THE ROLE OF PROTEIN SUPPLEMENT IN IMPROVEMENT OF ATOPIC DERMATITIS (AD) PATIENTS

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Abstract

Background: It is possible for AD patients to develop hypoproteinemia as a result of protein loss through severe skin sores, dietary restrictions due to various food allergies, or malnutrition.

Objectives: To evaluate the role of protein supplement in improvement of AD patients.

Patients and methods: This study was conducted as a clinical randomized Case control study. This study enrolled 34 patients with AD, then the 34 AD patients were randomized into 2 equal groups, the protein supplementation group and the non protein supplementation group but both received the routine AD treatment and followed up for 8 weeks. SCORAD were evaluated for all patients before treatment and at the end of therapy.

Results: the disease severity was studied before and after protein supplementation and it was found unfortunately by coincidence that baseline SCORAD was higher in the protein supplementation group with p value 0.007 than group B who didn't receive protein supplement. At the end of therapy there was good improvement but not statistically significant improvement of all patients in protein supplementation group compared to group B with p value 0.06.

Conclusion: protein supplementation to AD patients showed good clinical improvement but unfortunately it showed no statistically significant difference, this reveals our need for further studies for assessment of the efficacy of protein supplementation in AD.

Key words: Atopic dermatitis, Hypoproteinemia, protein, supplementation.

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INTRODUCTION

AD is extremely prevalent due to its nature as a chronic inflammatory condition. It affects 15-20% of children, affecting considerably their quality of life **(Rönmark, et al,2016)**

Some studies were done to estimate the role of protein supplementation in the treatment of AD. Some causes of hypoproteinemia in AD patients include protein loss through severe skin sores, dietary restrictions due to various food allergies, and malnutrition leading to high Scoring AD(SCORAD)indices **(Tan et al., 2017).**

Delayed improvement due to poor compliance of topical steroids, chronic protein leakage was thought to have a role in the development of hypoproteinemia, and dermatitis herpeticum was suggested to play a role as well **(LeeC et al, 2017)**

PATIENTS AND METHODS

This study was conducted as a clinical randomized Case control study. This study enrolled 34 patients with AD. The 34 AD patients were randomized into 2 equal groups, the protein supplementation group and the non protein supplementation group but both received the routine AD treatment and followed up for 8 weeks. SCORAD was evaluated for all patients before treatment and at the end of therapy.

Population of study: Pediatric AD Patients diagnosed or referred to pediatric dermatology clinic whose age<15years.

Study location: Abo-elreesh pediatric dermatology clinic.

Inclusion criteria: Pediatric Patients with AD with age<15 years at time of diagnosis. All types of AD e.g. (infantile, childhood). All grades of AD e.g.(mild, moderate, severe).

Exclusion criteria: Pediatric Patients with AD age more than 15 years. Patients accompanied by any systemic disease (e.g. SLE, etc.).

RESULTS

Demographic analysis of the study's findings shows; the mean duration of the disease from the first diagnosis is 3.2 years ±2.9 with a range from 0.2 year to 11 years, without significant results when correlated with age and gender (males equals females 50% each).

Table 1: comparison of disease severity score according to protein supplementation.

Protein supplement						
		Non protein supp. group		Protein supp. Group		
		Mean ± SD	Median (range)	Mean ± SD	Median (range)	P value
Baseline SCORAD		35.2± 7.6	36.5 (23-45.5)	47.5± 13.4	47 (26-70.5)	0.007
SCORAD baseline	Mild	1	5.90%	0	0.00%	0.009
	Moderate	16	94.10%	10	58.80%	
	Sever	0	0.00%	7	41.20%	
End of therapy (EOT) SCORAD		10.2± 7.2	10.5 (0-23.5)	19.9± 14.3	17.3 (0-44)	0.060
SCORAD End of therapy	Mild	15	88.20%	11	64.70%	0.051
	Moderate	0	0.00%	5	29.40%	
	N/A	2	11.80%	1	5.90%	

This study showed that baseline SCORAD was significantly different between studied groups which showed higher disease severity among subgroup using protein supplements with p value 0.007. At the end of therapy, with a p-value of 0.06, there was no discernible change in response to protein supplementation.

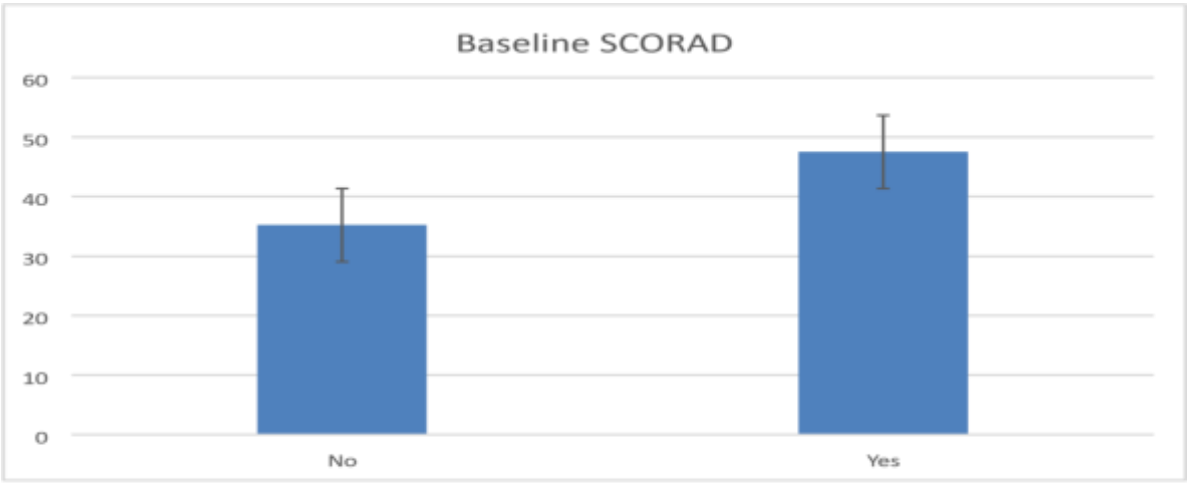

Figure 1: bar chart showing baseline SCORAD score according to protein supplementation

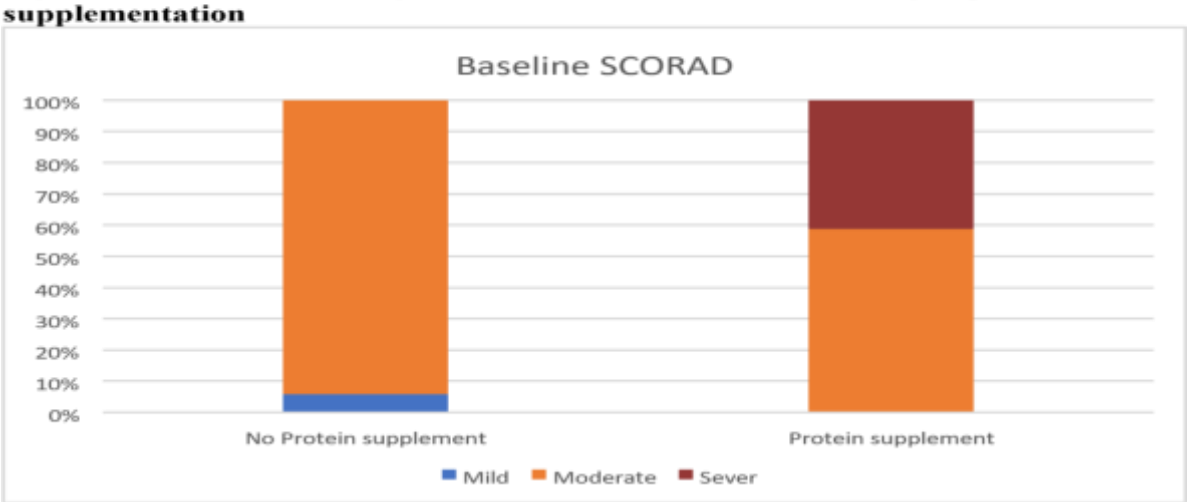

Figure 2: bar chart showing baseline SCORAD severity category according to protein supplementation.

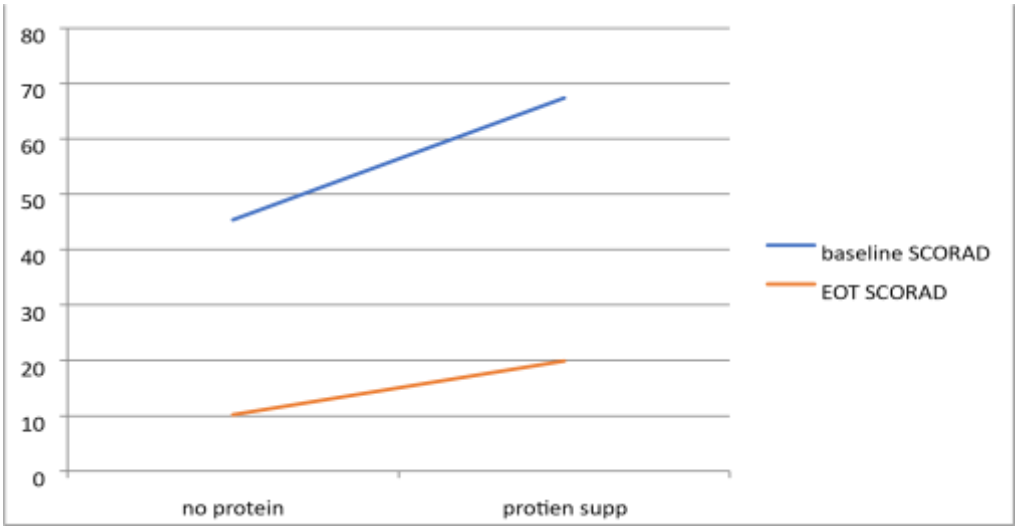

Figure 3: line chart illustrating SCORAD at baseline and end of therapy.

Table 2: comparison of improvement percentage according to protein supplementation.

Protein supplement						
		Non protein supp.		Protein supp.		
		N	%	N	%	P value
Improvement clinical	Excellent (>75%)	6	35.30%	7	41.20%	0.689
	Good (50-75%)	9	52.90%	8	47.10%	
	Fair (25-50%)	0	0.00%	1	5.90%	
	Dropped	2	11.80%	1	5.90%	

This table showed that there was no significance between the studied groups regarding protein supplementation.

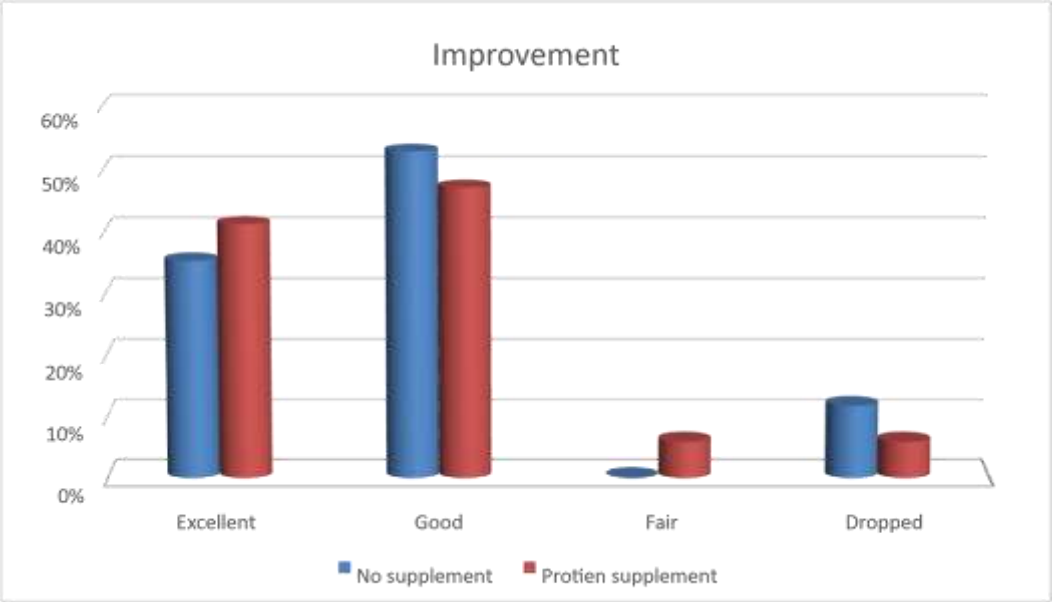

Figure 4: bar chart showing improvement rates among studied groups.

DISCUSSION

AD is a chronic relapsing and remitting inflammatory disease caused by a complex interaction of immune dysregulation, epidermal gene mutations, and environmental factors. This complex disrupts the epidermis causing intensely pruritic skin lesions **(Frazier et al., 2020).**

It has been observed that children with AD have hypoproteinemia, with serum protein level of 3-5 g/dl compared to a normal range of 6-7 g/dl in the similar age rangeof normal individuals. The route of protein loss was considered to be from the damaged skin and increased protein consumption by scaling from the skin lesion; Loss of protein from the gastrointestinal tract; or insufficient food intake. It was reported that rapid recovery of serum protein value is associated with the improvement of skin eruptions **(Nomura et al., 2002).**

In this study, 34 AD patients were enrolled; 17 of them received a protein supplement in addition to routine treatment and were reassessed after 8 weeks, the other 17 AD patients were enrolled as controls because they received routine treatment only. In this study, by comparing improvement after protein therapy, there was good clinical improvement, but unfortunately, statistically, there was no significant difference between the studied groups (protein and non-protein groups) with (p value 0.689). In the literature, Very few randomized controlled trials have assessed the efficacy of protein supplementation in treatment of AD, despite the presence of multiple studies discussed hypoprotienemia in atopic dermatitis, the fact which makes this study highly valuable.

The current study suggests that patients diagnosed with AD who took protein supplements noticed an improvement in their clinical signs and symptoms, then this improvement is proved by measurement of the clinical SCORAD Scoring .

In this study, the disease severity was studied before and after protein supplementation and it was found unfortunately by coincidence that baseline SCORAD was higher in the protein supplementation group with p value 0.007 than group B who didn't receive protein supplement. At the end of therapy there was good improvement but not statistically significant improvement of all patients in protein supplementation group compared to the non protein supplementation group with p value 0.06.

This study mainly based on the studies of **Tan et al., 2017 and Gibbs and Neil, in 2020.** Clinical pilot research conducted by **Tan** found that giving individuals with adultonset AD an oral L-histidine rich protein once daily for 4 weeks was associated with a reduction in clinical signs and symptoms of the disease, similar to what has been documented with the use of mid-potency (Group III) topical corticosteroids, there was a 40% reduction in AD activity over 4 weeks of treatment as measured by both clinician- and patient-scored measures of disease severity (SCORAD and POEM, respectively), proving that protein dietary supplementation may be a safe, simple, nonsteroidal strategy suitable for long-term usage in treatment of AD, especially in children. They reported increase in filaggrin formation after protein intake associated with improvement in the barrier function which was comparable to what is seen with the use of mid potency topical steroid only.

Similarly, Twenty-four AD patients were given a 4 g L-histidine base nutritional supplement daily for 8 weeks, and twenty-five young children were given 5 mL of an oral suspension formulation that delivered 0.8 g dose of L-histidine daily for 12 weeks, as part of Gibbs's pilot clinical study, Research indicated that considerable improvements and decreases in AD disease severity can be achieved with L-histidine. These reductions were 32% in adults and 49% in young children. These results are comparable to those reported for mid-potency topical corticosteroids. **(Gibbs and Neil, 2020).**

In the literature, approximately one hundred studies have been conducted to investigate the role of hydrolyzed formulas in the regression of atopic disease. Partial hydrolysis of formulas has been shown to have a modest effect on the delay and reduction of atopic disease in infants who are formula fed or fed on a mixed feeding of human milk and formula, There were no documented side effects in any of these investigations, not even among those with a high risk of developing an allergic condition, suggesting that more research is needed on the hydrolyzed formula **(Greer et al,. 2008)**. Another study showed the significant preventive effect on AD, with partial hydrolyzed formula persisted until 10 years without rebound **(von Berg et al., 2013).**

According to the recommendations of the European Food Safety Authority, in 2017 the United Kingdom released a dietary supplement containing 4 grams of L-histidine per day for those who are over the age of 12 and in 2018, a total of 352 users of the product were polled, with just 98 (or 28%) responding to the survey. 83% of patients with eczemaprone skin who took L-histidine supplements reported a 33% decrease in their use of topical corticosteroids, on average, with no serious adverse events noted. Unfortunately, it is un available at time of the study in Egypt, the fact which may explain the different results between this study and **gibbs and Neil, (2020)** study, because of the different formulas as we used whole protein formula, so further studies on L histidine intake only are needed.

Nomura found that in Japanese AD patients 11 out of 13 infants under the age of 12 months with severe AD, had hypoprotienemia with manifestations observed in some patients in the form of skin discharge, Skin edema, peripheral cyanosis, oliguria, and diarrhea also cerebral infarction was seen as a consequence of hypoprotienemia. The difference in results of both studies may be because

of the fact that Japanese population may have genetic risk to develop hypoprotienemia. He explained the cause of hypoprotienemia by three possible mechanisms: protein loss due to diarrhea and vomiting; protein loss due to severe skin lesions. The studied group of Japanese AD patients also had steroid phobia which considered a global phenomenon that exacerbates AD subsequently increases severity and exudate; or the insufficient food intake which may be due to the food allergy; or diarrhea; all can explain why is hypoproteienemia reported in those AD patients **(Nomura et al., 2002).** In this study; symptoms of hypoproteinemia aren't prevalent in the cases with good food and adequate protein intake; also the difference between the studied group populations and proper use of steroid in the treatment in this studied group, these decrease the incidence of hypoprotienemia in this study's cases; subsequently, can affect the significance of protein supplementation. But the study cases show insignificant but good clinical improvement this may be explained by the protein supplementation adding to the value of the original treatment, it isn't the main treatment because of our cases don't have manifestations of hypoproteinemia.

Another study enrolled 26 AD infants younger than 1 year predominantly boys, they showed hypoproteinemia that accompanies AD disease which may arise as a result of the gradual reduction of topical steroid medication or as a result of eczema herpeticum, according to their hypothesis. It's possible that this is because that study typically involved cases of high severity or major complications. This could be due to selection bias. They indicated that the higher prevalence of hyperproteinemia in newborns aged less than one year may be related to a greater presence of protein leakage through the skin as a result of an inadequate skin barrier. Male predominance in that study characterized by having more muscle bulk, may explain why that studied group affected more with hypoproteinemia, but in this study no sex predominance unlike the mentioned study; males equal females, it may explain the cause of protein intake insignificance in this study **(jo et al., 2018)**.

CONCLUSION

This study showed that protein supplementation to AD patients showed good clinical improvement but unfortunately it showed no statistically significant difference from the non protein supplementation group , this reveals our need for further studies for assessment of the efficacy of protein supplementation in AD.

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