Orginal Article

Hematological and Biochemical Parameter Changes Related to Methotrexate Therapy

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Abstract

A clinical trial was conducted to evaluate the hematological and biochemical changes related to methotrexate in the treatment of lichen planus. A total of forty four patients with lichen planus, attendign at the department of Dermatology and Venereology, Bangabandhu Seikha Mujib Medical University (BSMMU), Dhaka, Bangladesh durign the period of january 2009 to December 2010 were enrolled in this study purposively. Of them, 23 patients in group-A (case group) and 21 patients in group-B (control group) were selected randomly. The case group was treated with oral methotrexate and the control group was trated with betamethasone oral mini- pulse therapy. A decreasing trend of hemoglobin level and platet count was observed between two groups. An increasing trend of SGPT was observed among the case adn control up to 6th week of observation and then it decreased. This study also revealed abnormlity in platelet count and liver function test in both the groups. But the overall effects were less in cases than control. So it cand be concluded from this study that methtrexate can be used as an alternative saf drug therapy for the treatmetn of lichen planus.

Key words: Lichen planus, methotrexate, mini pulse betamethsone.

Introduction

Lichen planus is an inflammatory mucocutaneous condition characterized by shiny, violaceous, polygonal, flat topped, firm papules and plaques with Wickham's striae on the surfaces of lesions. It is highly pruritic. [1,2] T cells become activated via antigen-presenting cells such as Langerhans cells in conjunction with epidermal keratinocytes and co-stimulatory molecules. These activated T lymphocytes ply a pivotal role in regulating epidermal cell recognition, the licheniod response and basal cell damage. Lichen planus is an unpredictable disease that typically persists for l to 2 years, but may follow a chronic, relapsing course over many years.[3] Lichen planus may cause atrophic cicatricial alopecia and nail dystrophy with the involvement of scalp and nail respectively.[4] Skin lesions of lichen planus may be disfiguring. Involvement of the oral and genial mucosa in sever cases may be debilitating . Oral lichen planus may predispose to the development of squamous cell carcinoma within the lesions, Methotrexate is the most common dermatologist-prescribed oral immu nosuppressive agents.[5] Methotrexate is mainly related to its effect on epidermal cell proliferation. It has a more significant effect on lymphoid cells. Methotrexate exerts its anti-inflammatory effects via inhibition of lymphocyte proliferation. Treatment of lichen plaus is difficult and a lack of randomized controlled clinical trials makes evaluation of therapies challenging.[6] For the safe treatment option for the patients with lichen planus a prospective, randomized controlled clinical trial was aimed to find out and alternative first ling drug.

Materials and Methods

A clinical trial was conducted in the department of Dermatology and Venerology, BSMMU, Dhaka, Bangladesh. The patients with lichen planus attending at the department of Dermatology and Venereology, BSMMU, Dhaka during the period of January 2009 to December 2010 were enrolled in this study. A total of 44 patients of both sex were enrolled on the basis of following inclusion and exclusion criteria. Of them 23 patients in group-A (case group) and 21 patients in group-B (control group) were selected alternatively. A data collection sheet was used for research instrument.

Inclusion criteria of patient selection:

i. Clinically and histopathologically diagnosed cases of lichen planus.

ii. Baseline investigations including hemoglobin, liver and renal function tests of the patient were within normal limits.

iii. Patients of 18 years or older age of both sex.

Exclusion criteria of patient seletion

i. Patients of lichen planus co-existing with acute infections, neoplasia, uncontrolled hypertension and diabetes mellitus.

ii. Patients who have been suffering from hepatic, renal, cardiovascular and hematological diseases.

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iii. Patients with known hypersensitivity to methotexate and betamethasone.

iv. Pregnant women, lactating mother and those who were no-compliant for contraception

v. Patents who had a long history of alchol intake.

Study procedure

After taking and informed consent all patients with lichen planus were recruited for the study. According to the structured questionnaire, their particulars and history were taken. For women of reproductive age reproductive history, menstrual history, lactation and pregnancy plan were carfully judged. The duration of the disease, a detailed history of prior treatment, its duration and response were noted. All the patients for this study were selected on the basis of clinical examination, inclusion and exclusion criteria. Skin biopsy and histopathology were done to confirm the disease. Then haematogical and bicochemical baseline parameters including complete blood count (CBC), platelet count, random plasma glucose, liver function test [serum glutamic pyruvic transaminase (SGPT)], renal function test (serum creatinine) and routine urine test were done. Group –A (case group) patients were given oral methortrexate 10 mg (Tab. Methotrax® 10 mg) single morning dose after breakfast once in a week and oral folic acid 5 mg (Tab. Folison® 5mg) single morning dose after breakfast on the next day of methotrexate dose for 12 weeks. Group-B (control group) patients were given oral betamethasone 5 mg (Tab. Betnelan® 0.5 mg, 10 tablets at a time) in a single morning dose after breakfast on 2 consecutive days of every week for 12 weeks. None of the patient was allowed concurrent use of any topical or systemic drug. Topical emollients were advised if the skin was dry. Strict contraceptive measures were given to all married patients of reproductive age. The study period continued 12 weeks of treatments in both groups.

Follow up

Patients were followed up to find out the hematological and biochemical changes related to methotrexate therapy at 1st week,2nd week,6th week and 12th week. Random plasma glucose was done at baseline and after completion of 12 week's treametn.

Results

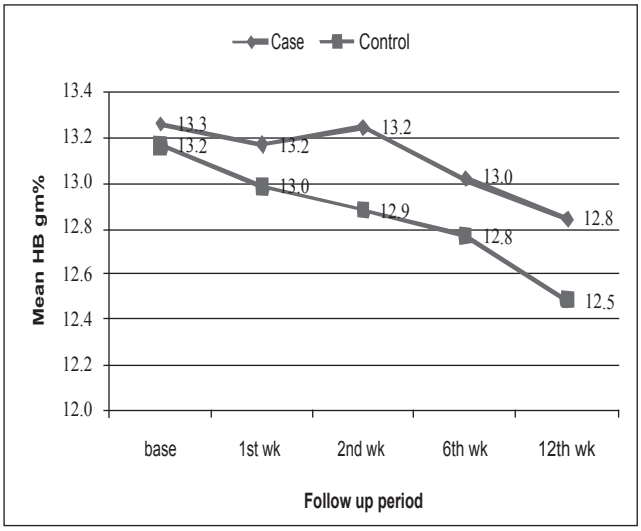
Table I shows that the mean (±SD) age of the cases was 34.9 (±13.4) years ranging from 18 to 60 years whereas the mean age (±SD) of the control was 32.9 (±11.4). years ranging from 18 to 61 years, but the mean difference was not statistically significant (p>0.05) though the mean age of the cases was higher than the control. On the contrary, no statistically significant sex difference was found between case and control (p>0.05) though the proportion of male patients were higher in case (39.1%) compared to control (33.3%).

Table I: Distribution of subjects at different age group and comparison of age and sex in case and control

Characteristics	Case (n=23)	Control (n=21)	Total (n=44)	p value
Age in years	**n (%)**	**n (%)**	**n (%)**	
<25	6 (26.1%)	4 (19.0%)	10 (22.7%)	
25-34	6 (26.1%)	9 (42.9%)	15 (34.1%)	
35-44	5 (21.7%)	5 (23.8%)	10 (22.7%)	
45-54	4 (17.4%)	1 (4.8%)	5 (11.4%)	
≥55	2 (8.7%)	2 (9.5%)	4 (9.1%)	
Mean (±SD)	34.9 (±13.4)	32.9 (±11.4)	33.9 (±12.4)	0.596€
Range	18-60	18-61	18-61	
Sex				
Female	14 (60.9%)	14 (66.7%)	28 (63.6%)	0.960*
Male	9 (39.1%)	7 (33.3%)	16 (36.4%)	

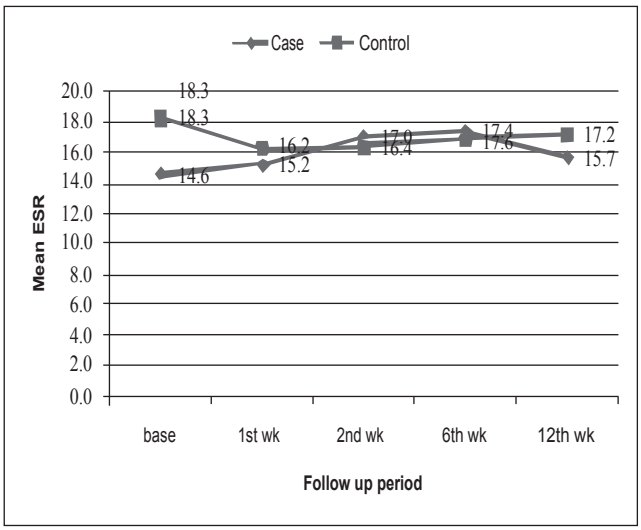
Case= Oral methotrexate, Control= Betamethasone oral mini- pulse

€p value reached form unpaired student's t test and *p value reached from Chi square test



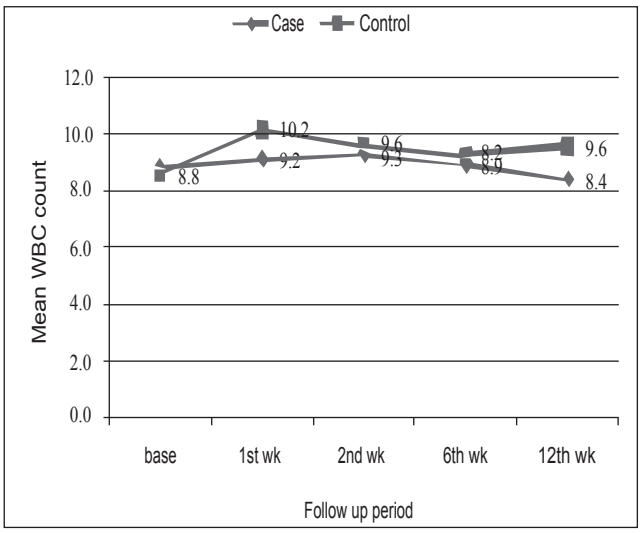
Case= Oral methotrexate, Control=Betamethasone oral mini- pulse

Figure I: Mean changes of hemoglobin level from baseline to 12th week follw up



Case= Oral methotrexate, Control= Betamethasone oral mini-pulse

Figure II: Mean changes of ESR from baseline to 12th week follow up



Case=Oral methotrexate, Control= Betamethasone oral mini- pulse

Figure III: Mean changes of WBC count from baseline to 12th follow up

Hemoglobin: A decreasing trend of hemogolobin level was observed. But no statistically significant mean difference was found between two levels such as basline to 1st week of observation, of 1st week to 2nd week observation and so on (p>0.05). Similarly no statistically significant mean difference was found between case and control in each level of observation (p>0.05).

ESR: A variable level of ESR was observed among the cases and control. However , no statistically significant mean difference was found in each observation form baseline to 1st week and so on within groups and also between groups (p>0.05).

WBC count: No statistically significant mean difference was observed within and between the cases and control from baseline to 1st follow up and so on (p>0.05).

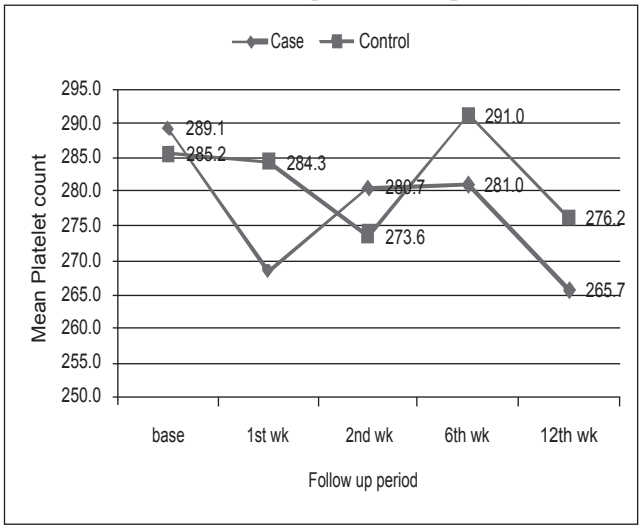


Figure IV: Mean changes of Platelet count form baseline to 12th week follow up

Platelet count: Amoung the cases the platelet count decreased from balseline data and then gradually increased up to 6th week followed by decrease. On the contrary, a decreasing trend of platelet counts was observed up to 2nd week and then increased at 6th week. But subsequently it decreased. Analysis indicated that there was no statistically significant mean difference of platelet count in different stages within and between the case and control groups (p>0.05).

Table II. Comparison of biochemical parameters between groups in different up

Characteristics	Case (n=23) Mean(±SD)	Control (n=21 Mean(±SD)	p value
SGPT U/L			
Base	24.2(±.7)	31.4 (±4.1)31.4 (±4.1)	>0.05
1st wk	29.7(±2.6)	28.7 (±3.1)	>0.05
2nd wk	29.3(±3.9)	37.1 (±8.2)	>0.05
6th wk	41.2(±10.9)	43.4 (±12.4)	>0.05
12th wk	28.0(±2.8)	34.2(±4.2)	>0.05
Random plasma glucose mmol/L			
Base	5.4 (±0.2)	5.3(±0.2)	>0.05
12th wk	5.3 (±0.2)	5.6(±0.3)	>0.05

Case=Oral methotrexate, Control= Betamethasone oral mini-pulse

P value reached form unpaired student's t test

SGPT: An increasing trend of SGPT was observed among the cases and control up to 6th week of observation and then decreased. However, no statistically significant mean difference was found within the group form baseline to 1st follow up to 2nd follow up and so on. Similarly, no statistically significant mean difference was found between cases and control in different follow up (p>0.05).

Random plasma glucose: No statistically significant mean difference of random plasma glucose was found within and between case and control in different level of observation (p>0.05).

Discussion:

This study was done to assess the hematological and biochemical parameter changes related to oral methorexate therapy in the treatment of lichen planus. In the present study, the mean age of all the study subjects was 33.9 ±12.4 years with a range of 18 to 61 years. It showed that 56.8% of the study subjects were within 25-44 years age group. Kachhawa et al. stated that lichen planus affected the middle-aged adults, which was consistent with this study.[7] Khondker et al. also showed that 62.56% were 30-50 years

age, 25% were 10-30 years and 13.33% were over 50 years of age with the mean age of the patient was 40±4 years.8 This study revealed that affected male were 36.4% and female were 63.6% which was similar to the report made by Katta that lichen planus had slight predominance in women.[1] But regarding sex, this study not consistent with the study by khondker et al. who showed 66.66% were male and 33.33% were female.[8] In this study piatelet count showed decreasing trend and increasing aend of SGPT in case group of patients but not in control group. Dr. Bob Goat in his article-'the side-effects of methotrexate injections' explained the pathophysiological basis of toxicities and side effects produced by Methotrexate and stated that Methotrexate inhibits cell production in the bone marrow and causes depression in levels of red blood cell (RBC), white blood cell (WBC) and platelet production. This can ultimately leads to low RBC (anemia), low WBC (leucopenia) and low platelets. Our studied haematological parameters support the above fact. He also mentioned that acute and chronic liver toxicity is reported most often due to large dosages or long-term exposure to methotrexate. Liver damage may result due to decreased cellular reactions (i.e., methylation) by the liver and suppressed proliferation.[9]

Conclusion

The hematological and biochemical parameter changes related to oral methotrexate therapy were measured. Though no statistical difference was observed but the overall adverse haematological and biochemical changes were less in cases (group-A) who were treated with methotrexate than control (group-B) who were treated with betamethasone. So, methotrexate can be used as an alternative safe drug therapy for the treatment of lichen planus. But it should be correlated with clinical outcome.

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