



Colchicine as a Steroid - Sparing Agent: A Novel Therapeutic Approach for Chronic Urticaria

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Abstract

Background

Chronic urticaria is defined as the occurrence of wheals and/or angioedema for at least six weeks. Till now, steroids, antihistaminic agents, antimalarial agents, and immunosuppressive agents were found to be useful in urticaria. Steroids were most commonly used. But steroids have got various adverse effects. Colchicine was used for treating gout and Mediterranean fever. But in our study, we would like to assess the role of colchicine, being an anti-inflammatory drug, in treating chronic urticaria.

Objective

To assess the efficacy of colchicine in treating chronic urticaria.

Methods

This interventional study was done at a tertiary care centre among 30 patients who came to the dermatology department of Fathima Institute of Medical Sciences, Andhra Pradesh, from January 2022 to December 2022 diagnosed with chronic urticaria. Pregnant and lactating women, patients with gout, and patients with acute serious illnesses that disturb data collection were excluded from the study.

Results

Most of the patients belonged to the age group 31-40 years. Most of the patients were females. The lesions were seen throughout the body in the majority of patients. There was a significant difference in the symptomatology and lesions before and after treatment with colchicine. Diarrhoea was seen in 4% of patients, which was self-limiting. There were no major side effects seen with colchicine among the remaining patients.

Conclusion

Colchicine acts as an effective novel therapeutic agent for treating chronic urticaria that is resistant to other therapies.

Keywords

Colchicine, steroid-sparing agent, urticaria, anti-histamine, Urticaria activity score.

Introduction

Chronic urticaria is defined as the occurrence of wheals and/or angioedema for at least six weeks.¹ These lesions usually develop throughout the body.² Patients with urticaria show papules and plaques, which are transient, pruritic, non-scaling, erythematous, and oedematous. The prevalence of chronic urticaria is approximately 0.1%–3% among the general population. Acute urticaria is commonly seen among children. But chronic urticaria may be seen at any age. Regarding gender, the prevalence was slightly more common among females. Urticaria is related to autoimmune disease and this was found when researchers reported an association between thyroid disease and chronic urticaria.³⁻⁴ Increased anti-thyroid antibodies can be seen among 12% of patients with chronic urticaria.⁵ Treatment of urticaria includes usage of antihistaminic agents, which are 1st line of medications. Steroids were used for patients who

won't respond to antihistaminic medications. Colchicine may be used, as steroids have various adverse effects like increased incidence of hyperglycemia, hypertension, skin atrophy, glaucoma, cataract, osteoporosis, gastric erosions etc.⁶⁻⁹ Previous literature suggested the use of colchicine for treating chronic urticaria. It was approved by the US food and drug administration for treating gout and familial Mediterranean fever only. But colchicine having many anti-inflammatory properties may be used in treating urticaria also. It acts by disrupting cytoskeletal functions, by inhibiting the polymerization of beta-tubulin into microtubules, preventing activation, degranulation, and finally migration of neutrophils. It blocks metaphase by disrupting mitotic spindle formation and sol-gel formation. Various side effects of colchicine are related to this anti-mitotic activity within skin, hair, and bone marrow, which are proliferative tissues.¹⁰⁻¹¹ It is given orally or applied topically as a gel. It is available as a 0.6mg tablet, capsule, and gel. It is obtained from *Colchicum autumnale*. Colchicine has a favorable safety profile at routinely prescribed doses. It is inexpensive and has a quick onset of action. Previously only a few studies were done on colchicine in chronic urticaria in western countries.¹²⁻¹³ But the literature is lacking in India. So, the current study was conducted. Till now, steroids, antihistaminic agents, indomethacin, antimalarial agents, and immunosuppressive agents like chlorambucil, azathioprine, and cyclophosphamide were found to be useful in chronic urticaria. The novelty of this study was that, we are evaluating the role and efficacy of colchicine in chronic urticaria.

Aim

This study was done to assess the efficacy of

colchicine in managing patients with chronic urticaria.

Materials and Methods

Source of data: This interventional study was done on patients coming to the Dermatology outpatient unit of a tertiary center named Fathima Institute of Medical Sciences, Kadapa, Andhra Pradesh, from January 2022 to December 2022 who were diagnosed to have chronic urticaria.

Inclusion Criteria

- Patients of any age and gender diagnosed to have chronic urticaria.
- Patients who received conservative treatment for at least 6 months but didn't respond to treatment
- Patients who provided informed consent to participate in the study.

Exclusion Criteria

- Pregnant and lactating women
- Patients with a known history of allergy to colchicine
- Patients with Gout
- Patients with acute severe illness, interfering with data collection
- Patients with incomplete data

Sampling: Simple random sampling method was used to select study population.

Sample size calculation: Lifetime prevalence of urticaria in India ranged from 7.8% to 22.3%.¹⁴

Considering this prevalence, the sample size is estimated as follows:

$$N=Z^2PQ/E^2$$

N=Sample size

P=Prevalence

Q=1-P

N=29

Confidence levels - 80% (power)

Error-10%

29 is the minimum sample size. So, we included 30 patients in this study.

Colchicine 0.6mg tablet was given once daily for all patients for 1 week. Response was assessed after 1 week. All patients were followed up till 3 months to check for any relapse.

Parameters Assessed

- Age
- Gender
- Duration of disease
- Presence of vasculitis
- Percentage of Responders – as per symptomatic improvement
- Steroid usage reduction during follow-up period
- UAS (Urticaria activity score) 7 score
- Adverse effects of colchicine
- Any relapse during follow-up

Urticaria activity score: It is commonly used diary-based patient-reported measure which estimates severity of itching and hive count in chronic urticaria.¹⁵

Score	Weals	Score	Itch
0	No	0	No
1	Mild (<20/24 hours)	1	Mild (present but not disturbing)
2	Moderate (20-50/24 hours)	2	Moderate (disturbing but not interfere with daily activities or sleep)
3	Severe	3	Severe(severe itching, interferes with daily activities or sleep)

UAS7: Urticaria activity score for 7 days; total (minimum 0-maximum 42)
 (UAS7≤6 may be evaluated as well controlled, 7-15 as mild, 16-27 moderate and 28-42 severe urticaria)⁵⁴

Figure 1: shows UAS-severity of score (mild, moderate and severe categories).¹⁶

Statistical Analysis

Data analysis was done using Epi Info software version 7.2.5. The results were expressed as mean ± S.D, percentages, and symptomatology before and after colchicine were compared using the chi-square test. ANOVA was used to compared steroid dosage reduction. P value < 0.05 was considered significant.

Ethical Considerations

Ethical committee approval was taken before

conducting the study. The informed consent form was taken from every patient who participated in the study.

Results

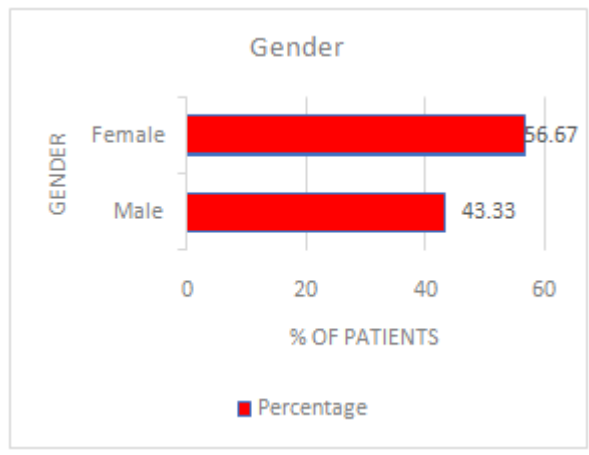
Demography

The mean age of patients was 36.2±1.2 years and most of the patients were females. Most of the patients (57%) belonged to the age group 31 to 40 years.

Age distribution	Frequency	Percentage
<20 years	4	13.33%
21-30	7	23.33%
31-40	11	36.67%
41-50	5	16.67%
above 50	3	10%

Table 1: illustrates age distribution of study patients.

Gender: Most of the patients were females.



Graph 1: shows the gender distribution the of study population

Duration of disease

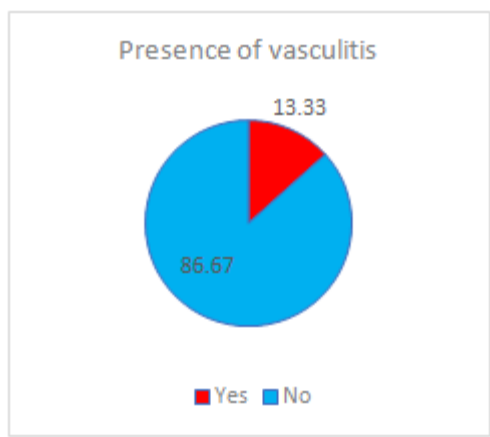
Most of the patients were suffering from chronic urticaria for more than 1 year.

Duration of disease	Frequency	Percentage
6 weeks - 6 months	7	23.33%
7-12 months	10	33.33%
Above 12 months	13	43.33%

Table 2: illustrates duration of chronic urticaria in study population.

Presence of vasculitis

Vasculitis was seen among 4 patients.



Graph 2: illustrates the presence of vasculitis among study patients.

Percentage of Responders

90% of patients responded well to colchicine as per the symptomatic improvement. There was complete

resolution of symptoms in 90% of patients and partial resolution in the remaining 10% of patients.

Symptomatic improvement	Frequency	Percentage
Complete resolution or response	27	90%
Partial resolution	3	10%

Table 3: illustrates symptomatic improvement among the study population.

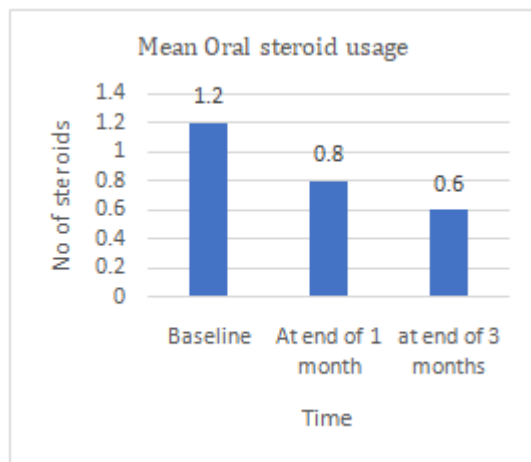
Steroid usage during follow-up

Most of the patients were using oral steroids -either prednisolone or methylprednisolone for their chronic urticaria. The mean no of doses of oral steroid usage before treatment with colchicine was 1.2 ± 0.3 . This

mean came down to 0.8 ± 0.2 by the end of 1 month and by 0.6 ± 0.25 by the end of 3 months. There is a significant reduction in the usage of oral steroids after treatment with colchicine as per ANOVA analysis. ($p=0.00$).

SS	df	MS	F	p
Between:	5.600	2	2.800	0.000
Within:	5.583	87	0.064	
Total:	11.183	89		

Table 4: illustrates ANOVA calculation for no of oral steroid usage before and after treatment with colchicine at the end of 1 and 3 months of follow up.



Graph 4: illustrates mean oral steroid usage from baseline to 3 months

Urticaria activity score

The mean score was 18.2 ± 2.4 before treatment with colchicine and it was 2.3 ± 0.9 after treatment with colchicine.

There is a significant improvement in the urticaria activity score as per the T-test. ($p=0.00$).

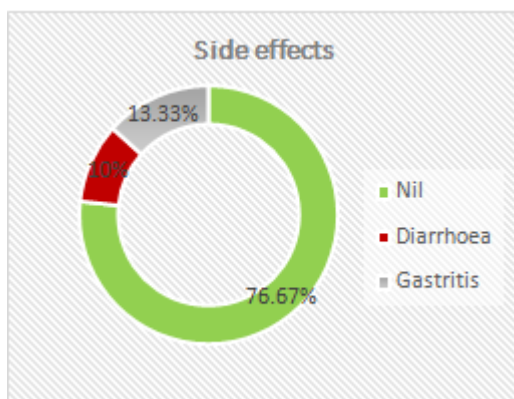
UAS	Mean±SD	P value
Before treatment	18.2 ± 2.4	0.000
After treatment	2.3 ± 0.9	

SS	df	MS	F	p
Between:	5.600	2	2.800	0.000
Within:	5.583	87	0.064	
Total:	11.183	89		

5 illustrates UAS before and after treatment

Adverse effects of colchicine

76.67% have no adverse effects due to colchicine. Diarrhoea seen in 10% patients subsided in 24 hours.



Graph 5: illustrates the side effects of colchicine (nil, diarrhoea and gastritis)

Relapse: Among 30 patients, relapse was seen in 4 patients within 3-month follow-up period.

Relapse of urticaria	Frequency	Percentage
Yes	7	23.33%
No	23	76.67%

Table 6: illustrates relapse among the study population.

Discussion

The study included 30 patients with chronic urticaria. The mean age of patients was 36 years and most of the patients were females in our study. Most of the patients had urticaria for more than 12 months and only 13% had vasculitis. Colchicine was given in the dose of 0.6mg orally once daily for 1 week. In the study of Martinez et al.¹⁷ the authors included paediatric patients aged 6 to 25 years. None had evidence of urticarial vasculitis. Patients were prescribed colchicine 0.6 mg or 1.2 mg daily. Results showed that each patient had significant improvement in symptoms after adding colchicine.

In the retrospective study of Pho LN¹³, the authors wanted to determine the efficacy and safety of colchicine among patients with chronic urticaria. 36

patients were included in their study. Duration of treatment ranged from one month to 17 months, while in our study, colchicine was given for 1 week. Therapy was said to be complete among 15 patients and partial among 5 patients. While in our study, a complete response was seen among 90% of patients. 15% of patients stopped colchicine due to diarrhoea and hematuria. In our study also, diarrhoea was seen among 10% of patients. 27% of patients had recurrence after colchicine was stopped. In our study, during a follow up period of 3 months after stopping colchicine, relapse was seen among 23.3% of patients, which is almost similar finding. Colchicine is generally safe but causes serious reactions very rarely.

Yonkof et al.¹⁸ reported hypocellular bone marrow or bone marrow suppression due to colchicine usage in a 19-year-old female suffering from chronic urticaria. Other novel treatment options for chronic urticaria include usage of calcineurin inhibitors like cyclosporin, UV therapy and Omalizumab according to some studies.¹⁹⁻²³

In the study of Nabavizadeh, 55 chronic urticaria euthyroid patients were included. Urticaria assessment was done using UAS score, similar to our study. They also assessed UQL- Q score and found that there was no significant statistical difference between cases and controls. The authors concluded that colchicine can effectively manage signs and symptoms of chronic urticaria, which improve the patient's quality of life. We also had the same opinion. In our study, we didn't assess the quality of life among urticaria patients after treating with colchicine. The strength of this study was we provided effective intervention to patients with chronic urticaria at free of cost. More studies and/or clinical trials are required to confirm the results reported in this research article. The main limitation is the small sample size.

We recommend studies on the comparison of corticosteroids, antimalarial agents, antihistaminic agents and immunosuppressants with colchicine among patients with chronic urticaria.

The study is self-sponsored.

There were no conflicts of interest.

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Conclusion

In the current study, we tested the efficacy of colchicine among patients suffering from chronic urticaria. Results showed that there was a significant

improvement in symptoms-after 1 week of treatment. Hence, we concluded that colchicine is a safe and effective relatively novel therapeutic strategy for patients suffering from chronic urticaria. It helps to reduce the usage of steroids.

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