with fatigue have reported difficulty with family and friends not understanding their fatigue and how SLE-related fatigue differs from regular fatigue (Connolly et al., 2014). Participants in this study reported that they get frustrated when they attempt to discuss their fatigue with family and work colleagues who, in response to these discussions, state that they also experience fatigue. This demonstrates a lack of understanding between SLE-related fatigue and regular fatigue. The study participants also stated that, at times, their family members, friends and/or colleagues put pressure on them to participate in social activities for which they lacked energy. This indicates a need for information sessions for family members, friends and work colleagues on fatigue in SLE, on factors that can increase fatigue and how fatigue impacts on daily activities. This may increase understanding of fatigue and facilitate positive support from immediate social networks on managing fatigue.

Causes of fatigue: summary

Many factors are believed to cause and compound fatigue in SLE. However, no research has as yet identified a linear cause and effect relationship for this symptom. The proposed causative factors range from other symptoms of SLE, for example joint and muscle pain, causing fatigue due to increased difficulty completing daily tasks. Fatigue is also believed to be aggravated by the biological actions of the SLE disease process, particularly during times of active disease. It has also been postulated that fatigue is exacerbated by the psychosocial impact of living with SLE and coping with the psychological impact of a chronic and enduring disease. However, despite the increased understanding of the many factors associated with fatigue in SLE, it can impact on all aspects of a person's daily activities.

Impact of fatigue on activities of daily living

People with SLE face a chronic and unpredictable disease course that may challenge their ability to cope with disease symptoms (Somers, 2012). This chronic disease may impact on all areas of activities of daily living. Activities of daily living are defined as tasks of everyday life that a person must perform to participate in social life, work roles and to live independently. These are categorized as self-care, productivity and leisure activities (Christiansen and Baum, 2005).

Self-care

Self-care activities are everyday activities that people do to look after themselves. These activities include dressing, personal care, shaving and bathing. Mattsson et al., (2012), conducted focus groups with individuals with SLE to analyse the effect of this diagnosis on self-care activities. Participants reported having to adapt and modify how they carried out their activities in order to manage the effect of pain and fatigue. In another qualitative study by Gallop et al., (2012), the impact of SLE on daily activities was also evaluated. In this study it was reported that symptoms such as fatigue, joint pain, swelling and muscle weakness had a substantial impact on participants' ability to carry out personal care activities particularly showering and bathing. In contrast to these findings, Connolly et al., (2014), reported little to no difficulty with self-care activities. Participants in that study discussed having experienced some difficulties prior to the diagnosis of their disease but these difficulties had then abated. Perhaps they started on medications which relieved symptoms which had caused these initial difficulties in their self-care activities.

Productivity

Productive activities are defined as activities that enhance the social and economic aspects of a community . In addition to employment, productive activities also consist of non-paid activities such as tasks undertaken for the upkeep of a person's home, volunteering and child minding responsibilities (Christiansen and Baum, 2005).

Work disability is a significant complication of SLE. The symptoms of SLE can adversely affect the ability to work which can result in loss of both current earnings and the ability to accumulate assets for retirement (Yelin et al., 2007). It is estimated that only 50% of people with SLE remain in employment resulting in the majority of the economic costs associated with SLE (Almehed et al 2010). Mattsson et al., (2012), reported that illness due to SLE was shown to affect work performance and resulted in periods of sick leave with subsequent financial implications. The opportunity to choose a job was limited and some participants reported being forced to work part time while others could not undertake any form of paid employment due to the symptoms of their disease.

Connolly et al., (2015) conducted semi-structured interviews with individuals in employment with SLE and who experienced fatigue. During the interviews participants discussed the negative impact of fatigue on their employment activities. They reported absenteeism, reducing their work hours, ceasing work

or having to take early retirement due to fatigue. Some participants described receiving considerable support and understanding from their employers. This enabled them to make changes to their work environment and/or to their work hours which in turn facilitated them to remain in employment. However, a number of the participants reported not disclosing their diagnosis in the work place for fear of a negative reaction from their employer or work colleagues. This resulted in increased anxiety and stress. This highlights the importance of people with SLE informing their employers of their diagnosis in order to avail of relevant supports and workplace accommodations to which they are entitled under employment legislation. Education is also required for employers and work colleagues on fatigue in SLE and on strategies for managing fatigue in the workplace.

Robinson et al., (2010), explored the impact of SLE on a range of productive activities with a convenience sample of people with SLE. Data collection methods were self-reported questionnaires, focus groups and individual interviews. Participants reported that signs and symptoms of SLE impacted on household responsibilities, parenting roles, and educational achievements. Connolly et al., (2014) also reported that as a result of reduced ability to participate in productive activities, participants were restricted in fulfilling what they considered important life roles. One woman discussed how her parenting activities were restricted with her young son because of her fatigue. Other roles affected included that of daughter, grandmother, friend, child-minder and volunteer. Society places great importance on individuals fulfilling work, family and social roles as it contributes to self-identity and community participation. Being unable to participate, or being restricted, in fulfilling valued roles can impact on psychological well-being (Boonen and Severns, 2011).

Leisure

Disability in chronic diseases such as SLE has been shown to result in decreased opportunities to socialize with peers. This can result in difficulties for the individual with SLE and their family (Yelin et al, 2007). Robinson et al., (2010), described how several of their study participants identified a progressive decline in participating in family, social and recreational events due to SLE symptoms particularly fatigue. In a qualitative study participants highlighted that leisure activities had been limited due to SLE related symptoms (Gallop et al., 2012). For example some participants reported that SLE related fatigue resulted in withdrawing participation in social and leisure activities that were physically demanding. In their qualitative study, Connolly et al., (2014) reported that almost all study participants had either given up leisure activities or altered them to accommodate fatigue. Study participants also described taking up new activities such as yoga or Pilates to replace lost leisure interests. Not only were these new hobbies and interests less physically demanding, but study participants also reported that Pilates and yoga improved their fatigue.

There is therefore evidence that SLE impacts on daily activities. However, Schmeiding and Schneider (2013) reported that detailed information on the impact of SLE on specific activities of daily living was scarce. They reported a need for large scale qualitative studies to identify how exactly SLE affects the daily

lives of people with SLE and to obtain a greater understanding of the impact of this disease on family members.

Impact of fatigue on quality of life

Quality of life is a subjective perspective on physical, emotional and social functioning (Fortin et al, 2004). Because of the nature of SLE, quality of life is an important factor to assess in a person's overall health. Given the multifaceted nature of fatigue it is also recommended to specifically consider the impact of this symptom on health-related quality of life (Moldovan et al., 2011).

People with SLE consistently report lower quality of life in comparison to healthy controls (Pettersen et al., 2015; Schmeding & Schneider, 2013). Despite the improvements in care they still experience long-term morbidity that adversely impacts on their quality of life (Pons-Estel et al, 2010). The most frequently reported symptoms that impact on quality of life for people with SLE include fatigue, joint pain and muscle weakness. Quality of life is also affected by difficulty in completing daily activities (Gallop et al., 2012).

Schmeding & Schneider (2013) conducted a systematic review on factors impacting on health-related quality of life. They examined 24 studies from Europe, North America and Australia. All studies had a minimum of 100 participants. They stated that the studies they reviewed consistently showed poorer quality of life for people with SLE than matched controls and population norms. Predictors of lower quality of life included older age, and co-morbid neurological or psychiatric disorders. Fatigue, pain, anxiety and cognitive impairments caused the greatest symptom burden on quality of life.

Measurements of fatigue in SLE

In order for individuals to learn to manage their fatigue and for health professionals to be able to treat fatigue, it is important to accurately measure the extent of an individual's fatigue in order to identify which elements of a person's life is most impacted by their fatigue. Given the subjective nature of fatigue the most common method for measuring fatigue is through self-report measures. When selecting a fatigue measure, a decision is needed on which type of measure best meets the needs, and time available, of the clinical cohort. This section will discuss a range of fatigue measures for people with SLE.

Fatigue measurement include (i) single item visual analogue scales (VAS), (ii) multi-item fatigue scales that explore broader issues of fatigue but produce a single global score of fatigue severity and (iii) multi-dimensional scales that provide sub-category scores in a number of different domains affected by fatigue (Hewlett et al., 2011). The shorter scales are often useful to obtain an overall perspective on the general impact of fatigue and to assess if a medical intervention has had an impact on severity of fatigue. The multidimensional scales, which take longer to complete, are indicated for designing and evaluating fatigue interventions.

An expert panel completed a systematic review of fatigue measurement scales used in SLE (Avina-Zubieta et al., 2007). Thirty-four studies which used 15 different fatigue measures were included in the final analysis. The measures reviewed ranged from single item visual analogue scales through to multidimensional scales examining the impact of fatigue on physical abilities, mental abilities, cognitive abilities, motivation and daily activities. Each measure was examined for construct validity, reliability and responsiveness. The panel recommended the Fatigue Severity Scale (FSS, Krupp et al., 1989) for evaluating SLE-related fatigue. The FSS is a 9-item scale that investigates the impact of fatigue on different areas of a person's functioning over a two-week period. It is measured on a scale of 1-7 where 1 = 'strongly disagree' to 7 = 'strongly agree'. Scores from the individual items are summed and are averaged by dividing by the total number of items. Higher scores indicate greater fatigue and a score of ≥ 4 is considered significant fatigue.

Although the FSS was the most commonly used measure of fatigue in the review, the FSS provides limited information for identifying which type of fatigue is causing the most difficulty for an individual. For this reason a multidimensional measure should be used to assess the extent of fatigue across a range of functional activities. For example, the Multidimensional Fatigue Inventory (MFI-20) (Smets et al., 1995) is a 20 item self-report questionnaire that measures different aspects of fatigue over a seven day period. The MFI contains five domains: general fatigue, physical fatigue, reduced activity, reduced motivation and mental fatigue. Scores range from a minimum of 4 to a maximum of 20 for each domain. Higher scores indicate more fatigue. The MFI-20 is used in research and clinical practice and has been found to be a reliable and valid measure of fatigue in chronic diseases (Thombs et al., 2008, Reeves et al., 2005). A score of 13 or above in the general fatigue category indicates severe fatigue (Reeves et al., 2005).

Fatigue management interventions

As discussed in this chapter fatigue is a frequent and debilitating symptom of SLE with no clear conclusions regarding the exact cause of this symptom. However many studies already discussed report the negative impact of fatigue on all elements of an individual's life. Given the pervasive nature of the symptom, management of fatigue is often a priority for those with SLE. However, Connolly et al., (2014), identified that people with SLE reported that their fatigue management strategies were mainly self-taught with little to no input from health professionals. Similarly, Peterson et al., (2015) stated that people with SLE reported a lack of knowledge and understanding of fatigue from health professionals. This indicates a need for health professionals to have knowledge of different approaches to managing and treating fatigue and to allocate time during clinic visits to address this symptom. Treatment of fatigue is generally considered under two categories: pharmacological and non-pharmacological.

Pharmacological interventions for fatigue

Pharmacological interventions involve the use of biologics to reduce fatigue. Yeun and Cunningham, (2014), in their review of pharmacological interventions discussed three different biologics trialed for their impact on fatigue severity: N-

acetylcysteine (NAC), an inhibitor of autoimmune inflammatory processes; Dehydroepiandrosterone (DHEA), a naturally occurring steroid and Belimumab which is a lymphocyte stimulator. The review reported that the use of NAC in SLE is in the early testing stages but that it shows a promising impact on reducing fatigue and disease activity. DHEA supplementation trialed for people with SLE reduced their disease activity, however, when compared to a placebo, it had no effect on reducing fatigue (van Vollenhoven et al., 2013). In a randomized control trial, there was a significant difference between Belimumab and a placebo in reducing fatigue. However, Yeun and Cunningham, (2014) stated that potential side effects and the high cost of the drug is a factor that must be considered in prescribing this drug for people with SLE.

Non-pharmacological fatigue interventions

Non-pharmacological interventions for fatigue are the most commonly used fatigue management strategies. They are aimed at reducing the impact of pain and fatigue for individuals with SLE by developing effective self-management strategies and thereby reducing psychosocial factors associated with fatigue (Yeun and Cunningham, 2014). Self-management interventions include cognitive-behavioural strategies, psychoeducation, counseling and psychotherapy. Other non-pharmacological interventions include exercise, dietary modifications, acupuncture and phototherapy.

Self-management interventions consist of developing skills in energy management, stress management, pain control, problem solving, positive coping strategies, effective communication and cognitive restructuring (del Pino-Sedano, 2016). These interventions are delivered through a range of modalities including group-based, on an individual basis, via telephone or through on-line modules. A core objective of these interventions is for individuals with SLE to become effective self-managers in order to become competent in addressing the on-going changes and fluctuations to their disease.

It is believed that people living with chronic health problems such as SLE benefit from self-management education (Park et al., 2013). Self-management is a dynamic process in which individuals are facilitated to develop the necessary knowledge and skills to actively manage their chronic illness. It involves the ability to monitor the illness over time and to develop cognitive, behavioural and emotional-based strategies to maintain a satisfactory quality of life (Barlow et al., 2005). For people with SLE, this is achieved by managing the symptoms, treatments and psychological effects of living with a chronic disease (Schulman-Green et al., 2012).

In a systematic review, occupational therapy-led fatigue management interventions have been identified as a promising approach to fatigue management (Smith and Hale, 2007). Due to the impact of persistent fatigue on daily functioning, occupational therapists, whose focus is on facilitating maximum participation in self-care, work and leisure activities, are often the profession who deliver fatigue focused self-management programmes. The overall aims of occupational therapy led interventions are to (i) increase understanding of fatigue, (ii) increase awareness of factors that exacerbate

fatigue, and (iii) facilitate development of effective fatigue management strategies (Connolly et al., 2013). This is achieved through people with fatigue analysing their daily routines in order to assess the energy expended on different activities and to examine if these activities can be carried out in a more energy-efficient manner. They are then informed of different methods for planning, pacing and prioritising activities in order to conserve energy.

Additionally occupational therapists advise on work simplification skills, body mechanics, environmental adaptations, appropriate assistive devices and sleep hygiene. Occupational therapy led fatigue self-management programmes have been shown to be effective for people with neurological conditions (Mathiowetz et al., 2005). However, further research is required on their effectiveness for people with rheumatic diseases including SLE.

In their review of six randomized control studies of psychological interventions for the management of fatigue in SLE, Liang et al., (2014), reported no significant differences in the level of fatigue. In contrast to this finding, in their systematic review del Pino-Sedano, (2016), reported that many psychosocial interventions are effective in reducing fatigue. However they also stated that the broad range of psychosocial interventions makes it difficult to reach definitive conclusions regarding the efficacy of specific interventions. They stated that further evaluations are needed of psychosocial interventions on their effects on fatigue management and cost effectiveness.

Exercise and dietary interventions for fatigue

Exercise is considered an effective intervention for people with SLE based on the significant association between inactivity and fatigue for people with SLE (Mancusco et al. 2011). Yuen and Cunningham (2014) reviewed exercise-based intervention studies for improving fatigue for people with SLE. The exercise interventions typically consisted of aerobic exercises and were aimed at increasing exercise tolerance, aerobic capacity and physical functioning in order to reduce fatigue. The reviewed studies included randomized control trials and quasi-experimental studies. Yuen and Cunningham (2014) concluded that exercise significantly improved fatigue severity however there were issues related to interpreting the findings of the studies due to the use of different fatigue measures and follow-up periods.

Yeun and Cunningham (2014) also reported however, that in most of the studies, there were a number of participants who were eligible for the study but were unwilling to take part in an exercise-based intervention. There were also problems with those who did participate, not continuing with the exercise programme after the study period had finished. They concluded that this could indicate a lack of enthusiasm of people with SLE to exercise. However this lack of motivation to engage in exercise could also be related to individuals' perceptions that engaging in an exercise programme would aggravate their joint and muscle pain. Connolly et al., (2015), reported that study participants avoided engaging in regular exercises due to this belief. This indicates the need for educational programmes on the benefits of exercise for fatigue and pain and for referral to relevant health professionals for advice regarding suitable exercise programmes.

Ahn and Ramsey-Goldman (2012) reported a 28-50% prevalence rate for obesity in people with SLE. Negative associations between obesity and physical functioning have been identified (Oeser et al., 2005). Yeun and Cunningham (2014) contended that obesity is likely to cause increased fatigue which in turn can impact on a person's mood and lead to depression. Davies et al., (2012), studied the impact of a low glycaemic index diet and a calorie restricted diet on weight loss and fatigue in SLE. Both diets resulted in weight loss and were equally effective in reducing fatigue. Correct nutritional advice early in the disease trajectory could therefore assist people with SLE to develop and maintain a healthy diet.

The range of interventions presented here indicates support for a combination of approaches to treating and managing fatigue in SLE. When deciding on the most appropriate fatigue management interventions, health professionals need to consider the burden of the intervention to the individual, the commitment required to carry out the intervention on a regular basis, and the cost of the intervention to the individual and healthcare services. Research also indicates that a multidisciplinary approach involving dieticians, occupational therapists, nurses and physiotherapy involvement is required for developing effective self-management strategies for fatigue in individuals with SLE.

Chapter summary

Fatigue is a prevalent symptom in SLE. It is often reported as the most difficult symptom to manage and the one that has the greatest negative impact on everyday activities. Research has attempted to identify the exact cause/s of fatigue in order to identify the most effective treatment for this troubling symptom. A wide range of international studies have investigated biological mechanisms of the disease process that could explain fatigue in order to identify suitable pharmacological interventions. Other symptoms of SLE such as joint pain, muscle weakness and depression have also been examined as causes for, or contributory factors to, fatigue. However, the findings are as yet inconclusive as to which of these symptoms explain the origin of fatigue.

Due to the subjective nature of fatigue, self-report measurement scales are the most frequently used method for assessing fatigue. These range from simple and quick visual analogue scales through to multidimensional measures that require the person with SLE to rate their fatigue across a number of physical, cognitive, social and work-related activities. The visual analogue scales are useful for a 'snapshot' of a person's fatigue however the more detailed multidimensional measures are recommended when information is required on the extent of a person's fatigue and which area of their life is most affected by their fatigue. Multidimensional measures are also warranted when designing and evaluating fatigue management interventions.

Similarly to the diversity of causes of fatigue in SLE, there are also a range of interventions recommended for reducing and managing fatigue. These interventions are aimed at improving and/or maintaining optimal physical, cognitive and emotional functioning in order to manage the impact of fatigue on

a daily basis. Intervention approaches include development of cognitive-behavioural strategies to manage the emotional impact of fatigue; exercise-based interventions to improve physical fitness; dietary advice to reduce the risk of developing co-existing chronic conditions, and energy management strategies to balance the energy demands of self-care, work and leisure activities. However, further research is required to test the effectiveness of these interventions used individually and in combination.

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