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Treatment of Sleep Disorders in Children with Atopic Dermatitis: What's New?

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Abstract

Atopic dermatitis (AD), also known as atopic eczema, is a chronic and inflammatory disease caused by an interaction of genetic, immunological, and environmental factors. It is characterized by skin lesions and itching and progresses with periods of improvement and worsening.

Patients with AD often experience sleep disorders, which leads to a worsening of the quality of life of patients and their families and may be associated with poorer school performance, behavioral and mood dysfunction, risk of short stature, metabolic syndrome, mental illness, neurocognitive dysfunction, psychiatric comorbidities such as anxiety, stress, depression, attention deficit hyperactivity disorder (ADHD). Furthermore, sleep disturbances in children with AD have been associated with pruritus and greater severity of dermatitis.

To this day, we do not have a curative treatment for this disease, but there is treatment, and it is possible to keep the disease under control. In these patients, controlling the condition is very important to improve the quality of sleep, at the same time, with better sleep there is greater control of AD.

Despite being very common in AD, we currently have few studies on sleep disorders and their treatment in this disease, and there is no consensus on the therapeutic approach. We carried out a descriptive study with a narrative review of the literature.

The research was based on studies published in English and Portuguese between January 2013 and October 2023, electronically in several databases, such as PubMed, Scientific Electronic Library Online, and Latin American and Caribbean Literature in Health Sciences.

The objective of this review is to describe possible treatments for sleep disorders in AD, in order to contribute to a better understanding and clinical management of these cases, seeking to minimize the impact on the lives of these patients.

Keywords: Sleep, Atopic dermatitis, Insomnia, Pruritus, Sleep efficiency

Introduction

The skin is the largest organ in the body and performs several functions such as: barrier against water loss, absorption of substances and infections, thermoregulation and tactile sensation. The integrity of the skin barrier is essential for maintaining skin homeostasis.

Atopic dermatitis (AD) is an inflammatory, chronic, recurrent, complex skin disease with multifactorial etiology, which is manifested by xeroderma, skin lesions, and itching, which is often disabling.

AD has a global distribution, being more common in childhood, generally manifests between 3 and 6 months of age and in the majority of cases, 70% to 90%, it tends to resolve spontaneously in adulthood [1].

The clinical presentation is variable, signs and symptoms can be observed in different locations of the body and may vary with the child's age. The diagnosis is clinical and there is no definitive diagnostic laboratory test. Treatment will be indicated according to the severity of each case, ranging from topical therapy in mild cases to immunosuppressants and immunobiologicals in moderate to severe cases.

High rates of sleep disorders have been described in these patients, generating consequences such as daytime fatigue, headache, neurocognitive and mood disorders, behavioral problems and compromised school and professional performance. The cause of sleep disorders in AD is discussed in the literature, it would be a vicious cycle caused by itching, some studies suggest that this can only partially explain this problem [1,2].

It is very important to understand and treat atopic dermatitis and associated sleep disorders to improve the quality of life of patients and families and reduce the negative impact on child development [2].

Materials and Methods

We carried out a narrative review of the literature, searching for studies published between January 2013 and October 2023, available in electronic media in several databases, such as PubMed, Scientific Electronic Library Online, and Latin American and Caribbean Literature in Health Sciences.

Health Sciences Descriptors "atopic dermatitis", "sleep" and "treatment" were used.

Justification

This review holds significance due to the prevalence of AD, particularly among children. AD can significantly diminish the quality of life for patients and their families, affecting physical, emotional, and social well-being. Sleep disturbances in AD contribute to the negative impact of the disease and we have few studies that address this topic and its treatment. The most frequently reported sleep problems in children with AD are delayed sleep onset, frequent nighttime awakenings, and decreased sleep duration. In this context, children's cognitive and behavioral development can be impacted in different intensities as a result of sleep disorders and current therapeutic options are scarce and aimed at controlling AD, demonstrating the importance of this review.

Literature Review

Atopic dermatitis

AD, also known as atopic eczema, is a common chronic skin disease characterized by skin inflammation that results in intense itching. It is considered an immunological and skin barrier disorder and is influenced by endogenous factors, such as genetic predisposition and exposure to environmental factors. Pathophysiology is still not fully understood. It is a heterogeneous disease and can present a wide variation in disease presentation and different phenotypes, which may be relevant for prognosis and treatment. The clinical presentation of the disease may change over time [3-5].

AD has become a global health problem, as it causes high healthcare costs worldwide and is associated with considerable morbidity and impaired quality of life. The estimated burden of the disease is comparable to other chronic conditions, such as epilepsy, diabetes mellitus, and cystic fibrosis [6].

AD lesions can occur anywhere on the body, but generally present a typical age-related distribution pattern. Infants generally present more acute skin lesions, characterized by erythema, edema, excoriations with secretion and crusts, mainly on the face and trunk. In childhood, AD becomes more localized and chronic, with more discrete erythema, xerosis and lichenification, commonly affecting the flexor surfaces. Adolescents and adults may have a diffuse pattern or localized lesions, affecting the hands, eyelids, and flexures [6].

It is extremely important to accurately assess the extent, intensity, and severity of the AD condition, as in addition to classifying the initial form, it helps in evaluating the therapeutic response. Severity criteria were established for monitoring, which evaluate parameters of extension, intensity of the lesions and subjective symptoms, such as itching and sleep. SCORAD (Severity scoring of atopic dermatitis) is based on the assessment of the affected body surface and the intensity of the lesions. According to the severity of the eruption elements, we classify them as: erythema, edema/papule, exudation/crust, lichenification, excoriations and xerosis. Subjective symptoms, itching and sleep are also evaluated [7].

AD can affect up to 20% of children worldwide and children with AD can experience worse quality of life, physical discomfort, behavioral changes, greater frequency of attention deficit/hyperactivity disorder, and more use of healthcare. Parents of children with AD may experience worsening quality of life, depression, anxiety, increased absenteeism from work and have a negative impact on the family [8].

The goals of treatment are to reduce itching and control the disease. The choice of treatment is mainly based on the severity of the disease, age, comorbidities, adherence, and costs [6].

Sleep disorders in atopic dermatitis

Sleep is fundamental to our overall health and well-being and plays a critical role in maintaining alertness. Atopic conditions in children can affect sleep, triggering changes in growth, concentration, behavior and school performance. Sleep disorders in children also directly affect the sleep of their caregivers [3,9].

Study evaluated the sleep pattern and development of 80 children aged 0 to 36 months with AD. Patients were evaluated using the Brief Infant Sleep Questionnaire and the International Child Development Monitoring Guide. 50% of those assessed had sleep problems. 12.5% of patients required support in one or more areas of development. Developmental delay was greater in patients with sleep problems. The study concluded that boys with moderate to severe AD in the first 3 months after diagnosis were at increased risk of sleep problems. Children with AD and sleep problems should be evaluated for developmental delays and monitored [10].

The assessment of a child's sleeping habits may vary from one family to another, whether the child sleeps in their own room or with their parents, consequently the report of nighttime awakenings and report of sleep duration may be underestimated or not valued in the case of children parents who do not sleep in the same room as their child [2].

The importance of sleep duration is a controversial issue. Sleep duration varies from individual to individual and the clinical repercussions on health are different, and may be associated with various sleep disorders, such as chronic and short-term insomnia and insufficient sleep syndrome. Excessive or insufficient sleep is associated with a greater risk of diseases such as high blood pressure, coronary disease, stroke, obesity, metabolic syndrome, and type 2 diabetes mellitus [3].

Three mechanisms have been proposed for the association of sleep disturbances in AD. One of them would be that the stress of having AD can precipitate acute insomnia, which can become chronic over time. Nighttime itching disrupts sleep and contributes to the cognitive and behavioral factors that reinforce insomnia as a response. Another possible mechanism would be the belief that itching disturbs sleep. Pruritus is in fact an important factor for an impaired quality of life and commonly worsens at night, with consequent scratching, which can disturb sleep. The "scratching cycle" can cause tissue damage and the release of inflammatory/pruritogenic mediators, further exacerbating sleep disorders. And a third possibility regarding sleep disturbances in AD is circadian variations in the production of cytokines and melatonin [11].

The causes of AD related insomnia are multifactorial and can be caused by itching and scratching, affecting both rapid eye movement (REM) and non-REM sleep. Some patients with AD also experience asthma, which increases sleep problems due to impaired nocturnal lung function. During AD remission, patients often still have difficulty sleeping due to AD sleep patterns developed during periods of exacerbation, leading to psychophysiological insomnia [12].

Sleep disorders significantly affect a child's daytime functioning, including behavior, social, emotional and cognitive relationships [8]. Furthermore, sleep disorders in AD are factors that negatively impact quality of life. Pruritus, a characteristic symptom in AD, is usually worse at night, resulting in itching that can contribute to sleep changes, interfere with sleep initiation, and cause sleep interruptions. Polysomnography and actigraphy studies have shown that children with AD are more agitated during sleep, wake up more frequently, and spend more time awake after sleep onset. Adequate sleep is essential for physical and mental well-being [13].

AD negatively impacts an individual's quality of life in several aspects, including sleep, which in most cases is unsatisfactory. However, sleep ends up being neglected in relation to AD control and sleep disorders are commonly present, with consequences for the patient's behavior and cognitive performance. Although the impact of sleep disorders is increasingly recognized, its pathophysiology is poorly understood. Currently, few studies have evaluated treatment methods and there is no consensus on the therapeutic approach to sleep disorders in patients with AD. Therefore, more studies are needed to better understand the pathophysiology of the disease, in order to formulate new treatment strategies [14].

Normally, the main reasons that lead to the difficulty of inducing and fragmenting sleep-in patients with AD is itching and the vicious cycle of itching. It is notable that repeated movements and abrasions during sleep are associated with greater fragmentation and reduced sleep effectiveness, correlating with disease severity. Furthermore, studies have shown that increased serum levels of IL-31, a potent itch inducer, were related to sleep disorders. However, the literature has shown that only 15% of nighttime awakenings are justified by scratching and this may partially explain sleep problems in AD [15].

There are several inflammatory cells and cytokines implicated in the pathophysiology of AD and they contribute to sleep-related problems. Type 2 immunity mediated by Th2 cells plays a fundamental role in AD, as during the allergic response macrophages and dendritic cells can activate Th2 cells and these will secrete cytokines, such as IL-4, IL-5, IL-13, IL-17, IL-22 and IL-31, leading to type 2 inflammation. Due to this mechanism of action, most treatments have been developed for the treatment of AD at different stages of evolution. However, for moderate to severe AD, current treatments have limited effects. Although the mechanisms are not fully elucidated, sleep deprivation has been implicated as

a predictor of a Th1/Th2 shift with a Th2 predominance, which could justify the association between sleep disturbances and more severe forms of AD. Thus, new studies and medications target specific cytokines, including IL-4, IL-13, IL-22 and immunoglobin E (IgE) [15,16].

Dupilumab is a human monoclonal antibody that antagonizes the alpha subunit of the IL-4 receptor, blocking the signaling of the Th2 cytokines IL-4 and IL-13. Approved by the United States Food and Drug Administration for moderate/severe AD. Several clinical trials have demonstrated the efficacy in improving the severity of AD and quality of life and presents safety profile in adults and children [17].

Difficulty falling asleep, frequent and prolonged nighttime awakenings, difficulty waking up, and excessive reduction in total daytime sleep duration were findings observed in children with AD [11].

The efficacy of bisdemethoxycurcumin (BDMC) in the inhibitory effect of skin lesions in AD mice induced by 2,4-dinitrochlorobenzene (DNCB) was demonstrated in a recent study. This finding suggests that BDMC may have long-term importance in the effective treatment of AD, however, more clinical studies are needed [18].

The most frequently reported sleep problems in children with AD are delayed sleep onset, frequent nighttime awakenings, and decreased sleep duration. We know that sleep is important and necessary for children's cognitive and behavioral development [10]. One study evaluated 10 children between 6 months and 15 years old diagnosed with moderate or severe AD. The patients received therapy for AD and were monitored by actigraphy for 14 days and reevaluated using SCORAD. It concluded that children with moderate to severe AD had changes in sleep quality, with decreased sleep duration, low sleep efficiency and increased awakenings. Improvement in AD severity after intensified AD treatment was associated with improved parental perception of sleep loss, but not with objective sleep quality assessed by actigraphy [2].

Study carried out by Chang et al., demonstrated that children with AD present the following sleep changes, through actigraphy and polysomnography: significant reduction in efficiency, longer latency time for sleep onset, greater fragmentation, and less non-rapid eye movement sleep compared to healthy individuals. Furthermore, sleep disturbances in children with AD have been associated with scratching and greater severity of dermatitis [19].

The study of a cohort of children and adolescents with moderate to severe AD aged between six and 17 years, using actigraphy assessment, demonstrated that sleep was altered in approximately 60% of participants [20].

Treatment of sleep disorders in AD

"Sleep disturbance" is a broad term encompassing poor sleep, disrupted sleep, sleep loss, or a specific sleep disorder like insomnia or obstructive sleep apnea. Sleep disorders have a negative impact on the quality of life of children with AD, however current therapeutic options are scarce and basically limited in controlling the dermatosis [11].

There is still no consensus regarding the treatment of sleep disorders in patients with AD. Management is carried out through AD guidelines that recommend control of the disease, with sleep disorders as a control measure. The clinical trials studied evaluated sleep as a secondary outcome. However, based on current evidence of sleep impairment in patients with AD, management should be focused on both disease control and sleep [21].

Treating symptoms of AD that can ease sleeping

Currently, the most commonly used medications for AD are first-generation sedative antihistamines. The secondary effect of this medication class is both sedation and itching control, resulting in improved sleep. This is because first-generation antihistamines can cross the blood-brain barrier and regulate histamine excitation in the central nervous system, causing a sedative effect. On the other hand, they also act by antagonizing the inflammatory effects of histamine released from mast cells and basophils, which may benefit the reduction of skin itching. Although there is a lack of studies and evidence to reduce itching in patients with AD. Sedative antihistamines can also interfere with sleep quality, as there is a decrease in REM sleep and consequently an impairment in daytime cognitive function and efficiency in daily activities [21].

The use of antihistamines for the primary treatment of AD is not recommended, although current guidelines suggest that sedating antihistamines are preferred over non-sedating antihistamines for the relief of severe pruritus. First generation antihistamines are used to control itching and act to induce sleep, due to their central action capacity, by crossing the blood-brain barrier and inhibiting the action of histamine. However, the sedative effect is not very effective in treating AD sleep in children [22].

Due to the lack of evidence on reducing the severity of the disease, the use of non-sedating antihistamines is not recommended by the American Academy of Dermatology (AAD) [22].

Directly treating sleep disorders

Other medications that promote sleep and are indicated for AD control lack scientific evidence and studies, such as: benzodiazepines, clonidine, chloral hydrate, etc. Benzodiazepines pose risks of sleep rebound on discontinuation, memory problems, and dependence. The risk of hepatotoxicity and respiratory depression has been linked to the use of chloral hydrate. The anticholinergic side effects

of clonidine require blood pressure monitoring and may also suppress REM sleep. Rapid disruption can also lead to REM sleep rebound [21].

While antidepressants may be the medicine of choice for depression, they are also used for other pathologies. Sometimes are used in dermatology because of some of their pharmacological properties that are not related to their antidepressant effect. Doxepin, a tricyclic antidepressant (TCA), has an affinity for the H1 receptor and H2 receptor antagonist, making it a potent antagonist and acting to control pruritus. The doxepin is 800 times more potent than diphenhydramine [23].

One study demonstrated that doxepin applied topically alone or in combination with triamcinolone acetonide is safe and effective for the effectual treatment of atopic dermatitis pruritus. Twenty-four individuals with atopic dermatitis received doxepin or doxepin with triamcinolone acetonide cream 4 times daily for 7 days in a randomized, double-blind, controlled study. The pharmacokinetic profile of doxepin and desmethyldoxepin was evaluated after topical application of doxepin hydrochloride 5% cream alone or in combination with triamcinolone acetonide 0.025%. It was concluded that topically applied doxepin is a safe and effective therapy for pruritus. Therefore, more research is needed [24].

Melatonin (N-acetyl-5-methoxytryptamine) is a neurohormone produced mainly by the pineal gland and is directly involved in the regulation of physiological processes, such as the circadian cycle, sleep induction, antioxidant activity, immune and cardiovascular regulation, and neuroprotective effect. In physiological conditions, plasma concentration of melatonin follows a circadian rhythm, low levels during the day and high levels at night. Decreased nocturnal secretion is associated with sleep disturbances and greater severity of AD in children. Due to its sleep-inducing and anti-inflammatory properties, melatonin may be useful in the treatment of AD [19,25].

Activation of the immune system leads to the production of free radicals associated with a decrease in melatonin levels and a decrease in the activity of antioxidant enzymes in several inflammatory diseases. Many skin diseases, including AD, are accompanied by infiltration and activation of mast cells, which release vasoactive and pro-inflammatory mediators. Experimental data suggest that melatonin inhibits the development of AD and reduces serum total IgE and IL-4 [26].

A study carried out by Chang et al., in Taiwan, aimed to evaluate the effectiveness of melatonin supplementation to improve sleep disorders and disease severity in children with AD. Seventy-three children and adolescents, aged 1 to 18 years old diagnosed with AD, involving at least 5% of the total body surface area, were evaluated. Forty-eight children were randomized 1:1 to treatment with melatonin 3 mg/day or placebo. The primary outcome was AD severity assessed by SCORAD. Secondary outcomes included sleep variables measured by actigraphy, subjective changes in sleep and dermatitis, sleep variables measured by polysomnography, nocturnal urinary 6-sulfatoxymelatonin levels, and serum IgE levels. No patients withdrew due to adverse events and no adverse events were reported during the study. The authors concluded that melatonin supplementation is a safe and effective way to improve sleep onset latency and disease severity in children with AD [25].

Psychological stress can aggravate AD symptoms, generating more stress and maintaining a cycle of worsening [5]. It has been shown that salivary melatonin levels are reduced in patients with AD compared to those without AD. At the same time, melatonin production is reduced by stress. However, a study carried out in Japan, with 24 patients with AD and an average age of 14 years, found an increase in salivary melatonin levels after stimulation, which in this case was "watching a humorous film" [27].

However, the effects of melatonin in controlling AD are not only explained by the control of the circadian rhythm or the sedative effect. According to the study carried out by Marseglia et al., it showed that melatonin could be an invaluable therapeutic option in the future in the treatment of AD, as it exerts immunomodulatory and anti-inflammatory effects and helps maintain the integrity of the skin barrier in patients with AD, acting to control skin inflammation [26].

Currently, the use of melatonin is only approved for adults, but according to its good safety profile, without association with serious adverse effects, it has become a favorable option in children, as an adjunct in the treatment of sleep disorders caused by AD in children. Therefore, more studies are needed to correctly indicate melatonin for the treatment of children, as well as the dose and therapeutic duration [15].

In addition to pharmacological therapies, there are non-pharmacological ones. The importance of implementing methods to improve sleep such as sleep hygiene, adhering to regular bedtime and wake-up times, routinely maintaining a relaxing and peaceful sleeping environment, and avoiding caffeine intake are fundamental in order to prevent insomnia. which may persist after the disease is controlled [28].

More studies are needed to evaluate the benefits of mindfulness meditation in improving sleep disorders in patients with AD. However, this practice has recently been used to treat insomnia in adults and adolescents and has been suggested that it could be useful in the treatment of other dermatological diseases [29].

Discussion

AD is one of the most common chronic inflammatory skin diseases and there are reports of the association of this with sleep disorders in 47% to 80% of children and are a worrying

problem that harms the quality of life of patients and their families. Poorer sleep quality makes these children more likely to itch, which will further aggravate skin inflammation and lead to increased severity of the skin disease [5,11,25].

In general, the greater the severity of AD, the greater the prevalence and severity of sleep disorders. It is described that during AD attacks, sleep disturbances increase from 60% to 83%. Sleep disorders have been linked to reduced happiness, impaired performance on neurobehavioral tasks, hyperactivity/inattention, behavioral and emotional disturbances, and stunted growth [11].

It is important to remember that correct and regular treatment of AD improves skin lesions, reduces pruritus, SCORAD and visual analogue sleep scales, but has not been associated with improvements in sleep duration, efficiency, latency, number of awakenings or awakenings after sleep onset [2].

Several studies have evaluated sleep in patients with AD, using subjective questionnaires or within eczema severity scores, such as SCORAD, which can generate assessment bias. Studies that applied sleep questionnaires to parents of children with AD observed that around 60% of patients with AD have sleep disorders, and this percentage increased to 83% during AD crises [11].

Cohort study carried out in the United Kingdom, evaluating children (N = 13,988) aged 1 year and monitored with AD and sleep until 16 years of age. Standardized measures of sleep duration were performed and composite measures of sleep quality, including nighttime awakenings, morning awakenings, difficulty initiating sleep, and nightmares, were repeated at various times. It concluded that AD appears to be associated with impaired sleep quality during childhood and suggested that clinicians consider sleep quality in all children with AD, especially those who also have asthma or allergic rhinitis and severe illness, and interventions are needed to improve sleep quality [13].

Treatment options for sleep disorders in AD are scarce in the literature. Pharmaceutical interventions for these conditions must be prescribed with caution and careful monitoring of possible adverse events must be carried out. Some authors recommend that the lowest possible dose be used to achieve the therapeutic effect. It is important to remember that some medications can trigger dependence and should therefore be used with caution, especially in pediatric patients [12].

Tricyclic antidepressants, such as doxepin and trimipramine, when prescribed in low doses, can improve sleep through sedative effects, leading to decreased sleep onset latency, prolonged sleep duration, and improved sleep efficiency. In addition to this effect, tricyclic antidepressants can also bring additional benefits in the treatment of depression and anxiety that may be comorbidities. In elderly patients, tricyclic antidepressants should be avoided or used with caution, in low doses, due to the sedative and anticholinergic effects that may be more pronounced in this age group. The indication of the age range for use varies according to some authors from 7 to 12 years old [12].

Itching is the most important symptom in AD and generates emotional impact. Most medications used to treat AD target inflammation and consequently will also have an effect on itching [30].

Antihistamines have been used for decades in attempts to relieve pruritus in patients with AD. However, only a few randomized controlled trials have been conducted and most of them have shown only a weak or no effect on reducing pruritus. Oral H1 antihistamines are widely used as a therapeutic adjunct in patients with AD and pruritus, despite the lack of evidence for their efficacy. First-generation antihistamines are used for sleep disorders in patients with AD because they can antagonize the inflammatory effects of histamine released by mast cells and basophils and can cross the blood-brain barrier resulting in a sedative effect. However, tolerance generally occurs after 4 to 7 days of treatment and the sedative effect disappears, which limits its usefulness in these patients. First-generation systemic antihistamines can compromise sleep quality and reduce REM sleep, and regular and prolonged use of sedating antihistamines is not recommended. Furthermore, anticholinergic adverse effects such as blurred vision and dry mouth should also be considered [25,30].

Mirtazapine is an adrenergic, histaminergic and serotonergic antagonist that can be indicated in patients with AD due to its antipruritic, anxiolytic, and sedative effects. Dry mouth and orthostatic hypotension are adverse effects described. Data are limited on pediatric dosing, but a dose of 7.5 mg per night and increase by 7.5 mg per week for individuals weighing less than 50 kg or 15 mg per week for individuals weighing more than 50 kg have been suggested up to a maximum daily dose of 45 mg [12].

Benzodiazepines, such as nitrazepam, are often prescribed for individuals who have difficulty sleeping. Benzodiazepines increase the opening frequency of the γ-aminobutyric acid (GABA) receptor to cause sedation; long-acting benzodiazepines are typically prescribed for insomnia and may decrease sleep latency and increase sleep duration and possibly affect sleep architecture by decreasing REM sleep. They have sedative and anxiolytic effects, but present risks of tolerance to sedative effects, rebound of sleep disorders after interruption and dependence. Muscle relaxation and memory problems can have adverse effects. Benzodiazepines are not recommended for use in children and should only be used as a last resource [12,25].

Chloral hydrate and clonidine have also been used, but supporting evidence has been limited [25].

A study carried out by Chang et al. demonstrated that

melatonin significantly reduces the latency to sleep onset by an average of 23.4 minutes (52.1%) and a significant increase in sleep induction time in children with AD, and this was quite important, as an increase in serum melatonin levels was observed and a positive impact on efficiency and lower sleep fragmentation, as well as an improvement in the quality of life of children with AD [25].

Melatonin is a neurohormone that influences the regulation of the circadian sleep-wake rhythm, in addition, melatonin appears to have other actions such as antioxidant action and an effect on immune modulation. In the context of sleep disorders melatonin appeared safe and effective in improving sleep in the studied children. Although the overall quality of the evidence is limited due to heterogeneity and inconsistency. Further research is needed [31].

Chang et al. found in a study that included 73 children and adolescents diagnosed with AD aged between 1 and 18 years, that when administering 3 mg of oral melatonin for 4 weeks at bedtime, it significantly reduced sleep latency time. Furthermore, it also observed a significant reduction in SCORAD in 66% of children. The study did not show an improvement in sleep quality, but this only reinforces the potential of melatonin as an anti-inflammatory and immunomodulatory agent in AD [25].

AD is a complex and multifactorial disease and the treatment of sleep disorders in children with AD remains a challenge, as previously reported, in some cases, despite the improvement of skin lesions, the sleep disorder persists. There are few studies and some series or case reports, and many medications are off label for use in the pediatric age group. More research is needed in this field to help with this frequent condition that has such an impact on patients' quality of life.

Conclusions

AD is a frequent, complex disease with many triggering and aggravating factors, compromising patients' quality of life and sleep. Treating this disease and sleep-disrupting treatments resulting from AD is challenging. Nowadays, there are still few studies and many medications are off-label for use in the pediatric age group, impacting the therapeutic arsenal. More studies are needed to expand the therapeutic possibilities.

Limitations

There are few studies regarding the treatment of sleep disorders in children with AD, which limits our knowledge and therapeutic options.

Acknowledgments

Despite the great impact it can have on the lives of patients with AD and their families, there are few studies on sleep disorders in this disease. Furthermore, many medications cited in the literature for the treatment of sleep disorders are prescribed off-label in the pediatric age group. We highlight these points as a limitation of our research and the need for greater efforts to contribute to the treatment of this challenging disease. No funding or sponsorship was received for this study or publication of this article.

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