ISSN 0975-2366
DOI:https://doi.org/10.31838/ijpr/2020.12.03.057

Research Article

Effectiveness of oral colchicine in the management of lichen planus

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Received: 24.01.20, Revised: 21.02.20, Accepted: 09.03.20

ABSTRACT

Aim and objectives: The goal of present work is to record the increase in the rate of lichen planus in Iraqi people and to study the effectivity and safety of colchicine as a therapeutic option among lichen planus patients. ***Materials and methods:*** This study in a design of a cross-sectional, 92 patients of lichen planus, were enrolled from those patients referred the outpatients clinic of section of dermatology and venereology in Merjan teaching hospital and Alhussein teaching hospital in Thi Qar , Iraq for a period extended from Jan. 2018 to Jan. 2019. Oral colchicine 1 g once daily was prescribed to every lichen planus patients in the study. Duration of therapy extended from one month to three months then follow up for another three months. Response to treatment was reported at every visit. Photographs were taken at both pre and post treatment visits. ***Results***: Out of the entire 92 patients involved in the study, 4 patients withdrew from the study because of gastrointestinal side effects of colchicine, while 3 patients were missed to follow up thus were omitted from the study. Beyond the residual 85 patients 39 were males (46%) and 46 females (54%) (female to male ratio 1.18:1). Age of patients ranged from 19-56 years. The most common type of lichen planus was classical type followed by actinic lichen planus, oral lichen planus was the third in frequency, while lichen planopillaris was the fourth making hypertrophic variant of lichen planus as the least common clinical variant. Enhancement in lichen planus lesions was more noticeable and obvious in patients who were under colchicine therapy for prolonged interval (the full three months). Good improvement (>70% reduction in the severity of lichen planus lesions) was noted clinically in 55 patients forming (64.7%) of all patients in the study. Moderate response (30-70% improvement) was detected in 22 patients forming (25.8%) out of total patients. Otherwise poor response to colchicine therapy (less than 30% improvement in lichen planus lesions) was seen in 8 patients only forming (11.7%) out of all patients in this study. ***Conclusion***: colchicine seems to be effective drug, safe and good choice for those challenging cases of lichen planus.

Keywords: colchicine, lichen planus, treatment modalities, Iraqi patients.

INTRODUCTION

Lichen planus (LP) is a public, inflammatory skin pathology that may involve hair follicles and mucous membranes. It is an idiopathic disease, with deteriorations and diminution phases[(1)]. Classic LP is patented by pruritic, violaceous papules that in favor the extremities [(2)], especially on the flexoral aspects in cutaneous LP and presents as trivial scratchy violaceous papules. The lesions are characteristically bilateral and symmetric[(3)].

There are plentiful variants of LP which can be recognized from the classical form based on morphology and lesions distribution[(4)].

Actinic or subtropical LP arises in kids or young adults with dusky skin living in warm conditions; nearly entire cases initiate from the Middle East, East Africa or India. Disease occur on unprotected face as distinct annular or discoid spots, which have an intensely hyper-pigmented center bordered by a prominent hypo-pigmented zone [(1)].

Oral LP can distress the skin and any coating mucosa, such as oral, esophageal, vaginal mucosa in addition to the skin. Habitually, it is initiate only in the oral cavity. It is the mucosal corresponding item of cutaneous LP, ensues recurrently in forties of age and disturbs females over and above males within ratio of 1.4:1[(5)]. Oral cavity, the buccal mucosa, tongue and the gingiva are regularly intricate even though further locations may be hardly involved. Lesions occurred solely on the mucosa of the oral cavity or with simultaneous skin scratches. Divergent clinical variants such as reticular, atrophic, hypertrophic and erosive are well familiar [(1)]. It might similarly exist with a burning impression in

the mouth, and as white lines adjacent sites of scratching (Wickham striae) [6].

Lichen planopilaris (LPP) is a comparatively scarce dermatopathy categorized by a long-lasting inflammatory status with lymphocyte infiltration that favorites to the discerning demolition of hair follicles, thus consequential in scarring alopecia [7]. LPP or Follicular LP lesions usually perform in the path of characteristic LP, nonetheless intermittently they preponderate and identification may then be challenging [8].

Even though autoimmunity is evidently proposed to be essential in LP, the precise pathological mechanisms are indistinct. LP is assumed to be an inflammatory autoimmune disease that is mediated by T-cell infiltration [9], which involves cytotoxic lymphocytes with a substantial fraction of γ-δ T lymphocytes, which are scarce in the skin[2,10].

Imperative aspects clinicians must reminisce when planning treatment practices for LP is the long-lasting course of the disease and the presence of contraindication for the first line therapy [11].

Colchicine consumes both antimitotic besides anti-inflammatory activity. Actually, it lessens flexibility, adhesiveness and chemotaxis of leukocytes. Moreover, since it has a suppressive action on the immune system, it constrains both cellular and humoral immunity [112]. It inhibits TNF-α receptors in macrophages and endothelial cells [13]. Colchicine usually prescribed in gout, familial Mediterranean fever, pericarditis, and Behçet's disease. Undesirable disadvantages of colchicine are predominantly GIT problems at elevated quantities.

MATERIALS AND METHODS

In the existing study, a cross sectional study design was implemented, 92 patients of LP, were registered from those patients joining the outpatients clinic of department of dermatology and venereology in Merjan teaching hospital and Alhussein teaching hospital in Thi Qar, Iraq for a period stretched from Jan. 2018 to Jan. 2019. All patients were identified basing on the distinctive clinical features by dermatologist (dermoscope aid the diagnosis for LPP cases), and for mistrustful cases biopsy was taken to confirm the diagnosis.

The demographic statistics such as age, gender and the duration of the disease was taken using a checklist, while information about the lesions such as type of lesion, site of involvement and numbers of lesions, itching and other associated symptoms were evaluated at the base time after taking the patients' verbal agreement. Exclusion criteria included those patients suspected of having drug-induced lichenoid eruptions, persons who contracted chronic liver problems, or chronic renal problems, or serious gastrointestinal disease, and those patients taking colchicine for other disease or had taken other treatment for lichen planus in the last month were also excluded from the study.

LP classified into variants or types according to different clinical presentations as classical, actinic, oral, lichen planopillaris (LPP), and hypertrophic LP. Patient's age ranged from 19 to 56 year-old (mean age 33.6 ± 12.3 years). Female: male ratio was 1.18:1. Extent of time the disease involved from I month to 2 years. All the patients involved in the study were given colchicine 1 g once daily. Duration of therapy extended from one month to three months then follow up for another three months. Reaction to treatment was reported at every visit. Photographs were reserved before and after the treatment regimen. Adversative effects correlated to the drug recorded if any such as diarrhea, nausea, cramping, abdominal pain, and vomiting. Complete evaluation regarding liver function test, renal function test, and complete blood picture were taken at baseline and after complete treatment course with colchicine for all patients. Reduction in the severity of LP as a response of the disease to colchicine was recorded as percentage: good improvement was indicated when there was >%70 improvement in the lesion. moderate improvement was indicated at 30-70% improvement, while poor improvement was stated when the reduction in lesion was <30%. Signs of response included: 1.decrease the itching, 2. no. of lesions (no appearance of new lesions and decrease in the number of old lesions), 3. lesion improvement and color changing, and 4. Dermoscopic improvement specially for LPP and hair regrowth were used as follow up indices. The statistical investigations using SPSS version were done. The results attained are deliberated significant at $p < 0.5$. Data used to evaluate the correlation between age, clinical type of LP and the gender of the patients.

RESULTS AND DISCUSSION

Out of the entire of 92 patients incorporated within the study, 4 patients withdrew from the study because of gastrointestinal side effects of colchicine, while 3 patients were missed to follow up thus were omitted from the study. Beyond the residual 85 patients 39 were males (46%) and 46 females (54%) (Female to male ratio 1.18:1). Age of patients ranged from 19-56 years. The age-gender distribution of patients through the present study presented in figure (1).

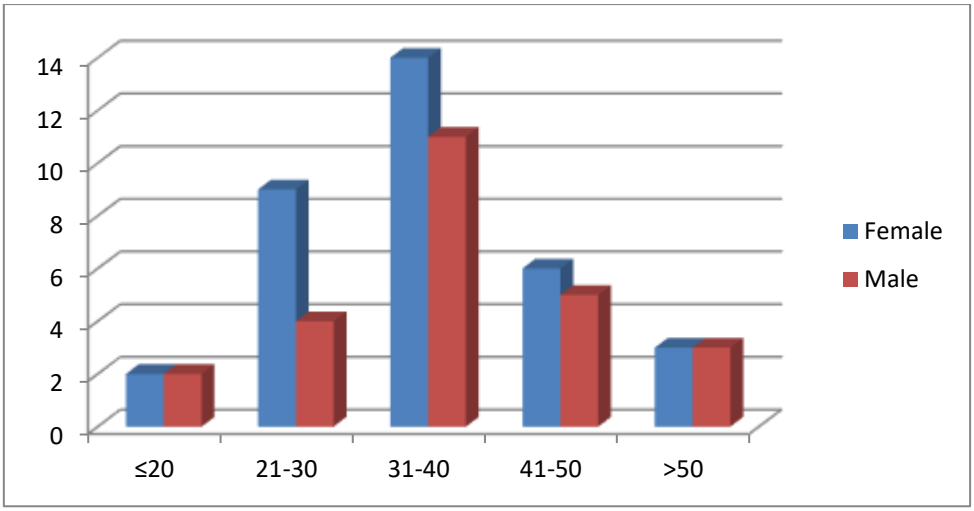

Fig.1: age/gender distribution of lichen planus patients

The pattern of LP detected and the age distribution vary among various genetic and geographic groups. In persons of European descent, it appears primarily after age 20, and peaks between 40 and 70. Very scarce cases appear after age 80. LP is infrequent in children and usually disturbs adults through their 4th to 6th decade [2] [1].

These results about the age-gender distribution of patients were supported by other researchers who found that onset of the disease is usually between 3rd and 4th decades, mostly seen in females [3]. Moreover, Strak, *et.al*. . 2015 in their study in Basra, Iraq noticed that most LP patients were in their 3rd decade and rare in children [14].

The clinical types or variants of lichen planus also studied according to the gender of patients. Results presented in table (1) showed that the most common type of LP was classical type followed by actinic and oral LP, while LPP was the fourth making hypertrophic variant as the least common clinical variant.

Table 1: Gender distribution of various clinical variants of lichen planus among all patients.

Gender	LP Clinical variants					Total no. (%)
	Classical LP no.(%)	Actinic LP no.(%)	Oral LP no.(%)	LPP no.(%)	Hypertrophic LP no.(%)	
Female	21	11	7	5	2	46 (54%)
Male	18	9	6	4	2	39 (46%)
Total	39(46%)	20(23.5%)	13(15.3%)	9(10.5%)	4(4.7%)	85 (100%)

Results of the present study about the gender distribution of diverse clinical kinds of LP amongst Iraqi patients was also confirmed by similar studies pointing generally on the predominance of classical type of LP tailed by actinic, and oral types, while the least common type was hypertrophic [3].

The most common detected clinical type of LP was classical type forming 39(46%) out the total 85 LP patient. Coming in line with the present study findings about classical LP distribution among different patients genders, a previous study done in eastern Turkey found that classical LP distresses patients at varying ages, but up to 95% of all cases ensue in adults, with utmost patients presenting between the 3rd and 6th decades of life[15].

Oral lichen planus is a mutual exhibition of lichen planus that may arise solitarily, nonetheless repeatedly occurs concurrently with other dermatopathies. In this study oral LP was the third clinical type as frequency of occurrence, oral LP patients found in 13 LP patients and formed (15.3%) out of all. This frequency of oral LP among different genders was supported by other study declaring that the oral clinical variant of LP affects females in excess of men and regularly disturbs middle-aged patients[4].

The current study established that females are more prone to LPP than males. Even though pathological generation is uncertain, various researchers repute such disease as a hair-specific autoimmune disease involves lymphocytic infiltration of follicular region of the hair follicle stem cells [16].

Hypertrophic LP mostly affect males as found in this study, lesions classically existing as grayish-yellow, or brownish-red papules and plaques,

most often on the pretibial region of the lower extremity and the ankles. Lesions may likewise disturbs other regions of the lower or upper limb, trunk, or in a universal manner [17].

The majority of patients with LP in a similar study in Iraq, had skin engrossment which was analogous to that initiate in other studies. Conversely, other researchers found that the two genders had generalized LP (skin and oral) while the least affected site was in genitalia and scalp [14].

Duration of colchicine treatment among LP patients in this study ranged from 1 month to 3 months. Gastrointestinal symptoms and diarrhea were the reason for extracting colchicine therapy for 4 patients out of the entire 92. The other 85 patients continue throughout this study on oral colchicine daily dose of 1 g and followed up by observing of their liver function test, renal function test, and complete blood picture before initiation and after termination of colchicine therapy. Improvement in LP lesions detected clinically, and dermoscopically for LPP patients.

Enhancement was further noticeable and obvious in patients under colchicine regimen for protracted interval (the full three months). Good improvement (>70% reduction in the severity of lichen planus lesions) was noted clinically in 55 patients forming (64.7%) of all patients in the study. Moderate improvement (30-70% reduction) was detected in 22 patients forming (25.8%) out of total patients. Otherwise, poor response to colchicine therapy (less than 30% reduction) was seen in 8 patients only forming (11.7%) out of all patients in this study as presented in table (2).

Table 2: Efficacy of colchicine on lichen planus patients

Improvement	Patients no. (%)		Total no.(%)
	Female	Male	
Good	31	24	55 (64.7%)
moderate	12	10	22(25.8%)
poor	3	5	8 (11.7%)
Total no.(%)	46 (54%)	39 (46%)	85(100%)

It is generally known that the maximum operative treatment modality to governor the signs and symptoms of LP is systemic steroids (prednisone) with a lot of side effects (most important dermatological changes includes skin thinning, purpura, acne, mild hirsutism, facial erythema, and striae besides other serious systemic adversative effects such as Cushing syndrome, osteoporosis, and impaired immune system) in addition to numerous contraindications such as diabetes mellitus, hypertension, and psoriasis). Numerous remedies described previously as incompletely operative such as retinoid, tacrolimus, oral diamino-diphenyl-sulfone (dapsone), and many other treatment modalities [18].

In addition, in the current study about the dependence of colchicine as a therapeutic option for LP, some studies established that colchicine been prescribed for skin conditions other than LP such as amyloidosis, Behcet disease, psoriasis and other dermatopathies with good results [19].

Finally, although the etiology of the LP is unknown exactly, with time it is becoming apparent that LP is being observed more and more in conjunction with diseases of altered or disturbed immunity. Serious hazards are concomitant with long-standing systemic corticosteroid use accompanying with several side effects. Throughout the former few years, colchicine has been publicized to be operative in managing a varied range of diseases, containing Behçet's disease, recurrent aphthous stomatitis, dermatitis herpetiformis and other skin diseases. Our study results about the efficacy and safety of colchicine as a therapeutic option for LP patients may help them to overlap the wide range of side effects of traditional systemic treatment such as steroids.

ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

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