Sleep disorders and atopic dermatitis: A 2-way street?

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Sleep disturbance is very common in patients with atopic dermatitis (AD) and is a major factor leading to impaired quality of life. Sleep disturbance is often viewed as one of the symptoms of AD and one of the measures of disease severity. In this review we describe a variety of sleep disorders associated with AD and a wide range of effect that sleep disorders have on patients with AD. We also discuss our current understanding of the mechanism of sleep disturbance in patients with AD. The relationship between sleep disorders and AD might be bidirectional and could form a vicious cycle. Therefore we suggest viewing sleep disorders as a comorbidity of AD for which regular screening and bidirectional management strategies are indicated, with equal focus on maintaining disease control and implementing specific strategies to improve sleep. (J Allergy Clin Immunol 2018;142:1033-40.)

Key words: *Sleep disturbance, atopic dermatitis, eczema, melatonin, sleep disorder*

Atopic dermatitis (AD) is a common allergic disease affecting 15% to 30% of children and 2% to 10% of adults.[1] It is a chronically relapsing pruritic inflammatory skin disease with complex pathophysiology that is still not fully understood.[2] It has long been known that sleep disturbance is very common in patients with AD and is a major factor leading to impaired quality of life.[3-5] Sleep disturbance is often viewed as one of the symptoms of AD. For instance, the SCORAD index, the most commonly used symptom score for AD, includes a visual analog scale for subjective sleep loss,[6] and studies assessing the effect of treatments for AD commonly evaluate whether the treatment improves sleep.[7-9] However, more and more studies have found that sleep disturbances have complex interrelationships with AD and a wide range of effect on patients with AD. Therefore we suggest that sleep disorders in patients with AD should instead be viewed as a comorbidity of AD and as an individual category to be regularly assessed and managed.

Abbreviations used
AD: Atopic dermatitis
HR: Hazard ratio
OR: Odds ratio
OSA: Obstructive sleep apnea
PSG: Polysomnography
REM: Rapid eye movement

SLEEP DISORDERS IN PATIENTS WITH AD

Sleep disturbance is reported in 47% to 80% of children with AD and in 33% to 87.1% of adults with AD (Table I).[1-21] The majority of studies in the literature describing sleep disturbance in patients with AD are based on questionnaires of subjective sleep problems. The most commonly reported sleep problems in both children and adults with AD include difficulty falling asleep, frequent nighttime awakenings, and excessive daytime sleepiness.[4,10,13,14,16-20] Children with AD also reported more wake time after sleep onset and difficulty waking up in the morning.[4,14,15,19-21] Chamlin et al[11] found that 30% of children with AD reported parent cosleeping, and cosleeping bothered 66% of these parents.

Only a few studies have taken objective measurements of sleep in patients with AD (Table I). Laboratory-based polysomnography (PSG), the gold standard assessment for sleep, has seldom been used to evaluate sleep in children with AD,[22-24] possibly because of the inconvenience of having to be performed at a sleep center overnight. The attachment of multiple leads and equipment during the PSG examination might also result in more skin irritation for the patient with AD. Of the few studies that assessed the sleep of patients with AD by using PSG, Hon et al[24] found that sleep efficiency (the proportion of time in bed spent asleep) was reduced in children with AD compared with control subjects (72% vs 88%, $P = .04$). Stores et al[25] reported that sleep in children with AD was at least 4 times more disrupted than that in control subjects on both brief (<2 minutes) and long (>2 minutes) periods of waking. Our group found that patients with AD had lower sleep efficiency (71.2% vs 76.2%, $P = .004$) and less non–rapid eye movement (non-REM) sleep than control subjects.[15]

Actigraphy involves a small wrist-worn device that uses activity-based monitoring to estimate sleep-wake patterns. Because of its ease of use, it is increasingly applied to provide objective sleep assessments in patients with AD.[3] Our group has validated that actigraphic measures had high correlation with the

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TABLE I. Sleep disorders in patients with AD

Sleep disorders in patients with AD	Prevalence/characteristics	Tool for assessment	References
Subjective sleep problems			
Eczema-affected sleep	Children: 47% to 80%; 86% during eczema flare-up Adults: 33% to 87.1%	Questionnaire; interview	1-7
Difficulty falling asleep	Children: 10.2% to 51.4%; average sleep onset latency, 39.8 minutes Adults: 76.2% with mild disease, 89% with moderate disease, and 100% with severe disease	Questionnaire	6-9
Nighttime awakenings	Children: 43% to 73%; average, 2.7-3.5 awakenings per night during eczema flare-up Adults: 4.8% with mild disease, 76.2% with moderate disease, and 92.6% with severe disease	Interview	1, 4, 5, 7, 9, 10
More wake time after sleep onset	Children: 38% stayed awake for 0.25-1 hours per night, 20% between 1-2 hours, and 11% for >2 hours; average, 88.3 minutes	Questionnaire	5, 10
Difficulty awakening in the morning	Children: 58% to 62.5%	Questionnaire	6, 8
Excessive daytime sleepiness	Children: 43.1% to 61.9% Adults: OR, 2.66 (95% CI, 2.34-3.01)	Questionnaire	6, 11, 12
Parent cosleeping	Children: 30%; 66% parents bothered by cosleeping	Questionnaire	2
Objective sleep problems			
Prolonged sleep onset latency	Children: average, 45 minutes	Actigraphy	6
More wake time after sleep onset	Children: average, 73.2-103.4 minutes Adults: average, 57.3 minutes	Actigraphy	6, 13, 14
Lower sleep efficiency	Children: average, 72% to 76.8% Adults: average, 90.6%	Actigraphy; PSG	6, 13-15
Others	Children: less NREM sleep Children and adults: more sleep fragmentation, more arousals and awakenings, more scratching and movement in sleep	Actigraphy; PSG; infrared video	6, 16, 17
Specific sleep disorders			
Sleep-disordered breathing	Children with eczema had increased risk of snoring (OR, 1.80; 95% CI, 1.28-2.54); children with AD had higher risk of OSA (HR, 1.86; 95% CI, 1.43-2.42) Adults with OSA more likely to have AD (HR, 1.5; 95% CI, 1.15-1.95); hazard risk was greater in male and young OSA patients (0-18 and 19-34 years)	Questionnaire; population-based cohort study	18-20
Insomnia	Adult patients with AD are more likely to have insomnia (OR, 2.36; 95% CI, 2.11-2.64)	Questionnaire, population-based	12
Others	Children with AD had more bedtime resistance and parasomnias	Children Sleep Habits Questionnaire	21

NREM, Non-REM.

gold standard PSG measures in patients with AD and suggest that actigraphy is a good and convenient method to assess the sleep of patients with AD in future studies.[15] Benjamin et al[26] showed that children with AD spent a mean of 46 minutes less sleeping at night than control subjects (468 ± 3 vs 422 ± 37 minutes). Hon et al[27] reported that actigraphic measures of activity were correlated with disease severity ($r = 0.52$, $P < .01$) and occurred most in the first 3 hours of sleeping in children with AD. Our group assessed the sleep of 72 children with AD and 32 control subjects with actigraphy and showed that children with AD had lower sleep efficiency (74.5% ± 9.2% vs 81.2% ± 7.6%, $P = .001$), more wake time after sleep onset (73.2 ± 45.7 vs 50.7 ± 29.9 minutes, $P = .004$), longer sleep onset latency (45 ± 29.3 vs 27 ± 16.2 minutes, $P < .001$), and a higher sleep fragmentation index score.[15]

Some specific sleep disorders have been reported to be associated with AD. Sleep-disordered breathing has been found to be associated with AD in several studies: Chng et al[28] reported that in preschool and primary school children in Singapore, habitual snoring was associated with AD (odds ratio [OR], 1.80; 95% CI, 1.28-2.54).[28] Population-based studies from Taiwan have shown that patients with obstructive sleep apnea (OSA) had a higher risk of AD (hazard ratio [HR], 1.5; 95% CI, 1.15-1.95), especially in male patients with OSA (HR, 1.53; 95% CI, 1.14-2.06), children less than 18 years old with OSA (HR, 4.01; 95% CI, 1.57-10.26), and young patients with OSA aged 19 to 34 years (HR, 1.75; 95% CI, 1.00-3.04; adjusted for allergic rhinitis and asthma).[29] In children less than 18 years old, patients with AD had a higher risk of OSA than those without AD (HR, 1.86; 95% CI, 1.43-2.42; adjusted for comorbidities of AD, such as rhinitis).[30] It is hypothesized that the association between AD and OSA could be due to common underlying pathways of oxidative stress and systemic inflammation.[29,30] A high sympathetic tone in patients with AD and resultant sleep fragmentation could also contribute to upper airway instability during sleep.[31] A US population-based study showed that in

adults eczema was associated with regular insomnia (OR, 2.36; 95% CI, 2.11-2.64).[20] Urrutia-Pereira et al[18] reported that in Latin American children, patients with AD had more bedtime resistance, sleep-disordered breathing, and parasomnias compared with control subjects. Cicek et al[32] reported that restless leg syndrome was more common in patients with AD than control subjects, although the underlying mechanism of this association is unclear. We suggest that patients with AD who complain of sleep problems should be carefully assessed for these associated sleep disorders to provide adequate treatment.

EFFECT OF SLEEP DISORDERS ON PATIENTS WITH AD

After itch, sleep disturbance has been ranked as the second highest factor leading to impaired quality of life in children with AD.[12] Children with AD have been reported to have lower quality of life than children with other chronic skin diseases, such as psoriasis, urticaria, and acne, and also other chronic diseases, such as renal disease, asthma, cystic fibrosis, epilepsy, and diabetes.[33]

The quality of life and sleep of family members are also affected by childhood AD. In parents of children with chronic illnesses, sleep disruption is most highly reported in parents of children with AD, affecting 54% to 86% of parents.[34] Mean reduction in parental sleep time during flare-ups in children with AD ranged from 0.66 to 2.6 hours per night.[13,35] Lawson et al[36] reported that 64% of parents of children with AD reported frustration and exhaustion caused by sleep problems, and 63% of siblings of children with AD were also losing sleep. Another study showed that the severity of sleep disturbance in the parents of children with AD was associated with the level of parental anxiety (maternal anxiety: $r = 0.58$, $P = .002$; paternal anxiety: $r = 0.59$, $P = .01$) and maternal depression ($r = 0.73$, $P < .001$).[35]

Sleep disturbance itself can have many negative consequences for children, including higher rates of behavioral problems, impaired neurocognitive function, and changes in mood.[37,38] A study found that 54% of parents of children with AD reported behavioral disturbances, such as irritability, bad temper, and being hurtful to other family members during flare-ups of AD.[36] A large cohort study including 1658 children showed that infant eczema with concurrent sleeping problems predicted emotional (OR, 2.63; 95% CI, 1.20-5.76) and conduct (OR, 3.03; 95% CI, 1.01-9.12) problems at 10 years of age.[39]

It has also been found that AD is associated with attention deficit hyperactivity disorder and short stature only when accompanied by sleep problems.[40,41] Because sleep is essential for growth and development and sleep disruption can result in poor concentration and disruptive behavior, it was suggested that sleep disturbance in patients with AD is an important link for these associations (Fig 1).[40,41]

Several studies also reported a significant effect of sleep problems on adults with AD. A US population-based study showed that sleep disturbances in adults with AD were significant predictors of poorer overall health status, number of sick days, and doctor's office visits.[20] In adults with AD, those with sleep disturbance and fatigue have also been reported to be more likely to have difficulty with instrumental activities of daily living (including concentrating, remembering, performing hobbies, doing finances, and driving), impaired quality of life, and negative effects on mental health and social functioning (Fig 1).[16]

MECHANISM OF SLEEP DISORDERS IN PATIENTS WITH AD

The pathogenesis of sleep disturbance in patients with AD is complex and not fully understood but likely involves several contributing factors.[42] Several studies have shown that disease severity is associated with sleep disturbance in children with AD.[3,15] Pruritus and scratching movements disrupting sleep seem to be the most straightforward reason for sleep disturbance in children with AD because the itch in these patients is often worse at night. The cause of itch in patients with AD has been suggested to be neuropeptide-mediated vasodilation and change in skin temperature[3] and sensory hypersensitivity caused by eosinophil-induced cutaneous nerve growth or increased skin levels of nerve growth factor.[43-45] IL-31, brain-derived neurotropic factor, and substance P have also been suggested to have a role in the pruritus seen in patients with AD.[1,46] However, studies to establish an association of itch or pruritogenic factors with sleep disturbance in patients with AD are either lacking or produced conflicting results.[42] It was also reported that scratching accounted for only 15% of arousals and awakenings in children with AD.[22] Therefore itch and scratching movements are contributing factors but are unlikely the only reason for sleep disturbance in patients with AD.

The circadian rhythm regulates immune function and cytokine production, cortisol secretion, and skin physiology, and these mechanisms could play a role in sleep disturbance in patients with AD. Various immune cell counts, immune cell function, and cytokine levels exhibit diurnal patterns.[42] Levels of proinflammatory cytokines, such as IL-1β, IL-2, TNF-α, IFN-γ, and IL-6, are increased at night and generally promote sleep, whereas anti-inflammatory cytokines, such as IL-4 and IL-10, are induced after awakening and could inhibit sleep.[47,48]

The pathogenesis of AD is complex. In acute lesions AD is characterized by profound increases of T_H2 and T_H22 responses. IL-4 and IL-13 seem to play key roles, but IL-5, IL-31, CCL18, and IL-22 levels are also increased. T_H17-associated molecules, such as IL-17A, peptidase inhibitor 3/elafin, and CCL20, are upregulated in both patients with acute and those with chronic AD. In chronic AD lesions T_H2 and T_H22 responses are intensified, but activation of the T_H1 axis is also found, with increased levels of IFN-γ, CXCL9, and CXCL10.[49] Histamine, thymic stromal lymphopoietin, IL-33, IL-31, IL-4, and IL-13 have been suggested to be key mediators of pruritus in patients with AD.[50] Serum IL-31, CCL17, CCL22, and CCL27 levels have been found to be correlated with AD disease activity.[49]

Because of the involvement of a wide range of cytokines and chemokines in patients with AD, it is possible that dysregulated levels of cytokines, such as IL-4, could contribute to sleep disturbance.[42,51] However, direct relationships between cytokine levels or immune cell activity during sleep in patients with AD have rarely been studied. Bender et al[52] reported that an increased differential between morning and evening IL-6 production by PBMCs stimulated with anti-CD3 was correlated with better sleep efficiency in adults with AD. Hon et al[27] reported that wrist activity during sleep was correlated with plasma concentrations of cutaneous T cell–attracting cytokine, thymus and activation-regulated chemokine, and macrophage-derived chemokine but did not correlate with subjective pruritus or sleep loss. Our group found that in children with AD, a higher morning serum IL-4 level was correlated with better sleep efficiency, and the ratio of

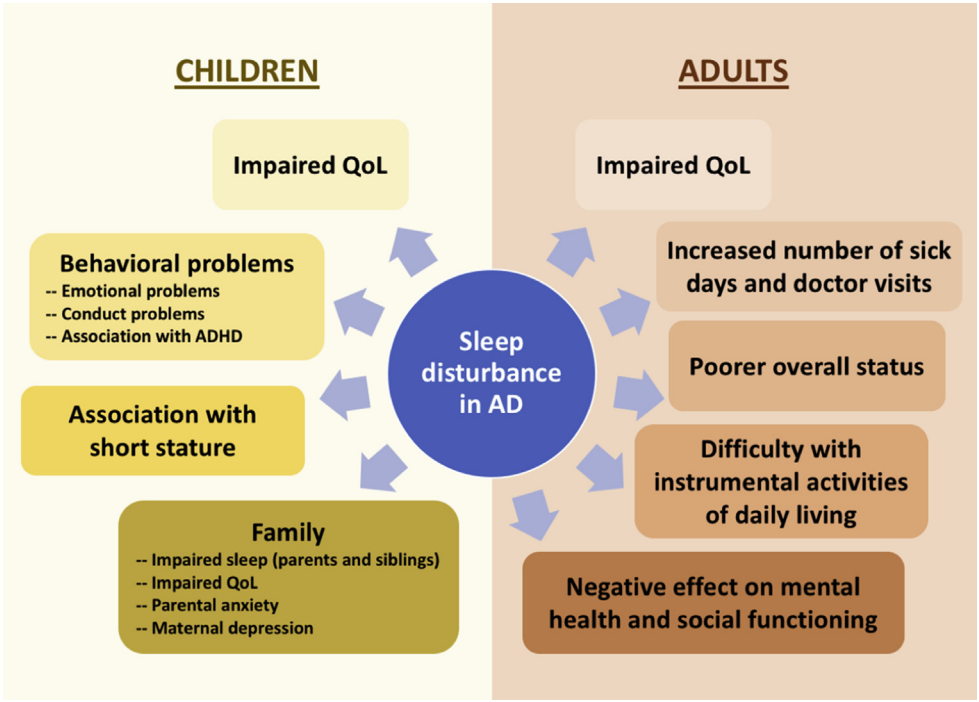

FIG 1. Effect of sleep disorders in patients with AD. Sleep disorders have a wide range of effects on both children and adults with AD. *ADHD,* Attention deficit hyperactivity disorder; *QoL,* quality of life.

IFN-γ/IL-4 was lower in those with poor sleep efficiency. We also found that morning serum IL-31 levels were correlated with a lower percentage of stage N1 sleep.[15]

Skin cells express circadian clock genes, such as circadian locomotor output cycles kaput *(CLOCK)* and brain and muscle aryl hydrocarbon receptor nuclear translocator-like 1 *(BMAL1)*, and skin barrier function is also regulated by the circadian rhythm. Skin blood flow rate is greater in the afternoon and early evening and has a second peak in the late evening before sleep onset.[53] Low sebum production at night and high transepidermal water loss in the evening could contribute to nocturnal itching in patients with AD.[54,55] Cortisol levels are lowest in the evening after sleep onset and could also contribute to increased pruritus at night.[54] However, studies directly investigating the relationship between cortisol levels or diurnal skin physiology and sleep disturbance in patients with AD are lacking and need further evaluation.

Melatonin is a hormone essential for regulating sleep and the circadian rhythm. It is mainly secreted by the pineal gland but also by other tissues, such as the skin, lymphocytes, and mast cells.[56] Melatonin has effects on sleep, immunomodulation, and antioxidant ability, and therefore it was suggested that it might play some role in patients with AD.[57] Schwarz et al[58] reported that the circadian melatonin rhythm was diminished in patients with AD. Our group found that nocturnal melatonin secretion was greater in patients with AD compared with that in control subjects and that in patients with AD, higher nocturnal melatonin levels were associated with better sleep efficiency, less sleep fragmentation, and milder disease.[15] In a randomized, double-blind, placebo-controlled trial, our group found that 3 mg of oral melatonin before bedtime for 4 weeks in children with AD improved sleep onset latency by 21.4 minutes compared with placebo (95% CI, −38.6 to −4.2; $P = .02$). AD disease severity was also improved after melatonin, decreasing the SCORAD score by 9.1 compared with that after placebo (95% CI, −13.7 to −4.6; $P < .001$). The improvement in SCORAD score was not correlated with the change in sleep onset latency.[59] This supports that in addition to sleep-promoting effects, other properties of melatonin, such as immunomodulation or antioxidation, could play a role in modulating AD.

There are few studies that examine the relationship between environmental factors and sleep disturbance in patients with AD. Our group found that serum allergen-specific IgE levels to dust mite (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinae*) were correlated with sleep disturbance in children with AD, including decreased sleep efficiency, higher percentage of time awake during sleep, and more sleep fragmentation.[15] Allergic sensitization and exposure to dust mite during sleep could also contribute to sleep disturbances in patients with AD. Roles of other allergens and the sleeping environment need further study.

Studies have shown that even when AD is in clinical remission, sleep disturbances, such as sleep fragmentation and frequent arousals, can persist.[22] It is possible that patients with AD acquire poor sleep habits because of their sleep disturbance during flare-ups, leading to behavior-related sleep problems that persist even without clinically evident disease. Cosleeping with parents is common in children with AD. Cosleeping has been found to be a predictor of nighttime waking in healthy children,[60] and it is unclear whether it could also contribute to further sleep disturbance in children with AD. Because of the skin condition, parents might also acquire a more permissive attitude toward the child's bedtime schedule or if the child has bedtime resistance, increasing the risk of behavioral insomnia.

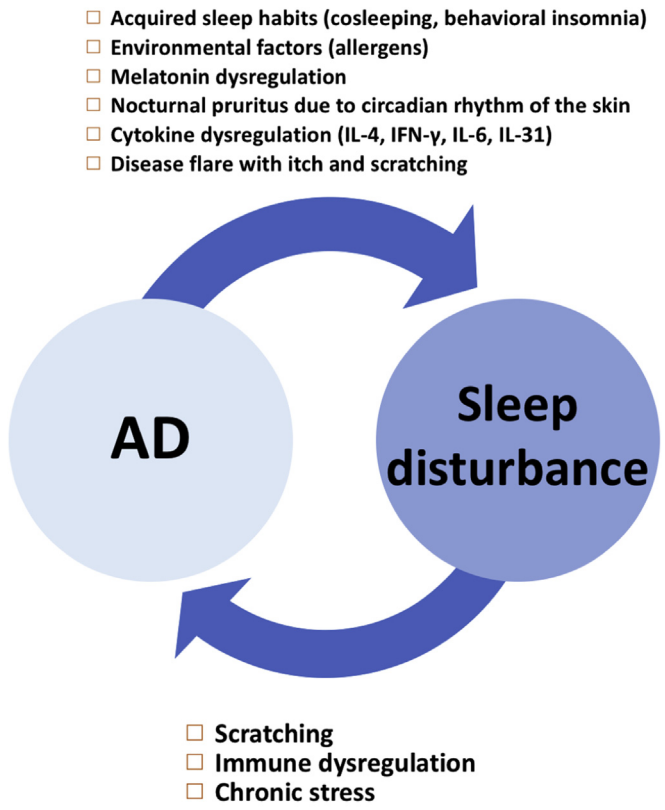

FIG 2. Bidirectional relationship between sleep disorders and AD. The mechanism of sleep disturbance in patients with AD is complex and involves multiple contributing factors. Sleep disturbance itself can also exacerbate AD, forming a vicious cycle.

DO SLEEP DISORDERS EXACERBATE AD?

Scratching leads to tissue damage and release of structural proteins, triggering an IgE response and resulting in an itch-scratch cycle that exacerbates AD.[1] Studies have found that in patients with AD, scratching occurs mainly in stage N1 sleep but is also not much suppressed during the deeper N2 and N3 sleep stages, when there is usually very little limb movement in healthy control subjects.[15,52] Compared with daytime, it is more difficult for patients to consciously suppress their scratching at night, and frequent awakenings during the night might also increase awareness of nocturnal pruritus, leading to more scratching. Clinically, parents also often report that it is harder to prevent their child from scratching during sleep and that AD often flares up after a night of poor sleep and intense scratching. It is possible that sleep disturbance itself exacerbates the itch-scratch cycle in patients with AD.

Sleep and the circadian rhythm have complex relationships with immune function. Numerous studies have shown that sleep loss could lead to dysregulation of the immune system. Immune responses to LPS stimulation, susceptibility to infection, and vaccination vary according to the timing of stimulation and can be altered with sleep loss.[61,62] Studies have found that IL-1β, IL-6, and TNF-α levels are increased during acute sleep deprivation, and IL-1β, IL-6, IL-17, and that high-sensitivity C-reactive protein levels are increased with chronic partial sleep deprivation.[63] In an animal model of psoriasis, those challenged with sleep deprivation had increased levels of proinflammatory cytokines, such as IL-1β, IL-6, and IL-12, and decreased levels of the anti-inflammatory cytokine IL-10. These cytokine levels were restored after 48 hours of sleep rebound.[64] Because of cytokine alterations, a chicken-or-egg relationship has also been suggested between sleep disorders and disease activity of inflammatory diseases, such as inflammatory bowel disease.[65]

Sleep deprivation could also disturb the functional rhythm of regulatory T cells[42,66] and could shift the T_H1/T_H2 balance toward T_H2 dominance.[67] Our group found that in children with AD, the IFN-γ/IL-4 ratio was lower in those with poor sleep efficiency.[15] This is compatible with the theory that sleep loss could shift the T_H1/T_H2 balance and suggests that sleep loss itself could probably also worsen AD.

Stress has been shown to worsen proinflammatory disorders, such as AD, through mechanisms like causing a shift to predominately T_H2 cells and impairing the response to stressful stimuli by the hypothalamic-pituitary axis. Skin cells could also produce corticotropin-releasing hormone in response to stress, which can lead to local inflammatory reactions and mast cell degranulation.[68] It is possible that chronic sleep disturbances could lead to chronic stress in patients with AD, which in turn further exacerbates AD.

In summary, there are reasons to believe that sleep disturbance itself could exacerbate AD and that there is a 2-way street between sleep disorders and AD, but studies establishing clear evidence are lacking, and further studies are needed to clarify whether the sleep disturbance in patients with AD worsens the itch-scratch cycle or causes immune dysregulations or stress which result in a vicious cycle in patients with AD (Fig 2).

MANAGEMENT OF SLEEP DISORDERS IN PATIENTS WITH AD

Currently, there is no consensus guiding the management of sleep disorders in patients with AD, and most treatment methods are based on expert opinion.[69] Guidelines for AD have recommended that treatment of AD should focus on disease control, with sleep disturbance as one of the measures of control.[70] Clinical trials that have assessed the effect of treatment on sleep in patients with AD are also mostly trials for disease-controlling agents, which evaluated sleep as a secondary outcome. Such trials include those using topical steroids, topical tacrolimus, cyclosporine, methotrexate, azathioprine, wet wraps, light therapy, and dupilumab for AD, and they all assessed sleep quality with subjective visual analog scales.[69-71] From current evidence, disease severity is associated with sleep disturbance in patients with AD, and pruritus and scratching are important contributing factors. Therefore optimal disease control is crucial in managing sleep problems in patients with AD. However, with the growing knowledge of the intertwining relationship between AD and sleep disorders, we suggest that management should be focused on both disease control and sleep (Fig 3).

The most commonly used sleep aids for AD are first-generation antihistamines, which can cross the blood-brain barrier and affect histamine's role in maintaining central nervous system arousal, resulting in a sedating effect, and might also have some benefit in pruritus by antagonizing the inflammatory effects of histamine released from mast cells and basophils, although high-level evidence for reducing itch in patients with AD is lacking.[68,72] Tolerance often occurs after 4 to 7 days of treatment, and anticholinergic side effects, such as blurred vision and dry mouth, can

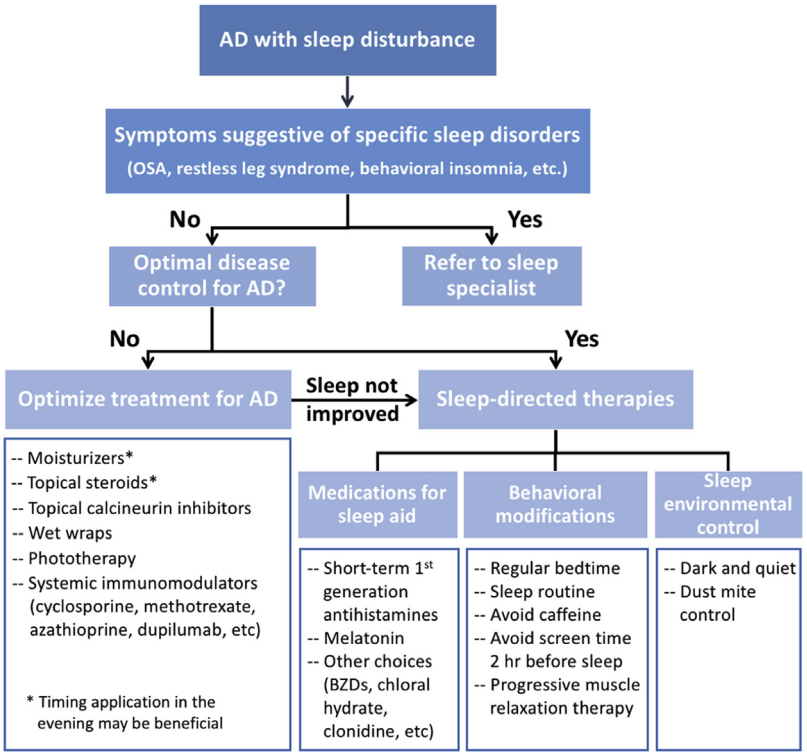

FIG 3. Proposed treatment strategy for sleep disorders in patients with AD. Patients with AD with sleep disturbance should first be screened for specific sleep disorders. Because of the intertwining relationship between sleep disorders and AD, management should be focused on both disease control and strategies to improve sleep. *BZDs*, Benzodiazepines.

occur.[73] Sedating antihistamines can also reduce sleep quality, decrease REM sleep, and impair daytime cognitive function and work efficiency.[72]

Other sleep-promoting agents that have been suggested for AD, such as benzodiazepines, chloral hydrate, and clonidine, all lack supporting evidence.[70,74] Benzodiazepines carry the risks of tolerance to sedating effects, rebound worsening of sleep on discontinuation, addiction, and memory problems.[74] Chloral hydrate use has risks of hepatotoxicity and respiratory depression.[70] Clonidine use requires blood pressure monitoring and could also have anticholinergic side effects. Clonidine could also suppress REM sleep, and rapid discontinuation could lead to REM rebound.[68]

Oral melatonin supplementation has been found to improve both sleep onset latency and disease severity in children with AD in a randomized controlled trial.[59] Melatonin also has a good safety profile and might be a favorable choice for children. However, the optimal dose and duration of treatment need further study.

The importance of implementing methods to improve sleep hygiene and sleep-directed behavioral therapies should be stressed for the purposes of both improving sleep and preventing acquired behavioral insomnia, which could persist after disease control. General measures for improving sleep hygiene include adhering to regular bedtimes and wake-up times, performing a relaxing bedtime routine, keeping a quiet sleeping environment, and avoiding caffeine intake.[69] Because of the effect of the circadian rhythm on AD, applying moisturizers and topical steroids in the evening could be advantageous because transepidermal water loss is greatest and skin blood flow rate is most affected by topical steroids at this time.[42] Use of moisturizers and topical medications could also be incorporated into the bedtime routine. Light, particularly blue light, suppresses melatonin secretion, and therefore it is important to avoid screen time 2 hours before sleep and maintain a dark sleeping environment.[42]

Dust mite sensitization might have a role in the sleep disturbance seen in patients with AD,[15] and therefore dust mite control in the sleeping environment should be encouraged. Progressive muscle relaxation therapy, which involves cycles of tensing a target muscle group for 10 seconds and then relaxing the muscle group for 20 seconds, has also been shown to be helpful in reducing pruritus, sleep loss, and anxiety in patients with AD and could be tried in older children or adults with AD.[75]

If behavioral insomnia occurs, referral to a psychologist or sleep medicine specialist is suggested for behavioral modification strategies, such as extinction, graduated extinction, scheduled awakenings, bedtime fading, and response cost.[69] Mindfulness meditation has recently been used to improve insomnia in adults and adolescents,[76,77] and it has been suggested that it could be helpful for treating psoriasis or other dermatologic diseases.[78-80] Further study is needed to explore whether mindfulness meditation could improve sleep disorders in patients with AD.

Screening for specific sleep disorders that have been found to be associated with AD is also important. Frequent snoring, apneas or choking during sleep, mouth breathing, or abnormal sleeping positions, such as being propped up on pillows or sleeping with the neck hyperextended, could suggest OSA. Uncomfortable sensations in the lower extremities accompanied by an almost

irresistible urge to move the legs exacerbated by resting or lying in bed and partially relieved by movement could indicate restless leg syndrome.[81] If symptoms are suggestive of specific sleep disorders, referral to a sleep specialist is recommended for further evaluation and management (Fig 3).

CONCLUSIONS

Sleep disorders are very common in patients with AD and have a wide range of effects. The relationship between sleep disorders and AD seems to be bidirectional and likely forms a vicious cycle. Instead of regarding sleep disorders as only one of the symptoms or disease severity measures for AD, we suggest viewing sleep disorders as a comorbidity of AD for which one should screen regularly, and specific treatments for sleep disorders should be incorporated into management strategies.

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