Section 11 Discussion

Symptoms, risk and diagnosis

Atopic dermatitis (AD) is a chronic, inflammatory skin condition with clinical features varying based on age of the patient.[1] It is associated with other atopic manifestations such as asthma, rhinitis and food allergy.[2-4] It presents in varying degrees of severity from a mild disease treated with over-the-counter products to severe disease requiring treatment with systemic immunosuppressive agents.[5] AD can be classified into either intrinsic or extrinsic AD with the classification of disease depending on co-existence with allergic features.[6] Common symptoms of AD include itchiness, red to brownish-grey patches on the skin, small, raised bumps, which may leak fluid and crust over when scratched, and/or thickened, cracked, dry, scaly skin.[7] Onset of AD occurs most commonly in infants and children, however it can occur at any age with clinical features varying with age of onset.[8]

In this PEEK study, the most common symptoms leading to diagnosis were rash-like symptoms and thickened, cracked, dry, scaly skin, which is consistent with the literature. An additional condition that led to the diagnosis of AD was allergies. This is an important observation as it demonstrates a common pathway in which eczema is diagnosed.

People with AD are at risk of infectious, systemic, and psychosocial comorbidities.[9] Infectious complications in AD have been reported with majority of secondary infections being bacterial.[10] AD patients are at higher risk of developing disseminated viral infections such as herpes virus and coxsackie virus[11]and they are also at a higher risk of developing other atopic diseases such as asthma, food allergy and allergic rhinitis, which is sometimes referred to as “atopic march”[12] People affected by AD and their caregivers often experience sleep disturbances[13] and patients may be self-conscious about their appearance and may avoid public appearances which leads to an increased emotional burden.[14] Stress is known to trigger itch and general flares in AD patients thereby exacerbating their condition.[14]

The main diagnostic features of AD are chronic relapsing dermatitis with pruritus (itch), xerosis (dry skin) and eczematous lesions along with specific clinical criteria.[15] Diagnosis can be aided by presence of dermatographism (raised welts), keratosis pilaris (small, hard bumps), hyperlinear palms (increased marking on the palms), periorbital (area around the eye) changes, perifollicular (area around hair follicle) accentuation, and pityriasis alba (pale pigmentation of the skin).[10] It is crucial to exclude these skin conditions to confirm AD diagnosis.[16]

In this PEEK study, the most common tests recalled were skin examination only followed by skin examination, blood test, patch test and review of medical history. There were very few instances where there was a misdiagnosis suggesting that the diagnostic pathway for this cohort of patients was relatively linear.

Treatment

The main goal of AD management is restoring the disrupted epithelial barrier, with topical therapy the most common method of current treatment.[17] These include emollients, topical corticosteroids, antihistamines, topical calcineurin inhibitors and antimicrobial and antiseptic measures with some patients requiring additional oral immunosuppression therapy. [17]

A systematic review conducted by Nankervis et al. in 2016 assessed a total of 541 randomised control trials including 92 interventions for AD treatment.[18] The results of this review indicated that very few treatments were of significant benefit. The review showed that widely used treatments such as emollients, impregnated bandages and topical corticosteroids did not result in any significant benefit, however, the authors note that ceasing treatment would not benefit patients as more research is still needed on the potential drawbacks and harms of each treatment.[18]

Therapies including Atopiclair ® emollient,[19-23] ultraviolet light therapy,[24,25] cilcosporin[26-29] for severe AD and azathioprine for moderate to severe AD[30,31] have been observed through clinical trials to offer benefit, while oral prednisolone, methotrexate, mycophenolate mofetil, biological therapies (omalizumab; mepolizumab), intravenous immunoglobulin and montelukast have potential of benefit but require more research.[32-51]

Targeted immune therapy is an emerging area and offers a new form of treatment for patients with AD. There are a number of target biologics being investigated for the treatment of moderated to sever AD[52-57], however dupilumab is the most advanced in relation to studies conducted and proven efficacy.[17]

While new therapies are emerging, the most common treatment experienced by participants in this PEEK study was corticosteroid cream. In relation to quality of life while using treatments, all treatments score relatively poorly with mean quality of life scores ranging from 'life was distressing' to 'Life was a little distressing'. In addition, participants found current treatments to be between ineffective to moderately effective only. It is therefore not surprising that there was a clear and reasonable call from participants in this study for new treatments to offer a more holistic approach and the expectation that treatments would be safe and not be detrimental to their long-term health.

Biomarkers

The current classification of AD inadequately reflects the pathophysiology and diversity of the disease.[58] The current treatment for patients not responding to topical therapy is systemic immunosuppressive therapy[17] and biomarkers have the potential to aid in predicting treatment outcomes of immunosuppressive therapy by monitoring the pharmacogenetics and therapeutic effect of drugs been given.[58] Biomarker-based stratification can also help in predicting the response of the new targeted therapies.[58]

Filaggrin gene mutations, which have the potential to be used as a prognostic biomarker, are frequently found in patients with severe AD and in patients who have an early onset AD.[59] The use of biomarkers is scarce in AD treatment but has the potential to optimise and personalise treatment,[58] for example, monitoring isoenzymes CYP34A and CYP3A5 which control bioavailability and systemic clearance of cylcosporin, can be used as biomarkers to guide AD treatment.[60] There are currently no predictive biomarkers available and the adequacy of these measures requires additional research.[58]

The results of this PEEK study are consistent with the availability and progress made in the area of biomarker research. The majority of participants had not had a discussion about biomarker, however it is important to note that if and when a test does become readily available, the majority of patients are likely to be interested in accessing it.

Complementary therapies

The interplay between genetic predisposition, skin barrier defects, environmental factors and immune dysfunction, contribute to the complexity of AD.[61] Due to the recurrent nature of AD throughout life, it is often managed it with complimentary therapies in conjunction with conventional therapies.[61]

Some common complementary therapies include vitamins and probiotics, however the research to support their use in alleviating AD remains limited.[62,63] Herbal therapies in the form of tea or tinctures, creams and lotions have been used to reduce inflammation in AD.[61] Acupuncture and acupressure which stimulate certain points in the body have also been used to reduce symptoms of AD.[61,64]

Stress and anxiety, which are known as triggering factors of AD, may be reduced by massage therapy.[65,66] Some studies also show that hypnotherapy can aid in healing of eczema by influencing the subconscious.[64,67] Essential oils like German chamomile and yarrow can

possibly help in reducing inflammation when used in aroma therapy [61,64] However, it is important to note that with these complementary therapies, further research is needed to confirm their effectiveness in relation to AD symptom alleviation.[61]

The main treatments that participants in this PEEK study considered as complementary therapies was using various creams and gentle soaps as complementary therapies and dietary changes. Food exposure has been associated with triggering AD[63] and patients are often recommended to avoid foods such as dairy, gluten and sugar.[61] There are however no specific overall diet that have been demonstrated to control the symptoms of AD beyond avoiding foods that individuals are allergic to.[64]

Quality of life

As AD is known to have both a physiological and psychological impact and it is important to have tools which can measure QOL and disease severity.[68-71] A systematic review conducted in 2016 indicated that there is an absence of a single, standard measurement for QoL in AD, rather there is a large number varied instruments measuring QOL and disease severity.[69] AD is also known to have a significant, negative on quality of life (QoL) and is also associated with poor health related quality of life (HRQoL).[70,72]Patients with moderate to severe AD have been observed to have a more significant impact on their QoL in contrast to those with mild AD[70,72] which can include significant financial losses due to inability to go to work.[72] AD treatment also adds a financial burden to the patient and their families including specialist consultations, medications and over the counter treatments.[73]

Individuals suffering from AD often experience sleep deprivation and tiredness, with sleep and mood disorders reported more frequently in people affected by AD affected patients compared to the general population.[74] The theme of impact on sleep was explored in this PEEK study where close to half of all participants described AD having an impact on sleep and this primarily referred to itchiness.

The psychological impact of AD has also been recorded, with patients experiencing embarrassment due to their appearance thereby reducing their social interaction and often leading them to alienate themselves from society.[75-77] This may in turn results in psychological problems due to isolation.[78] The impact on relationships in relation to self-esteem and confidence/being embarrassed was certainly a theme within this PEEK study and an area where interventions to ameliorate this are greatly needed.

AD is known to be a time-consuming condition as patients and their care givers often need to spend more than an hour in management of it.[69,75] Participants in this PEEK study spoke about the time required to shower and get ready, which was anywhere between 20 minutes to over one hour, while other participants spoke about the routine that they needed to adhere to in order to get ready each day. The descriptions provided by participants of this process in itself gives us insights into what people with AD go through each and every day and we would encourage decision-makers to read through these descriptions and indeed this report so that they have a better understanding of the impact that AD has on individuals.

Comordities associated with AD such as allergic rhinitis, asthma and food allergy also negatively impact quality of life.[75] An overall assessment of the patient's condition by enquiring about physical symptoms and its impact on their work/school life and sleep may help in better assessment of QOL of the patient.[79] It is also important to educate patients and their families about the chronic relapsing nature of AD to help them have a better understanding of the disease and reduce their subsequent frustration during treatment.[79]

This concept was noted by a number of participants in this PEEK study that called for more follow-up and care planning to manage their AD and also, more information and support to both identify triggers leading to flares, and how to manage them.

Health professional communication and multidisciplinary approaches

It has been suggested that it is important to have standard nomenclature for AD to avoid unnecessary confusion and so that patients can easily recall the disease they might be suffering from and have better understanding of the skin disorder.[80] Standard nomenclature is also important for entering the disease in clinical trials,[80] and a systemic review conducted in 2016, showed that AD was the most common term used overall.[81] It was also recommended to use only AD across all publications, health care clinician training and in patient education to avoid confusion.[81]

Management of AD requires a multidisciplinary approach due to the complex nature of the disease. Patients and their families require a wide range of information, skills and support to be able to cope with the condition.[82] This is particularly important as there is often a lack of knowledge and skills needed to follow treatment plans which hinders disease management.[83]

As noted previously, there was a call for more follow-up and care planning from AD patients in this PEEK study, suggesting an active interest in maintaining control over their condition. A multi-disciplinary approach includes an AD specialist to medically evaluate and manage the patient, provision of psychological and behavioural support, education and nursing care and nutritional assessment and guidance.[84] A multidisciplinary approach has been observed to be beneficial in decreasing the severity of disease and improving QoL, however more research is needed to identify those patients with AD that will benefit most from a multidisciplinary approach and to evaluate its cost-effectiveness. [83]

Information and education

Technology can play an important role in informing and educating patients about any disease. Social media platforms are also being used exchange information and engage in online discussions on different health topics.[85] Scientific journals and professional organisations are also using these platforms to disseminate information about treatments and support and patient decision making is increasingly influenced by the information available online.[85] It follows that with the growing use of internet it essential for the information available to be correct and consistent. A study by Corcimaru (2017) revealed that, recent google media trends in relation to AD have shown that the term eczema is more popular than AD.[86] The study recommends using word eczema in online education materials to improve communication.

This is in contrast to the study by Kantor (2016) that was previously discussed where the recommendation was to use only AD across all publications, health care clinician training and in patient education,[81] and while the rationale for this was to avoid any more confusion, there was no evidence presented to demonstrate that confusion existing from a patient perspective.

The participants in this PEEK study consistently used the term eczema to describe their condition, and there were no themes that emerged to suggest that the use of various terms was problematic. However, this was not a specific area of investigation within the study. It is also important to note that while participants in this PEEK study primarily accessed information online, their preference was to talk to someone about their condition.

Support/Psycho-social care

The overall, negative impact on QoL of AD affected patients and care givers needs to be managed in an effective manner.[87] Patients have identified challenges in having short appointments with their dermatologist causing them to have limited information about their treatment and reducing adherence to AD treatment.[87] The chronic nature of AD also

causes negative psychological impact and patients may experience depression, anxiety and frustration.[88]

In order to improve QoL, treatment of AD requires a multidisciplinary approach that includes behavioural therapy and psychotherapy in addition to dermatological therapy.[89] Therapeutic patient education (TPE) is an approach which includes patient centred care and can help in improving adherence, health outcome and QOL of life of AD affected patients and their families.[88] This approach helps healthcare providers to transfer information and skills needed by to cope and self-manage the disease and is a multidisciplinary including physicians, nurses, dieticians and psychologists.[88] An integral part of TPE is shared decision making where the patient and caregivers get to share their experience, concern and preferences regarding the treatment.[88] This information sharing process helps in identifying barriers faced by patient and can help in finding the solutions tailored to the needs of the patient and caregiver. There is also evidence that managing patient's expectations and discussing realistic outcomes of the treatment can increase adherence to treatment and lower psychological impact on the patient.[89]

A key feature of AD within this PEEK study was the impact of the condition on QoL where close to half of all participants described a significant impact in relation to self-esteem and confidence, often leading to social isolation. This is a significant observation and one that warrants intervention so that the impact of the physiological presentation of AD does not result in psychological disturbance.

Conclusion and characterisation of this patient population

People with AD are commonly diagnosed after observing rash-like symptoms and thickened, cracked, dry, scaly skin, with the presence of allergies also leading to the diagnosis of AD. To reach a diagnosis, common tests include skin examination, blood test, patch test and review of medical history and there is a relatively linear diagnostic pathway for this patient population. While new therapies are emerging, corticosteroid creams remain the most common form of treatment, however most treatments score relatively poorly in relation to how they impact the QoL of a patient. In addition, most treatments are considered to be ineffective to moderately effective only. As a result, this population of patients are reasonably calling for new treatments that offer a more holistic approach and are safe and not detrimental to their long-term health.

This is also a patient population that is significantly affected by the psychological impact of their condition, including patients experiencing embarrassment due to their appearance, reduction in social interaction and increased alienation from society. This is an area where interventions to ameliorate this are greatly needed so that the impact of the physiological presentation of AD does not result in psychological disturbance.

An area of future development in the care for patients with AD is coordinated and multidisciplinary care, and this was identified by the patient population who called for more follow-up and care planning.

AD is also known to be a time-consuming condition and this patient population is required to conduct a regular and diligent routine in order to maintain their health. This is sometimes a difficult concept for people who do not have AD to understand, and we encourage people to take the time to read through this report so that more empathy and compassion can be shown to those suffering with AD.

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