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PROBIOTICS IN TREATMENT OF ATOPIC DERMATITIS – KNOWLEDGE AND ATTITUDE AMONG SERBIAN PHYSICIANS

PROBIOTICI U TERAPIJI ATOPIJSKOG DERMATITISA – ZNANJA I STAVOVI SRPSKIH PEDIJATARA

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Summary Introduction: Since the 1970s, AD incidence has increased 2- to 3-fold in industrialized nations, impacting approximately 15% to 20% of children, 5% to 20% of adolescents.

Materials and methods: This was 6 months (January to June 2024) retrospective study collecting data through a web-based questionnaire designed to measure knowledge and attitude of Serbian physicians towards AD diagnosis, treatment and prevention strategies. The participants were healthcare professionals, specialists who are treating patients with AD. Surveys can reveal gaps in knowledge, concerns about safety or effectiveness, and the need for further training or support. This insight can help improve clinical guidelines, promote evidence-based practices, and ensure patients receive comprehensive and up-to-date care.

Results: Patients with Atopic Dermatitis in Serbia were mostly treated by physicians specialized in pediatrics and dermatology (210 dermatologist and 218 pediatricians were included). Virtually all participants agreed that discovering and avoiding triggering factors are crucial to keep AD under control. Among our participants diagnosing and staging of AD are mostly based on clinical criteria including assessment of itching intensity and sleep disturbance using visual analogue scales and overall quality of life.

Discussion: Results of our survey has the potential to identify current knowledge gaps and attitudes of physicians who are treating patients with atopic dermatitis. Physicians who experience less difficulties while treating AD have more positive practice attitudes and treatment satisfaction rates.

Conclusion: Continuous medical education, open-mindedness to evolving evidence, and a genuine commitment to understanding the patient's lived experience are essential for elevating care quality in this challenging and burdensome condition.

Keywords: atopic dermatitis, children, probiotics

Sažetak Uvod: Od 1970-ih, incidenca atopijskog dermatitisa (AD) se povećala 2 do 3 puta u industrijalizovanim zemljama, pogađajući približno 15% do 20% dece i 5% do 20% adolescenata.

Materijali i metode: Ovo je bila retrospektivna studija u trajanju od 6 meseci (od januara do juna 2024. godine) koja je prikupljala podatke putem veb upitnika osmišljenog da proceni znanje i stavove srpskih lekara prema dijagnozi, lečenju i strategijama prevencije AD. Učesnici su bili zdravstveni radnici, specijalisti koji leče pacijente sa AD. Ankete mogu otkriti praznine u znanju, zabrinutost u vezi sa bezbednošću ili efikasnošću i potrebu za daljom obukom ili podrškom. Ovo istraživanje može pomoći u poboljšanju kliničkih smernica, promovisanju praksi zasnovanih na dokazima i osiguravanju da pacijenti dobijaju sveobuhvatnu i ažurnu negu.

Rezultati: Pacijente sa atopijskim dermatitisom u Srbiji uglavnom su lečili lekari specijalisti pedijatrije i dermatologije (uključeno je 210 dermatologa i 218 pedijatara). Gotovo svi učesnici su se složili da je otkrivanje i izbegavanje faktora koji izazivaju AD ključno za držanje AD pod kontrolom. Među našim učesnicima dijagnostikovanje i određivanje stadijum atopijskog uglavnom se zasnivaju na kliničkim kriterijumima, uključujući procenu intenziteta svraba i poremećaja spavanja korišćenjem vizuelnih analognih skala i ukupnog kvaliteta života.

Diskusija: Rezultati našeg istraživanja imaju potencijal da identifikuju trenutne praznine u znanju i stavove lekara koji leče pacijente sa atopijskim dermatitisom. Lekari koji imaju manje poteškoća tokom lečenja Alchajmerove bolesti imaju pozitivniji stav prema praksi i stopu zadovoljstva lečenjem.

Zaključak: Kontinuirano medicinsko obrazovanje, otvorenost prema novim dokazima i istinska posvećenost razumevanju životnog iskustva pacijenta su neophodni za podizanje kvaliteta nege u ovom izazovnom i teškom stanju.

Ključne reči: atopijski dermatitis, deca, probiotici

INTRODUCTION

Since the 1970s, AD incidence has increased 2- to 3-fold in industrialized nations, impacting approximately 15% to 20% of children, 5% to 20% of adolescents. The natural course of the disease could be either relapsing-remitting or persistent and even mild to moderate.

Chronic itch, sleep deprivation, and stigmatization in AD can cause heavy disruption of the quality of life of patients and their families (1,2). Genetic (eg, filaggrin [FLG] mutations), chemical (increase in pH), and immunologic (shift toward TH2 cell response) factors in addition to microbial dysbiosis play an important role in complex pathophysiology mechanism of atopic dermatitis (3-6). Recently a plenty of new therapeutical modalities more focus on the underlying

disease mechanism has been developed, rather than focusing on symptom control like the old once. As an integral part of the healthy skin barrier, the skin microbiome constitutes a promising therapeutic target relevant to the pathophysiology of AD and barrier integrity. The skin microbiome is established even prenatal with a further development in the first two years of life under the influence of both genetics and environmental factors (7-9). Afterwards the skin microbiome remains relatively stable in healthy individuals (7,10,11). The skin is made up of different microenvironment with different levels of sebum, moisture, and differences in pH. These factors strongly influence the ecologic niche and microbial composition. Current data suggest that gut dysbiosis, especially if it happens early in life, contributes to the development of inflammatory conditions including allergies (atopic dermatitis, food allergies and finally respiratory allergies) (12-14). Probiotics are living, nonpathogenic microorganisms that are used to promote a healthy microbial ecosystem (15). There is ongoing debate regarding the impact of probiotics on the prevention and progression of AD, as well as their potential therapeutic value. However, the significance of probiotics in topic application and food supplementation as an alternative treatment approach in the emerging “postantibiotic” era is gaining considerable attention and significance (16-18).

METHODS

Design and Study Setting

This was 6 months (January to June 2024) retrospective study collecting data through a web-based questionnaire designed to measure knowledge and attitude of Serbian physicians towards AD diagnosis, treatment and prevention strategies. The participants were healthcare professionals, specialists who are treating patients with AD. Ethics committee approval was not required for this research.

Participants

Physicians were recruited through an independent online database Medscape of validated physicians who had consented to participate in research. Physician anonymity was maintained throughout the survey. Surveying physicians' attitudes toward treating atopic dermatitis (AD) is crucial for understanding how they approach both conventional and emerging treatment options. With the growing availability of advanced therapies like biologics and JAK inhibitors, as well as increased interest in supplements such as probiotics and vitamins, it's important to assess physicians' knowledge, acceptance, and use of these treatments. Their attitudes directly influence treatment choices, patient education, and overall quality of care. Surveys can reveal gaps in knowledge, concerns about safety or effectiveness, and the need for further training or support. This insight can help improve clinical guidelines, promote evidence-based practices, and ensure patients receive comprehensive and up-to-date care.

RESULTS

Of total 575 participants, 451 were included in the final sample (only those who are dermatologist n=210, general practitioner n=23 and pediatricians n=218). Results are presented as count (%), mean (SD) or median (minimum, maximum,

25th and 75th percentile). Groups based on specialization were compared using parametric (ANOVA) and non-parametric (Pearson chi square) tests. All p values less than 0.05 were considered significant. Patients with Atopic Dermatitis in Serbia were mostly treated by physicians specialized in pediatrics and dermatology (210 dermatologist and 218 pediatricians were included for analysis). Average age of the participants were 51.2 years with average work experience of 24 years, 68 males and 360 females. Almost 40% of responders treated patients with AD on daily basis, while 54.7% see 1-10 patients per week Table 1.

Table 1 Demographic characteristics of participating physicians

		N	%
Participants	Dermatologist	210	49.1%
	Paediatricians	218	50.9%

	N	Mean	SD	Min	P25	Median	P75	Max
Age	428	51.2	7.6	27.0	46.5	50.0	55.0	75.0
How long have you been working?	428	24.0	7.7	1.0	19.0	23.0	28.0	46.0

		N	%
Gender	Male	68	15.9%
	Female	360	84.1%

More than half of the physicians in our survey used clinical symptoms and/or laboratory tests to diagnose AD in their patients. Virtually all participants (100 99% and 93.1% respectively) agreed that discovering and avoiding triggering factors are crucial to keep AD under control. They marked cold weather, cosmetics and baths, the main triggers for AD relapse and exacerbation in their patients. Basic skin care and topical treatment have been chosen as the first line treatment for up to 96% responders. Among our participants diagnosing and staging of AD are mostly based on clinical criteria including assessment of itching intensity and sleep disturbance using visual analogue scales and overall quality of life. An adaptation of the diagnostic approach to the patients' age is required. The recommended diagnostic tool should be simple and could be supported by digital applications in the future. Criteria for AD severity scoring should consider the distribution pattern (localized vs. widespread, extent and localization of affected body surface area), the need for daily treatment for several weeks, the need for high potency steroids, the response to treatment, the recurrence of symptoms, infections, the presence of comorbidities, the age of disease onset, and the impact on quality of life. Dupilumab was the first specific therapeutic monoclonal antibody approved for the treatment of AD in 2017, in our survey only 9.8% of responders treated their patients with biologics and 11% were using cyclosporine.

According to the answers around half of the patients were satisfied or partly satisfied with the AD treatment. In responders' opinion the main reasons for unsatisfactory were treatment costs and fear of corticosteroids (31.8% and 30% respectively).

DISCUSSION

Progress in understanding the underlying pathophysiology and risk factors of atopic dermatitis could lead us to new preventive (prevention) strategy with primary goal of alleviating

symptoms. Results of our survey has the potential to identify current knowledge gaps and attitudes of physicians who are treating patients with atopic dermatitis. Physicians who experience less difficulties while treating AD have more positive practice attitudes and treatment satisfaction rates. When physicians consider that "it is possible to achieve good long-term control of AD," they achieve better treatment outcomes. In other words, differences in treatment goals affect physicians' practice and treatment outcomes. Prevention strategy with specialized formulation of three probiotics strains in combination with vitamin D3 and Zn could be aimed to induce deep and therapy free remission with probability on impacting associated comorbidities. However, to reach this goal, key areas require further exploration, including the definitions of disease modification and disease activity index, further understanding of disease mechanisms including the role of microbial dysbiosis and the potential windows of opportunity for prevention (primary and secondary).

Atopic dermatitis is a chronic, relapsing condition, and while treatments can effectively reduce or eliminate symptoms, there is no known cure that permanently eliminates the disease. In atopic dermatitis, "cured" is generally not used to describe the outcome. Instead, the condition is considered managed, meaning that symptoms are controlled and the disease is in remission, but it can still potentially return.

Double blind placebo-controlled trails and open label follow up studies gave us promising results regarding the possibility of specific probiotics to modify skin inflammation. Certain probiotics formulations might impact the pathological mechanisms and the natural course of the disease leading to a sustained remission long after cessation of treatment. In our study formulation of three probiotic strains *Lactobacillus casei* (*Lactocaseibacillus casei*) BL 2401, *Lactobacillus salivarius* (*Ligilactobacillus salivarius*) BL 2201, *Bifidobacterium Breve* BL 3406 (3×10^9 CFU) combination with 7mg Zinc and 1200 IJ Vitamin D3 were used in patients with atopic dermatitis, once daily for 3 months (19). The aim of this real-life intervention in intention to treat population was follow up long term efficacy of probiotic formulation enriched with Zinc and Vitamin D3 (Imunolak Kids D3+Zn) in the group of children who have previously add on treatment for atopic dermatitis with this probiotic formulation in duration of 3 months. Total of 75 children with mild to moderate AD which has been treated with Imunolak Kids D3+Zn were followed up for relapse (SCORD index) and quality of life (VAS scale) for 6 months after cessation of the probiotic enriched formulation supplementation.

Our findings were that 6 months after cessation of the treatment AD was under control, almost all of patients were still in remission. Although we noticed less respiratory tract symptoms during the study period, 3 months of probiotic supplementation did not have prolonged effect on respiratory allergies after treatment cessation. 3 months of probiotic treatment could have prolonged and adequate effects for AD control, but if we want to try to prevent atopic march overall particularly respiratory allergies, probiotic supplementation should be prolonged for at least 6 months to one year.

Future studies should be more focused on possibility of probiotics to successfully prevent the development and progression of atopic co-morbidities e.g. food allergies and/or allergic rhinitis before or during their manifestation. The aim of further research should be more focus on optimal duration of the treatment with probiotics and long-term efficacy.

The general objective of our survey was to provide a pragmatic and practical support to optimally manage of atopic dermatitis and its comorbidities at national level. The main aim was to strengthen national prevention programs and help to improve knowledge and attitudes of physicians who are treating patients with Atopic Dermatitis. Further activities will be organizing education through lectures and seminars in order to translate findings into practice and improve patient care in real-world settings. Surveys like this one might improve clinician-patient communication and patient satisfaction, could empower patients and their caregivers, engaging them to follow concept of shared decision making. As it has been shown both in our previous intervention trial (20) from patients point of view and in our latest survey, adherence to AD therapy is often poor, particularly for adequate moisturizer application and topical corticosteroid (TCS) treatment, the latter mainly due to the fear of side effects and steroid withdrawal symptoms (21). Food allergies and immunodeficiencies must be considered in patients with severe and/or persistent disease refractory to treatment, particularly in patients with an early onset. During our intervention study (20) we observed that children with more severe form of AD often have accompanying food allergies, particularly to peanuts, and are more likely to develop other allergic diseases such as asthma and AR later in life (22). Broader therapeutic strategies, including dietary interventions with specific probiotic formulations, psychological support, and lifestyle modifications (e.g., stress management, allergen avoidance), can play pivotal roles in disease control. Interdisciplinary collaboration with dermatologists, allergists, psychologists, and nutritionists enhances the comprehensiveness of care. Moreover, clinicians should remain informed about emerging research and alternative therapies with evidence-based support, as patient interest in integrative approaches continues to grow (23).

CONCLUSION

To improve long-term outcomes and patient satisfaction, physicians must broaden their clinical perspective in treating atopic dermatitis. This entails a shift toward holistic, personalized, and multidisciplinary management strategies that reflect the complexity of the disease. Continuous medical education, open-mindedness to evolving evidence, and a genuine commitment to understanding the patient's lived experience are essential for elevating care quality in this challenging and burdensome condition.

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