

# Role of Folic Acid Supplement in Reduction of Methotrexate's Side Effects in Treatment of Plaque Psoriasis

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## ABSTRACT

**Objective:** To determine the role of folic acid (FA) supplement in reduction of methotrexate's side effects in treatment of plaque psoriasis.

**Study Design:** Cross sectional study.

**Place and Duration of Study:** This study was conducted at the Department of Dermatology at Liaquat University Hospital Hyderabad from January to June 2016.

**Materials and Methods:** Cases >18 years age, and diagnoses with chronic plaque psoriasis of severe-to-moderate intensity were selected in the study after clinical examination. Each of the patients underwent oral methotrexate treatment along with folic supplementation. Cases were divided in two groups according to folic supplementation as 5mg and 10mg FA, and side effects of methotrexate were noted in both groups. All the information was recorded in the proforma.

**Results:** Mean age of the patients in this study was 44.34±3.14 years. Male were found in the majority 69.10%. In this study cases were divided in two groups according to folic acid supplementation, 41.82% cases were on 5mg, and 58.20% cases were on 10mg folic acid out of 55 patients. Side effects were noted in 40 cases out of 55, 6 patients were not come for follow-up and 9 cases were without complains of side effects. Side effects were noted as; uneasiness, loss of appetite, nausea and vomiting, fatigue, dizziness and others with percentage of 28(70.0%), 31(77.5%), 18(45.0%), 31(77.5%), 27(67.5%) and 20(50.0%) respectively. As well as reduction of the side effects were found in cases under supplement of 10mg folic acid as compare to 5mg, while no significant difference was found, P-value 0.09.

**Conclusion:** It is concluded that side effects of Methotrexate were decreased due to folic acid supplement but not significant.

**Key Word:** Plaque psoriasis, Methotrexate, folic acid

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## INTRODUCTION

Psoriasis is primarily a skin inflammatory problem with reactive irregular epidermal discrepancy as well as hyper proliferation prevalent in 2-3% peoples worldwide.<sup>1</sup> Pathophysiology of disorder includes mostly the stimulation and migration of T cells towards dermis triggering the cytokines release (specifically TNF- $\alpha$ , tumor necrotic factor) which causes inflammation as well as quick formation of skin cells.<sup>1</sup>

Incidence of psoriasis within 7500,000 cases which were enrolled to a general medical practitioner in UK remained 1.5%.<sup>2</sup> In a research carried out in America through national psoriasis established an incidence of 2.1% in adults, as well as survey established that 25% peoples had psoriasis and possibly graded as moderate to severe psoriasis.<sup>3</sup> Almost 1/3rd of peoples had psoriasis family history, and investigators have detected genetic loci correlated with the disorder.<sup>4</sup>

Methotrexate is the effective therapy choice for cases suffering from moderate-to-severe of psoriasis. As psoriasis is an incurable disease, the target of the Methotrexate therapy is the suppression of psoriasis, accomplishing lasting diminutions with least therapeutic side effects.<sup>4</sup> Methotrexate is a well proven, time tested drug applied for severe psoriasis. Its application yet comprising low dose, once per week plan for psoriasis is frequently correlated with unfavorable side effects; particularly substantial, are side effects concerning gastrointestinal functions observed in up to 30% cases.<sup>5</sup> The process by which methotrexate treatment with low dose instigates these symptoms hasn't been entirely explained. The therapy option for such adverse effects as well stay vague.

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Supplementation with folate either folic acid (FA) or folic acid can possibly lessen side effects form ethotrexate treatment. There are no consistent, evidence-based guidelines for folate supplementation in this clinical setting. Data concerning the impact of folic supplementation on the safety and efficacy of MTX therapy for psoriasis has been done.<sup>6</sup> Therefore currant study was performed to evaluating the reduction in side effects by folic supplementation in patients with psoriasis treated by methotrexate.

**MATERIALS AND METHODS**

Currant cross sectional case series study was conducted in department of dermatology at Liaquat university hospital Hyderabad. Study duration was 6 months through January to June 2016. Every case with >18 years age, both the genders, having chronic plaque psoriasis with moderate – severe condition and had not previously been provided methotrexate treatment, were selected for currant study. Cases were underwent complete clinical examination & medical history. Each patient having severe comorbidities history for example cerebral, or neurologic disorder, DM, liver disease; anemia, serologic positive test in terms of HBV or HCV, CVD, cancer, pulmonary disease, thrombocytopenia, leukemia, hematological disorders, and hypertension were not selected for study. Diseased women was also not included such as: breast-feeding, on contraceptive therapy. All the selected caes underwent oral methotrexate treatment, and further these cases were divided in two groups according to folic acid supplement 5mg and 10 mg. Overall data was recorded through a pre-intended proforma for each diseased personas well as included demographic profile (age & gender), duration of disorder in addition to side effects of treatment. Medical history per week, routine skin and laboratory examination were held to perceive the side effects of methotrexate. Data was analyzed in SPSS version 16.0.

**RESULTS**

The current study contributing patients mean age as 44.34+3.14 years, with range of 18 to 76 years. Table:1 Men were observed to be in majority 69.10% as contrasted to women 30.90%. Fig: 1

In this study cases were divided in two groups according to folic acid supplementation, 41.80% cases were on 5mg, and 58.20% cases were on 10mg folic acid out of 55 patents. Fig:2.

In present study side effects were noted in 40 cases out of 55, 6 patients were not come for follow-up and 9 cases were without complains of side effects. Side effects were noted as uneasiness, loss of appetite, nausea and vomiting, fatigue, dizziness and others with percentage of 28(70.0%), 31(77.5%), 18(45.0%), 31(77.5%), 27(67.5%) and 20(50.0%) respectively. As

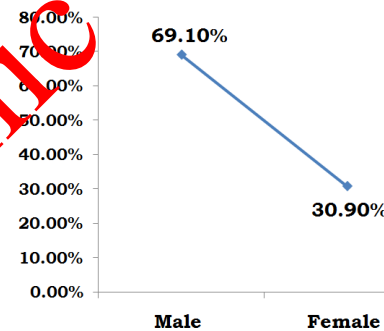
well as reduction of the side effects were found in cases under supplement 10mg folic acid as compare to 5mg, while no significant difference was found, P-value 0.09. Table:2.

**Table No.1: Cases distribution according to age n=55**

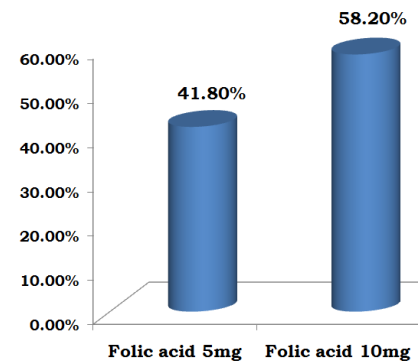
Mean	44.34 years
Std. Deviation	4.64 years
Minimum	18.00 years
Maximum	76.00 years

**Table No. 2: Side effects comparison according to folic acid supplement=40**

	FA 5mg n=19	FA 10mg n=21	Total n=40	P-value
Uneasiness	15	13	28(70.0%)	
Loss of appetite	16	15	31(77.5%)	0.09
Nausea and vomiting	12	08	20(50.0%)	
Fatigue	17	14	31(77.5%)	
Dizziness	14	13	27(67.5%)	
Other	10	08	18(45.0%)	



**Figure No.1: Cases distribution according to gender n=55**



**Figure No.2: Cases distribution according to Folic acid supplement n=55**

**DISCUSSION**

Methotrexate as foliate antagonist is an established treatment for inflammatory & autoimmune situation.<sup>7</sup> In

certain cases, methotrexate is correlated with substantial toxicity & side effects.<sup>7</sup> We found mean age of the patients in this study 44.34±3.14 years, with range of 18 to 76 years. Similarly Chládek J et al<sup>8</sup> reported that mean 45.6 years, with range of 37–59 years. Likewise Karn D et al<sup>9</sup> demonstrated that most of cases 31.25% were with age group of 40 & 49 years, and > 80% patients had infected in the age of 49 years. Haider S et al<sup>10</sup> reported that mean age 40.0±12.6 years and male gender was most common 45(61.6%) and 28 (38.4%) female. As well in this study male were found in the majority 69.10% as compare to females 30.90 %. In our study side effects were noted in 40 cases out of 55, because 6 patients were not come for follow-up and 9 patients were without complains of side effects. Side effects were noted as uneasiness, loss of appetite, nausea and vomiting, fatigue, dizziness and others with percentage of 28(70.0%), 31(77.5%), 18(45.0%), 31(77.5%), 27(67.5%) and 20(50.0%) respectively. Duhraet al<sup>11</sup> found similar results, they were capable of using methotrexate without gastrointestinal problems. It is as well tricky to explain that how non-gastrointestinal side effects can be dealt with supplementation of folic acid. A folic acid dosage of 10mg /day did not cooperation methotrexate's efficacy. These findings are in accordance with the findings of the other controlled studies.<sup>12</sup> In many other studies it is reported that the MTX application is interruption due to intolerance "fatigue, diarrhea, nausea, and headache" as well as organ toxicity (bone-marrow suppression, hepatotoxicity, pulmonary fibrosis). Furthermore, the antipsoriatic outcome intensity varies among individuals because of numerous factors, comprising a huge inter-patient inconsistency in MTX pharmacokinetics.<sup>7,13,14</sup>

In this study reduction in side effects were found in cases underwent supplement 10mg folic acid as compare to 5mg, while no significant difference was found, P-value 0.09. This may due to short sample size as well as short period of study. Similarly in the findings of Salim A et al<sup>15</sup> concluded that due to small sample size and little time duration, cannot reported accurately the FA may decrease side effects of methotrexate. While Strober BE et al<sup>10</sup> stated that supplements of folate in cases managed with methotrexate drops the prevalence of gastrointestinal intolerance & hepatotoxicity without impaired methotrexate efficacy. Chládek J et al<sup>8</sup> reported that antipsoriatic effect of the methotrexate treatment can influenced through FA and can reduced with its combined therapy. This supports that the methotrexate may precede the beneficial effects in psoriasis through mechanism except dihydrofolate reductase. Neutrophil chemotaxis is inhibited by Methotrexate,<sup>16</sup> and effects the. Activity/production of interleukin 1 & 2,

leucotriene B4, T8 - positive cells and natural killer cells.<sup>5</sup> Though insolvent of methotrexate on these controlling side effects independently in psoriasis is not clear till now.<sup>5</sup>

## CONCLUSION

It is concluded that side effects of Methotrexate were decreased due to folic acid supplement but not significant. More big sample size studies are required to achieved the more accurate findings. Additionally folic acid should be advised with methotrexate treatment in the much better way.

**Conflict of Interest:** The study has no conflict of interest to declare by any author.

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