Cross Current International Journal of Medical and Biosciences
Abbreviated Key Title: Cross Current Int J Med Biosci
ISSN: 2663-2446 (Print) & Open Access

OPEN ACCESS

Volume-2 | Issue-2 | Mar, 2020 |

Research Article

An Exploration of the Pulmonary Complication of the Treatment in Psoriatic Patients Receiving Topical, PUVA and Methotrexate Therapy

Dr. Tunergina Akhter[1], Prof. Shelina Begum[2], Dr. Afroza Khanam[3], Dr. Syeda Muslema Akhtary[4], Dr. SM Akhter –Ul-Alam[5], Dr. Lt. Col. Mst. Nasrin Nahar[6], Dr. Khandakar Nadia Afreen[7]

[1]Assistant Professor, Department of Physiology, Army Medical College, Bogura, Bangladesh
[2]Professor & Chairman, Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh
[3]Associate Professor, Department of physiology, Marks Medical College, Dhaka, Bangladesh
[4]Associate Professor, Department of physiology, Dhaka Center International Medical College, Dhaka, Bangladesh
[5]Assistant Professor, Department of Skin & VD, Pabna Medical College, Pabna, Bangladesh
[6]Assistant Professor, Department of Physiology, Armed Forces Medical College, Dhaka, Bangladesh
[7]Associate Professor, Department of Physiology, ZH Sikder Women Medical College, Dhaka, Bangladesh

***Corresponding author:**
Dr. Tunergina Akhter

Received: 16.02.2020
Accepted: 25.03.2020
Published: 29.03.2020

Abstracts: ***Background:*** In Bangladesh the prevalence rate of psoriasis is 1.49%. Although this rate of prevalence rate is not so high but in patient's traditional treatment procedure, physicians have to aware about the exploration of the pulmonary complication of the treatment in psoriatic patients receiving topical, PUVA and Methotrexate Therapy. ***Aim of the study:*** The aim of this study was to compare the lung function test results among the psoriatic patients receiving topical, PUVA and Methotrexate therapy in order to explore the pulmonary complication of the treatment. ***Methods:*** This cross-sectional study was carried out in the Department of Physiology of Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka, from July 2012 to June 2013. A total number of 120 subjects were selected, among which 30 were apparently healthy subjects (control group-A) for comparison and 90 were diagnosed male Psoriatic patients (study Group-B). Controls were selected from the community and the patients from the Indoor and Out Patient Department (OPD) of Dermatology and Venereology, BSMMU, Dhaka. Based on treatment, these study subjects were further divided into three groups consists of 30 male subjects in each group. These were group B_1 (30 diagnosed male Psoriatic patient receiving only topical therapy), B_2 (30 male Psoriatic patients receiving PUVA therapy, B_3 (30 male Psoriatic patients receiving Methotrexate therapy). ***Results:*** In this study, all the control subjects (A) were with normal lung function tests (LFT). On the contrary, 19, 20 and 29 psoriatic patients were with abnormal lung function tests in the experimental groups B_1, B_2 and B_3 respectively. The results were shown in Table IV. Decreased FVC was detected in patients of Psoriasis belonged to total 48(53.33%) out of 90 patients. Among them 10(33.33%) were in group B_1, 13 (43.33%) in group B_2 and 25 (83.33%) in group B_3. Decreased FEV_1 was detected in patients of Psoriasis belonged to total 43(47.78%) out of 90 patients. Among them 9(30%) were in group B_1, 10 (33.33%) in group B_2 and 24(80%) in group B_3. ***Conclusion:*** From this study it may be concluded that, the lung function test results among the psoriatic patients receiving topical, PUVA and Methotrexate therapy is very potential. For more specific result we would like to recommend for conducting more studies on the same issue with larger sized sample.

Keywords: Pulmonary, Venereology, Methotrexate Therapy, Psoriatic, Lung Function.

INTRODUCTION

In Bangladesh the prevalence rate of psoriasis is 1.49%. Psoriasis has been linked to multiple clinical outcomes including Hypertension; Ischemic heart disease; diabetes; dyslipidemia; cerebral stroke; cancer and depression (Mallbris *et al.*, 2004; Daniel *et al.*, 2005; Pearce *et al.*, 2005; Sommer *et al.*,2006; Dreiher *et al.*,2008). A few studies found an association

Quick Response Code

Journal homepage:

http://crosscurrentpublisher.com/ccijmb/

between lung function and psoriasis (Mallbris *et al.*, 2004; Dreiher *et al.*,2008; He *et al.*, 2010; Chiang and Lin 2011). However, the association of the disease with other systems especially respiratory has not been evaluated clearly. Pulmonary infiltrates are the most commonly encountered form of methotrexate pulmonary toxicity and these infiltrates resemble hypersensitivity lung disease (Cited by Lateef, Shakoor and Balk 2005). Patients with methotrexate-induced lung toxicity usually demonstrate a restrictive pattern on pulmonary function tests with decreased carbon monoxide diffusing capacity and increased alveolar-arterial gradient with hypoxemia(Cooper, White and Matthay 1986; Cottin *et al.*, 1996; Limper 2004)·Pulmonary function tests are the most sensitive means of detecting any pulmonary involvement in any disease. Spirometry is probably the most important tool for screening of pulmonary disease and most frequently perform pulmonary function test (Searles and McKendry 1987). Various ventilatory variables like FVC, FEV_1, FEV_1/FVC ratio, PEFR, $FEF_{25-75\%}$ can be measured by Spirometry (Hargreave, Mowat and Benson 1992; Cottin, Tebib and Massonnet *et al.*, 1996; Bedi, Kaur and Behera 1999; Khadadah *et al.*, 2002). Acute pneumonitis and interstitial fibrosis have been reported in psoriasis receiving Methotrexate (Filip *et al.*,1971; Sostman *et al.*,1976; Kaplan and Waite 1979; Lewis and Walter 1979; Bedrossian, Miller and Luna 1979; Philips and Jones 1987; Mckenna and Burrows 2000). Bedi, Kaur and Behera (1999). Reported a mild not significant decline in $FEF_{25-75\ \%}$, residual volume (RV) and RV/TLC % values after six months of treatment with Methotrexate in psoriatic patients. Some researchers of different countries observed that FVC, FEV_1 values were significantly decreased on long term low dose methotrexate therapy in patients with rheumatoid disease (Hargreave , Mowat and Benson 1992; Cottin *et al.*,1996;Khadadah *et al.*, 2002). In a prospective study, Khadadah *et al.*, (2002) also observed that FEV_1/FVC% was significantly higher and PEFR value was non significantly lower over two years period of Methotrexate therapy in patients with Rheumatoid arthritis. No published data was available regarding lung function test in newly diagnosed psoriatic patient receiving only topical therapy and the patients receiving PUVA therapy. However with the best of our knowledge, no such study has been undertaken to explore the lung function status in diagnosed psoriatic patients and the effects of antipsoriatic medication (Like Topical therapy, PUVA therapy, MTX therapy) on lung function status in Bangladesh. No published data is available comparing the lung function test in patient receiving PUVA therapy with that of the patient receiving methotrexate therapy. Small studies suggest deterioration of pulmonary function with chronic methotrexate therapy, particularly in patients with pre-existing obstructive lung disease (Gerber et al 1996). Therefore these study aims to observe the lung function status in these groups of patients and also to evaluate the effect of topical, PUVA therapy and methotrexate therapy on lung function in psoriatic patients. This study will also compare the lung function status of patients receiving topical therapy and PUVA therapy with that of the patients receiving Methotrexate therapy. The outcome of this study will reveal the importance of screening of the pulmonary functions in diagnosed psoriatic patients receiving only topical therapy and also in patients receiving systemic anti-psoriatic therapy for early diagnosis of pulmonary involvement and better management of these patients.

Objectives

a) General objective:

- To compare the lung function test results among the psoriatic patients receiving Topical, PUVA and Methotrexate therapy in order to explore the pulmonary complication of the treatment.

b) Specific Objectives:

- To assess spirometry lung function status in psoriatic patients after antipsoriatic medication.
- To measure all these pulmonary function variables in apparently healthy subjects for comparison.

METHODOLOGY AND MATERIALS

A total number of 120 subjects were selected, among which 30 were apparently healthy subjects (control group-A) for comparison and 90 were diagnosed male Psoriatic patients (study Group-B). On the first day of enrollment, the objectives, nature, purpose and potential risk of all the procedures used for the study were explained in detail to each subject, with a cordial attitude giving emphasis on the benefits he might obtain from this study. He was encouraged for voluntary participation & was allowed to withdraw himself from the study even after participation, whenever he felt uneasy. If he agreed to enroll in the study, an informed written consent was taken in a prescribed form. Detailed family history, medical history and thorough physical examination of each patient were done and all the information was recorded in a standard questionnaire. Then all the patients were requested to attend the Department of Physiology of BSMMU, in fasting state at 8 am on the day of biochemical and Spiro metric examination. For statistical analysis Independent sample 't' test, ANOVA, Chi-square and Pearson's correlation coefficient test were performed, as applicable. Protocol was approved by Institutional Review Board, BSMMU, Shahbag, Dhaka.

➢ **Inclusion Criteria**

- Age range 25-45 years.
- Psoriatic patients diagnosed by the physicians of Dermatology and Venereology.
- Psoriatic patients under treatment with Topical (eg.Corticosteroid cream/ointment, Coal Tar,

Dithranol, Tazarotene, VitaminD_3 etc.)therapy, PUVA therapy and Methotrexate medication.

➢ **Exclusion Criteria**

- Other type of dermatological disorders.
- History of any type of smoking (Cigarettes, Hookah, Biri, Tobacco etc).
- Patients with acute or chronic lung & chest wall disease e.g. Pneumonia, Tuberculosis, Asthma, COPD, Malignancy etc.

RESULTS

The results are shown in Table I and Figure 1. The means age were 33.5±1.424, 34.5±1.401, and 35.27±1.44 and 34.8±1.212 years in group A, B_1, B_2 and B_3 respectively and ranging from 25 to 45 years. All the values were almost similar and the differences among the groups were statistically non-significant. Therefore, all the groups were matched for age. The mean± SE BMI were 23.557±0.584, 23.089±0.721, 23.986±0.579 and 23.155±0.595 years in group A, B_1, B_2 and B_3 respectively. In this study we found the mean±SE score of socioeconomic status were 2±0.203, 1.9±0.175, 1.967±0.189and 1.833±0.192in group A, B_1, B_2 and B_3 respectively. The mean score difference of socioeconomic status in all the groups of the subjects were not statistically significant. Therefore, all the groups were matched for socioeconomic status. In this study, all the control subjects (A) were with normal lung function tests (LFT). On the contrary, 19 (63.33%), 20 (66.67%) and 29(96.67%) Psoriatic patients were with abnormal lung function tests in the experimental groups B_1, B_2 and B_3 respectively. Decreased FVC was detected in patients of Psoriasis belonged to total 48(53.33%) out of 90 patients. Among them 10(33.33%) were in group B_1, 13 (4333%) in group B_2 and 25 (83.33%) in group B_3. Decreased FEV_1 was detected in patients of Psoriasis belonged to total 43(47.78%) out of 90 patients. Among them 9(30%) were in group B_1, 10 (33.33%) in group B_2 and 24(80%) in group B_3. Decreased FEV_1/FVC% was detected in patients of Psoriasis belonged to total 0 (0%) out of 90 patients. Among them 0 (0%) were in group B_1, 0 (0%) in group B_2 and 0 (0%) in group B_3. PEFR was detected in patients of Psoriasis belonged to total 40(44.44%) out of 90 patients. Among them 14 (46.67%) were in group B_1, 12 (40%) in group B_2 and 14 (46.67%) in group B_3. Decreased FEF_{25-75} was detected in patients of Psoriasis belonged to total 0 (0%) out of 90 patients. Among them 0(0%) were in group B_1, 0 (0%) were in B_2 and 0 (0%) in group B_3. In group B_1, restrictive disorder was found in 9(30%) patients, small airway obstruction was in 0(0%) patients and large airway obstruction in 0 (0%) patients. In group B_2, restrictive disorder was found in 10 (33.33%) patients, small airway obstruction was in 0 (0%) patients and large airway obstruction in 0 (0%) patients. In group B_3, restrictive disorder was found in 23(76.67%) patients, small airway obstruction was in 0(0%) patients and large airway obstruction in 0 (0%) patients. In this study, among those 90 Psoriatic patients 42(46.67%) were diagnosed as restrictive disorder; where 12 Psoriatic patients were presented with different type of pulmonary symptoms and rest 30 were without any pulmonary complain.

Table I: Frequency distribution of subjects by lung function tests (normal/ abnormal LFT) in different groups

Groups	n	With normal LFT	With abnormal LFT
		no. (%)	no. (%)
A	30	30 (100%)	**0 (0%)**
B_1	30	11 (36.67%)	**19 (63.33%)**
B_2	30	10 (33.33%)	**20 (66.67%)**
B_3	**30**	**1(3.33%)**	**29 (96.67%)**

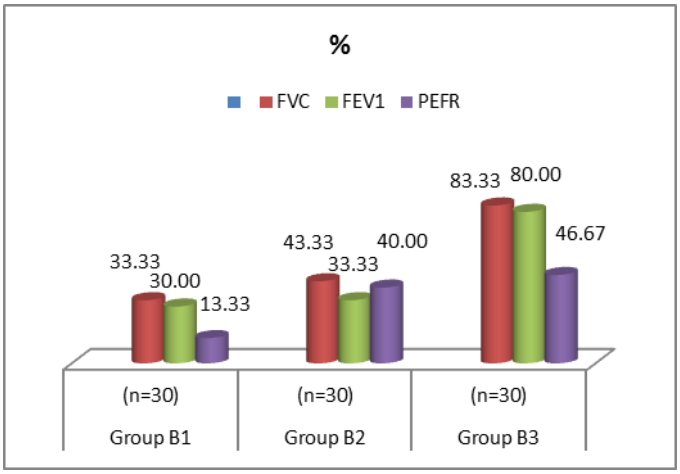

Figure I: Distribution of subjects (%) by abnormal pulmonary function variables in different study groups (n=90)

Table II: Frequency distribution of Psoriatic patients by the type of pulmonary disorders in different study groups (n=90)

Groups	Large airway obstruction (LAO)	Small airway obstruction (SAO)	Restrictive disorder (RD)
B1 (n=30)	0 (0%)	0 (0%)	9 (30%)
B2 (n=30)	0 (0%)	0 (0%)	10 (33.33%)
B3 (n=30)	0 (0%)	0 (0%)	23 (76.67%)
Total=90 (B1+B2+B3)	0(0%)	0(0%)	42(46.67%)

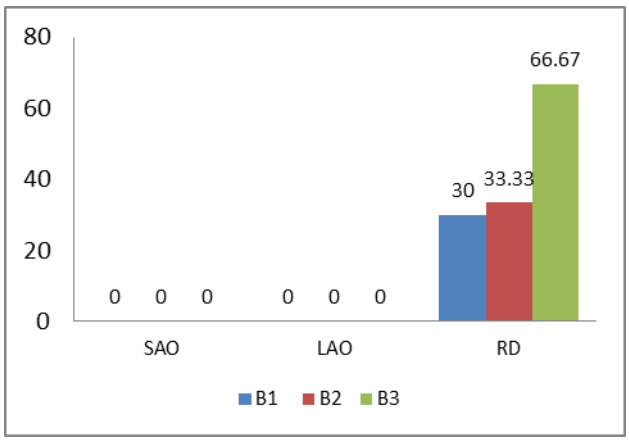

Figure II: Frequency (%) distribution of Psoriatic patients by the type of pulmonary disorders in different study groups (n=90)

DISCUSSION

In this study, values of lung function variables of healthy subjects were within normal limit and were almost similar to those reported by different investigators abroad . Again, both the groups (control and study) were comparable, as there was no significant difference in the confounding variables such as age, BMI, socioeconomic status and occupation, between two groups. However, to exclude the effect of age and BMI on the values of different Spirometric variables, measured value as percentage of predicted values were used for analysis. Acute pneumonitis is the most common pulmonary toxicity associated with methotrexate. However, studies also suggest an association between methotrexate and bronchiolitis obliterans organizing pneumonia, non-cardiogenic pulmonary oedema, rapidly progressive pulmonary fibrosis and bronchitis with hyper-reactive airway (Snyderman, William and Rice 1985,Cooper; White and Matthay 1986; Zitnik and Cooper 1990; Ohoson , Okano and Kameda 1997; Dawson, Clewes and Hendry 2004). In this study, 19(63.33%), 20(66.67%) and 29(96.67%) diagnosed Psoriatic patients after medication with only topical therapy, PUVA therapy and Methotrexate therapy respectively were with abnormal lung function test. On the other hand, none of the control subjects were with abnormal lung function tests. No similar observation was available for comparison. In this study, among the 90 Psoriatic patients after antipsoriatic only 42 (46.67%) were diagnosed with restrictive type of pulmonary disorder. However, among them 9(30%), 10(33.33%) and 23(76.67%) patients were treated by topical therapy, PUVA therapy and Methotrexate therapy respectively. On the other hand, none of the patients of different study groups were diagnosed with any type of obstructive disorder, either small airway obstructive disorder or large airway obstructive disorder. Patients with methotrexate induced lung toxicity usually demonstrate a restrictive pattern on pulmonary function tests with decreased carbon monoxide diffusing capacity and increased alveolar-arterial gradient with hypoxemia (Cooper, White and Matthay 1986; Cottin, Tebib and Massonnet *et al.,* 1996; Limper 2004). In addition, all of our study subjects were without respiratory complaints, though the spirometric test showed presence of silent restrictive change within them. However, the exact mechanism for this change cannot be delineated from this study, but the importance

of routine pulmonary function tests in this group of patients is outlined from our study.

Limitations of the study

It was a cross-sectional type study with small sample size, which doesn't reflect the scenario of the whole country.

CONCLUSION

From this cross sectional study, it's going to be finished that, the spirometry variables might decrease a lot of in male psoriatic patients when antimetabolite medication compared to topical or PUVA medical care. These decrement could also be related to silent pulmonic disorders. Psoriatic patients square measure unremarkably suffering from restrictive sort of pulmonic disorder. To be a lot of conclusive the subsequent recommendations square measure projected for additional studies: Prospective sort of study may be drained recently diagnosed Psoriatic patients and when half-dozen months of antimetabolite medical care. Similar sort of study may be through with massive sample size and additionally in feminine Psoriatic patients.

REFERENCES

1. Bedi, G.K., Kaur, I., & Behera, D. (1999). Pulmonary function changes in patients with psoriasis on methotrexate therapy. *J. Dermatol. 26*(7), 423-427.
2. Bedrossian, C.W.M., & Miller, W.C., & Luna, M.A. (1979). Methotrexate induced diffuse interstitial pulmonary fibrosis.*South Med. J. 72*, 313-318
3. Beyeler, C., Jordi, B., & Gerber, N.J. (1996). Pulmonary function in rheumatoid arthritis treated with low-dose methotrexate: a longitudinal study. *Br J Rheumatol. 35*, 446–452.
4. Chiang, Y.Y., & Lin, H.W. (2012). Association between Psoriasis and Chronic obstructive pulmonary disease: a population based study in Taiwan. *J Eur Acad Dermatol Venereol. 26*(1), 59-65
5. Cooper Jr, J. A. D., White, D. A., & Matthay, R. A. (1986). Drug-induced pulmonary disease: Part 1: Cytotoxic drugs. *American Review of Respiratory Disease*, *133*(2), 321-340.
6. Cottin, V., Tébib, J., Massonnet, B., Souquet, P. J., & Bernard, J. P. (1996). Pulmonary function in patients receiving long-term low-dose methotrexate. *Chest*, *109*(4), 933-938.
7. Dawson, J.K., Clewes, A.R., & Hendry, J. (2004). Pulmonary effects of low dose methotrexate therapy. *Clin. Plum. Med. 11*, 307-317.
8. Dreiher, J., Weitzman, D., Davidovici, B., Shapiro, J., & Cohen, A. D. (2008). Psoriasis and dyslipidaemia: a population-based study. *Acta dermato-venereologica*, *88*(6), 561-565.
9. Filip, D.J., Logue, G.L., & Harle, T.S. (1971). Pulmonary and hepatic complications of methotrexate therapy of psoriasis. *JAMA. 216*, 881-883
10. Hargreaves, M. R., Mowa, A. G. T., & Benson, M. K. (1992). Acute pneumonitis associated with low dose methotrexate treatment for rheumatoid arthritis: report of five cases and review of published reports.*Thorax. 47*, 628-633
11. He, Z., Chen, Y., Chen, P., Wu, G., & Cai, S. (2010). Local inflammation occurs before systemic inflammation in patients with COPD. *Respirology*, *15*(3), 478-484.
12. Kaplan, RL, & Waite, D.H. (1978). Progressive interstitial lung disease from prolong methotrexate therapy. *Arch Dermatol. 114*, 1800-1802.
13. Khadadah, M.E., Jayakrishnan, B., Gorair, S.A., Mutairi, M.A., Maradni, N.A., Onadeko, B., & Malaviya, A.N. (2002). Effect of methotrexate on pulmonary function in patients with rheumatoid arthritis a prospective study. *Rheumatol Int. 22*, 204–207
14. Lateef, O., Shakoor, N., & Balk, R. A. (2005). Methotrexate pulmonary toxicity. *Expert opinion on drug safety*, *4*(4), 723-730.
15. Lewis, W.L., & Walter, J.F. (1979). Methotrexate-induced pulmonary fibrosis.*Ach dermatol. 115*, 1169-70
16. Limper, A. H. (2004). Chemotherapy-induced lung disease. *Clinics in chest medicine*, *25*(1), 53-64.
17. Mallbris, L., Granath, F., Hamsten, A., & Ståhle, M. (2006). Psoriasis is associated with lipid abnormalities at the onset of skin disease. *Journal of the American Academy of Dermatology*, *54*(4), 614-621.
18. McKenna, K. E., & Burrows, D. (2000). Pulmonary toxicity in a patient with psoriasis receiving methotrexate therapy. Blackwet science Ltd. *Clinical and experimental Dermatology. 25*(1), 24-27.2
19. Ohosone, Y., Okano, Y., & Kameda, H. (1997). Clinical characteristics of patients with rheumatoid arthritis and methotrexate induced pneumonitis. *J. rhematol. 24*, 2299-2302.
20. Pearce, D. J., Morrison, A. E., Higgins, K. B., Crane, M. M., Balkrishnan, R., Fleischer Jr, A. B., & Feldman, S. R. (2005). The comorbid state of psoriasis patients in a university dermatology practice. *Journal of Dermatological Treatment*, *16*(5-6), 319-323.
21. Philips, T.J., Jones, D.H., & Baker, H. (1987). Pulmonary complications following methotrexate therapy. *J Am Acad Dermatol. 16*, 373-375.
22. Searles, G., & McKendry, R. J. (1987). Methotrexate pneumonitis in rheumatoid arthritis: potential risk factors. Four case reports and a review of the literature. *The Journal of rheumatology*, *14*(6), 1164-1171.
23. Snyderman, R., William, E., & Rice, J.R. (1985). Pneumonitis complicating low dose methotrexate

therapy in rheumatoid arthritis. *Arch. Intern. Med. 145*, 2035-2038.

24. Sommer, D. M., Jenisch, S., Suchan, M., Christophers, E., & Weichenthal, M. (2007). Increased prevalence of the metabolic syndrome in patients with moderate to severe psoriasis. *Archives of dermatological research*, *298*(7),321-328.
25. Sostman, H.D., Matthay, R.A., Putman, C.E, Smith, G.J.W. (1976). Methotrexate pneumonitis. Medicine. 55, 371-388.
26. Zitnik, R.J., & Cooper, J.A. Jr. (1990). Pulmonary disease due to anti-rheumatic agents. *Clin. Chest Med.* *11*,139-150.