MAŁOLEPSZA, Aleksandra & DEMBOWSKI, Tomasz. Probiotics and gut-skin axis - new look on factors affecting skin condition. Journal of Education, Health and Sport. 2023;31(1):55-60. eISSN 2391-8306. DOI http://dx.doi.org/10.12775/JEHS.2023.31.01.005
https://apcz.umk.pl/JEHS/article/view/43683
https://zenodo.org/record/7944234

The journal has had 40 points in Ministry of Education and Science of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of December 21, 2021. No. 32343.
Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical Culture Sciences (Field of Medical sciences and health sciences); Health Sciences (Field of Medical Sciences and Health Sciences).
Punkty Ministerialne z 2019 - aktualny rok 40 punktów. Załącznik do komunikatu Ministra Edukacji i Nauki z dnia 21 grudnia 2021 r. Lp. 32343. Posiada Unikatowy Identyfikator Czasopisma: 201159.
Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).

The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 24.04.2023. Revised: 10.05.2023. Accepted: 17.05.2023. Published: 17.05.2023.

Probiotics and gut-skin axis - new look on factors affecting skin condition

Aleksandra Małolepsza
Bonifraterskie Centrum Medyczne sp. z o.o Oddział w Krakowie, ul. Trynitarska 11, 31-061 Kraków
ORCID: 0000-0002-0645-7824
ola.malolepsza@onet.pl

Tomasz Dembowski
Bonifraterskie Centrum Medyczne sp. z o.o Oddział w Krakowie, ul. Trynitarska 11, 31-061 Kraków
ORCID: 0000-0002-3323-4036
tomaszdembowski@gmail.com

SUMMARY

Introduction and purpose

The human gut microbiota consists of trillions of microscopic organisms, mostly bacterias. They play a significant role in nutrient metabolism, maintenance of structural integrity of the gut mucosal barrier, immunomodulation and protection against pathogens. Many factors can influence the composition of the intestinal microbiota, for example antibiotics, diet or stress. These factors may lead to dysbiosis which causes activation of neurotransmitters. It can results in the entry of metabolites to the blood stream, systemic immune dysregulation and alteration of skin microbiota. The aim of the study was to review the literature and determine the effects of intestinal microbiota and probiotics in selected skin diseases and what is new - skin aging process.

State of knowledge

We analyzed numerous studies which indicate that disturbed gut microbiota can be related to some chronic diseases, including skin disorders such as atopic dermatitis, acne vulgaris, psoriasis and rosacea. Additionally, it has been proven that bacterial dysbiosis can intensify the skin aging proces. In order to reproduce normal gut microbiota probiotics are used. Despite the fact that there are only a few studies showing the unequivocal effect of probiotics on skin diseases, their results seem to be encouraging.

Conclusions

Proper composition of the intestinal microbiome determines the homeostasis of the human body. Disturbance of the gut microbiome play a significant role not only in development and aggravation of many skin diseases, but also have an impact on the skin aging. Despite quite a lot number of studies assessing the impact of microbiota on certain skin disorders, there is still a need to evaluate impact of probiotics. Researches indicate that they can be used as a helpful therapeutic tool. Taking this into account, it is worth considering it in the treatment process.

Key words: gut microbiota; probiotics; gut-skin axis; skin aging; dermatology

Introduction and purpose

The human gut microbiota consists of trillions of microscopic organisms, mostly bacterias [1]. They play a significant role in nutrient metabolism, maintenance of structural integrity of the gut mucosal barrier, immunomodulation, and protection against pathogens [2]. Many factors can influence the composition of the intestinal microbiota, for example antibiotics, diet, hygiene, stress, immunodeficiency and hyperimmunity. These factors may lead to dysbiosis which causes activation of neurotransmitters. It can result in the entry of metabolites to the blood stream, systemic immune dysregulation and alteration of skin microbiota. In fact, the relation between the intestinal microbiota and skin homeostasis is two-way. The aim of the study was to review the literature and determine the effects of intestinal microbiota and probiotics in selected skin diseases and what is new - skin aging process. There are numerous studies which indicate that disturbed gut microbiota can be related to some chronic diseases, including skin disorders such as atopic dermatitis, acne vulgaris, psoriasis, hidradenitis suppurativa and rosacea [3, 4]. Additionally, it has been proven that bacterial dysbiosis can intensify the skin aging proces [5]. Skin microbiome is composed of bacterias such as Cutibacterium, Corynebacterium, Staphylococcus and Streptococcus and, exactly like the gut microbiome, plays an important role in protection from pathogens and regulation of the immune system.

Over century ago, Elie Metchnikoff, the Nobel Prize winner in Medicine, was the first who noticed the effect of what is now called „probiotic" [6]. Current definition of probiotics is ’live microorganisms which, when administered in adequate amounts, confer a health benefit on the host established by Food and Agriculture Organization of the United Nations/World Health Organization [7]. Oral intake of probiotics restore human gut microbiota and therefore - homeostasis.

Despite the fact that there are only a few studies showing the unequivocal effect of probiotics on skin diseases, their results seem to be encouraging [8].

Description of the state of knowledge

Atopic dermatitis (AD)

Atopic dermatitis (AD) is a chronic inflammatory skin disease caused by dysregulation of the immune system and gene mutations [9]. Symptoms that may occur are redness, irritation and thickening of the skin. AD treatment depends on the patient's age and severity of skin lesions. Severity of AD can be assessed by SCORAD scale. The greater the value, the greater the severity of the skin changes. Watanabe et al. conducted the study in which they

compared AD patients with healthy patients in terms of microbiome diversity [10]. When it comes to *the* gut microbiota, patients with AD had lower counts of Bifidobacterium and higher counts of Staphylococcus than in control group. Decrease in the amount of Bacteroides fragilis and Streptococcus, responsible for anti-inflammatory function, correlates with the severity of skin eczema [11]. The role of probiotics supplementation, both in the prenatal and the postnatal period, was assessed by Li et al. in meta-analysis, which proved that this action reduced the risk of AD in children [12]. Apart from this, it has been shown that using certain probiotics such as Bifidobacterium lactis CECT 8145, B longum CECT 7347, and Lactobacillus casei CECT 9104 reduced SCORAD value in adult patients with moderate AD [13]. Most likely, the mechanism of action of the probiotics is improvement in the lymphocytes Th1/Th2 ratio and reducing proinflammatory cytokines [14]. To sum up, this can be an additional element of the therapy of AD.

Acne

Acne is a common chronic inflammatory skin disease in which hair follicles become plugged with oil and dead skin cells. It usually appears in the form of closed and opened plugged pores, papules, pustules and cystic lesions. Acne therapy involves the use of continuous skin care, paying attention to the position of retinoids. Therapy is often long-term, and even after a long period of remission, the changes may recur.

Even though exact mechanisms by which the gut microbiota influence acne is unknown, there are some studies that emphasize this relation. Results of the study comparing microbiome of patients with acne and healthy control population was that the first group has decreased Firmicutes and increased Bacteroidetes amounts [15]. It can be assumed that disturbed intestinal microbiota affects acne. The results of various studies using probiotics in acne are promising [15]. They indicate anti-inflammatory effects and maintaining the integrity of the colon mucosa.

Psoriasis

Psoriasis is a chronic inflammatory skin disease where the inadequate reaction of the immune system is activated. It leads to elevation of pro-inflammatory cytokines. Symptoms of psoriasis are:

- heterogenous rash that varies in different people
- dry skin
- itching of the skin
- raised skin patches covered with scales.

The disease often affects various aspects of life, significantly impairing its quality. Research shows that the intestinal microbiota of people with psoriasis differs from healthy people [16]. Interestingly, people diagnosed with a specific type of psoriasis (pustular psoriasis vs psoriasis vulgaris) have diverse gut microbiota [17]. The results of research on the effect of probiotics on the course of psoriasis also seem to be very promising. Bifidobacterium infantis 35624 administration provided TNF-α reduction in psoriasis patients comparing to the placebo group [18]. Patients with a severe pustular psoriasis also benefited from administration Lactobacillus sporogenes [19]. Taking this into account, the inclusion of probiotics in psoriasis therapy may be considered.

Rosacea

Rosacea is a chronic inflammatory skin disorder manifesting by facial flushing, persistent facial erythema, telangiectasia or papules and pustules. Certain factors such as stress, alcohol (especially red wine), cigarettes, spicy and hot foods and drinks, foods containing histamine can exacerbate skin inflammation. What is more, patients with rosacea demonstrated increased amount of Demodex brevis and Demodex folliculorum on the skin. There is a theory that assumes that bacterial dysbiosis is involved in the development of rosacea through activation of plasma kallikrein-kinin pathways [20]. Various studies present concepts of the relation between the role of Helicobacter pylori in rosacea and

they tend to hypothesis that its eradication significantly improves the course of the disease [21, 22]. Probiotics are considered to be helpful tool in rosacea therapy [20].

Skin aging

Due to the development of medicine and the extension of lifetime, there is a need to look for solutions to delay the aging process. Aesthetic medicine and plastic surgery are often used for this purpose. It is worth to remember about basic methods of prevention, such as using sun protection creams. All in all, it is important not only in the context of skin aging, but also in the prevention of skin cancer.

The diversity of the composition of the intestinal microbiome decreases with age. These changes cause intestinal barrier impairment and leakage into the bloodstream of certain substances such as interferon-gamma (IFN-γ), IL-1, IL-6, matrix metalloproteinases (MMPs). It leads to chronic proinflammatory state and, in consequence, impair the removal of senescent cells [5].

It is estimated that the skin surface pH is on average 4.7. This acidic environment provides barrier homeostasis and antimicrobial defense [23]. Recent studies show that oral probiotics have a beneficial effect on its maintenance. Additionally they have a positive result on oxidative stress and photodamage. According to the latest research, all of these changes have favorable impact on skin aging [5].

Conclusions

Proper composition of the intestinal microbiome determines the homeostasis of the human body. Disturbance of the gut microbiome plays a significant role not only in development and aggravation of many skin diseases, but also have an impact on the skin aging process. Despite quite a lot number of studies assessing the impact of microbiota on certain skin disorders, there is still a need to evaluate impact of probiotics. Researches indicate that they can be used as a helpful therapeutic tool. Taking this into account, it is worth considering it in the treatment process.

References:

- DAS B, Nair GB. Homeostasis and dysbiosis of the gut microbiome in health and disease. J Biosci. 2019 Oct;44(5):117. PMID: 31719226.
- Jandhyala SM, Talukdar R, Subramanyam C, Vuyyuru H, Sasikala M, Nageshwar Reddy D. Role of the normal gut microbiota. World J Gastroenterol. 2015 Aug 7;21(29):8787-803. doi: 10.3748/wjg.v21.i29.8787. PMID: 26269668; PMCID: PMC4528021.
- Vijay A, Valdes AM. Role of the gut microbiome in chronic diseases: a narrative review. *Eur J Clin Nutr* **76**, 489–501 (2022). https://doi.org/10.1038/s41430-021-00991-6
- De Pessemier B, Grine L, Debaere M, Maes A, Paetzold B, Callewaert C. Gut-Skin Axis: Current Knowledge of the Interrelationship between Microbial Dysbiosis and Skin Conditions. Microorganisms. 2021 Feb 11;9(2):353. doi: 10.3390/microorganisms9020353. PMID: 33670115; PMCID: PMC7916842
- Ratanapokasatit Y, Laisuan W, Rattananukrom T, Petchlorlian A, Thaipisuttikul I, Sompornrattanaphan M. How Microbiomes Affect Skin Aging: The Updated Evidence and Current Perspectives. Life (Basel). 2022 Jun 22;12(7):936. doi: 10.3390/life12070936. PMID: 35888025; PMCID: PMC9320090.
- Amara AA, Shibl A. Role of Probiotics in health improvement, infection control and disease treatment and management. Saudi Pharm J. 2015 Apr;23(2):107-14. doi: 10.1016/j.jsps.2013.07.001. Epub 2013 Jul 18. PMID: 25972729; PMCID: PMC4421088.

- Food and Agriculture Organization/World Health Organization (FAO/WHO), 2001. Health and nutritional properties of Probiotics in food including powder milk with live lactic acid bacteria, Report of a Joint FAO/WHO Expert Consultation on Evaluation of Health and Nutritional Properties of Probiotics in Food including Powder Milk with Live lactic acid bacteria, Córdoba, Argentina. Available at: http://www.who.int/foodsafety/publications/fs_management/en/probiotics.pdf.
- Szántó M, Dózsa A, Antal D, Szabó K, Kemény L, Bai P. Targeting the gut-skin axis-Probiotics as new tools for skin disorder management? Exp Dermatol. 2019 Nov;28(11):1210-1218. doi: 10.1111/exd.14016. Epub 2019 Aug 28. PMID: 31386766.
- Frazier W, Bhardwaj N. Atopic Dermatitis: Diagnosis and Treatment. Am Fam Physician. 2020 May 15;101(10):590-598. PMID: 32412211.
- Watanabe S, Narisawa Y, Arase S, Okamatsu H, Ikenaga T, Tajiri Y, Kumemura M. Differences in fecal microflora between patients with atopic dermatitis and healthy control subjects. J Allergy Clin Immunol. 2003 Mar;111(3):587-91. doi: 10.1067/mai.2003.105. PMID: 12642841.
- Zheng H, Liang H, Wang Y, Miao M, Shi T, Yang F, Liu E, Yuan W, Ji ZS, Li DK. Altered Gut Microbiota Composition Associated with Eczema in Infants. PLoS One. 2016 Nov 3;11(11):e0166026. doi: 10.1371/journal.pone.0166026. PMID: 27812181; PMCID: PMC5094743.
- Li L, Han Z, Niu X *et al.* Probiotic Supplementation for Prevention of Atopic Dermatitis in Infants and Children: A Systematic Review and Meta-analysis. *Am J Clin Dermatol* **20**, 367–377 (2019). https://doi.org/10.1007/s40257-018-0404-3
- Umborowati MA, Damayanti D, Anggraeni S, Endaryanto A, Surono IS, Effendy I, Prakoeswa CRS. The role of probiotics in the treatment of adult atopic dermatitis: a meta-analysis of randomized controlled trials. J Health Popul Nutr. 2022 Aug 17;41(1):37. doi: 10.1186/s41043-022-00318-6. PMID: 35978397; PMCID: PMC9386980.
- Rusu E, Enache G, Cursaru R, Alexescu A, Radu R, Onila O, Cavallioti T, Rusu F, Posea M, Jinga M, Radulian G. Prebiotics and probiotics in atopic dermatitis. Exp Ther Med. 2019 Aug;18(2):926-931. doi: 10.3892/etm.2019.7678. Epub 2019 Jun 14. PMID: 31384325; PMCID: PMC6639913.
- Sánchez-Pellicer P, Navarro-Moratalla L, Núñez-Delegido E, Ruzafa-Costas B, Agüera-Santos J, Navarro-López V. Acne, Microbiome, and Probiotics: The Gut-Skin Axis. Microorganisms. 2022 Jun 27;10(7):1303. doi: 10.3390/microorganisms10071303. PMID: 35889022; PMCID: PMC9318165.
- Buhaș MC, Gavrilaș LI, Candrea R, Cătinean A, Mocan A, Miere D, Tătaru A. Gut Microbiota in Psoriasis. Nutrients. 2022 Jul 20;14(14):2970. doi: 10.3390/nu14142970. PMID: 35889927; PMCID: PMC9321451.
- Zhang, X., Shi, L., Sun, T. *et al.* Dysbiosis of gut microbiota and its correlation with dysregulation of cytokines in psoriasis patients. *BMC Microbiol* **21**, 78 (2021). https://doi.org/10.1186/s12866-021-02125-1
- Alesa DI, Alshamrani HM, Alzahrani YA, Alamssi DN, Alzahrani NS, Almohammadi ME. The role of gut microbiome in the pathogenesis of psoriasis and the therapeutic effects of probiotics. J Family Med Prim Care. 2019 Nov 15;8(11):3496-3503. doi: 10.4103/jfmpc.jfmpc_709_19. Retraction in: J Family Med Prim Care. 2021 Feb;10(2):1076. PMID: 31803643; PMCID: PMC6881942.
- Metikurke Vijayashankar M, Raghunath N. Pustular psoriasis responding to probiotics – A new insight. *Our Dermatol Online.* 2012;3:326–8.
- Weiss E, Katta R. Diet and rosacea: the role of dietary change in the management of rosacea. Dermatol Pract Concept. 2017 Oct 31;7(4):31-37. doi: 10.5826/dpc.0704a08. PMID: 29214107; PMCID: PMC5718124.

- Daou H, Paradiso M, Hennessy K, Seminario-Vidal L. Rosacea and the Microbiome: A Systematic Review. Dermatol Ther (Heidelb). 2021 Feb;11(1):1-12. doi: 10.1007/s13555-020-00460-1. Epub 2020 Nov 10. PMID: 33170492; PMCID: PMC7859152.
- Yang X. Relationship between Helicobacter pylori and Rosacea: review and discussion. BMC Infect Dis. 2018 Jul 11;18(1):318. doi: 10.1186/s12879-018-3232-4. PMID: 29996790; PMCID: PMC6042414.
- Ali SM, Yosipovitch G. Skin pH: from basic science to basic skin care. Acta Derm Venereol. 2013 May;93(3):261-7. doi: 10.2340/00015555-1531. PMID: 23322028.