# EFFICACY AND SAFETY OF METHOTREXATE IN LICHEN PLANNUS

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## ABSTRACT

**Background:** Lichen planus is a common inflammatory disease that can involve the skin, nails, mucous membrane, and hair follicles. There is a long list of topical and systemic therapies for its treatment. Methotrexarte can be a very good substitute for systemic corticosteroids, especially in old ages and patients with systemic diseases.

**Patients And Method:** This pilot study was carried out in Out Patients Department of Dermatology Unit Hayatabad Medical Complex from June 2011 to May 2012. Patients of Lichen Plannus (diagnosed clinically) were selected by non-probability purposive sampling method after obtaining an informed written consent.

**Results:** A total of 37 patients were enrolled in the study. Out of these, 34 patients completed the study. There was exclusion of six patients from the study due to adverse events. There were 12 (35.3%) males and 22 (64.7%) females. Female to male ratio was 1.8:1.The age of patients ranged from 17 to 60 with a mean of 34.26(±10.77) years. The drug was found safe and well tolerated as only six patients showed side effects. Side effects were observed in 6 patients,5 female and one male. Excellent response was seen in 20 patients ( M 7, F13),moderate in 9 patients (M4, F5) and mild response in 5 patients (M1,F4).

**Conclusion:** Methotrexate is safe and efficient drug for treating lichen plannus. Larger studies with follow up is required to see the effectiveness of Methotrexate in preventing relapse after initial excellent response

## INTRODUCTION

Lichen planus is a mucocutaneous inflammatory disorder characterized by shiny, violaceous, and flat-topped polygonal papules, which are most profuse on the ankles and in the lumbar region, the legs and neck are also frequently involved. The skin and oral mucosa are the most frequently involved areas. Other mucous membranes (including the genitalia, esophagus, and conjunctiva) and skin appendages (e.g., scalp, hair and nails) can also be affected[1].

Although the exact etiology of lichen planus is unknown, an autoimmune pathogenesis is postulated with activated T-cells directed against basal keratinocytes2. The existence of rare cases of familial lichen planus and the over representation of certain HLA haplotypes (e.g. HLA-DR1 in cutaneous lichen planus) suggest that genetic factors have a role in susceptibility to this disease. There is a significant association between lichen planus and infection with the hepatitis C virus[1].

According to population-based data from Sweden, the prevalence of cutaneous lichen planus among men is 0.3 %(3) and the prevalence of oral lichen planus is 1.5%14; the respective prevalences among women are 0.1%13 and 2.3%[4].

Despite the good results with corticosteroids, recurrence is quite common and sometimes leads to long-term use of such medications.

Other systemic treatments that have been tried in cutaneous LP with variable response rates include oral retinoids, azathioprine, Tetracycline,cyclosporine, mycophenolate mofetil, thalidomide,low molecular weight heparin, PUVA or UVB,metronidazol, and biologic agents[5,6,7].

Methotrexate ,an old drug with lot of uses in dermatology was found to be effective and safe in lichen plannus.It can be a very good substitute for systemic corticosteroids, especially in old ages and patients with systemic diseases. Methotrexate (MTX) inhibits the action of Dihydrofolate reductase which is a necessary enzyme in the synthesis of thymidylate and purine nucleotides required for DNA/RNA synthesis.

The most important side effects of MTX include pancytopenia and hepatotoxicity. Pancytopenia typically develops earlier, as compared to hepatic fibrosis and cirrhosis which take years to develop.

Therefore, in the case of lichen planus, the risk of liver fibrosis is low because of the short period of consumption[2].

MTX is not difficult to use and oral administration achieves reliable blood levels unaffected by food intake.

Therefore, the aim of this study was to investigate

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the effect of low dose methotrexate (MTX) for the treatment of generalized lichen planus.

## PATIENTS AND METHODS

This pilot study was carried out in Out Patients Department of Dermatology Unit Hayatabad Medical Complex from June 2011 to May 2012.Patients with generalized LP presented to Private clinic were also included in study. Patients of Lichen Plannus(diagnosed clinically) were selected by non-probability purposive sampling method after obtaining an informed written consent. Both sexes were included with generalized Lichen Plannus after fulfilling the inclusion criteria.

The patients were screened for hepatitis serology and the other hepatic diseases before initiation of MTX. If patient found to be positive for hepatitis they were excluded from study. Excellent response was considered as the complete resolution of pruritus and the disappearance of cutaneous lesions. Moderate response was considered as more than 50% improvement, and mild response was defined as less than 50% clearance of cutaneous lesions and relief of pruritus.

Therapy will be considered successful if there is excellent response, improvement in lesions at 12th weeks after starting the treatment.

### Inclusion criteria:

Generalized lichen planus involving atleast 20% of total body area

Pts 15-60 years of age.

### Exclusion criteria

Pregnant and lactating mothers.

Pts with active hepatic disease.

Pts with active renal disease.

Pts less than 15 yrs of age.

Inability to attend the clinic for follow up visits.

The above factors are confounders and will make the study results baised if included.

### Data collection procedure

All patients meeting the inclusion criteria i.e. generalized lichen planus involving atleast 20% of total body area The purpose and benefits of the study will be explained to the patients and they will be assured that the study is done purely for data publication and research purpose and a written informed consent will be obtained. All patients will be subjected to detailed history and clinical examinations .Patients were given oral methotrexate 15 mg taken once weekly for 12 weeks The results will be assessed 4, 8, and 12 weeks after starting the treatment.

Treatment was tapered after the 12 week or whenever a complete response was achieved. A response rate less than 75% at 12th week was regarded as treatment failure. Treatment was stopped if any side effect of treatment appear in patient.

All of the above information including name, age, gender will be recorded in a pre designed Proforma. Exclusion criteria will be followed to control confounders and bias in study results.

### Data analysis

Data will be analyzed in SPSS version 19. Mean ± SD will be calculated for numerical like age, total body area involvement at presentation, associated pruritis, and at 12th week follow up. Frequencies and percentages will be calculated for categorical variables like gender, response to treatment and efficacy. Results will be presented in form of tables, graphs and charts.

## RESULTS

A total of 37 patients were enrolled in the study. Out of these, 34 patients completed the study. There was exclusion of six patients from the study due to adverse events (rise in the levels of ALT twice the upper normal limit and decreased WBC count <3500/mm3). Three patients lost to follow up after Ist visit. Patients who lost follow up after their induction were not included in data collection.

There were 12 (35.3%) males and 22 (64.7%) females. Female to male ratio was 1.8:1.The age of patients ranged from 17 to 60 with a mean of 34.26 (±10.77) years.Most of the patients was between 17 to 40 years of age group. Pruritis was present in 29(85.3%) patients.

The drug was found safe and well tolerated as only six patients showed side effects. Side effects were observed in 6 patients, 5 female and one male. There were eleven patients with age less than 30, out of which one patient develop side effect.14 patients were in between 31-40yr,out of which one patient developed side effect. Between 41-50 yr there were 4 patients and one developed side effect. Above 50 years three patients showed side effect out of four.

Excellent response was seen in 20 patients (M7, F13),moderate in 9 patients (M4 F5) and mild response in 5 patients (M1F4).

## DISCUSSION

This is the first study regarding the efficacy and safety of the MTX in LP in Khyber Pukhtoonkhwa. Internationally, only two pilot studies one by Turan H et al[8] from Turkey and other by Malik zaid et al[2] has been published till date, using oral MTX as monotherapy for LP.

In our study the incidence of LP was higher in females than males with a ratio of 1.8:1 The literature

**TABLE 1: LICHEN PLANUS-DISTRIBUTION OF PATIENTS ACCORDING TO AGE GROUPS Age (in years) * Response**

Crosstab

| | Response | | | |
|---|---|---|---|---|
| | Mild | Moderate | Excellent | Total |
| Age (in years) <= 30.00 Count % within Age (in years) | 3 | 6 | 2 | 11 |
| | 27.3% | 54.5% | 18.2% | 100.0% |
| 31.00 - 40.00 Count % within Age ( in years) | 4 | 9 | 2 | 15 |
| | 26.7% | 60.0% | 13.3% | 100.0% |
| 41.00 - 50.00 Count % within Age (in years) | 0 | 2 | 2 | 4 |
| | .0% | 50.0% | 50.0% | 100.0% |
| 51.00+ Count % within Age (in years) | 1 | 2 | 1 | 4 |
| | 25.0% | 50.0% | 25.0% | 100.0% |
| Total Count % within Age (in years) | 8 | 19 | 7 | 34 |
| | 23.5% | 55.9% | 20.6% | 100.0% |

**TABLE 2: EFFICACY OF METHOTREXATE IN LICHEN PLANUS**

Gender * Response Crosstabulation

| | Response | | | |
|---|---|---|---|---|
| | Mild | Moderate | Excellent | Total |
| Gender Male Count % within Gender | 1 | 4 | 7 | 12 |
| | 8.3% | 33.3% | 58.3% | 100.0% |
| Female Count % within Gender | 4 | 5 | 13 | 22 |
| | 18.2% | 22.7% | 59.1% | 100.0% |
| Total Count % within Gender | 5 | 9 | 20 | 34 |
| | 14.7% | 26.5% | 58.8% | 100.0% |

**TABLE 3: SAFETY OF METHOTREXATE IN LICHEN PLANUS**

Side Effect

| | Frequency | Percent | Valid Percent | Cumulative Percent |
|---|---|---|---|---|
| Valid Yes | 6 | 17.6 | 17.6 | 17.6 |
| No | 28 | 82.4 | 82.4 | 100 |
| Total | 34 | 100.0 | 100.0 | |

supports this epidemiological data. Boyd AS et al[9] described that LP affects women preferentially.

In present study, the maximum incidence of disease was seen in 17-60 years of age group which is comparable with other studies. Abdallat SA et al[10] reported that majority of LP patients were between 34-59 years.

In our study 85.3% cases showed moderate to excellent response, whereas more than 90% reduction was found in 91% cases in the pilot study conducted by Hakan T et al[8] in Turkey. Mild resonse was seen in 14.7% in our study compared to 9% of patients in the study conducted by Hakan T. This difference may be due to the fact that in Hakan's study, the patients with generalized LP were enrolled only and generalized LP is a variant which responds well to therapy. In contrast, in our study the patients with different types of LP were enrolled. The literature shows that few variants of LP like LP hypertrophicus, follicular LP and LP pigmentosus, are highly resistant to treatment. Moreover, Hakan used MTX dose in the range of 15-20mg/week according to the severity of disease while we used a standard dose of 15mg/week irrespective of severity or type of the disease which may explain the reason of higher percentage of non-efficacy of the drug in our study.

In our study safety and tolerability (82.4% patients) was found to be very good. The side effects (nausea, rise in transaminases twice the upper normal limit and decrease in the white cell count less than 3500/mm3) were reported in five (17.6%) cases.Study by Malik zaid et al[2] showed side effects in 11.1% of patients..This

difference may be due more number of patients in our study.

MTX in a short course has proved beneficial regarding its good tolerability and minimal side effects. Large controlled trials are needed to determine the efficacy of MTX in oral/ mucosal LP also. Being an effective, safe, cost effective, and readily obtainable drug, MTX can be a good option for treatment of LP in developing countries like Pakistan.

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