Fatigue in Rheumatologic Diseases

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KEYWORDS

• Fatigue • Fatigability • Rheumatoid arthritis
• Cognitive behavioral therapy • Fibromyalgia
• Chronic fatigue syndrome • Exercise

Fatigue is a universally shared experience and a significant component of rheumatologic diseases. The fact that rheumatologic patients experience fatigue that negatively affects their quality of life has been well documented. What is less clearly understood are the multifactorial physical and emotional mechanisms that contribute to this fatigue and, as a result, limit effective treatment strategies, which to date still remain mostly empiric. Fatigue is often rated by patients with rheumatologic disease as one of the key factors leading to decreased quality of life. Fatigue is poorly correlated with the severity of disease. Despite the omnipresence of and the stress caused by fatigue, it is surprising how infrequently it is addressed by both patients and physicians. Rheumatologic patients often believe that fatigue is an expected part of the disease process or a side effect of medications. Physicians, however, either dismiss the fatigue as functional in origin or focus more on joint and muscle involvement or abnormal laboratory values.

DEFINITION

There are many definitions of fatigue offered in the medical literature. However, for the purpose of discussing rheumatologic disease, a more global, biopsychosocial orientation is applied. As quoted in the *Physiologic Basis of Rehabilitation Medicine*,[1] Dill offered the following definition: "The various unmistakably disagreeable sensations commonly referred to the word fatigue are in fact the accompaniment of a great variety of physiologic conditions, which have in common only this, that the physiologic equilibrium of the body is breaking down." A distinction should also be made between

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fatigue and fatigability, the latter being defined as progressive weakness of muscle with repetitive use followed by recovery after a brief period of rest. Fatigability has also remained underdiagnosed and may be an additional component of the global picture of fatigue in rheumatologic disorders.

Despite the pervasive and negative impact that fatigue can have on quality-of-life issues in the patient with rheumatologic disease, it does serve an important function as the body's ''warning signal,'' forcing an individual to stop what he is doing and evaluate what is wrong.[2]

This article reviews fatigue as it occurs in 4 common rheumatologic disorders: fibromyalgia syndrome (FMS), chronic fatigue syndrome (CFS), rheumatoid arthritis (RA), and osteoarthritis (OA).

ASSESSMENT OF FATIGUE

History

Despite the significant negative impact fatigue imposes on the rheumatologic patient, it is often not addressed in clinical settings. Wolfe and Pincus reported that 89.7% of rheumatologists do not usually assess fatigue in their offices, and fewer than 15% collect any formal quantitative information regarding fatigue, psychological distress, and functional disability.[3] Patient self-report questionnaires have been found to be a valuable tool in assessing fatigue and monitoring functional status. Wolfe and colleagues[3,4] advocated the routine use of questionnaires as an integral part of patient care, which correlated with traditional measures, such as laboratory tests and radiographs. Moreover, questionnaires can be more effective in predicting long-term mortality and morbidity than measurements such as grip strength, walk time, or joint count. Multidimensional health status questionnaires such as Modified Health Assessment Questionnaire and Health Assessment Questionnaire (HAQ) have both been shown to be strong predictors of mortality in rheumatologic diseases. In 1 study involving 7760 patients, Wolfe showed that a single question asking patients to rate their fatigue in the past week on the visual analog scale (VAS) performed as well as 3 other significantly longer questionnaires. The single-item VAS fatigue scale was even more sensitive in detecting change in fatigue level than longer questionnaires.[5] To use patient questionnaire effectively, it should be administered to all patients attending the clinic on a sequential basis.

A large number of fatigue scales exist, and there is no consensus on which fatigue-measuring scales are most appropriate for use in assessment of fatigue in rheumatologic disease.[6] Fatigue is multidimensional in expression, with influence on physical, emotional, cognitive, and even social aspects of life. This created a challenge in its measurement. Many recent articles have focused on a questionnaire called functional assessment of chronic illness therapy (FACIT).[7] This instrument was initially employed to evaluate fatigue in anemia and cancer patients. Recent studies, however, have evaluated its efficacy in rheumatologic disease. The FACIT-fatigue is an abbreviated 13-item measure of fatigue that has showed good internal consistency in patients with RA when compared with other extensive scales (**Table 1**).

This scale is easy to administer, patient-friendly, and provides reliable insights into the causes of fatigue. It can be easily adapted to other rheumatologic diseases such as fibromyalgia and OA.[8]

Physical Examination

Fatigue is frequently not addressed in physical examinations during routine office visits, primarily due to its complex physiologic and psychosocial nature. To better

Table 1
FACIT-Fatigue Scale (Version 4)

Below is a list of statements that other people with your illness have said are important. Please circle or mark 1 number per line to indicate your response as it applies to the *past 7 days*

	Not at all	A little bit	Somewhat	Quite a bit	Very much
I feel fatigued.	0	1	2	3	4
I feel weak all over.	0	1	2	3	4
I feel listless ("washed out").	0	1	2	3	4
I feel tired.	0	1	2	3	4
I have trouble *starting* things because I am tired.	0	1	2	3	4
I have trouble *finishing* things because I am tired.	0	1	2	3	4
I have energy.	0	1	2	3	4
I am able to do my usual activities.	0	1	2	3	4
I need to sleep during the day.	0	1	2	3	4
I am too tired to eat.	0	1	2	3	4
I need help doing my usual activities.	0	1	2	3	4
I am frustrated by being too tired to do the things I want to do.	0	1	2	3	4
I have to limit my social activity because I am tired.	0	1	2	3	4

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delineate the objective physical manifestation of fatigue, the term *fatigability* has been used, which is defined as diminished strength as exercise of muscle groups proceeds. Experimental studies that test for fatigability have employed dynamometer, electrical stimulation of peripheral nerves, and transcranial magnetic stimulations. In routine clinical settings, fatigability can be assessed by manual muscle testing after repetitive movement of functionally important muscles. Dobkin offered the following approach:[9]

The examiner could choose 10 to 15 repetitions of (1) raising the extended arms overhead or reaching and lifting an item, followed by retesting the strength of the isolated deltoids at 60° of abduction; (2) repetitive extension of the fingers against the modest resistance of an examiner's finger; (3) repetitive 30° hip flexor movements with the patient supine and leg extended at the knee followed by retesting strength of the iliopsoas at 20° of hip flexion; (4) repetitive 20° hip extensor movements against gravity or a modest force with the patient prone; (5) repetitive 60° knee flexor movements while prone against only gravity or modest resistance, followed by retesting the hamstrings with the knee flexed 30°, and so on. Retesting that reveals any decline from the initial torque and that resolves after a minute of rest would be consistent with exercise-induced fatigability.

Laboratory tests are not routinely used for the monitoring of fatigue, since fatigue has been found to correlate with pain and depression and not with disease activity as reflected by laboratory tests such as erythrocyte sedimentation rate or rheumatoid factor.[10]

FATIGUE IN FIBROMYALGIA

Perhaps no rheumatologic disorder is more associated with fatigue than FMS, the most common widespread pain disorder in the United States. Fibromyalgia affects 2% of 4% of the general population, and between 76% and 81% of people with fibromyalgia suffer from the symptom of chronic fatigue.[11,12] FMS is a syndrome without known pathologic agents, whose cardinal symptoms include pain, fatigue, and nonrestorative sleep. Specific criteria for the diagnosis of FMS were established in 1990 by the American College of Rheumatology (ACR) [**Table 2**].

Pain and Fatigue

Although a distinct cause for FMS is unknown, the most commonly accepted theories include the following: (1) central sensitization, with dysfunctional processing of pain by the central nervous system, (2) suppression of descending inhibitory pain pathways, (3) various neurohumoral dysregulations, especially those involving serotonin, norepinephrine, and substance P, (4) suppression and dysregulation of the hypothalamic-pituitary-adrenal axis.[13–17] Regardless of the pathologic mechanism(s), the result is widespread body pain, which, in turn, is closely associated with overwhelming fatigue. Common patient complaints often reflect this inter-relationship between pain and fatigue, for example, "The pain wears me down" or "When I'm tired I hurt all over." Fibromyalgia patients often describe the fatigue as overwhelming, exhaustive, debilitating, or incapacitating. Patients literally describe having to stop what they are doing and lie down. Wolfe and Pincus in a study in Rheumatology 1999 noted that in multivariate analysis, the strongest independent predictors for fatigue were pain, sleep disturbance, depression, tender point count, and HAQ.[3] In a 2007 study, pain was confirmed as among the strongest predictors of fatigue: "Individuals with higher average level of pain reported greater fatigue and daily increase in pain were related to daily increase in fatigue, including elevation of fatigue on the next day."[18] A 2008

Table 2
Criteria for the classification of fibromyalgia[66]

1. History of widespread pain

Definition. Pain is considered widespread when all of the following are present: pain in the left side of the body, pain in the right side of the body, pain above the waist, and pain below the waist. In addition, axial skeletal pain (cervical spine, anterior chest, thoracic spine, or low back) must be present. In the definition, shoulder and buttock pain is considered as pain for each involved side. "Low back" pain is considered lower segment pain.

2. Pain in 11 of 18 tender point sites on digital palpation

Definition. Pain, on digital palpation, must be present in at least 11 of the following 18 tender point sites:

- Occiput: bilateral, at the suboccipital muscle insertions
- Low cervical: bilateral, at the anterior aspects of the intertransverse spaces at C5–C7
- Trapezius: bilateral, at the midpoint of the upper border
- Supraspinatus: bilateral, at origins, above the scapula spine near the medial border
- Second rib: bilateral, at the second costochondral junctions, just lateral to the junctions on upper surfaces
- Lateral epicondyle: bilateral, 2 cm distal to the epicondyles
- Gluteal: bilateral, in upper outer quadrants of buttocks in anterior fold of muscle
- Greater trochanter: bilateral, posterior to the trochanteric prominence
- Knee: bilateral, at the medial fat pad proximal to the joint line

For classification purposes, patients will be said to have fibromyalgia if both criteria are satisfied. Widespread pain must have been present for at least 3 months. The presence of a second clinical disorder does not exclude the diagnosis of fibromyalgia. Digital palpation should be performed with an approximate force of 4 kg. For a tender point to be considered "positive," the subject must state that the palpation was painful. "Tender" is not to be considered "painful."

workshop sponsored by the National Institute of Aging noted that physical functioning in FMS, RA, and OA was predicted by pain and fatigue but not by pain alone.[2]

Nonrestorative Sleep and Fatigue

Nonrestorative, fragmented sleep is a constituent of the fibromyalgia syndrome and a significant contributor to the fatigue experienced by the fibromyalgia patient. Nearly all patients suffering from FMS experience poor sleep quality,[19] and the fatigue that follows is so pervasive that half of the patients who meet ACR criteria for FS also meet criteria for CFS.[20] Fibromyalgia patients were also reported to have higher stress responses to a variety of stimuli, which in turn compromise sleep and in turn exacerbate fatigue.[21,22]

Mental Fatigue ("Fibrofog")

Cognitive deficits involving memory and mental clarity referred to as ''fibrofog'' are common in FMS.[23–25] However, formal cognitive testing often does not support deterioration. FMS patients can experience dissociation or disengagement, which refers to the separation of parts of experience from the mainstream of consciousness. A common example is highway hypnosis.[23]

Evaluating Fatigue in Fibromyalgia

In evaluating fatigue in the fibromyalgia patient, there is a temptation to ascribe fatigue to the disease itself, rather than looking for alternative causes. Although no longer considered a diagnosis of exclusion, many conditions can mimic and occur concurrently with FMS and produce significant fatigue (**Table 3**).

Table 3
Conditions that simulate fibromyalgia or occur concurrently with fibromyalgia[20]

Common
Hypothyroidism
Medications (especially lipid-lowering drugs, antiviral agents)
Polymyalgia rheumatica
Hepatitis C
Sleep apnea
Parvovirus infection
Cervical stenosis/Chiari malformation
Less common
Autoimmune disorders (eg, systemic lupus erythematosus, rheumatoid arthritis)
Endocrine disorders (eg, Addison disease, hyperparathyroidism)
Lyme disease
Eosinophilia-myalgia syndrome
Tapering of corticosteroids
Malignancy

Failure to identify another disease process responsible for the fatigue will significantly compromise both treatment and outcome. An initial laboratory analysis for patients who present with fatigue and have criteria consistent with FMS should include the following: complete blood count, urine analysis, erythrocyte sedimentation rate, and thyroid-stimulating hormone. Other tests such as antinuclear antibody, rheumatoid factor, serum complement levels, Lyme titers, Epstein-Barr virus test, muscle enzymes, radiographs, or other imaging studies are warranted only if the history and physical examination suggest a particular diagnosis.[20]

Treatment of Fatigue in Fibromyalgia

As described, the causes of fatigue in rheumatologic disease are multifactorial. Therefore, comprehensive treatment programs that incorporate pharmacologic and nonpharmacologic treatment strategies would appear to be the most efficacious.

Pharmacologic treatment of fatigue in FMS

Numerous medications, including serotonin specific reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, psychostimulants, and so on, have been employed in the management of fatigue. Four of the most currently prescribed medications are discussed. The tricyclics amitriptyline (Elavil) and cyclobenzaprine (Flexeril) have been considered mainstay agents in the management of FMS for many years. Although considered an antidepressant and muscle relaxant, respectively, both are structurally tricyclic compounds.

Amitriptyline A systematic Medline Cochrane review of amitriptyline in the management of FMS noted that at 25 mg a day, fatigue, in addition to pain and fragmented sleep, was improved but short lived. No positive effects were noted at 12 weeks. As such, the author stated, "A definitive clinical recommendation regarding the efficacy of amitriptyline for fibromyalgia symptoms cannot be made."[26]

Cyclobenzaprine A 2004 meta-analysis of the effectiveness of cyclobenzaprine noted no reduction in fatigue but some general overall improvement in well-being.[27]

Pregabalin (Lyrica) Approved by the FDA in June 2007, pregabalin is the first medication approved for the treatment of FMS. A 2008 randomized, double-blind, placebo-controlled study reported that pregabalin at 300, 450, and 600 mg a day was safe and effective in the treatment of fibromyalgia, but no significant improvement in fatigue was noted.[28] This lack of improvement in fatigue was felt to be due to pregabalin's side effect of daytime somnolence.[29]

Duloxetine (Cymbalta) Approved by the FDA in June 2008, duloxetine was the second medication approved for FMS. A 2008 study in *Pain* reported that duloxetine at 600 mg a day appears to be safe and efficacious in the treatment of FMS, with mental fatigue score improved at the end of the 6-month trial period.[30]

A difficulty with many of these studies is that they evaluate the efficacy of a particular medication compared with placebo. What is lacking are studies comparing these medications to each other or comparing combinations of medications or combined pharmacologic and nonpharmacologic programs.

Cognitive-behavioral therapy for fatigue in FMS

Cognitive-behavioral therapy (CBT) is a stress inoculation training that involves the teaching of life and coping skills to minimize fatigue, pain, and stressful events.[31] A 2006 study compared the efficacy of CBT to pharmacologic intervention. The authors concluded that CBT was efficacious and must be considered a primary treatment in FMS.[32]

CHRONIC FATIGUE SYNDROME

CFS is a condition similar to, and often confused with, FMS. The overlap between these 2 syndromes is striking.[20] CFS has been described as a subset of FMS or as a distinct entity.[33] Women are diagnosed as having CFS 2 to 4 times as often as men, and the condition occurs most commonly in patients in their 40s and 50s.[34] The underlying pathophysiology of CFS is currently believed to be similar to that of FMS and includes atypical sensory processing in the central nervous system and dysfunction of skeletal muscle nociception and the hypothalamic-pituitary axis.[35] The specific diagnostic criteria for CFS are outlined in **Table 4**.[36]

The hallmark of CFS is the presence of overwhelming fatigue of at least 6 months' duration that is not restored with rest. As outlined in **Table 4**, CFS also includes symptoms of sore throat, lower-grade fever, and lymph node tenderness, suggesting a possible viral etiology. Despite these findings, the specific cause(s) of CFS remain unclear. It should be noted that FMS patients may also complain of viral-like symptoms, making the distinction between CFS and FMS difficult. In fact, the 2 symptoms may overlap or even occur concurrently.

Like FMS, there is no confirmatory laboratory test for CFS, and, therefore, the diagnosis rests exclusively on the patients presenting symptoms. Currently, there are no approved medications for the treatment of CFS. However, duloxetine is currently being investigated for the treatment of fatigue in CFS in a double-blind, randomized, control study in collaboration with its manufacturer, Eli Lilly. Study completion is scheduled for December 2009.[37] Trials of the psychostimulant modafinil (Provigil) have provided inconsistent results and, therefore, cannot be recommended for CFS.[38] CBT has been proven efficacious in reducing the symptoms of fatigue in CFS and may be more effective in reducing fatigue symptoms compared with other psychological therapies.[39] Like FMS, many research articles lend support to the effectiveness of CBT in the management of fatigue in CFS. The Cochrane Collaboration advises a *graded* exercise program for patients with CFS. Overstrenuous exercise

Table 4
1994 International Research Case Definition of Chronic Fatigue Syndrome[36]

CFS is a syndrome characterized by fatigue that is
Medically unexplained
Of new onset
Of at least 6 mo duration
Not the result of ongoing exertion
Not substantially relieved by rest
Causes a substantial reduction in previous levels of occupational, educational, social, or personal activities
In addition, there must be 4 or more of the following symptoms:
Impaired memory or concentration
Sore throat
Tender neck (cervical) or armpit (axillary) lymph nodes
Muscle pain (myalgia)
Headaches of a new type, pattern, or severity
Unrefreshing sleep
Postexertional malaise (lasting more than 24 h)
Multijoint pain (arthralgia without swelling or redness)
Conditions that would exclude a diagnosis of CFS include other medical disorders known to cause fatigue, major depressive illness, medications that cause fatigue as a side effect, and alcohol or substance abuse.

should be avoided, because it can exacerbate symptoms and promote immune system dysfunction.[40] The combination of graded exercise, CBT, which emphasizes *active* coping skills, paced daily activities, adequate rest, and a healthy life style appears to be the most efficacious and practical plan for managing CFS.

FATIGUE IN RHEUMATOID ARTHRITIS

Predictors of Fatigue in Rheumatoid Arthritis

Fatigue is a common symptom in RA, reported in 80% to 93% of individuals with RA, and can be perceived as the most problematic aspect of the disease.[41] In one study, pain and depressive symptoms were found to be the best predictors of fatigue in RA patients, whereas longer symptom duration, less perceived adequacy of social support, and less disease activity were also significant predictors of fatigue.[41] In another study comparing fatigue in RA, OA, and FMS, pain was found to be the strongest predictor of fatigue.[18] In a large study involving 24,831 patients, Wolfe and colleagues[42] concluded that pain, functional loss, depression, and sleep disturbance, and not inflammation, were the proximate causes of fatigue. Similar findings were also reported by Pollard and colleagues[10] in a cross-sectional study evaluating RA patients on anti-tumor necrosis factor (TNF) or disease-modifying antirheumatic drug (DMARD) treatment, which concluded that fatigue was associated with pain and changes in mental health, particularly depression, and not disease activity.

Treatment of Fatigue in Rheumatoid Arthritis

Improvement in fatigue as a consequence of effective treatment in pain has been widely reported. In a randomized controlled trial (RCT) involving 271 RA patients, Weinblatt and colleagues[43] showed that patients receiving Adalimumab, an anti-TNF

antibody, plus methotrexate, had significantly less fatigue and pain than those in patients receiving placebo plus methotrexate. In an observational study with 30 patients receiving anti-TNF and 54 patients receiving DMARDs, Pollard and colleagues[10] showed that both treatments resulted in a decrease in fatigue, which correlated with improvement in pain. In an RCT by Cohen and colleagues, RA patients who had failed anti-TNF agents received rituximab plus methotrexate (n = 311) and had significantly less fatigue and better quality of life than patients receiving placebo plus methotrexate (n = 209).[44] Similar results with rituximab were also reported in other RCTs.[45,46] Chronic interpersonal stress is associated with greater stimulated cellular production of interleukin 6 along with impaired capacity of glucocorticoids to inhibit the cellular inflammatory response, leading to increased fatigue in RA patients.[47] Despite the apparent efficacy of TNF inhibitors in ameliorating fatigue, there are conflicting studies that do not support the positive studies noted here. Wolfe investigated 21,016 RA patients participating in the National Data Bank for Rheumatic Diseases and found that patients receiving anti-TNF therapy did not have lower fatigue scores compared with those of patients not treated with anti-TNF agents.[42] Therefore, the known efficacy of TNF inhibitor in the treatment of RA remains controversial when specifically applied to the treatment of fatigue.

OSTEOARTHRITIS

Fatigue in OA is not routinely evaluated. However, a growing number of studies have shown that fatigue is a crucial component of the disease.[48–50] Murphy and colleagues[48] measured ambulatory OA patients' physical activity by wrist-worn accelerometers and demonstrated that fatigue is strongly associated with physical inactivity in OA patients. Wolfe reported that OA patients had a similar level of fatigue as that of RA patients, and the 2 diseases shared the same predictors for fatigue: pain, depression, and functional loss.[5] In a qualitative study, Power and colleagues[51] also identified pain and depression as major factors in OA fatigue. Zautra and colleagues[18] noted that there are important differences between OA, RA, and FMS patients in both everyday manifestation and the bio-psychosocial correlates of fatigue. Fatigue in OA is influenced by daily pain fluctuation but to a lesser extent than that in RA or fibromyalgia.

EXERCISE

Exercise in Fibromyalgia

There is emerging evidence that exercise is beneficial in reducing fatigue in fibromyalgia. In a 2008 review article, the Ottawa Panel considered 13 RCTs and 3 controlled trials using aerobic fitness exercises for managing fibromyalgia. Grade A recommendations (based on RCT showing statistically significant clinical importance >15%) were given to aerobic exercise in relieving pain and depression, reducing VAS score for ''lack of energy'' by 30% and improving cardiopulmonary function, endurance, and positive affect. However, direct measurement of fatigue in 2 trials only received grade C recommendation (not statistically or clinically significant). In addition, the Ottawa Panel considered 5 RCTs using strengthening exercises in fibromyalgia and gave grade A recommendation for fatigue, depression, muscle strength, and short-term pain relief.[52,53] The article mentioned that most trials were rated low quality, but the panel still recommended the use of aerobic fitness as well as strengthening exercises based on the emerging evidence. A study involving postmenopausal women with FMS lends further support to the benefit of concurrent strength and endurance training in reducing fatigue in FMS. This study reinforces the concept that low-intensity

strength training and aerobic exercises can decrease fatigue even though the amount of training was too low to improve general strength and not intensive enough to improve Vo_{2max}.[54]

Exercise in Chronic Fatigue Syndrome

The exercise program outlined for FMS is the same for CFS, which is a graded exercise program incorporating aerobic and strength training.

Exercise in Rheumatoid and Osteoarthritis

Exercise has been found to decrease fatigue in OA and RA. The Ottawa Panel Evidence-Based Clinical Practice Guidelines recommend the use of therapeutic exercises for OA after considering 26 RCTs.[55] Both strengthening exercises and general fitness exercises were recommended. The same panel also recommended whole-body, low-intensity exercises for RA patients based on 16 RCTs.[56] The Ottawa Panel used pain and function as outcomes and did not specifically address fatigue. However, knowing that pain, along with depression, is one of the strongest predictor of fatigue in OA and RA, it is reasonable to hypothesize that exercise significantly reduces fatigue. This result was confirmed in an RCT of 220 RA patients using low-impact, aerobic, group and home exercises, which showed that fatigue, pain, and depression decreased after 12 weeks of exercise.[57]

High- versus Low-Intensity Exercise for Rheumatoid Arthritis

For RA patients, traditionally, low-intensity, isometric, muscle strengthening, and range-of-motion exercises have been advocated. High-intensity, dynamic exercises were considered inappropriate because of fear of exacerbating inflammation and creating more joint damage.[56] However, current studies support the principle that high-intensity exercise is beneficial. An RCT with 281 patients in 2004 by de Jong and colleagues showed that patients receiving high-intensity, weight-bearing exercises actually developed less radiological damage during a 2-year period than that of patients not receiving such a structured exercise program.[58] In another RCT, van den Ende and colleagues[59] also showed that patients hospitalized because of an exacerbation of their disease did better with an intensive exercise program than patients performing a conservative program; no deleterious effects on disease activity were found. Similar results were also reported by other RCTs.[60,61]

An example of a high-intensity, 12-week outpatient exercise program for patients with well-controlled RA is as the following: Patients attend 1-hour group exercise sessions 3 times a week, which includes warming up, bicycling for 20 minutes, dynamic weight-bearing exercises such as knee bending, step-ups, walking at fast speed, and muscle strengthening for trunk and upper extremities. Every 4 weeks, patients are introduced to a new set of exercises with a higher exercise load. During bicycling, heart rate was maintained at 70% to 85% of the age-predicted maximum heart rate.[60]

Bracing, Energy Conservation, and Adaptive Equipment

There is some evidence that knee bracing in patients with unicompartmental OA reduces pain, improves gait, and reduces compartmental load.[62] Taping of the patella was also shown to produce clinically meaningful decrease in chronic OA knee pain.[63] For RA patients, a joint protection educational program that focuses on energy conservation techniques and adaptive equipments has been shown to reduce pain and improve activities of daily living.[64,65] These studies did not directly evaluate the effect of intervention on patient fatigue. However, recognizing that pain is one of the

strongest predictors of fatigue, these interventions may empirically be beneficial in rheumatologic patients with significant fatigue.

SUMMARY

Today, fatigue still remains an under-reported symptom in rheumatologic diseases, infrequently addressed by patient and physician. Although not all of the causes of fatigue in rheumatologic diseases have been fully elucidated, recognizing the multifactorial components is essential in formulating targeted, effective treatment strategies. Deconstructing rheumatologic diseases into discrete symptoms such as fatigue in an effort to identify specific causes and formulate targeted treatments remains a daunting task. High-quality RCTs will be required to evaluate the effectiveness of combined pharmacologic and nonpharmacologic strategies, which empirically appear to be the most promising. To date, this research is lacking.

CLINICAL PEARLS

1. Always ask patient about fatigue—use VAS and short fatigue questionnaire.
2. Rule out nonrheumatologic causes of fatigue.
3. Identify and treat causative factors of fatigue, especially pain and depression.
4. Make the treatment individualized and multidimensional and inclusive of the following:
   - Appropriate medications (ie, duloxetine, pregabalin for FMS)
   - Combined aerobic exercise and strength training
   - CBT
5. Reassure the patient that significant improvement can occur over time with active participation and an effective treatment strategy.

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