Sleep Disorders and Psoriasis: An Update

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Psoriasis alters patients’ quality of life. Among the disorders associated with psoriasis, sleep disorders are common, although they are not directly assessed by most quality-of-life scores. Thus, the specific evaluation of sleep disorders using dedicated scores is necessary, especially because such disorders alter patients’ physical and psychological health. The relationship between psoriasis and sleep disorders has been shown in numerous studies, but has not yet been fully elucidated. The aim of this study was to update knowledge of sleep disorders in patients with psoriasis, through a review of the scientific literature since 1980. This work covers several topics of interest, such as sleep assessment methods, the prevalence of sleep disorders in patients with psoriasis, factors predictive of sleep disorders in patients with psoriasis, the impact of sleep disorders on comorbidities and quality of life, pathogenic mechanisms, obstructive sleep apnoea and restless leg syndromes, and the impact of biotherapy treatments on sleep disorders in patients with psoriasis.

Key words: psoriasis; sleep quality; sleep disorders.

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Psoriasis is a common chronic inflammatory dermatological condition, affecting 0.6–4.8% of the world’s population (1), the aetiopathogenesis of psoriasis involves genetic, immunological and environmental factors (2, 3). The study of sleep disorders (SDs) in patients with psoriasis began in the early 1990s (4). This area of study in psoriatic patients is of particular interest, because good-quality sleep has been shown to play a fundamental role in health and well-being, including restoration of physiological and mental function at all stages of life (5). Conversely, SDs have negative consequences on physical and mental health, including an increased risk of fatigue and daytime sleepiness, loss of productivity, absenteism, accidents at work and on the roads, and an increased risk of behavioural disorders and depression (6–9). Sleep deprivation also has an impact on the immune system (10–16). SDs are considered an independent risk factor in the pathogenesis of several chronic diseases considered to be comorbidities of psoriasis, such as type 2 diabetes, hypertension (17), metabolic syndrome (18) and cardiovascular disease (8, 19–24). The associations between psoriasis and SDs are wide and multidirectional. The aim of this study is to review the literature regarding SDs in patients with psoriasis.

METHODS

A systematic literature search was conducted in PubMed and EM-Base databases, using the search terms “psoriasis” and “sleep” to identify peer-reviewed journal articles published between 1980 and 2020. The literature search was limited to work carried out in adults.

RESULTS

Means of assessing sleep disorders in patients with psoriasis

Studies evaluating SDs in patients with psoriasis were carried out on the basis of specific sleep interviews or questionnaires, such as the Pittsburgh Sleep Quality Index (PSQI). The PSQI is a validated self-assessment questionnaire that measures sleep quality and sleep patterns in adults, using a score ranging from 0 (undisturbed) to 21 (highly disturbed). The PSQI explores 7 components of sleep: “Subjective quality of sleep”, “Sleep latency”, “Sleep duration”, “Usual sleep efficiency”, “Sleep disorders”, “Use of sleep medication” and “Poor daytime sleepiness”. Other studies have been carried out using other SD assessment tools, such as the Functional Outcome of Sleep Questionnaire (FOSQ) (25), the Insomnia Severity Index (ISI) (26), the General Sleep Disturbance Scale (27), and the Medical Outcomes Study Sleep Scale (MOS-SS) (28–30).

SIGNIFICANCE

The aim of this study was to review the literature covering the last 40 years regarding sleep disorders in patients with psoriasis. Sleep disorders should be considered as a crucial comorbidity of psoriasis, acting as both a mediator and an effect. The early detection and management of sleep disorders could significantly improve the quality of life of such patients, hence it is important to assess sleep quality and the existence of sleep disturbances in patients with psoriasis. Therefore, it is essential to include questions about sleep disorders in examinations of patients with psoriasis.
Table I. Prevalence of sleep disorders (SDs) among psoriatic patients

| Study                        | Year  | Total number of patients | Prevalence of SDs (%) | Method for evaluating SDs |
|------------------------------|-------|--------------------------|-----------------------|---------------------------|
| Shutty et al. (26)           | 2013  | 35                       | 77.1                  | PSQI                      |
| Melikoglu et al. (33)        | 2017  | 58                       | 60.3                  | PSQI                      |
| Henry et al. (34)            | 2017  | 186                      | 76.8                  | PSQI                      |
| Wong et al. (35)             | 2017  | 62                       | 69.3                  | PSQI                      |
| Jensen et al. (36)           | 2018  | 179                      | 53.6                  | PSQI                      |
| Delfino et al. (37)          | 2008  | 40                       | 55                    | Interview                 |
| Sliens et al. (38)           | 2009  | 135                      | 34                    | Interview                 |
| Duffin et al. (31)           | 2009  | 420                      | 49.5                  | Interview                 |
| Hu et al. (39)               | 2010  | 100                      | 60                    | Interview                 |
| Tsu et al. i (40)            | 2011  | 51,800                   | 0.05                  | Interview                 |
| Nyunt et al. (41)            | 2013  | 223                      | 40.9                  | Interview                 |
| Sanchez-Carazo et al. (42)   | 2014  | 1,022                    | 12.2                  | Interview                 |
| Chiu et al. (43)             | 2016  | 99,628                   | 2.2                   | Interview                 |
| Duvetor et al. (44)          | 2019  | 911                      | 16.3                  | Interview                 |
| Ljosa et al. (27)            | 2012  | 139                      | 62.6                  | GSDS                      |
| Sharma et al. (45)           | 2001  | 30                       | 56.7                  | GHQ-H                     |

PSQI: Pittsburgh Sleep Quality Index; GSDS: General Sleep Disturbance Scale; GHQ-H: General Health Questionnaire.

Prevalence of sleep disorders in patients with psoriasis

According to a study carried out in 2005 by the National Psoriasis Foundation (US) among 420 psoriatic patients, SDs with episodes occurring at least once a month were reported in 49.5% of the patients, while 11.3% experienced episodes on more than 15 days a month (31, 32). The prevalence of SDs in patients with psoriasis varies from 0.05% to 77.1% in different studies (33–45) (Table I).

Five case-control studies found that the mean PSQI score of patients with psoriasis was significantly higher than that of control subjects (Table II, 46–48). One case-control study using the ISI reported a 4.3-fold increased risk of insomnia in patients with psoriasis (26). A polysomnographic study of psoriatic patients showed a decrease in durations of stage 1 and deep sleep and an increased frequency of snoring.

Predictors of sleep disturbance in patients with psoriasis

Severity of psoriasis. Several studies have found that the clinical severity of psoriasis is associated with an increased risk of developing SDs (26, 33, 49–52). A study by Melikoglu et al. of 48 psoriatic patients showed that PSQI scores were significantly correlated with psoriasis severity assessed by the Psoriasis Area and Severity Index (PASI) (p = 0.03) (33). A study of psoriatic patients with jet lag found a relationship between clinical severity assessed by the PASI and the importance of SDs (53), which is probably explained by pain and pruritus. On the other hand, studies by Gezer et al. (54), Callis Duffin et al. (31), Nowowiejska (55) et al. and Stinco et al. (47) did not find such a relationship.

Psoriatic arthritis. The prevalence of SDs in psoriatic arthritis varies from 15.1% to 85.4% depending on the study (Table III). A Danish study reported more SDs in patients with psoriatic arthritis (45.1%) than in patients with psoriasis (16%) (44). The severity of SDs, as assessed by the PSQI score, is greater in patients with psoriatic arthritis than in patients with psoriasis (31, 35). Two studies found that sleep quality in patients with psoriatic arthritis decreased with increasing C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) (56, 57).

Pain. Pain is a major cause of sleep disturbance in psoriatic arthritis (31, 56, 61, 62). Pain is associated with an increased risk of SDs in patients with psoriasis (27). The impaired quality of life in patients with psoriatic arthritis has been shown to be partly due to SDs caused by pain (27). The intensity of pain measured with an analogue scale correlates with the severity of SDs measured with the PSQI (50).

Impact of pruritus. Pruritus in patients with psoriasis is associated with an increased risk of difficulty falling asleep and frequent nocturnal awakenings causing sleep fragmentation (31, 63, 64), which can result in daytime fatigue (65). However, sleep helps limit the intensity of itching associated with psoriasis (57% or 65% according to different studies) (64, 66). Several studies have established a relationship between pruritus intensity and the severity of SDs (29, 49, 67), but such a relationship was not found with pain.

Impact of sleep disorders on co-morbidities and quality of life

Many comorbidities associated with psoriasis, such as cardiovascular disease (68–72), diabetes (73–76) and hypertension (77–79), are associated with an increased risk of SDs. Insomnia is a major symptom of depression, which occurs in patients with psoriasis in 10–58% of cases (80–85). In addition, persistent SDs are a risk factor for the development of diabetes (86), cardiovascular disease (87, 88), high blood pressure...
Table III. Prevalence of sleep disorders (SDs) among psoriatic arthritis patients

| Study                        | Number of patients | Prevalence of SDs (%) | Method for evaluating SDs |
|------------------------------|--------------------|-----------------------|---------------------------|
| Duffin et al. 2009 (57)      | 86                 | 15.1                  | PSQI                      |
| Duruz et al. 2013 (58)       | 40                 | 44.8                  | PSQI                      |
| Wong et al. 2017 (35)        | 113                | 84                    | PSQI                      |
| Gezer et al. 2017 (54)       | 41                 | 85.4                  | PSQI                      |
| Economic and Social Councils 2018 (50) | 62           | 67.7                  | PSQI                      |
| Palominos et al. 2020 (59)   | 396                | 39.6                  | PSAID-12                  |
| Haugeberg et al. 2020 (60)   | 137                | 38                    | Questionnaire             |

PSQI: Pittsburgh Sleep Quality Index; PSAID-12: Psoriatic Arthritis Impact of Disease questionnaire.

In addition, many studies have established that SDs are an independent factor altering quality of life (27, 95–100). In a study of 152 patients with psoriasis, SDs assessed by the Medical Outcomes Study Sleep Scale (MOS-SS) were significantly associated with an altered quality of life, as determined by the Dermatology Life Quality Index (DLQI) (27). Another study found that jet lag was likely to worsen the quality of life of patients with psoriasis (53). Nowowiejska et al. considered that a “vicious circle” occurs between SDs and the severity of skin lesions. Subjective symptoms caused by psoriasis decrease daily quality of life and induce SDs. Decreased sleep quality exacerbates stress and further worsens quality of life (55).

The importance of considering sleep disorders in patients with psoriasis

Patients with psoriasis should be questioned about SDs. If SDs are reported, patients should be questioned precisely to assess the type of SD (sleep disturbance, difficulty maintaining sleep, early awakening), the presence or absence of a triggering event or factor, the duration of insomnia (acute or chronic), the length of time that the disturbance has been present, daytime consequences (professional, social, or family repercussions), and previous or current hypnotic treatments. Meticulous questioning must be coupled with the use of questionnaires specialized for the evaluation of SDs and a diary (or calendar), which allows objective sleep disorder assessment over several weeks. In cases of severe SDs, and especially cases of suspected obstructive sleep apnoea (OSA) and restless leg syndromes (RLS), the patient should be referred to a sleep specialist who will use certain paraclinical examinations (polysomnography or actimetry).

Pathogenesis

The reciprocal relationship between SDs and psoriasis is also explained by the aetiopathogenic role of proinflammatory cytokines and neurotransmitters in the immune system (101). An animal study in a laboratory-bred strain of albino mice (BALB/c mice) with and without psoriasis found that 48 h of sleep deprivation resulted in an exacerbation of psoriasis, which is explained by an increase in plasma proinflammatory cytokines, such as interleukin-1β and tumour necrosis factor-α (TNF-α) (101). Other studies in animal models have shown an increase in psoriasis-related inflammation during acute sleep deprivation, as well as an increase in inflammatory mediators following restriction from 25% to 50% of the normal sleep time (set at 8 h) (102).

Psoriatic patients are known to have lower melatonin levels and lack a night-time peak (35), while melatonin receptors have been found in the skin, suggesting that melatonin plays a role in skin physiology.

SDs aggravate skin inflammation (103) through central and peripheral circadian mechanisms that modulate cytokine secretion (104, 105) and act on the skin structure by altering the pH, insensible water loss and permeability (106–108). Thus, disturbances in skin thermoregulation and disturbances in the permeability of the stratum corneum may partly explain the pathogenesis of SDs in psoriasis (103, 109). However, increased levels of proinflammatory cytokines, such as TNF-α and interleukin 6, play a fundamental role in the occurrence of SDs in psoriasis (110–112). Serum and skin levels of TNF-α and interleukin 6 are increased in psoriasis and in cases of sleep restriction (109, 113, 114). TNF-α and interleukin 6 have also been shown to cause keratinocyte hyperproliferation in patients with psoriasis (110–112). In addition, these 2 substances play a role in the regulation of sleep, and appear to be responsible for increases in drowsiness and fatigue in humans (115, 116).

The role of several neurotransmitters has also been considered, such as substance P, which is present in high concentrations in the lesional skin of patients with psoriasis (117, 118) and promotes keratinocyte multiplication, skin inflammation and lymphocyte activation (119).

The role of substance P has been established in various biological processes, such as pain transmission and sleep physiology (120, 121). It plays a role in the pathogenesis of SDs and in a number of chronic inflammatory diseases (4, 45, 122). The role of inflammatory cytokines in the development of metabolic syndrome has also been reported due to activation of the autonomic nervous system secondary to sleep deprivation (101), which may explain the increased frequency of metabolic syndromes in certain dermatological conditions (123).
**Sleep apnoea syndrome**

OSA syndrome is characterized by repeated episodes of complete or partial collapse of the upper airways, which occur during rapid eye movement sleep (REM sleep or REMS) and are responsible for interruptions or decreases in respiratory flow. Intermittent hypoxia, hypercapnia and sleep fragmentation caused by OSA are associated with an increased risk of accidents caused by daytime sleepiness. Patients with OSA have an increased risk of cardiovascular disease (particularly hypertension), metabolic syndrome and diabetes, which are all comorbidities of psoriasis (124). Psoriasis is known to increase the risk of obesity, one of the major risk factors for OSA (125). The reported prevalence of OSA among patients with psoriasis varies across studies from 36% to 81.8% compared with 3–7% in the general population (63, 126–128) (Table IV).

The rate of OSA increases with the duration of psoriasis (125) and is higher in cases of severe psoriasis (135, 136) and psoriatic arthritis. A recent study found no significant relationship between PSQI score, risk of OSA, and severity of psoriasis assessed by the PASI (55).

A study based on nocturnal polysomnography showed a similar sleep pattern and similar total sleep time and sleepiness scores in patients with psoriasis with and without OSA (135).

Studies have shown that treatment of OSA with continuous positive airway pressure (CPAP) can improve psoriatic lesions and result in a decrease in TNF-α and interleukin-6 (134, 136), which has led to the possibility of a link between improved sleep, reduced inflammatory syndrome and improved psoriasis (134). The link between OSA and psoriasis is not clearly established, but may be explained by activation of the sympathetic nervous system and inflammatory signalling pathways (63, 103, 126, 127, 136, 137). Recurrent nocturnal arousal caused by OSA may lead to activation of the sympathetic nervous system and inflammatory reactions, followed by secretion of proinflammatory cytokines (136–138), resulting in the recrudescence of psoriasis lesions and exacerbation of symptoms, such as pruritus and pain (127, 139).

**Restless legs syndrome**

RLS, which manifests as abnormal leg movements during sleep, is reported in patients with psoriasis at rates of 15.1% to 18% depending on the study (57, 140, 141) and 5–10% in control populations (127, 142). RLS disturbances interfere with sleep patterns, causing difficulties in falling asleep or waking up and leading to deterioration of sleep quality in patients with psoriasis (55).

The aetiopathogeny of RLS in patients with psoriasis is thought to be related to an inflammatory disorder (143, 144). One study showed that the occurrence of moderate or severe RLS was significantly more common in patients with psoriatic arthritis (68.7%) than in patients with psoriasis (30%, p < 0.001) (145). Similar results were obtained by Nowowiejska et al. (55).

**Impact of biotherapy treatments on sleep disorders in patients with psoriasis**

Several studies have examined the impact of biotherapies on sleep. Two of these studies have investigated the effects of adalimumab (ADA) on sleep in psoriasis (25, 28):

- In a study of 152 patients, Strober et al. found a 15% improvement in PSQI scores after 16 weeks of ADA treatment, which was partly explained by an improvement in the PASI score. ADA also improved quality of life, pain and productivity at work (28).
- A second study in 20 patients with chronic plaque psoriasis and OSA treated with ADA did not show an improvement in OSA after 8 weeks of treatment (25).

Three studies have shown an improvement in sleep quality after treatment of psoriasis with etanercept (30, 146). The impact of the treatment on pruritus, skin discomfort and pain may explain this beneficial action on the quality of sleep.

The discomfort of topical treatments, particularly sticky, greasy sensations, has also been suggested to contribute to sleep disturbance in patients with psoriasis.

**Conclusion**

SDs are particularly frequent during psoriasis, with a consequent significant alteration in patients’ quality of life. A close relationship exists between psoriasis and SDs, the pathophysiological mechanisms of which are not fully understood. SDs in patients with psoriasis are still underdiagnosed and often remain a common complaint that is not systematically reported to dermatologists. SDs should be considered a crucial comorbidity in psoriasis, acting as both a mediator and an effect. Assessing the quality of sleep and the existence of SDs in patients with psoriasis is important. Patients with psoriasis sometimes do not consider it necessary to discuss the issue of SDs with their dermatologist. Early detection, using one of the available validated screening questionnaires, and the management of SDs, can significantly improve the quality of life of psoriatic patients. Therefore, including questions about SDs in examinations of patients with psoriasis is essential.

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**Table IV. Prevalence of obstructive sleep apnoea (OSA) among psoriasis patients**

| Study                                      | Psoriatic patients, n | Prevalence of OSA (%) |
|--------------------------------------------|-----------------------|-----------------------|
| Kabeloglu Ilbay et al. 2019 (129)          | 57                    | 61.4                  |
| Bissonnette et al. 2012 (130)              | 20                    | 81.8                  |
| Karaca et al. 2013 (131)                   | 33                    | 54.5                  |
| Papadavid et al. 2010 (132)                | 15                    | 66.7                  |
| Woodcock et al. 2010 (133)                 | 12                    | 53                    |
| Buslau et al. 1999 (134)                   | 25                    | 36                    |
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