Austin Journal of Dermatology

Austin Publishing Group

Open Access Full Text Article

Perspective

Considering the Gut-Skin Axis for Dermatological Diseases

Ali IA[1], Foolad N[2] and Sivamani RK[2]*

[1]School of Medicine, University of California-Davis, USA

[2]Department of Dermatology, University of California-Davis, USA

***Corresponding author:** Sivamani RK, Department of Dermatology, University of California, Davis, 3301 C Street, Suite 1400, Sacramento, CA 95816, USA

Received: August 08, 2014; **Accepted:** September 30, 2014; **Published:** October 02, 2014

Abstract

Assessment of dermatological ailments may require attention to the health of the gastrointestinal tract (GI, gut). Skin manifestations are well reported with certain diseases that affect the gastrointestinal tract such as Crohn's disease, ulcerative colitis, and dermatitis herpetiformis [1]. However, alterations in gut functions are starting to be recognized for primary dermatological diseases. Understanding the interplay between this gut-skin axis for cutaneous diseases may serve as a new avenue for developing novel therapeutic strategies.

Introduction

Skin disease and gut function

Several dermatoses appear to have a gut-skin connection, including acne vulgaris, Atopic Dermatitis (AD), psoriasis, and ichthyosis vulgaris. Acne vulgaris was first postulated to have GI connection approximately 80 years ago [2]. A 2013 study reported that the prevalence of Small Intestine Bacterial Overgrowth (SIBO) was higher in those with rosacea and 46% of these patients said their rosacea cleared or markedly improved upon treatment of SIBO with rifaximin [2,3]. Small intestinal biopsy samples taken from children with AD evaluating gut mucosa barrier function demonstrated enhanced transfer of intact and degraded proteins through the barrier relative to controls, increasing the antigenic load [4]. Multiple studies report that probiotic supplementation may improve AD [5-8], further supporting a gut-skin connection.

Psoriasis is an inflammatory skin disorder with associated inflammation of the internal organs and musculoskeletal system [9-12]. GI disorders are present in 28% of patients with psoriasis [13]. Common abnormalities in psoriasis patients include changes in the mucous membrane of the duodenum [14]. Psoriasis may cause dermatogenicenteropathy and intestinal inflammation [15]. Khardikova et al. evaluated the gastric and duodenal mucosa cells of 20 psoriasis patients and found degeneration of the epithelium of the intestinal villi and crypts [16]. Chronic duodenitis was reported in 25% of patients. In a study of psoriatic patients, 46% (12/26) had convoluted jejunal mucosa [15].

Ichthyosis results in thick and scaly skin [17]. A study by Fry et al. found alterations in the morphology of the mucosa of the jejunum in patients with ichthyosis [18]. Intestinal biopsies suggested that ichthyosis vulgaris altered the metabolic activity of the intestine due to the decrease of succinic dehydrogenase [18]. Ichthyosis can result in intestinal malabsorption of substances such as fats [19]. Individuals with Netherton syndrome, a severe form of ichthyosis had GI malabsorption due to jejunal villous atrophy [20,21]. A study of children with ichthyosis reported growth failure due to an impaired skin barrier [17]. A majority of the children had a history of constipation, elevated serum calcium and magnesium levels.

Microbiome of the gut and skin

Breastfeeding exposes infants to a diversity of antigens that have been processed by the mother's GI tract reducing their allergenic potential and aiding in oral tolerance; in addition, it provides non-pathogenic bacteria that will become the first colonizers for the infant's developing microbiome [7]. A study comparing the microbiota of Estonian and Swedish two-year olds with and without allergies found that allergic children in both countries had less colonization with commensal lactobacilli, *Bifidobacteria* and *bacteriodes* and greater colonization with aerobic bacteria, particularly coliforms and Staphylococcus aureus [22]. *In vitro* studies have shown that seven strains of sonicated *Bifidobacteria* were able to inhibit the growth of S. aureus S.P.-N2, and three strains were able to reduce the viability of P. acnes, the causative organism of acne vulgaris [23]. The exact mechanism by which *Bifidobacteria* exerts its antimicrobial action has yet to be delineated. Furthermore, different case studies reported contradictory findings for the role of *Bifidobacteria*, leading to the likeliness that specific species of the bacteria are beneficial while others are associated with atopy [24]. Kalliomäki et al. showed a 50% reduction in AD occurrence in children of at risk mothers who were treated with probiotics pre- and postnatal [8].

Gut and skin communication

Communication between the gut and the skin are not well described. Recent studies have shown how the epithelial cells of the intestine not only have a role in absorption and digestion, but in both immune and inflammatory response through secretion of cytokines [25-32]. The epithelium of the intestine secretes cytokines, which regulate inflammation [33]. T helper 17 cells (Th17) are controlled by the small intestine and are eliminated by the intestinal lumen [34]. Th17 are one source of IL-22, a cytokine that binds to receptors on keratinocytes and thus plays a role in the clearance of skin infections by increasing the antimicrobial defense of skin keratinocytes [35-38]. Further research will be needed to assess whether Th17 cell clearance in the gut is impaired in psoriasis, suggesting another mechanism for how the gut-skin axis is coordinated.

The mechanisms for how the gut and skin communicate are still poorly understood. For example, while probiotics have been shown to improve AD [5-8], it remains disputed whether this is due

Citation: Ali IA, Foolad N and Sivamani RK. Considering the Gut-Skin Axis for Dermatological Diseases. Austin J Dermatolog. 2014;1(5): 1024.

to an increase [39] or a decrease [40] in systemic inflammation. A variety of GI cells such as epidermal cells, Paneth cells, enterocytes, and macrophages synthesize various inflammatory cytokines, such as tumor necrosis factor [41]. It is not known how many of these peptides enter the bloodstream and may modulate dermatological disease. Future research will help better describe any potential communication between the gut and the skin.

Conclusion

There is growing evidence for a gut-skin connection. Inflammation and barrier defects in the gut appear to have correlation diseases of the skin. However, this is still an emerging field and there is much research that needs to be conducted to have a better understanding of the relationship between the gut and the skin. Understanding the role of the gut microbiome and its modulation is still in its infancy. Although several studies point to the promise of using probiotics for skin disease, we have not determined which strains of bacteria are best for barrier maintenance in the gut nor is it known what formulation, dosing and timing would be most helpful for probiotics that are orally ingested [7]. The building knowledge of the gut, gut microbiome, and how gut health may be related to skin health is a new paradigm for skin care research [7].

References

1. Marzano AV, Borghi A, Stadnicki A, Crosti C, Cugno M. Cutaneous manifestations in patients with inflammatory bowel diseases: pathophysiology, clinical features, and therapy. Inflamm Bowel Dis. 2014; 20: 213-227.
2. Bowe W, Patel NB, Logan AC. Acne vulgaris, probiotics and the gut-brain-skin axis: from anecdote to translational medicine. Benef Microbes. 2014; 5: 185-199.
3. Weinstock LB, Steinhoff M. Rosacea and small intestinal bacterial overgrowth: prevalence and response to rifaximin. J Am Acad Dermatol. 2013; 68: 875-876.
4. Majamaa H, Isolauri E. Evaluation of the gut mucosal barrier: evidence for increased antigen transfer in children with atopic eczema. J Allergy Clin Immunol. 1996; 97: 985-990.
5. Kim SO, Ah YM, Yu YM, Choi KH, Shin WG, Lee JY. Effects of probiotics for the treatment of atopic dermatitis: a meta-analysis of randomized controlled trials. Ann Allergy Asthma Immunol. 2014; 113: 217-226.
6. Panduru M, Panduru NM, Sălăvăstru CM, Tiplica GS. Probiotics and primary prevention of atopic dermatitis: a meta-analysis of randomized controlled studies. J Eur Acad Dermatol Venereol. 2014;.
7. da Costa Baptista IP, Accioly E, de Carvalho Padilha P. Effect of the use of probiotics in the treatment of children with atopic dermatitis; a literature review. Nutr Hosp. 2013; 28: 16-26.
8. Kalliomäki M, Salminen S, Arvilommi H, Kero P, Koskinen P, Isolauri E. Probiotics in primary prevention of atopic disease: a randomised placebo-controlled trial. Lancet. 2001; 357: 1076-1079.
9. Hannuksela-Svahn A, Pukkala E, Läärä E, Poikolainen K, Karvonen J. Psoriasis, its treatment, and cancer in a cohort of Finnish patients. J Invest Dermatol. 2000; 114: 587-590.
10. Khardikova SA, Beloborodova EI, Pesterev PN. Psoriasis and intestinal absorption. Tomsk. 2000.
11. Roenigk HH, Maibach HI. Psoriasis. New York. 1990.
12. Skripkin YK. Skin and Venereal Diseases. Moscow. 1995.
13. Krinitsina YM. Morphogenesis, Clinical Signs, and Several Aspects for Correction of Psoriasis in Modern Ecological Situation. Abstract of Doct. Med. Sci. Dissertation: Novosibirsk. 1998.
14. Pietrzak A, Lecewicz-Torun B, Kadziela-Wypyska G. Changes in the digestive system in patients suffering from psoriasis. Ann Univ Mariae Curie Sklodowska Med. 1998; 53: 187-194.
15. Shuster S, Watson AJ, Marks J. Small intestine in psoriasis. Br Med J. 1967; 3: 458-460.
16. Khardikova SA, Nepomnyashchikh GI, Aidagulova SV, Lapii GA. Ultrastructural characteristics of cell populations in the gastric and duodenal mucosa during psoriasis. Bull Exp Biol Med. 2002; 134: 489-493.
17. Fowler AJ, Moskowitz DG, Wong A, Cohen SP, Williams ML, Heyman MB. Nutritional status and gastrointestinal structure and function in children with ichthyosis and growth failure. J Pediatr Gastroenterol Nutr. 2004; 38: 164-169.
18. Fry L, McMinn RMH, Shuster S. The small intestine in skin diseases. Archives of Dermatology. 1966; 93: 647-653.
19. Marks J, Shuster S. Intestinal malabsorption and the skin. Gut. 1971; 12: 938-947.
20. Judge MR, Morgan G, Harper JI. A clinical and immunological study of Netherton's syndrome. Br J Dermatol. 1994; 131: 615-621.
21. Pradeaux L, Olives JP, Bonafe JL, Le Tallec C, Pigeon P, Ghisolfi J. [Digestive and nutritional manifestations of Netherton's syndrome]. [Article in French]. 1991; 48: 95-98.
22. Björkstén B, Naaber P, Sepp E, Mikelsaar M. The intestinal microflora in allergic Estonian and Swedish 2-year-old children. Clin Exp Allergy. 1999; 29: 342-346.
23. Lee DK, Kim MJ, Ham JW, An HM, Cha MK, Lee SW, et al. *In vitro* evaluation of antibacterial activities and anti-inflammatory effects of Bifidobacterium spp. addressing acne vulgaris. Arch Pharm Res. 2012; 35: 1065-1071.
24. Penders J, Stobberingh EE, van den Brandt PA, Thijs C. The role of the intestinal microbiota in the development of atopic disorders. Allergy. 2007; 62: 1223-1236.
25. Seydel KB, Li E, Swanson PE, Stanley SL Jr. Human intestinal epithelial cells produce proinflammatory cytokines in response to infection in a SCID mouse-human intestinal xenograft model of amebiasis. Infect Immun. 1997; 65: 1631-1639.
26. Crabtree JE, Peichl P, Wyatt JI, Stachl U, Lindley IJ. Gastric interleukin-8 and IgA IL-8 autoantibodies in Helicobacter pylori infection. Scand J Immunol. 1993; 37: 65-70.
27. Eckmann L, Kagnoff MF, Fierer J. Epithelial cells secrete the chemokine interleukin-8 in response to bacterial entry. Infect Immun. 1993; 61: 4569-4574.
28. Jung HC, Eckmann L, Yang SK, Panja A, Fierer J, Morzycka-Wroblewska E, et al. A distinct array of proinflammatory cytokines is expressed in human colon epithelial cells in response to bacterial invasion. J Clin Invest. 1995; 95: 55-65.
29. Kelly CP, Keates S, Siegenberg D, Linevsky JK, Pothoulakis C, Brady HR. IL-8 secretion and neutrophil activation by HT-29 colonic epithelial cells. Am J Physiol. 1994; 267: G991-997.
30. Kim JM, Jung HC, Im K, Cho YJ, Kim CY. [Interleukin-8 gene expression in the human colon epithelial cell line, HT-29, exposed to Entamoeba histolytica]. Korean J Parasitol. 1995; 33: 357-364.
31. McCormick BA, Hofman PM, Kim J, Carnes DK, Miller SI, Madara JL. Surface attachment of Salmonella typhimurium to intestinal epithelia imprints the subepithelial matrix with gradients chemotactic for neutrophils. J Cell Biol. 1995; 131: 1599-608.
32. Eckmann L, Reed SL, Smith JR, Kagnoff MF. Entamoeba histolytica trophozoites induce an inflammatory cytokine response by cultured human cells through the paracrine action of cytolytically released interleukin-1a. J Clin Invest. 1995; 96: 1269-1279.
33. Stadnyk AW. Intestinal epithelial cells as a source of inflammatory cytokines and chemokines. Can J Gastroenterol. 2002;16: 241-246.
34. Esplugues E, Huber S, Gagliani N, Hauser AE, Town T, Wan YY, et al. Control of TH17 cells occurs in the small intestine. Nature. 2011; 475: 514-518.

35. Pan HF, Li XP, Zheng SG, Ye DQ. Emerging role of interleukin-22 in autoimmune diseases. Cytokine Growth Factor Rev. 2013; 24: 51-57.

36. Akdis M, Palomares O, van de Veen W, van Splunter M, Akdis CA. TH17 and TH22 cells: a confusion of antimicrobial response with tissue inflammation versus protection. J Allergy Clin Immunol. 2012; 129: 1438-1449.

37. Wolk K, Witte E, Wallace E, Döcke WD, Kunz S, Asadullah K, et al. IL-22 regulates the expression of genes responsible for antimicrobial defense, cellular differentiation, and mobility in keratinocytes: a potential role in psoriasis. Eur J Immunol. 2006; 36: 1309-1323.

38. Bedoya SK, Lam B, Lau K, Larkin J 3rd. Th17 cells in immunity and autoimmunity. Clin Dev Immunol. 2013; 2013: 986789.

39. Viljanen M, Pohjavuori E, Haahtela T, Korpela R, Kuitunen M, Sarnesto A, et al. Induction of inflammation as a possible mechanism of probiotic effect in atopic eczema-dermatitis syndrome. J Allergy Clin Immunol. 2005; 115: 1254-1259.

40. Jung BG, Cho SJ, Koh HB, Han DU, Lee BJ. Fermented Maesil (Prunus mume) with probiotics inhibits development of atopic dermatitis-like skin lesions in NC/Nga mice. Vet Dermatol. 2010; 21: 184-191.

41. De Smet K, Contreras R. Human antimicrobial peptides: defensins, cathelicidins and histatins. Biotechnol Lett. 2005; 27: 1337-1347.

Austin J Dermatolog - Volume 1 Issue 5 - 2014
ISSN : 2381-9197 | www.austinpublishinggroup.com

Citation: Ali IA, Foolad N and Sivamani RK. Considering the Gut-Skin Axis for Dermatological Diseases. Austin J Dermatolog. 2014;1(5): 1024.