Use of nutricosmetic based on proteoglycan in non-cicatricial alopecia in children and adolescents

Uso de nutricosmético à base de proteoglicanos em alopecias não cicatriciais em crianças e adolescentes

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ABSTRACT

Introduction: Nutricosmetics have been used as supplements for hair growth in the treatment of non-cicatricial alopecia. However, there are no studies on using of these products in individuals under 18 years of age.

Objective: To assess the efficacy and tolerability of using a nutricosmetic product based on proteoglycans in individuals under 18 years of age with non-cicatricial alopecia.

Methods: This is a clinical, uncontrolled, and prospective trial. Patients with non-cicatricial alopecia, of both sexes, aged between 6 years and 18 years, received nutricosmetics containing proteoglycan for six months. Three dermatologists independently evaluated standardized pre and post-treatment photos. A hair count was performed in a scalp area of 1 cm^2, and the patients answered a questionnaire about improvement or worsening.

Results: Eleven patients (100% women) were included. Ten (91%) showed improvement after six months, observed through photographic evaluation, hair count, and self-assessment. No patient presented allergies. Two patients had transient epigastric pain.

Conclusions: The use of proteoglycans-based nutricosmetics was effective and well-tolerated in children and adolescents with non-cicatricial alopecia.

Keywords: Alopecia; Hair follicle; Proteoglycans; Treatment outcome

RESUMO

Introdução: *Nutricosméticos têm sido utilizados como suplementos para crescimento capilar no tratamento de alopecias não cicatriciais, porém não existem estudos sobre o uso desses produtos em indivíduos abaixo de 18 anos de idade.*

Objetivo: *Avaliar a eficácia e a tolerabilidade do uso de um produto nutricosmético à base de proteoglicanos em indivíduos menores de 18 anos, portadores de alopecias não cicatriciais.*

Métodos: *Ensaio clínico, não controlado e prospectivo. Portadores de alopecias não cicatriciais, de ambos os sexos, com faixa etária entre seis e 18 anos, receberam nutricosmético contendo proteoglicano por seis meses. Fotos padronizadas pré e pós-tratamento foram avaliadas independentemente por três dermatologistas. Foi realizada contagem de fios em área de 1cm^2 do couro cabeludo, e os pacientes responderam a questionário sobre melhora ou piora.*

Resultados: *Foram incluídas 11 pacientes (100% do sexo feminino), nas quais 10 (91%) apresentaram melhora após seis meses, constatada por meio de avaliação fotográfica, contagem de fios e autoavaliação. Nenhuma paciente apresentou alergia. Duas pacientes apresentaram desconforto epigástrico transitório.*

Conclusões: *O uso de nutricosmético à base de proteoglicanos foi eficaz e bem tolerado em crianças e adolescentes portadores de alopecias não cicatriciais.*

Palavras-chave: *Alopecia; Folículo piloso; Proteoglicanas; Terapêutica*

Original Articles

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INTRODUCTION

Hair does not play a vital role in humans. Still, aesthetic impairment can bring psychological damage to patients, due to its loss or rarefaction (alopecia), especially in children and women.[1,2,3] Hair loss is a frequent complaint in the dermatological office.[4,5]Alopecia can be subdivided into two large groups: non-scarring, potentially reversible; and scarring, characterized by permanent damage to the hair follicle.[1,6] Non-scarring alopecia is the most common form.[7]

Nutricosmetics (NC) contain vitamins, minerals, collagens, proteoglycans, and other substances, that work with food supplements. They are not considered drugs.[8,9,10] NCs have been widely used as an adjuvant therapeutic option in the treatment of alopecia, with the advantage, according to the pharmaceutical industry, [10-13] of presenting good results with few adverse events. However, few clinical studies support their use.[11,12] They have even been studied in pregnant women,[14] but there are no studies involving children and adolescents.

OBJECTIVE

The study's objective was to evaluate the efficacy and tolerance of a nutricosmetic based on proteoglycans in individuals under 18 years of age with non-scarring alopecia.

METHODS

We conducted an open, prospective, and uncontrolled clinical trial.

By convenience sample, we selected patients with non-scarring alopecia, of both sexes, less than 18 years old, seen at the Specialties Clinic of the Hospital Universitário de Londrina from November 2016 to October 2019. Participants received nutricosmetics (NC) based on specific 300 mg proteoglycans (versicans, decorins, and syndecans) in addition to acerola extract (118 mg), biotin (30 mcg), and silicon (75 mg).

The exclusion criteria were: allergy to fish (one of the product's components), scarring alopecia, and current use of any treatment for alopecia or other supplements.

Figure 1: Instrument with 1 cm2 for counting hair strands.

The institution provided the NC, and it was self-administered in two daily doses (tablets could be macerated for ingestion, if necessary).

Hair counting was performed in an area of 1 cm^2 at the scalp's most affected area due to alopecia before and after treatment. The principal investigator counted all the hair strands inside the mold with tweezers' aid through a 1cm x 1cm square hole made in a plate (Figure 1). There was no cutting or shaving of the hair.

Three dermatologists, members of the Brazilian Society of Dermatology and not involved in the research, evaluated standardized photos before and after treatment. The photos were as-

Table 1: Distribution by sex, age, phototype and diagnosis

	Sex	Age	Fothotype	Diagnosis
01	F	16a +1m+4d	III	Eflúvio telógeno
02	F	13a+11m+8d	IV	Eflúvio telógeno
03	F	17a+2m+21d	III	Eflúvio telógeno
04	F	11a+2m	IV	Tricorrinofalangiano-1
05	F	17a+1m	III	Eflúvio telógeno
06	F	17a+4m+26d	III	Tricorrinofalangiano-1
07	F	9a+9m+25d	III	Alopecia areata
08	F	16a+2m+28d	II	Eflúvio telógeno
09	F	9a+11m+19d	III	Alopecia areata
10	F	13a+9m+19d	IV	Alopecia areata
11	F	13a+6m+16d	III	Moniletrix

F=female a=age; m=months; d=days;

Table 2: Main results of the use of nutricosmetics consisting of proteoglycans for the treatment of non-scarring alopecia in individuals less than 18 years of age.

Paciente		T0	T6	*p-valor*
Densidade capilar (fios/cm2)				
	01	82	126	
	02	106	178	
	03	104	166	
	04	136	204	
	05	168	174	
	06	84	146	
	07	12	86	
	08	94	154	
	09	11	92	
	10	06	84	
	11	56	86	
Densidade média dos participantes *		**78**	**136**	**0,02**
Avaliação fotográfica (3 dermatologistas)**				
Piora importante		-	0/33	
Leve piora		-	0/33	
Inalterado		-	3/33	
Leve melhora		-	16/33	
Melhora importante		-	14/33	
Avaliação melhora leve/importante		-	30/33	**0,02**

**(média de fios e contagem de fios por paciente): T0(pré-tratamento); T6 (após 6 meses de tratamento)*
***(avaliação de 3 dermatologistas cegos independentes no total de 33 respostas possíveis)*

sessed both in chronological order (pre and post-treatment) and inverted to reduce the evaluator's bias. The dermatologists were informed about it and assessed the photos without knowing their chronological order. Scores were: -2 (significant worsening); -1 (slightly worsening); 0 (unaltered); +1 (slight improvement); + 2 (important improvement). The analysis only considered pre and post-treatment assessments.

Patients also answered a self-assessment questionnaire at the end of 6 months, indicating worsening, no change, and improving.

The following data were collected and entered into an Excel spreadsheet: name, hospital patient registration number, gender, age, phototype, duration of hair loss, previous treatment, laboratory tests (blood count, platelets, ferritin, TSH, blood glucose, creatinine, and transaminases).

The data were analyzed and processed using the GraphPad Instat and Excel 2007 software. Statistical significance was performed using the chi-square test, considering the 5% significance level ($p < 0.05$) and applied to compare sex and improvement. The outcomes were: density of hair in the target area, photographic evaluation, and self-evaluation of patients.

The Institution's Ethics and Research Committee approved the research, C.A.A.E number 57073416.9.0000.5231. The parents or guardians of the study participants signed the informed consent.

RESULT

Eleven patients were included, and their serum tests were normal. Although the study was not gender exclusive, subjects were 100% women, significant compared to men ($p = 0.001$). Age ranged from 9 years to 17 years (average of 13.2 years). Table 1 presents the diagnoses, with telogen effluvium being more prevalent (5/11).

Ninety-one percent (10/11) of the patients improved after six months of treatment when considering hair count and photo evaluation (Table 2 and Figures 2-5).

The invited dermatologists' evaluation of photographs pointed to an improvement in most cases (16 responses for slight

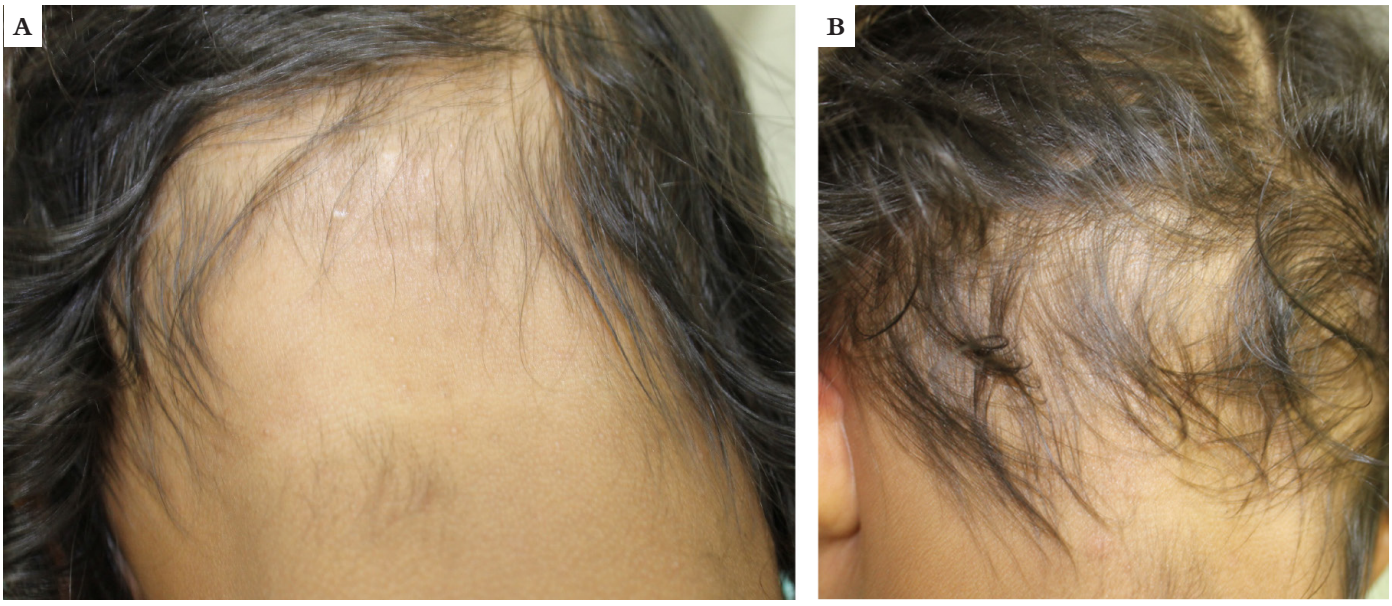

Figura 2: A - Patient with occipital alopecia areata (ophiasis). **B.** After 6 months of treatment

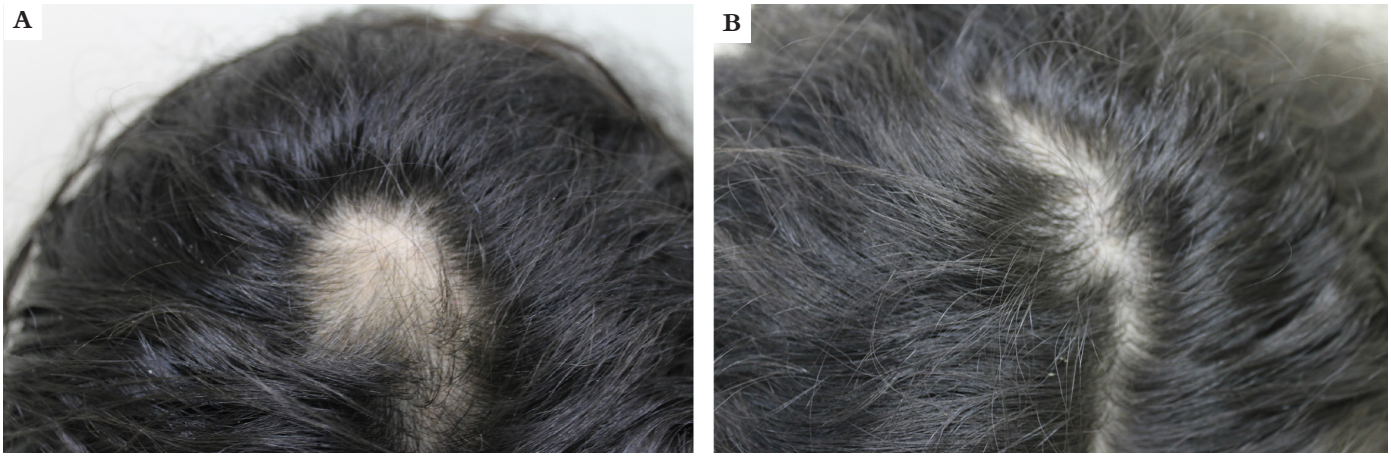

Figure 3: A - Patient with alopecia areata on scalp vertex. **B.** After 6 months of treatment

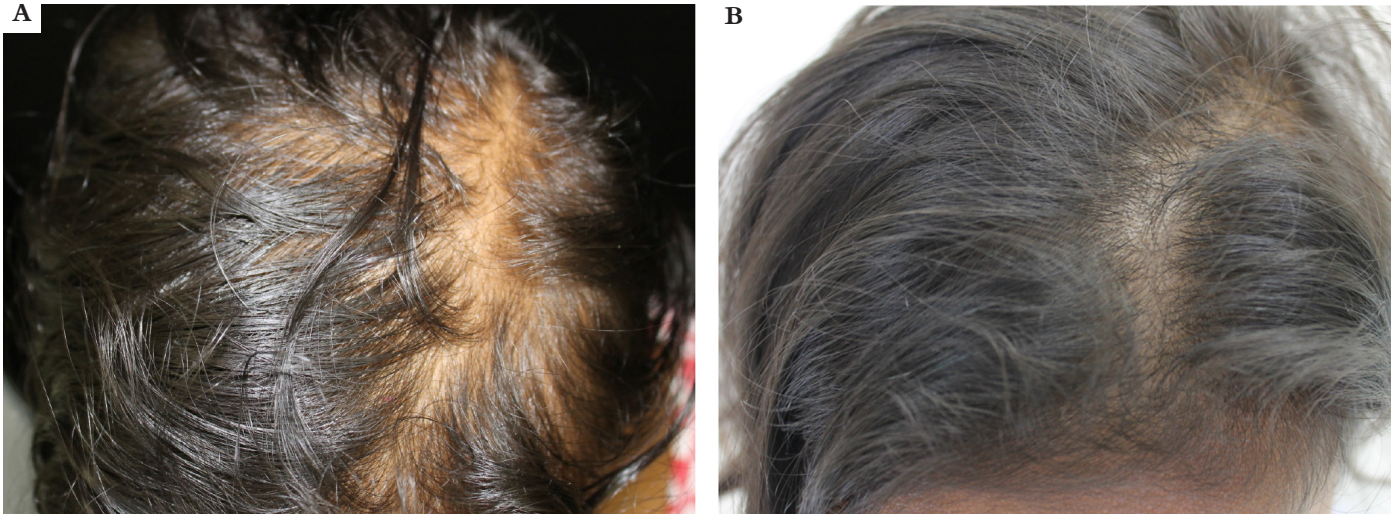

Figura 4: A - Patient with telogen effluvium **B.** After 6 months of treatment

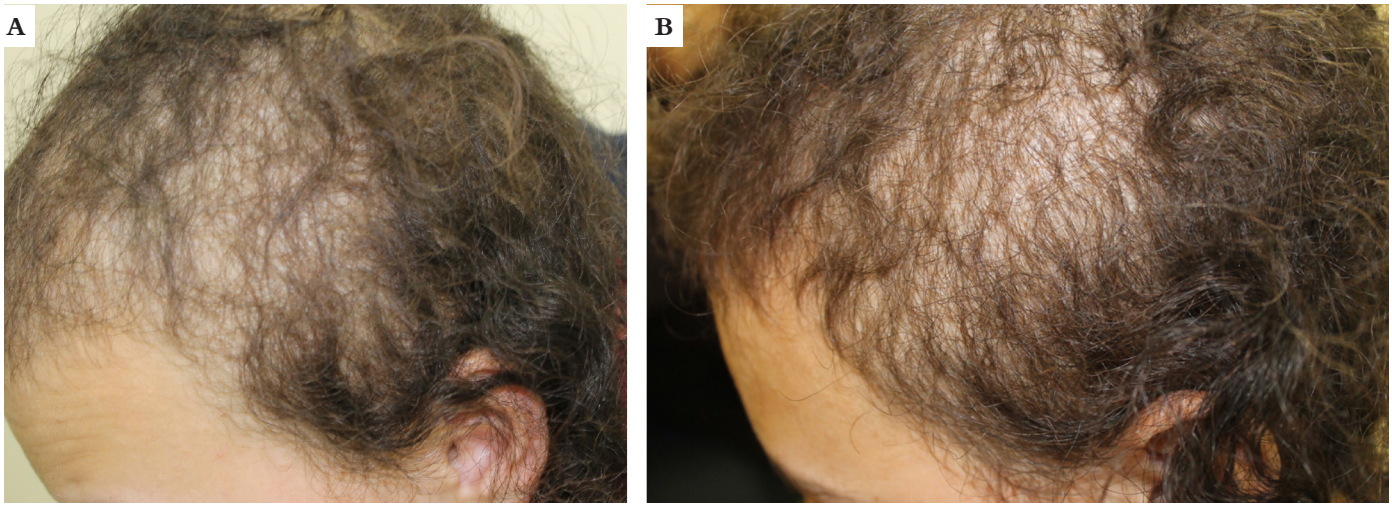

Figure 5: A - Patient with monilethrix. **B.** After 6 months of treatment

improvement and 14 responses as a significant improvement, in 33 possible responses). Three responses were left unaltered (Table 2).

The monilethrix patient (Figure 4) answered a questionnaire stating no improvement during the six months. However, the photographs and hair count showed improvement.

One patient (Figure 5) answered the questionnaire stating no improvement. The photographs showed no significant increase in volume. The increase in 6 hair strands (168 per cm^2 to 174 hair strand) was not significant when compared to the increase in other patients ($p = 0.59$), with consistency between the three points of evaluation (hair count, clinical and self-evaluation).

No patient reported allergies. The two youngest patients had an initial epigastric discomfort (nausea without vomiting) upon the ingestion of the nutricosmetic. None of the patients had abdominal pain or diarrhea related to product administration.

DISCUSSION

Alopecia can bring psychological harm to patients, especially children, adolescents, and women.[1,3] The 100% women sample can prove this (underage girls) since the study's objective was not to exclude the men population.

Hair growth supplements are NC containing different vitamins, minerals, collagens, proteoglycans, and other substances.[8,11,12,15] Even pregnant women have been evaluated in previous studies,[11] but there are no studies involving children and adolescents. It could be motivated by the difficulty in taking pills, little voluntary demand by children and adolescents for medical services, preference for topical treatments, and the difficulty in releasing parents for clinical trials.

The NC used in the present study contains 300 mg of proteoglycans (versicans, decorins, and syndecans) extracted from fish, in addition to acerola extract (118 mg), biotin (30 mcg), and silicon (75 mg), which help in the hemostasis of the human hair follicle.

Proteoglycans (PG) are the main components of the extracellular matrix (ECM), with direct and indirect cell signaling, presenting independent roles in regulating the hair follicle's growth state. They can control the activation of growth factors and other anagen inducers. Therefore, their concentration is a determining factor for the interaction cascades that lead to anagen initiation.[8]

Another key PG with anagen-inducing properties is decorin. It acts as a signal through the canonical insulin-like growth factor (IGF) signaling cascade and directly regulates cell death and the synthesis of other matrix constituents. Decorin actively blocks the transformation of growth factor-beta 1 (TGF-β1), a potent inducer of apoptosis and catagen, making it a potential anagen inducer.[8]

Also, PGs increase the stability of collagen fibrils and protect them from proteolytic cleavage. Thus, they are key modulators of fibrillogenesis. Versican has been shown to enhance the expression of fibronectin and β1-integrin that facilitates cell-ECM adhesion.[8]

The NC's adverse events are dyspepsia (gastric discomfort) and itching, especially in people allergic to fish.[11]

Telogen effluvium is a frequent cause of hair loss. [1,7] However, there are no data on its incidence in children and adolescents. The diagnosis was based on clinical history, traction test, normal trichoscopy, and removal of other causes. The presence of the TRPS-1 gene confirmed Trichorhinophalangeal syndrome type-1.[17] Clinical[18] and dermoscopic examination diagnosed the alopecia areata and monilethrix.

At the beginning of the medication, the participants' age range did not exceed 17 years + 6 months + 29 days to not reach the full 18 years after six months of treatment (Table 1). According to photographic evaluation, capillary density, and self-assessment questionnaire, 91% of the patients improved after

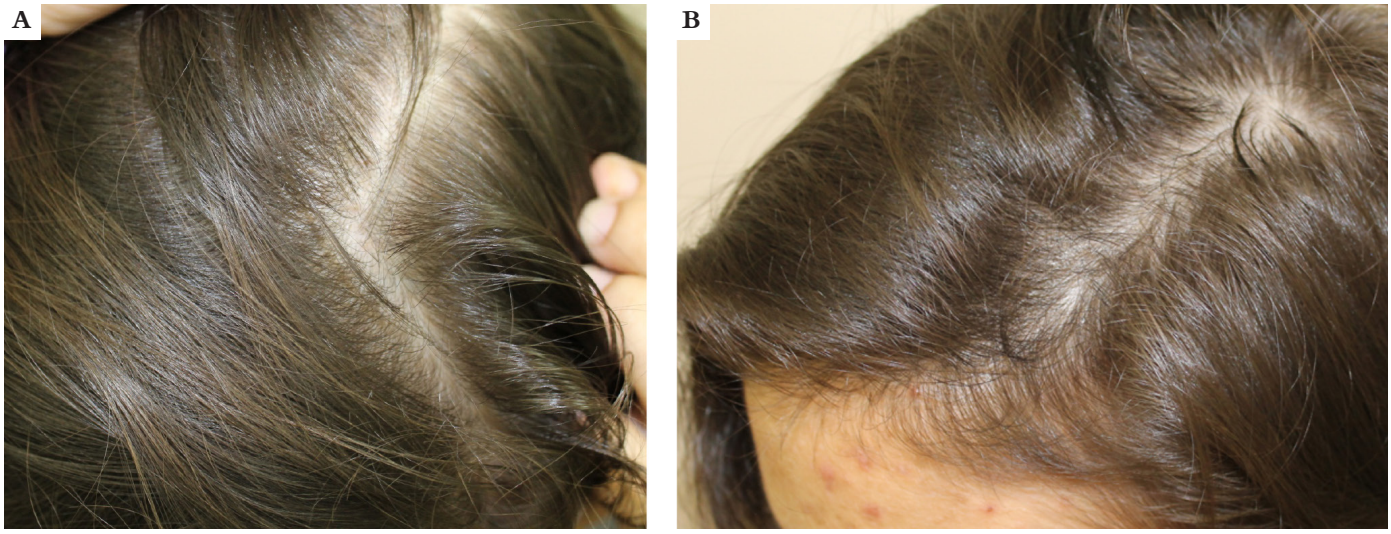

Figure 6: A - Patient with telogen effluvium. **B.** Patient after 6 months. Apparently no volume improvement.

six months of treatment (Table 2 and Figures 2, 3, 4, and 5). Only one case showed no improvement (Table 2 and Figure 6).

The dermatologists' evaluations of the photographs were in agreement with the result of the assessment of the capillary density of the most affected area. The option of not knowing which ones were the pre and post-treatment photos was meant for not inducing their responses.

None patient presented allergies. Two patients (the youngest) had to macerate the product and had nausea without vomiting at the beginning of the treatment, but completed the study. There were no complaints of epigastric pain, abdominal pain, or diarrhea.

The main limitations of the study are a small sample, not being controlled, the inclusion of participants with different diagnoses, and the possibility of spontaneous improvement of alopecia areata and telogen effluvium.[16,19]

CONCLUSION

The use of NC based on proteoglycans in monotherapy to treat children and adolescents with non-scarring alopecia proved to be effective and well-tolerated. These preliminary findings need to be confirmed by controlled, larger sample studies. ●

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