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Serum Uric Acid in Patients with Psoriasis Vulgaris and the Therapeutic Effect of Colchicine

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ABSTRACT

Background: Psoriasis is a chronic, proliferative, and inflammatory skin disorder that manifests as erythematous plaques coated in silvery scales, most often on the body's extensor surfaces, scalp, and lumbosacral area. Psoriasis individuals may potentially benefit from the antioxidant properties of SUA. Some evidence of colchicine's effectiveness in treating psoriasis has been gathered.

Objective: To compare the serum uric acid level in psoriasis vulgaris individuals with that of healthy controls and to evaluate the effect of the addition of colchicine to the ordinary treatment of psoriasis on the level of serum uric acid and the degree of improvement of psoriasis.

Patients and Methods: This prospective case-control research included 51 individuals with psoriasis, and conducted at outpatient clinic of the Dermatology, Andrology, and STDs Department at Mansoura University Hospitals.

Results: There was a statistically significant variance among the patients concerning PASI score after treatment and uric acid level after treatment, while there was no statistically significant variance regarding PASI score before treatment and baseline uric acid. Non-smoking and receiving colchicine were associated with a better PASI score in univariable analysis. However, in multivariable analysis, receiving colchicine was considered a predictor of a better PASI score.

Conclusion: Hyperuricemia was detected in psoriasis vulgaris cases, which showed improvement after the addition of colchicine to the treatment of hyperuricemia. Elevated serum uric acid levels didn't affect psoriasis severity. While receiving colchicine was considered a predictor of a better PASI score.

Keywords: Psoriasis vulgaris, Serum uric acid, Colchicine, Hyperuricemia.

INTRODUCTION

Psoriasis is a skin, nail, and joint condition that causes persistent inflammation. Elbows, knees, scalp, and lower back are popular sites for the red, scaly plaques that characterize this condition, but any area of skin is fair game [(1)].

Activated T cells infiltrate the skin, where they spur the growth of keratinocytes and contribute to the disease's pathogenesis. The accumulation of plaques is a direct outcome of the abnormal turnover of keratinocytes. Epidermal hyperplasia and parakeratosis are also common symptoms [(2)].

The Psoriasis Area and Severity Index (PASI) is the gold standard for quantifying the extent of the disease and gauging the success of therapy [(3)]. The metabolism of adenosine and guanosine, two purines, results in the production of uric acid. High uric acid levels are strongly correlated with insulin resistance and the onset of metabolic syndrome (MetS), which is thought to result from insulin resistance [(4)].

By stimulating the production of inflammatory chemokines, serum uric acid (SUA) mediates the inflammatory response [(5)]. Psoriasis individuals may potentially benefit from the antioxidant properties of SUA; as has been suggested [(6)].

Colchicine, a member of the alkaloid family, is found in plants like Colchicum autumnale that are in the lily family. Colchicine's cellular effects are principally brought about by blocking microtubule polymerization [(7)].

Some evidence of colchicine's effectiveness in treating psoriasis has been gathered from case series and cross-over studies. Pustular psoriasis and palmoplantar pustulosis are examples of psoriasis that are notoriously difficult to treat, and the medicine may be more effective in these cases [(8)].

The purpose of this research was to compare the serum uric acid level in psoriasis vulgaris individuals with that of healthy controls and to evaluate the effect of the addition of colchicine to the ordinary treatment of psoriasis on the level of serum uric acid and the degree of improvement of psoriasis.

PATIENTS AND METHODS

This was prospective case-control research to compare SUA in patients with that in controls and an extended clinical trial to assess the efficacy of adding colchicine to the ordinary treatment of psoriasis. The study included 51 patients with psoriasis and was conducted at an outpatient clinic of the Dermatology, Andrology and STDs Department at Mansoura University Hospitals.

Sample size: The required sample size was calculated using the IBM[a] SPSS[a] Sample Power[a] version 3.0.1 (IBM[a] Corp., Armonk, NY, USA). Based on an exhaustive literature review, **Yilmaz *et al.*** [(4)] found that the mean serum uric acid level in psoriasis cases was 5.08 mg/dl (SD 1.33) compared to 4.59 mg/dl (SD 1.26) in the control group. This distinction among the categories was used to determine the sample size. At a

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significance level of 95 percent and a power of 80 percent, the minimum sample size required for each group was calculated to be 44 individuals.

Patients group: included 51 patients with psoriasis; the patients were divided at random into 2 equal subgroups: **Subgroup A:** received treatment using topical corticosteroid (betamethasone 0.1% betaderm cream) twice daily + NBUVB 3 times/week for 12 weeks. **Subgroup B:** received treatment using topical corticosteroid + NBUVB + colchicine tablets (0.025 mg/kg/day) divided on 2 doses/day for 3 months (colchicine 0.6 mg tab) [(9)].

The **control group** included 50 apparently healthy, age- and gender-matched subjects. They were chosen not to have any autoimmune illness and on no interfering medications, not suffering from any disease, nor receiving any medications that may affect their SUA level.

Inclusion criteria: age ≥18 years, both genders, and patients with mild and moderate psoriasis (Chronic plaque psoriasis vulgaris).

Exclusion criteria: age ≤18 years, patients having other autoimmune diseases and individuals who had acute illness, patients with medical conditions known to affect serum UA such as renal disease and cancer, and history of excessive consumption of alcohol and caffeine.

Method of randomization

Using computer-generated random tables, cases were randomly divided into two equal groups in accordance with the employed method.

Methods

All cases in the study were subjected to the following: Complete history-taking, complete physical examination (general and full dermatological examination).

Biochemical analysis

Serum uric acid was estimated by the automated chemistry analyzer Cobas 111 using the uricase method (Germany) [(10)]. Peripheral blood samples were obtained from all study subjects (4 ml). The blood samples were allowed to clot at room temperature for ten to twenty minutes before centrifugation for twenty minutes at a speed of 2000–3000 rpm. Serum samples were collected and stored at -20°C until the time of the assay.

Follow-up: The patients were followed up every 2 weeks, and PASI score was assessed at every visit, and the patient was asked about his satisfaction. After the treatment, the serum level of uric acid was assessed again in the patients' group.

Ethical consideration:

All participants provided written informed consent prior to inclusion in the investigation, which included an explanation of the significance of the research and the procedures that were initiated. An approval from the institutional review board (IRB), Faculty of Medicine, Mansoura University, was obtained before the start of the study. At all stages of the investigation, confidentiality and individual privacy were upheld. Patients were permitted to disengage from the study at any time with no repercussions and the data collected was utilized exclusively for scientific purposes. The Helsinki Declaration was followed throughout the study's conduct.

Statistical analysis

The collected data were coded, processed, and analyzed utilizing the SPSS (Statistical Package for the Social Sciences) version 26 for Windows® (IBM SPSS Inc., Chicago, IL, USA). Qualitative data were described in the form of numbers and percentages and were compared by Chi-Square test. Quantitative data were expressed as mean± standard deviation (SD) or standard error (SE), or median (range) in accordance with normality. They were compared by student T test, Mann-Whitney test (U test), and Wilcoxon signed rank sum test. Correlation analysis, and regression analysis were also used and $P< 0.05$ was considered statistically significant.

RESULTS

There was significant between cases and healthy control regarding gender and age (Table 1).

Table (1): Comparison of patients with psoriasis vulgaris and control groups regarding demographic data

	Psoriasis vulgaris n = 51		Control n = 50		Test (p)
	No.	%	No.	%	
Gender					
Male	22	43.1%	21	42.0%	X^2=0.013 P=0.908
Female	29	56.9%	29	58.0%	
Age (years)					
Mean ± SD	38.04 ± 11.46		36.72 ± 11.11		Student t-test=0.587 p=0.559
Median (Range)	38.0 (19.0 – 59.0)		36.5 (19.0 – 59.0)		

SD. Standard deviation Range: Min.-Max. X^2, Chi-Square

PASI score was assessed; no significant difference was found before treatment, while after treatment, both groups showed significant improvement. On comparing PASI scores after treatment between both groups, those who received colchicine had a significantly better PASI score when compared to those who did not receive colchicine (Table 2).

Table (2): Comparison of patients with psoriasis vulgaris who received colchicine and didn't receive colchicine regarding PASI.

	Psoriasis vulgaris n = 51		Test (p1)
	Received colchicine n=26	Did not receive colchicine n=25	
PASI start of treatment			
Mean ± SE	6.46 ± 0.71	7.00 ± 0.76	U=355.0 p=0.572
Median (Range)	6.9 (1.6 – 17.7)	6.9 (0.8 – 15.1)	
PASI after 12 weeks			
Mean ± SE.	4.43 ± 0.51	6.52 ± 0.70	U=438.5 p=0.032*
Median (Range)	4.3 (0.7 – 9.9)	6.5 (0.7 – 14.1)	
P2	<0.001*	<0.001*	

SE: Standard Error, Range: Min. – Max. *: Significant ≤0.05
P1: Comparison between cases who received and those who did not receive colchicine.
P2: Comparison among before and after treatment in each group.

Baseline uric acid differed significantly between psoriasis vulgaris cases and the control group. Moreover, uric acid levels after treatment decreased significantly when compared to before treatment. In addition, after treatment, uric acid did not decrease to the control level and was still higher than the control group (Table 3).

Table (3): Comparison of patients with psoriasis vulgaris and control groups regarding uric acid.

	Psoriasis vulgaris n = 51		Control n = 50	P1	P2	P3
	Before treatment	After treatment				
Uric acid (mg/dL)						
Mean ± SE	7.10 ± 0.24	6.22 ± 0.22	5.36 ± 0.50	<0.001*	<0.001*	<0.001*

SE. Standard Error, Range: Min. – Max. *: Significant ≤0.05
P1: Comparing between start and end of treatment by Wilcoxon test.
P2: Comparing between psoriasis vulgaris at start of treatment and control by Mann-Whitney.
P3: Comparing between psoriasis vulgaris at end of treatment and control by Mann-Whitney.

No significant differences were found between patients who received colchicine and those who didn't receive colchicine regarding baseline uric acid. After treatment, uric acid decreased significantly in both groups. On comparing uric acid levels after treatment between both groups, it was significantly lower in those who received colchicine when compared to those who did not receive colchicine (Table 4).

Table (4): Comparison of patients with psoriasis vulgaris who received colchicine and didn't receive colchicine regarding uric acid.

Uric Acid (mg/dL)	Psoriasis vulgaris n = 51		Test (p1)
	Received colchicine n=26	Did not receive colchicine n=25	
Before treatment			
Mean ± SE	7.10 ± 0.34	7.09 ± 0.33	U=312.5 p=0.814
After treatment			
Mean ± SE	5.67 ± 0.24	6.79 ± 0.33	U=449.0 p=0.019*
P2	<0.001*	0.004*	

SE: Standard Error, Range: Min. – Max. *: Significant ≤0.05.

P1: Comparing between cases who received and those who did not receive colchicine by Mann-Whitney test.
P2: Comparing between start and end of treatment by Wilcoxon test.

No significant association was found among uric acid level versus gender, smoking, drug use, or family history among patients with psoriasis vulgari

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Table (5): Association between uric acid and different parameters among patients with psoriasis vulgaris.

		N	Patients with Psoriasis vulgaris n = 51					
			Uric acid before treatment			Uric acid after treatment		
			Mean ± SE.	Median	Range	Mean ± SE.	Median	Range
Sex	**Male**		6.4± 0.4	6.3	1.4–16	5.7± 0.2	6	3.9– 7.3
	Female		6.1± 0.4	5.7	1.3–14.5	6.6± 0.3	6.3	3.5– 11.2
	^{U}p			**0.516**			**0.106**	
Smoker	**No**	**41**	7.07 ± 0.29	6.90	4.0 – 11.9	6.31 ± 0.26	6.20	3.5 – 11.3
	Yes	**10**	7.23 ± 0.28	7.25	6.0 – 9.1	5.85 ± 0.27	5.80	4.2 – 7.1
	^{U}p			**0.420**			**0.426**	
Drug history	**No**	**8**	6.23 ± 0.44	6.25	4.0 – 7.8	5.16 ± 0.43	5.45	3.5 – 7.1
	Yes	**43**	7.26 ± 0.26	7.00	4.3 – 11.9	6.41 ± 0.23	6.20	3.9 – 11.3
	^{U}p			**0.169**			**0.131**	
Family history	**Negative**	**34**	6.82 ± 0.27	6.90	4.0 – 11.9	5.88 ± 0.21	6.00	3.5 – 8.6
	Positive	**17**	7.65 ± 0.45	7.30	5.1 – 11.3	6.89 ± 0.47	6.80	3.9 – 11.3
	^{U}p			**0.147**			**0.087**	

SE. Standard Error; Range: Min. – Max. *: Significant ≤0.05; ^{U}p, p value for Mann Whitney (U) test.

We used age, sex, family history, smoking, baseline PASI, uric acid, and the addition of colchicine to treatment as confounders in regression analysis to try to predict which patients would improve their PASI scores the most. Non-smoking and receiving colchicine were associated with a better PASI score in univariable analysis. However, in multivariable analysis, receiving colchicine was considered a predictor of a better PASI score.

Table (6): Regression analysis for prediction of better PASI score improvement.

	Univariable		Multivariable	
	β	p	β	p
Age	0.021	0.927		
Gender	8.601	0.189		
Positive family history	-3.973	0.465		
Smoking	-6.925	0.005*	0.241	0.110
Age of onset	0.179	0.446		
Baseline PASI	0.109	0.877		
Baseline uric acid	-0.043	0.978		
Colchicine addition	1.488	<0.001*	1.433	<0.001*

β, regression coefficient, *: Significant ≤0.05.

DISCUSSION

The present research demonstrated that the mean age of psoriasis cases was 38, ranging from 19 to 59 years. They were 43.1% males and 56.9% females. No other skin disease was found among all the studied cases. In the same line as **Armstrong *et al*.** [11] who examined a total of 12,625 participants with psoriasis, their mean (SD) age was 32.8 (24.1) years; of them, 6492 were women (51.4%) and 6133 were men (48.6%), which agreed with our results regarding female predominance and the mean age group.

The present study showed that, regarding the addition of colchicine to their treatment, cases who received and those who did not receive colchicine were matched regarding all baseline data, with no significant differences between both groups regarding systemic diseases, drug and family history, age of onset, and their baseline PASI. After treatment, cases who received colchicine had significantly better PASI scores when compared to those who did not receive colchicine. **Taguchi *et al.*** [12] combined the use of secukinumab and guselkumab with colchicine to treat relapses in two patients with generalized pustular psoriasis who had shown improvement while using the biologics. Pustular psoriasis treatments include cyclosporine, acitretin, and biologicals; however, colchicine might be administered first if necessary. The treatment may be more useful in resistant or difficult-to-treat psoriasis, such as pustular psoriasis and palmoplantar pustulosis [8].

The current research showed that baseline uric acid was higher in PV cases than the control group (median was 6.9 versus 4.2, respectively). Moreover, uric acid levels after treatment with colchicine decreased significantly when compared to before treatment (median = 6.1 versus 4.2). A hospital-based cross-sectional study was performed by **Gui *et al.*** [13], containing 117 psoriatic cases and 117 controls matched for age, sex, and body mass index. Psoriatic cases had higher levels of serum uric acid (6.25 ± 1.62 vs. 5.71 ± 1.35 mg/dl) and significantly higher incidence of hyperuricemia (31.6% vs. 16.2%) than cases without psoriasis, which agreed with our results.

The current research indicates that serum uric acid levels were significantly lower in those who received colchicine when compared to those who did not receive colchicine. While **Isha *et al.*** [14] evaluated uric acid levels in twenty-four individuals both before and after psoriasis therapy for a period of twelve weeks. Individuals whose psoriasis improved also showed statistically significant decreases in blood uric acid levels. Psoriasis patients with hyperuricemia are at a higher risk for acquiring inflammatory comorbidities, including cardiovascular disease, and may experience the onset of gouty arthritis and debilitating pain. Monitoring uric acid levels on a regular basis and treating hyperuricemia as soon as it causes changes is crucial.

The current research revealed no significant association was found among uric acid level versus gender, smoking, drug and family history local examination of skin, nail and hair among patients with psoriasis vulgaris.

Zhang *et al.* [6] widened their search for evidence that links psoriasis with hyperuricemia, and they found a possible link among the morbidity of cardiovascular and metabolic disorders as well as SUA elevation in psoriasis cases.

In this study, regression analysis was used to predict who would improve their PASI score the most, taking into account factors like age, gender, family history, smoking, baseline PASI, uric acid, and the addition of colchicine to their treatment. Receiving colchicine was considered a predictor of a better PASI score.

In another report, multivariate logistic regression analysis presented that psoriasis can be a strong predictor of hyperuricemia; psoriasis was a significantly positive predictor of hyperuricemia after adjusting for associated baseline characteristics such as age, gender, BMI, and other features of metabolic syndrome. Convincing evidence has indicated that psoriasis is independently associated with hyperuricemia [15, 16].

CONCLUSION

In conclusion, hyperuricemia was detected in psoriasis vulgaris cases, which showed improvement after the addition of colchicine to the treatment of hyperuricemia. Elevated serum uric acid levels didn't

affect psoriasis severity. While receiving colchicine was considered a predictor of a better PASI score.

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