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CLINICAL EFFICIENCY OF SYNBIOTIC THERAPY (PROBIOTICS AND PREBIOTICS) IN THE COMPLEX TREATMENT OF MICROBIAL ECZEMA

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ABSTRACTS: Background: Microbial eczema is a chronic inflammatory dermatosis closely linked to skin and gut dysbiosis. Emerging evidence regarding the "gut-skin axis" suggests that modulating the intestinal microbiota with probiotics and prebiotics (synbiotics) may influence skin inflammation and immune response to *Staphylococcus aureus*. Objective: To evaluate the clinical efficacy of adding a synbiotic supplement (containing *Lactobacillus rhamnosus*, *Bifidobacterium longum*, and Fructooligosaccharides) to the standard treatment regimen of microbial eczema. Methods: A randomized controlled clinical trial was conducted at Andijan State Medical Institute involving 90 patients with microbial eczema. Patients were divided into two groups: the Control Group (n=45) received standard topical and systemic therapy, while the Main Group (n=45) received standard therapy plus an oral synbiotic complex once daily for 30 days. Efficacy was assessed using the SCORAD index, Dermatology Life Quality Index (DLQI), and recurrence rates over a 6-month follow-up. Results: By day 30, the Main Group showed a significantly greater reduction in SCORAD scores (72% reduction) compared to the Control Group (55% reduction, $p<0.05$). Patients receiving synbiotics reported faster relief from pruritus and a marked improvement in DLQI. Furthermore, the recurrence rate at 6 months was significantly lower in the synbiotic group (22%) compared to the control group (48%). Conclusion: The inclusion of synbiotics in the treatment of microbial eczema enhances clinical response, accelerates symptom resolution, and reduces the frequency of relapses, likely by normalizing the gut-skin immune axis.
Keywords: Microbial eczema, probiotics, prebiotics, synbiotics, gut-skin axis, *Staphylococcus aureus*, Andijan State Medical Institute.

MIKROBLI EKZEMANI KOMPLEKS DAVOLASHDA SINBIOTIK TERAPIYA (PROBIOTIK VA PREBIOTIKLAR)NING KLINIK SAMARADORLIGI

ANNOTATSIYA: Kirish: Mikrobli ekzema teri va ichak disbiozi bilan chambarchas bog'liq bo'lgan surunkali yallig'lanishli dermatozdir. "Ichak-teri o'qi" bo'yicha yangi dalillar shuni ko'rsatadiki, ichak mikroflorasini probiotik va prebiotiklar (sinbiotiklar) bilan modulyatsiya qilish teri yallig'lanishiga va *Staphylococcus aureus* ga bo'lgan immun javobga ta'sir qilishi mumkin. Maqsad: Mikrobli ekzema standart davolash rejimiga sinbiotik qo'shimchasini (*Lactobacillus rhamnosus*, *Bifidobacterium longum* va Fruktooligosaxaridlar) qo'shishning klinik samaradorligini baholash. Usullar: Andijon davlat tibbiyot institutida 90 nafar mikrobli ekzemasi bo'lgan bemor ishtirokida randomizatsiyalangan nazoratli klinik sinov o'tkazildi. Bemorlar ikki guruhga bo'lindi: Nazorat guruhi (n=45) standart mahalliy va tizimli davo oldi, Asosiy guruh (n=45) esa standart davo plyus kuniga bir marta og'iz orqali sinbiotik kompleksini 30 kun davomida qabul qildi. Samaradorlik SCORAD indeksi, Dermatologik hayot sifati indeksi (DLQI) va 6 oylik kuzatuv davomida qaytalanish darajasi yordamida baholandi. Natijalar: 30-kuniga

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kelib, Asosiy guruhda SCORAD ko'rsatkichlarining pasayishi (72%) Nazorat guruhiga (55%) nisbatan sezilarli darajada yuqori bo'ldi (p<0,05). Sinbiotik qabul qilgan bemorlarda qichishish tezroq yo'qoldi va DLQI sezilarli yaxshilandi. Bundan tashqari, 6 oylik qaytalanish darajasi sinbiotik guruhida (22%) nazorat guruhiga (48%) qaraganda ancha past bo'ldi. Xulosa: Mikrobli ekzemani davolashda sinbiotiklarni qo'llash klinik javobni kuchaytiradi, simptomlarning yo'qolishini tezlashtiradi va qaytalanish chastotasini kamaytiradi, bu ehtimol ichak-teri immun o'qining normallashuvi bilan bog'liq.
Kalit so'zlar: Mikrobli ekzema, probiotiklar, prebiotiklar, sinbiotiklar, ichak-teri o'qi, *Staphylococcus aureus*, ADTI.

КЛИНИЧЕСКАЯ ЭФФЕКТИВНОСТЬ СИНБИОТИЧЕСКОЙ ТЕРАПИИ (ПРОБИОТИКОВ И ПРЕБИОТИКОВ) В КОМПЛЕКСНОМ ЛЕЧЕНИИ МИКРОБНОЙ ЭКЗЕМЫ.

АННОТАЦИЯ: Введение: Микробная экзема — это хронический воспалительный дерматоз, тесно связанный с дисбиозом кожи и кишечника. Появляющиеся данные о «оси кишечник-кожа» свидетельствуют о том, что модуляция кишечной микрофлоры с помощью пробиотиков и пребиотиков (синбиотиков) может влиять на воспаление кожи и иммунный ответ на *Staphylococcus aureus*. Цель: Оценить клиническую эффективность добавления синбиотической добавки (содержащей *Lactobacillus rhamnosus*, *Bifidobacterium longum* и фруктоолигосахариды) к стандартной схеме лечения микробной экземы. Методы: В Андижанском государственном медицинском институте было проведено рандомизированное контролируемое клиническое исследование с участием 90 пациентов с микробной экземой. Пациенты были разделены на две группы: контрольная группа (n=45) получала стандартную местную и системную терапию, тогда как основная группа (n=45) получала стандартную терапию плюс пероральный синбиотический комплекс один раз в день в течение 30 дней. Эффективность оценивалась с использованием индекса SCORAD, дерматологического индекса качества жизни (DLQI) и частоты рецидивов в течение 6 месяцев наблюдения. Результаты: К 30-му дню в основной группе наблюдалось значительно большее снижение показателей SCORAD (снижение на 72%) по сравнению с контрольной группой (снижение на 55%, p<0,05). Пациенты, получавшие синбиотики, отмечали более быстрое облегчение зуда и заметное улучшение DLQI. Кроме того, частота рецидивов через 6 месяцев была значительно ниже в группе синбиотиков (22%) по сравнению с контрольной группой (48%). Заключение: Включение синбиотиков в лечение микробной экземы усиливает клинический ответ, ускоряет разрешение симптомов и снижает частоту рецидивов, вероятно, за счет нормализации иммунной оси кишечник-кожа.
Ключевые слова: Микробная экзема, пробиотики, пребиотики, синбиотики, ось кишечник-кожа, *Staphylococcus aureus*, АГМИ.

INTRODUCTION

Microbial eczema (also known as microbial-associated nummular dermatitis) accounts for approximately 12-25% of all eczema cases treated in outpatient dermatological practices in Uzbekistan. The pathogenesis of this condition is multifactorial, primarily involving a defect in the epidermal barrier, allergic sensitization to bacterial antigens (most notably the exotoxins of *Staphylococcus aureus*), and autoinoculation.

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Traditionally, the therapeutic strategy has relied heavily on the "Germ Theory"—the eradication of the causative agent using topical or systemic antibiotics combined with anti-inflammatory corticosteroids. While effective in the acute phase, this approach has significant long-term limitations. The widespread and repeated use of antibiotics contributes to the development of resistant bacterial strains (e.g., MRSA) and, crucially, exacerbates dysbiosis in the host's microbiome. This destruction of commensal flora can leave the host more vulnerable to future colonization by pathogens.

Recent scientific literature highlights the "Gut-Skin Axis"—a bidirectional communication pathway between the gastrointestinal tract and the skin, mediated by immune cells, circulating cytokines, and microbial metabolites. Intestinal dysbiosis can lead to increased intestinal permeability (often termed "leaky gut"), allowing bacterial lipopolysaccharides (LPS) and other pro-inflammatory molecules to enter the systemic circulation. This "metabolic endotoxemia" promotes a state of chronic subclinical inflammation and Th2-immune dominance, which directly aggravates eczematous processes and impairs skin barrier function.

In the Fergana Valley region, specific dietary patterns (such as high carbohydrate and animal fat intake) combined with frequent antibiotic use may contribute to a high prevalence of gut dysbiosis among dermatology patients. Therefore, restoring intestinal homeostasis could be a key strategy in managing chronic dermatoses. This study aims to investigate whether the addition of a synbiotic (a synergistic combination of probiotics and prebiotics) to standard therapy can not only improve immediate clinical outcomes but also reduce long-term recurrence rates in patients with microbial eczema treated at the Andijan State Medical Institute.

MATERIALS AND METHODS

Study Design and Ethical Considerations This was a prospective, randomized, comparative clinical trial conducted at the Department of Dermatovenereology of Andijan State Medical Institute between January 2023 and January 2024. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants in accordance with the Declaration of Helsinki.

Patient Selection A total of 90 patients (52 males, 38 females) aged 18 to 65 years were enrolled.

Inclusion criteria - Clinical diagnosis of microbial eczema (nummular, paratraumatic, or varicose types); moderate to severe disease activity (SCORAD > 25); history of recurrent episodes (≥2 per year).

Exclusion criteria - Systemic antibiotic or corticosteroid use within 4 weeks prior to enrollment; primary immunodeficiency; severe gastrointestinal pathology (e.g., Crohn's disease, Ulcerative Colitis); pregnancy or lactation; known hypersensitivity to probiotic components.

Treatment Protocol Patients were randomized into two groups using a computer-generated sequence:

1) Control Group (n=45): Received standard guideline-based therapy: Systemic - Desloratadine 5 mg once daily (10 days); Calcium gluconate 10% IV (10 days). Antibiotics (Azithromycin 500mg) were prescribed only if frank purulence/fever was present (5 days). Topical - Combined betamethasone dipropionate + gentamicin sulfate cream twice daily for 14 days, followed by a neutral emollient.

2) Main Group (n=45): Received the exact standard therapy as above plus Synbiotic therapy. Synbiotic Agent: A capsule containing *Lactobacillus rhamnosus* GG ($3x10^9$ CFU), *Bifidobacterium longum* ($3x10^9$ CFU), and Fructooligosaccharides (FOS) as a prebiotic substrate.

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Regimen - 1 capsule daily, taken 2 hours after antibiotic administration (if applicable), for a total of 30 days. Clinical Efficacy - The SCORAD (SCORing Atopic Dermatitis) index was used to objectively assess the extent (Area) and severity (Intensity of erythema, edema, crusting, excoriation, lichenification, and dryness) of lesions. Assessments were performed at Baseline (Day 0), Day 15, and Day 30. Symptomatic relief - Pruritus (itching) was evaluated using a Visual Analog Scale (VAS) from 0 to 10.

Quality of Life - The dermatology Life Quality Index (DLQI) questionnaire was administered at Day 0 and Day 30. Long-term Follow-up - Patients were contacted monthly for 6 months to record any recurrence of skin lesions.

Statistical analysis - Data were analyzed using IBM SPSS Statistics v.26. Continuous variables (SCORAD, VAS) were presented as mean ± standard deviation (SD) and compared using Student's t-test. Categorical variables (recurrence rates) were compared using the Chi-square (X^2) test. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline characteristics the two groups were homogenous at baseline regarding age, gender distribution, disease duration, and initial severity scores (Table 1).

Table 1. Baseline Clinical Characteristics

Parameter	Control group (n=45)	Main group (n=45)	p-value
Age (years)	34.2 ± 11.5	35.8 ± 10.9	>0.05
Gender (Male / Female)	25 / 20	27 / 18	>0.05
Disease Duration (years)	4.1 ± 2.3	3.9 ± 2.5	>0.05
Baseline SCORAD	44.8 ± 6.2	45.2 ± 5.9	>0.05

Comparative efficacy analysis - The study demonstrated a clear advantage for the Main Group across all primary endpoints by the end of the treatment period (Day 30). While acute inflammation resolved in both groups, the synbiotic group showed superior resolution of chronic signs like lichenification and dryness.

Table 2. Comparison of Clinical Outcomes at Day 30

Clinical Parameter	Control group (n=45)	Main group (n=45)	P-value
SCORAD Index (Mean ± SD)	20.1 ± 4.5	12.6 ± 3.1	< 0.001
Reduction in SCORAD (%)	55.4%	72.1%	< 0.05
Pruritus Intensity (VAS 0-10)	2.8 ± 1.2	0.9 ± 0.5	< 0.001
DLQI Score (Quality of Life)	7.8 ± 2.1	4.2 ± 1.5	< 0.01
Resolution of Edema (Days)	8.4 ± 1.5	6.1 ± 1.2	< 0.05

Dynamics of clinical symptoms - Day 15: The Main Group showed a faster reduction in erythema and exudation. This early separation suggests that gut modulation may enhance the anti-inflammatory efficacy of standard treatments. Day 30: The Main Group achieved a marked reduction in lichenification and dryness. The final SCORAD in the Main Group was significantly lower, indicating a more complete remission.

Relapse Rates (6-Month Follow-up) The most significant clinical finding was the prophylactic effect of the synbiotic regimen. In the Control Group, 22 patients (48.9%) experienced a flare-up of microbial eczema within 6 months, often requiring a new course of topical steroids. In the

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Main Group, only 10 patients (22.2%) experienced a relapse. This represents a greater than twofold reduction in recurrence risk (OR = 0.30,95% CI: 0.12 - 0.74).

DISCUSSION

The results of this randomized controlled trial conducted at Andijan State Medical Institute provide compelling evidence for the efficacy of synbiotics in microbial eczema. While standard therapy effectively suppresses local inflammation and reduces bacterial load on the skin, it does not address the systemic background of the disease.

Immunological Mechanisms We propose that the observed benefits are mediated through specific immunological pathways:

Treg stimulation - Probiotic strains like *L. rhamnosus* GG are potent inducers of regulatory T-cells (Tregs) in the Gut-Associated Lymphoid Tissue (GALT). These Tregs release IL-10 and TGF-beta, cytokines known to suppress the Th2-type allergic inflammation that characterizes eczema.

Reduction of "Leaky Gut" - Chronic eczema is often associated with increased intestinal permeability. The synbiotic combination helps tighten epithelial junctions in the gut, preventing the translocation of bacterial endotoxins (LPS) into the bloodstream. Reducing systemic LPS levels lowers the baseline inflammatory state of the skin.

Impact on *Staphylococcus aureus* Although synbiotics are ingested orally, they impact skin colonization. The fermentation of Fructooligosaccharides (FOS) by *Bifidobacteria* produces Short-Chain Fatty Acids (SCFAs) like butyrate and propionate. Circulating SCFAs have been shown to inhibit the formation of *S. aureus* biofilms and enhance the production of antimicrobial peptides (defensins) by skin keratinocytes. This creates a "hostile environment" for the pathogen, preventing recolonization without the use of antibiotics.

Comparison with Existing Literature Our findings align with international studies (e.g., *Kim et al., 2014*; *Salem et al., 2018*) which suggest that the gut microbiome is a major regulator of skin health. However, this study is unique in demonstrating these effects specifically in *microbial eczema*, a subtype often overlooked in favor of atopic dermatitis. The high recurrence rate in our control group (48.9%) is consistent with the natural history of the disease in the Uzbek population, while the reduction to 22.2% in the study group represents a significant clinical breakthrough.

Clinical Implications The study highlights that treating the skin alone is insufficient for chronic microbial eczema. The addition of a 30-day course of synbiotics is a cost-effective, safe, and easily compliant intervention that significantly alters the disease trajectory. It reduces the reliance on repeated courses of topical steroids, thereby minimizing the risk of skin atrophy and steroid addiction.

CONCLUSION

Based on the results of the studies, we conclude that: 1) Enhanced clinical efficacy - The inclusion of synbiotics (Probiotics + Prebiotics) in the complex therapy of microbial eczema is pathogenetically justified. It significantly accelerates clinical recovery, reducing SCORAD scores by 72% compared to 55% with standard therapy alone. 2) Improved quality of life - Synbiotic therapy provides faster and more sustained relief from pruritus, the most debilitating symptom of eczema, significantly improving the patients' DLQI scores. 3) Potent prophylactic effect - The most critical benefit is the reduction of the 6-month recurrence rate from 48.9% to

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22.2%. This suggests that modulating the gut-skin axis confers long-term resilience against disease flares.

Recommendation - We strongly recommend incorporating a 1-month course of synbiotics into the standard treatment protocol for recurrent microbial eczema in dermatological practice in Uzbekistan. Future research should focus on identifying the optimal duration of therapy and specific probiotic strains for different eczema phenotypes.

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