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Combined Permethrin and Salt Water Immersion Effects on Eosinophils, Immunoglobulin E, Histamine, and C3 Complement in Scabies Patients

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Abstract

Background: Scabies reduces quality of life due to intense nocturnal pruritus. Pruritus is associated with hypereosinophilia, increased immunoglobulin E (IgE), histamine release, and complement C3 activation. This study aimed to determine the effectiveness of combined permethrin and salt-water immersion therapy in reducing eosinophil counts, IgE, histamine, and complement C3 levels in patients with scabies.

Methods: A quasi-experimental pre-test–post-test control group study was conducted among 92 students with scabies at an Islamic boarding school in Banten Province, Indonesia, from December 2024 to December 2025. Participants were selected using purposive sampling and divided into intervention and control groups. The intervention group received combined permethrin and warm salt-water immersion therapy, while the control group received permethrin alone. Eosinophil count, IgE, histamine, and complement C3 levels were measured before and after treatment. Data were analyzed using paired and independent t-tests.

Results: Significant reductions were observed in the intervention group after therapy in eosinophils ($t=65.0$; $p<0.001$), IgE ($t=152.9$; $p<0.001$), histamine ($t=152.1$; $p<0.001$), and complement C3 ($t=152.4$; $p<0.001$). Post-treatment comparisons showed significant differences between groups for eosinophils ($t=2.07$; $p<0.05$), IgE ($t=2.66$; $p<0.05$), histamine ($t=2.09$; $p<0.05$), and complement C3 ($t=4.25$; $p<0.001$).

Conclusions: Combined permethrin and warm salt-water immersion therapy significantly reduced inflammatory and immunological markers in patients with scabies and may help alleviate nocturnal pruritus.

Keywords: Complement C3, eosinophils, histamine, immunoglobulin E, scabies

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Introduction

The *Sarcoptes scabiei* mite, which causes scabies, can dig tunnels in human skin and lay eggs in them, causing itching and rashes. Scabies has globally affected 200 million people worldwide[1]. The estimated global annual incidence rate in 2019 reached 565 (499-634) million cases with a disease burden measured at 4.84 million Disability-Adjusted Life Years (DALYs), with a very high burden spread across Asia, Oceania, and Latin America[1,2]. Scabies is also included in the skin Neglected Tropical Diseases (NTDs) which are targeted for control by the World Health Organization (WHO) until 2030.[3,4]

Scabies is more common in developing countries than in developed countries, particularly in tropical regions with limited resources and high population densities.[1,4] The prevalence of scabies varies by region. In Southeast Asia, the prevalence of scabies reached 11.4%, the second highest according to WHO regional classification after the Western Pacific.[1] In Indonesia, the prevalence of scabies reached 5.60-12.95% in 2018, and Indonesia bears the largest scabies burden of 195 countries worldwide. Scabies is also the third most common skin disease out of 12 in Indonesia.[3]

Scabies impacts a decline in healthy quality of life due to unbearable itching. Pruritus

can persist for months in untreated patients, ranging from mild, moderate, to severe itching. This pruritus is triggered by hypereosinophilia, which increases the production of IgE antibodies, histamine, and complement C3.[5] Furthermore, chronic scabies accompanied by secondary infections can lead to dangerous systemic complications.[6] This condition can trigger severe systemic complications, such as kidney infections and rheumatic heart disease. Meanwhile, the pharmacological therapy available so far, although 91% effective and reducing pruritus symptoms, still causes complaints from some patients due to side effects such as burning sensations and post-application skin irritation.[7] Therefore, non-pharmacological therapy or complementary medicine is needed as an additional solution to reduce itching.

Salt-water immersion therapy is proposed in this study based on the evidence base of previously studied pharmacological reviews, namely eosinophil hyposensitization, neutralization of IgE levels, histamine factor depletion, and complement C3 degradation.[8] However, there has been no research evaluating salt therapy based on immunological parameters in scabies patients. Research on the administration of warm salt-water immersion has so far only evaluated subjective healing.[9] Therefore, more objective and measurable markers are needed through immunological parameters. The aim of this study is to evaluate the effectiveness of combined permethrin and salt-water immersion as complementary therapy in scabies patients in Banten Province.

Methods

This study used a quasi-experimental design with a control group. The purpose of this study was to examine variables involving the control and intervention groups. This study evaluated the impact of salt therapy intervention on the incidence of nocturnal pruritus in scabies patients at a boarding school. A pre-test and post-test interventions were conducted on the treatment and control groups. The intervention involved a combination of permethrin treatment and salt-water immersion, while the control group received permethrin alone. This study was conducted at a boarding school in Banten from December 2024 to December 2025.

The sampling technique used in this study was non-probability sampling. More specifically, this study employed purposive sampling, which is a technique for determining respondents for sampling based on certain criteria until a minimum sample size is met. By using purposive sampling, this study involved 92 respondents. The study subjects were part of the accessible population who met the researcher's inclusion and exclusion criteria. The inclusion criteria for this study were students registered as boarding school students in Banten Province, new students at the junior and senior high school levels residing at the boarding school, students who were willing to participate in the study and signed an informed consent form and students diagnosed with scabies by a physician. The exclusion criteria for this study were students with a history of allergies or other skin conditions, MTs and MA students who did not reside on the boarding school grounds, students currently taking medication used (antihistamines, corticosteroids), and/or students with chronic illnesses.

This research protocol has passed ethical review by the ethics committee of the YARSI University Graduate School, with letter number 391/KEP-UY/EA.10/XI/2024. The clinical diagnosis is conducted by a general practitioner, established by finding two of the four cardinal signs of scabies, namely nocturnal pruritus; the presence of mites in laboratory examinations; a group of people suffering from the same disease; the presence of tunnels, papules, vesicles or pustules in predilection areas or distributed throughout the body.[6] Then the subjects were divided randomly into 46 subjects each for the control and intervention groups. The type of salt used in this study was sea salt. The amount of salt used was 35 grams and was dissolved in 1 liter of warm water to maintain the NaCl concentration in optimal conditions as a therapeutic modality.[10] The water temperature applied to both groups was 36–37°C to maximize the absorption process through the skin.[11]

After receiving salt-water immersion therapy, blood samples were collected from the respondents and examined in the laboratory. From the collected specimens, a peripheral blood eosinophil differential count was performed, namely the relative number of eosinophils in the differential count of peripheral blood leukocytes.[12] Blood sampling was carried out twice, on the first day when scabies was first clinically diagnosed, and on the seventh day after administering salt-water therapy. The obtained blood samples were then centrifuged at 3500 rpm for 10 minutes at a temperature of 5–10°C to measure IgE levels, histamine factors, and complement

C3 concentrations. The centrifugation results were then examined using a kit based on an indirect ELISA examination.[13] The data obtained was then conducted a normality test using Kolmogorov-Smirnov. After that, the normal data analyzed using independent t-test on SPSS.

Results

Eosinophils can be distinguished from other types of leukocytes through visual observation using a microscope on peripheral blood smears. Next, a bivariate analysis was performed to compare eosinophil counts between intervention groups using an independent t-test at a 95% significance level. The average difference in eosinophil counts between the intervention groups before and after treatment was 64 with a standard deviation of 0.26 and a standard error of 2.9. Therefore, it can be concluded that the administration of 5% permethrin and saline immersion water can significantly reduce eosinophil counts (t=65.2; p<0.001). These results were then compared with the control group using an independent t-test (Figure 1).

Figure 1 shows that the average difference in eosinophil counts between the two groups (intervention and control) after treatment was 9.043. Since the calculated t (2.07) is greater than the t table (0.38), it can be concluded that there is a significant difference in eosinophil counts between the group given Permethrin 5% + saline immersion water and the group given only Permethrin 5%. This can be interpreted as meaning that there was a significant decrease in eosinophil counts after administration of saline immersion water.

Immunoglobulin E is declared positive in subjects if the IgE in the sample binds to the allergen. After obtaining the levels, a bivariate analysis was performed to compare IgE levels between the intervention groups using an independent t-test using a 95% significance level. It was found that the average difference in IgE levels in the intervention group before and after treatment was 0.26 with a standard deviation of 0.011 and a standard error of 0.001. Therefore, it can be concluded that the administration of 5% Permethrin and saline immersion water can significantly reduce IgE levels (t=152.9; p <0.001). These results were then compared with the control group using an independent t-test (Figure 2).

Figure 2 shows that the mean difference in IgE levels between the intervention and control groups after treatment was 0.079. Since the calculated t (2.66) is greater than the t table (0.02), it can be concluded that there is a significant difference in IgE levels between the group given Permethrin 5% + salt immersion water and the group given only Permethrin 5%. This can be interpreted as meaning that there was a significant decrease in IgE levels after the administration of salt immersion water.

Histamine measurements were performed on 48 wells from the treatment group using an ELISA test with a human RnD system kit. After obtaining the levels, a bivariate analysis

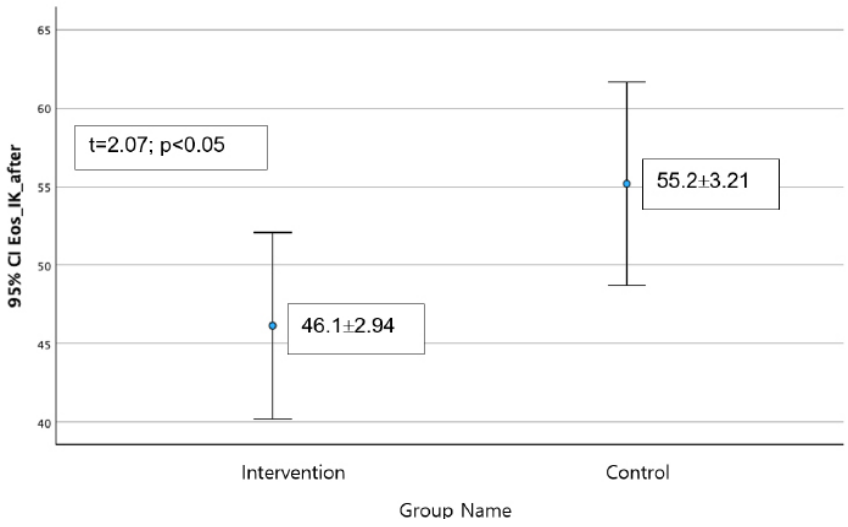

Figure 1 Comparison of Eosinophil Counts Between the Two Groups

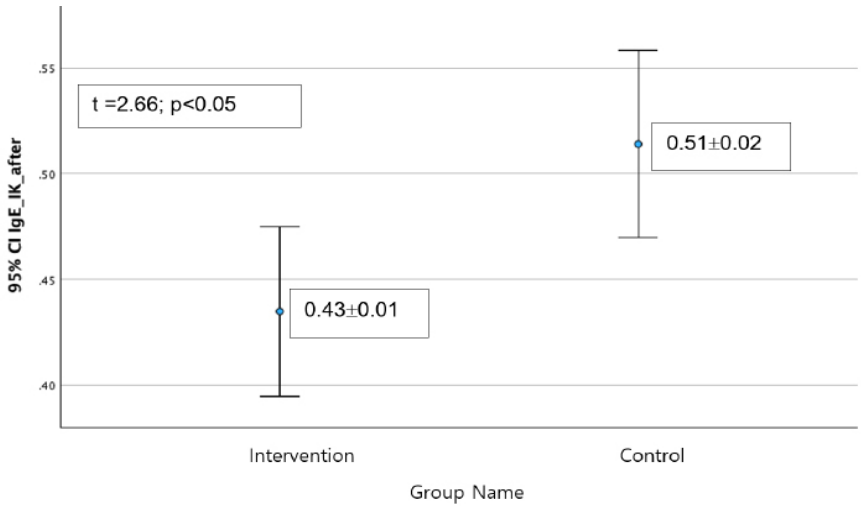

Figure 2 Comparison of IgE Levels Between the Two Groups

was performed to compare histamine factor levels between intervention groups using an independent t-test using a 95% significance level. The average difference in histamine factor levels in the intervention group before and after treatment was 0.27 with a standard deviation of 0.012 and a standard error of 0.002. Therefore, it can be concluded that the administration of 5% Permethrin and salt immersion water can significantly reduce histamine factor levels (t=152.1; p<0.001). These results were then compared with the control group using an independent T-test (Figure 3).

Figure 3 shows that the average difference in histamine factor levels between the two groups (intervention and control) after treatment was 0.054. Because the calculated t (2.09) is greater than the t table (0.03), it can be concluded that there is a significant difference in histamine factor levels between the group given Permethrin 5% + salt immersion water and the group given only Permethrin 5%. This can be interpreted that there was a significant decrease in histamine factor levels after the administration of salt immersion water.

Serum complement C3 concentrations were measured using a commercially available complement C3 assay using the ELISA method on an automated biochemical analyzer. After obtaining the levels, a bivariate analysis was performed to compare complement C3 concentrations between the intervention groups using an independent t-test at a 95% significance level. The average difference in complement C3 concentrations between the

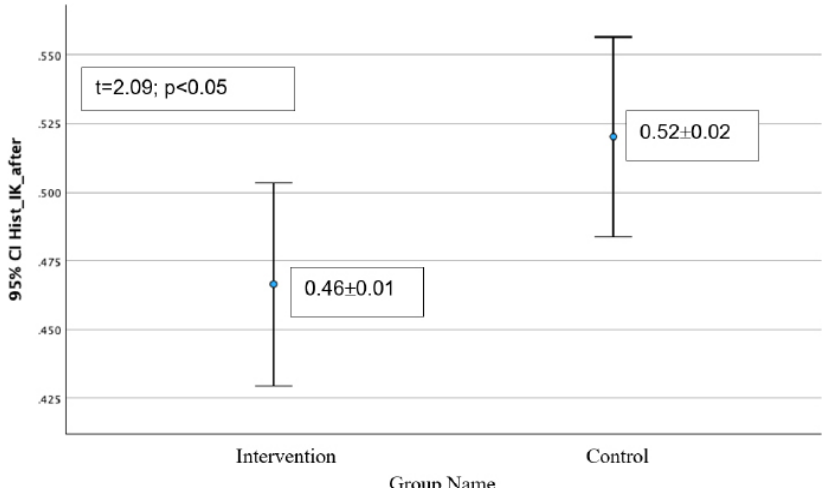

Figure 3 Comparison of Histamine Factors in the Two Groups

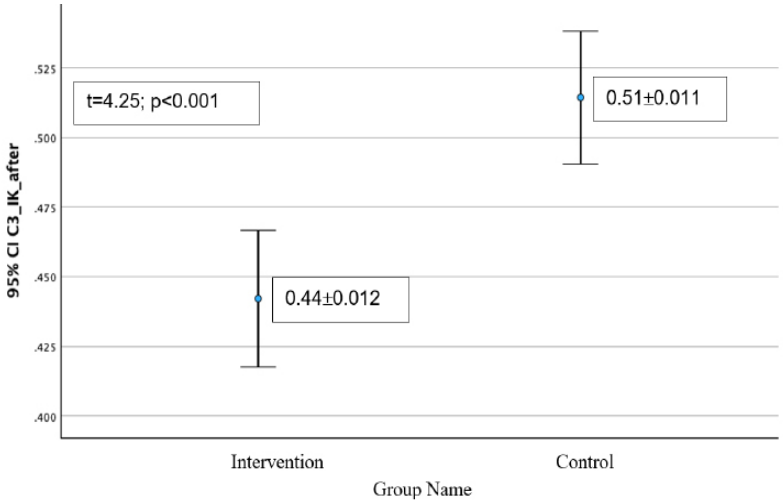

Figure 4 Comparison of Complement C3 Concentrations in the Two Groups

intervention groups before and after treatment was 0.35 with a standard deviation of 0.015 and a standard error of 0.002. Therefore, it can be concluded that the administration of 5% Permethrin and saline immersion water can significantly reduce complement C3 concentrations (t=152.4; p<0.001). These results were then compared with the control group using an independent T-test (Figure 4). Figure 4 shows that the average difference in complement C3 concentration between the two groups (intervention and control) after treatment was 0.072. Since the calculated t (4.25) is greater than the t table (0.04), it can be concluded that there is a significant difference in complement C3 concentration between the group given Permethrin 5% + saline immersion water and the group given only Permethrin 5%. This can be interpreted as meaning that there was a significant decrease in complement C3 concentration after administration of saline immersion water.

Discussion

The administration of 5% permethrin combined with salt-water immersion therapy significantly reduced eosinophil counts. Previous studies have suggested that the efficacy of salt therapy is associated with direct immunological effects, including increased activity and proliferation of T lymphocytes stimulated by cytokines released from eosinophils.[14] In addition, the results of this study are also in line with the cytobacteriological study by Chervinskaya *et al.*[15] which showed the fact that salt therapy promotes a reduction in neutrophils and increases skin epithelial macrophages, where the expression of both immune cells is stimulated by mediators released by eosinophils.

There was a significant difference in eosinophil counts between the group given 5% permethrin + saline immersion water and the group given only 5% permethrin. This indicates a significant decrease in eosinophil counts after the saline immersion water treatment. Based on previous research, a decrease in eosinophil count was found from 3.500/uL to 2.000/uL in pediculosis patients treated with permethrin shampoo.[16] Similar findings have also been reported in psoriasis patients, where salt-water immersion therapy enhanced macrophage reactivity and phagocytic activity through immune mediators associated with eosinophilic inflammation.[17]

Administration of 5% permethrin and saline immersion significantly reduced IgE levels. This is consistent with a study by Kim *et al.* which found that saline positively affected humoral and cellular immunity in patients with chronic dermatoses, with a significant decrease in IgE levels being the most visible humoral immunity effect. This decrease is also particularly significant in atopic patients.[18] Other studies suggested that salt-water therapy reduces basophil and mast cell activity, both of which are involved in IgE-mediated allergic and inflammatory responses associated with mite infestations.[19]

There was a significant decrease in IgE levels after administration of salt immersion water. According to Bhat *et al.,*[20] both

basophils and mast cells detected in skin lesions of scabies patients will produce IL-6 and TNF-alpha, then trigger Th2 to increase the production of IL-13, IL-5 and IL-4 which are the main molecules for B cell expansion to produce IgE.Referring to previous research, IgE is important in host immunity against mites along with eosinophils, basophils, and mast cells. The increase in IgE in scabies patients is based on an ELISA study that showed that 2% of 91 cases of scabies patients had circulating IgE binding to *S. scabiei* antigens. Immunoblot results from patients' serum with crusted scabies showed a significant increase in IgE binding to 21 *S. scabiei* antigens. However, the allergens contributing to this reaction still require further investigation.[21]

The administration of 5% Permethrin and salt immersion water can significantly reduce histamine levels. This is consistent with research by Chervinskaya *et al.* which stated that salt immersion therapy can reduce histamine factors in patients with atopic dermatitis. According to the study, the reduction in histamine after salt-water therapy is quite promising in treating various skin conditions due to the physiological effects that can be adjusted to the patient's condition. Approximately 65–75% of patients in the study reported a decrease in symptoms such as itching, lichenification, improvement of cracked skin, and a reduction in sympathicotonia after completing salt-water therapy. Patients who experienced a remission phase of acute inflammatory exudative events were more likely to benefit from treatment (reduced vascular infiltration and stenosis).[22] Similar improvements were also reported in pyoderma patients, where reductions in histamine levels contributed to decreased itching and enhanced skin healing.[23]

Complement C3 concentrations significantly decreased after administration of 5% permethrin combined with salt-water immersion therapy. Previous studies in eczema patients suggested that salt-water immersion therapy may improve skin barrier integrity and normalize skin pH through activation of skin ion channels and electrophysiological mechanisms, thereby reducing complement C3 activity.[24] This finding aligns with research by Lazarescu *et al*., which showed that salt-water immersion therapy can reduce complement C3 protein concentrations in onychomycosis patients. According to the study, the reduction in complement C3 after salt-water immersion therapy increases blood flow to the skin and stimulates cell membrane function, thus having an anti-inflammatory effect.[25]

The limitation of this study is that it has not been able to explore the deeper immunological mechanisms of salt-water immersion therapy, including its effect on other inflammatory mediators to understand the biological pathways involved. Based on the results of this study, it can be concluded that administration of combination permethrin and salt-water immersion as complementary therapy in the intervention group statistically significant reduced eosinophil counts, IgE levels, histamine factor levels, and complement C3 concentrations compared to the control group. The results of this study are expected to reduce the symptoms of nocturnal pruritus in scabies patients, supported by direct outcome reframed as a potential clinical implication. Therefore, this study may provide potential complementary therapy solutions in overcoming the problem of nocturnal pruritus as the main manifestation of scabies, in addition to improving clean and healthy lifestyles in preventing scabies transmission.

Authors' Contributions

RFT conducted the study, collected and analyzed the data, and drafted the manuscript. EP, TYA, and SWH supervised the research, provided methodological guidance, contributed to manuscript development, and reviewed the final manuscript. All authors approved the final version of the manuscript.

Conflict of Interest

The authors declare no conflict of interest.

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Generative AI Disclosure Statement

All analyses, interpretations, and manuscript writing were conducted solely by the authors without the use of generative artificial intelligence (AI) or AI-assisted technologies.

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