Original Article

Comparison of Atorvastatin and 0.1% Betamethasone Valerate in Psoriatic patients

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Objective: To compare effects of Atorvastatin (40mg/80mg) and 0.1% Betamethasone Valerate on progress of psoriasis with cardiovascular complications.

Methodology: This study was comparative interventional randomized clinical trial conducted in Pharmacology Department of Basic Medical Sciences Institute, Jinnah Postgraduate Medical Center (JPMC), with the collaboration of Dermatology department of JPMC, Karachi. The study period was from June 2013 to June 2016. A total of 225 patients were divided into group A, B and C. Post treatment effects of drugs were evaluated by different parameters (Psoriasis Area and Severity Index (PASI), High Sensitivity C-Reactive Protein (hsCRP), Lipid profile, Liver Function Test (LFT) Creatine Phosphokinase (CPK)). The quality of life was evaluated in those patients by Dermatological Life Quality Index(DLQI).

Results: The mean percentage change of PASI and hsCRP showed highly significant changes at twelve and twenty weeks. Before and after the treatment mean Lipid profile and DLQI also showed significant changed. LFT and adverse event had non-significant change at the end of treatment.

Conclusion: Atorvastatin had remarkable results on psoriasis disease severity and cardiovascular complication were same as standard therapy 0.1% Betamethasone Valerate. When the combination of drugs was used, more significant results were seen as compared to single therapy. (Rawal Med J 202;45:282-286).

Keywords: Atorvastatin, Betamethasone Valerate, Psoriasis.

INTRODUCTION

Psoriasis is an immune mediated inflammatory diseases associated with genetic inheritance. It is an ideal disease for researcher in clinical trials. The prevalence of psoriasis in Pakistan was 5.1% out of 22-27% skin diseases. Psoriasis has many co-morbidities like obesity, dyslipidaemia, irritable bowel syndrome, diabetes mellitus and the most common cardiovascular diseases. The hallmark of psoriasis and cardiovascular events is inflammation which involves discharge of inflammatory cytokines and inflammatory cell activation. It is associated with number of psychological issues which produce great influence on patient's quality of life.

Atorvastatin has dual action on psoriasis; first it decreases the progress of disease and secondly it reduces its co-morbidities especially cardiovascular risk. It inhibits HMG-CoA reductase enzyme, which interferes with cholesterol synthesis. It has pleotropic effect to inhibit prenylated protein and play important role in immune-inflammatory diseases like psoriasis. Topical corticosteroid remains first line treatment in all grades of psoriasis.[7] Betamethasone has anti-inflammatory, immunosuppressive and anti-proliferative effects and decreases proliferation of cells and inhibits pro-inflammatory cytokines release, however it has toxic effects like adrenal gland suppression and cushing syndrome. This objective was to evaluate the effect of Atorvastatin on psoriasis disease progression and cardiovascular risk.

METHODOLOGY

The interventional clinical trial was conducted in Pharmacology Department, BMSI, JPMC, with the collaboration of Dermatology Department JPMC, Karachi. Informed consent by patients and ethical approval by Ethical committee of JPMC was taken. The sample size was 225 patients, calculated by on the basis of a previous study, as in this study the 75%

PASI score achieved by psoriatic patients treated by Atorvastatin. The confidence interval was 95% and absolute precision was 15 in this study. The duration of the study was from June 2013 to June 2016. The patients were randomized through serial envelopes having stickers of three groups.

Patients were enrolled of both genders from aged of 25-65years having PASI of <12 and hsCRP ≥3. Individuals who had current statin and corticosteroids therapy in past four weeks, pregnancy, lactation or chronic illness were excluded. Study period was 180 days with six follow ups. Total subjects were 225 randomly allocated into three groups: Group A was (n=66/75) prescribed 40mg of tablet atorvastatin for three months then followed by 20 mg for next three months in addition of topically applied betamethasone valerate 0.1% once daily for six months with three weeks applied and one-week interval. Group B was (n=70/75) prescribed placebo in addition of topically applied betamethasone valerate 0.1% twice daily then once daily for next three months with three weeks applied then one-week interval. Group C was (n=70/75) prescribed 80mg tablet Atorvastatin for three months then 40mg for next three months.

Psoriasis Area and Severity Index (PASI) was used to measure the effects of drugs. If PASI score was <7 means mild, 7-12 means moderate and >12 was severe. FDA has defined that if this change is 50% means the drug is effective. C reactive protein (hsCRP) was monitored (n= 1mg/L). Quality of life was measured pre and post treatment by Dermatology Life Quality Index (DLQI0.

Statistical Analysis: We used SPSS Version 21. Demographic variables were evaluated by Chi square. Age, weight, Lipid profile, LFT CPK PASI, DLQI, hsCRP were measured by One-way ANOVA. $p<0.05$ was considered significant.

RESULTS

A total of 225 patients were enrolled with 75 in each group. Nine patients in group A and 5 in group B and C were lost to follow up. There were no significant differences between demographic characteristics (Table 1). At baseline, no significant difference was found between the PASI, hsCRP and DLQI in three groups. At third and sixth month, there were significant change found between the PASI, hsCRP, DLQI and also mean percentage of these variables in three groups. At the end of study, 69 and 65 patients reached PASI 50 in group A and B, respectively. 68 patients at PASI 75 in group C and one patient in PASI 75 in each A and B groups (Table 2).

Table 1. Demographic characteristics.

Variable	Group A n (%)	Group B n(%)	Group C n (%)	p-value
Age (years)	47.8 ± 8.23	46.5 ± 7.84	47.9 ± 8.42	0.528
Gender				0.280
Male	54 (77.15)	57 (86.37)	52 (76.48)	
Female	16 (22.86)	9 (13.64)	16 (23.53)	
Weight (Kg)	68.5 ± 6.71	69.5 ± 5.75	69.07 ± 4.68	0.573
Family History	37 (52.85)	36 (54.50)	35 (51.47)	0.938
Itching	70 (100)	66 (100)	68 (100)	1.000
Decreased in sleep	70 (100)	66 (100)	68 (100)	1.000
Smoking History	44 (62.86)	42 (63.64)	43 (63.24)	0.995

Table 2. Outcomes variables.

Variable	PASI			
	Group A	**Group B**	**Group C**	**P- Value**
Baseline	10.892 ±1.192	11.227 ±0.729	10.988 ± 0.711	0.092
Third Month (% Change)	3.821 ± 0.448 (64.918 ±1.509)	3.910 ±0.272 (65.176 ±0.424)	2.725 ± 0.178 (75.193 ± 0.609)	0.0001 (0.0001)
Six Month (% Change)	2.718 ± 0.315 75.073 ±0.369	2.806 ±0.183 75.001 ±0.563	1.45 ± 0.585 86.749 ± 0.547	0.0001 0.0001
hsCRP				
Baseline	3.96 ± 0.55	4.00 ± 0.31	3.98 ± 0.33	0.846
Third Month (% Change)	3.26 ± 0.53 (17.617 ±4.93)	3.372 ± 0.41 (15.767 ± 5.67)	3.11 ± 0.38 (21.879 ± 6.48)	0.004 (0.001)
Six Month (% Change)	2.57 ± 0.58 35.156 ± 8.78	2.65 ± 0.40 33.692 ±7.980	2.37 ± 0.38 40.37 ± 8.51	0.002 0.001
DLQI				
Baseline	19.6 ± 1.98	20.2 ± 1.16	19.77 ± 1.43	0.076
Six Month (% Change)	5.63 ± 0.515 71.053 ±3.464	5.55 ± 0.531 72.215 ±3.17	3.41 ± 0.521 82.69 ± 2.61	0.001 0.001

*PASI=Psoriasis Area and Severity Index, hsCRP=High Sensitivity C-Reactive Protein, DLQI= Dermatological Life Quality Index

Table 3. Comparison of lipid profile of patients at different intervals.

Variable	Group A	Group B	Group C	p-values
	mg/dl			
Baseline				
TCHOL	193.73 ± 4.98	194.15 ± 3.88	193.5 ± 4.67	0.712
TRIG	145.71 ± 2.81	145.64 ± 2.51	145.79 ± 2.84	0.945
HDL	38.16 ± 1.33	38.02 ± 1.42	38.24 ± 1.73	0.691
LDL	140.90 ± 5.00	141.29 ± 4.56	141.62 ± 4.13	0.655
Third month				
TCHOL	174.30 ± 4.92	193.76 ± 4.35	183.78 ± 5.17	0.001
TRIG	138.62 ± 2.88	145.09 ± 2.68	139.85 ± 3.26	0.001
HDL	39.30 ± 1.21	38.27 ± 1.53	39.07 ± 1.49	0.001
LDL	130.19 ± 4.24	140.91 ± 4.83	135.03 ± 3.99	0.001
Six month				
TCHOL	139.16 ± 5.10	192.83 ± 5.26	163.87 ± 5.19	0.001
TRIG	119.61 ± 3.19	144.98 ± 2.55	132.96 ± 3.61	0.001
HDL	42.37 ± 0.98	38.14 ± 1.39	40.18 ± 1.44	0.001
LDL	107.83 ± 4.88	140.24 ± 5.20	126.19 ± 4.35	0.001

*TCHO=Total Cholesterol, TRIG=Triglycerides, HDL=High Density Lipoprotein, LDL = Low Density Lipoprotein.

Table 4. Comparison of safety profile between groups at different intervals.

Variable	Group A	Group B	Group C	p-value
	U/L			
Baseline				
ALT	34.900±5.43	34.060±3.27	33.544±4.24	0.087
AST	35.457±3.31	35.090±3.404	34.544±3.435	0.272
Gamma GT	37.514±3.802	38.015±3.159	37.926±4.042	0.206
ALP	94.014±12.492	94.469±11.294	94.323±6.374	0.299
TBLU	0.577±0.121	0.609±0.118	0.583±0.105	0.210
CPK	82.814±14.505	80.439±8.770	79.941±10.52	0.299
Third months				
ALT	35.085±5.38	34.196±3.41	33.823±3.35	0.087
AST	35.614 ±3.19	35.257±3.64	34.779±3.56	0.272
Gamma GT	37.600±4.31	38.257±3.13	38.132±4.11	0.206
ALP	94.085±12.63	94.515±11.04	94.455±6.27	0.299
TBLU	0.592±0.144	0.627±0.172	0.602±0.142	0.210
CPK	83.042±14.272	80.560±8.686	80.147±10.258	0.272
Six months				
ALT	35.228±5.35	34.242±3.36	33.941±3.13	0.157
AST	35.600±3.79	35.303±3.71	34.720±3.656	0.373
Gamma GT	37.885±4.42	38.439±3.34	38.191±4.19	0.724
ALP	94.114±12.863	94.560±11.44	94.617±6.13	0.954
TBLU	0.163	0.640±0.175	0.611±0.172	0.400
CPK	82.128±17.139	80.954±8.626	80.279±10.038	0.683

*ALT=Alanine Transaminase, AST= Aspartate Aminotransferase, Gamma GT= Glutamytransferase, ALP=Alkaline Phosphatase, TBLU= Total Bilirubin, CPK= Creatine Phosphokinase

There was no significant difference found in three groups at baseline but at six month's significant change found in Lipid profile of three groups (Table 3) and no significant difference found between LFT and CPK (Table 4). There were no significant differences found in adverse events between the three groups like arthritis 0% in all three groups, nausea 8.57%,0%, 13.24% in group A, B and C, respectively. Furthermore, myalgia 5.71% in group A, 0% in group B, 3% in group C, and others skin problems 0% (group A), 16.67% (group B), 7.35% (group C).

DISCUSSION

Psoriasis associated with cardiovascular complications in this study, which improved by single or combination therapy of Atorvastatin and Betamethasone, as reported by a study. In this study, almost all of the patients were of 47 years of age mostly male and associated with family history, smoking and all gave the history of disturbed sleep and itching. These results in line with other studies.

We found that there were no significant differences between the baseline means PASI score of three groups and most of the patients having mild-moderate disease. At sixth month, the mean percentage change of PASI between three groups showed highly significant p-value (0.0001). In mild-moderate type of psoriasis, Betamethasone is the first line treatment. Atorvastatin reduces immune-mediated inflammation in psoriasis and decreases pro-inflammatory cytokines (TNF α and INF) thus reduces the severity of disease.

We found that 69 and 65 patients in group A and B showed PASI 50% and 68 patients in group C had PASI 75% at the end of therapy. Therefore, the combination group showed improved results as compared to other groups, as seen in other studies. Faghihi et al reported 40mg of statin had 75% change of PASI, but the sample size was small.[8]

The base line hsCRP was increased in this study but no significant differences were found between all three study groups. This significantly decreased in third and sixth month.[18] The significant change was found between three groups but combination group showed highly significant results. Hence these results similar to a clinical trial by Philippine Dermatological Society as they were comparing Atorvastatin to topical betamethasone and showed that combination

therapy produce their effect by two mechanisms. Firstly decreases severity of disease and secondly reduces cardiovascular complications.[19] Another study reported that statin decreases the LDL and CRP with reduces IL1 and INFα which modulate the inflammatory process.[20]

In our study, comparison of mean DLQI at base line were non- significant. The mean change of DLQI were 71.05±3.6, 72.215±3.1 and 82.69±2.6 in group A, B and C, respectively at the end of study (p=0.001), the combination group showing more significant results as compared to others group. These results are similar to a study which reported that psoriasis produced negative influence on psychological, physical and social life of patients.[21]

In this study, the base line lipid profiles of patients were raised and most of the people were not aware of it. Our results showed higher LDL and lower HDL, suggesting that psoriasis was associated with dyslipidaemia which is one of the other risk factor of cardiovascular diseases. Significant difference were found between three groups and from base line to end of treatment in lipid profile. These changes were significant but not above the normal range of lipid profile.

The base line parameters of safety profile of study drugs like LFTs and CPK between group A, group B and group C were statically non-significant as shown in table 4, and similar results were noted in another study.[22] Statin in group A showed greater change as compared to group C due to higher doses in group A, as in other studies.[23]

The limitation of the study is that the Atorvastatin was not continued more than three months. There is need to evaluate the effects of Atorvastatin in higher doses for longer duration in psoriasis and also compared it with other oral treatments of disease.

CONCLUSION

Atorvastatin produced significant outcomes on psoriasis and when used in combination with Betamethasone produced more significant results as compared to alone.

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REFERENCES

1. Piruzian ES, Sobolev VV, Abdeev RM, Zolotarenko AD, Nikolaev AA., Sarkisova MK, et al. Study of molecular mechanisms involved in the pathogenesis of immune-mediated inflammatory diseases, using Psoriasis as a model. Acta Naturae 2009;3:125-35.
2. Bajaj DR, Devrajani BR, Yousfani A, Shah SZA, Devrajani T, Bibi I. Evaluation of chronic skin diseases at Liaquat University Hospital Hyderabad (The six months' descriptive study). Med Chan 2009;15:59-62.
3. Jagannath S, Meera S, Jayaram S, Sahithya CS. Study of high sensitive C-reactive protein and lipid profile in Psoriasis. IJCBR 2014;1:1-6.
4. Ridker PM. Psoriasis, inflammation, and vascular risk: A problem more than skin deep. Eur Heart J 2010;31:902–4.
5. Kilic A, Cakmak S. Psoriasis and comorbidities. Eur Med J Dermatol 2013; 1:78-85.
6. Greenwood J, Steinman L, Zamvil SS. Statin therapy and autoimmune disease: from protein prenylation to immunomodulation. Nat Rev Immunol 2006;6:358-70.
7. Pittlekow M, Genebriera J. Psoriasis In: Pharmacology and therapeutics: Principles to practice, expert consult Ed. Waldman SA. Elsevier Health Sciences 2008; 1:983-1005.
8. Faghihi T, Radfar M, Mehrabian Z, Ehsani AH, Hemami RM. Atorvastatin for the treatment of plaque-type Psoriasis. Pharmacother 2011;31:1045-50.
9. Schmitt J, Wozel G. The psoriasis area and severity index is the adequate criterion to define severity in chronic plaque – type psoriasis. Dermatology 2005;210:194-9.
10. Feldman S, Krueger G. Psoriasis assessment tools in clinical trials. Ann Rheum Dis 2005;64(Suppl 2): ii65–ii68.
11. Vadakayil AR, Dandekeri S, Kambil SM, Ali MA. Role of C-reactive protein as a marker of disease severity and cardiovascular risk in patients with psoriasis. Indian Dermatol Online J 2015;6:322-5.
12. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI): a simple practical measure for routine clinical use. Clin Exp Dermatol 1994;19:210-6.
13. Kurt T, Gokmen F. Cardiovascular risk in patients affected by autoimmune diseases early diagnosis and

treatment. Inflamm Cell Signal 2015;2:1-6.
14. Reich A, Welz-Kubiak K, Rams L. Apprehension of the disease by patients suffering from Psoriasis. Postepy Dermatol Alergol 2014;31:289-93.
15. Thawornchaisit P, Harncharoen K. A comparative study of Tar and Betamethasone valerate in chronic plaque Psoriasis: A study in Thailand. J Med Assoc Thai 2007;90:1997-2002.
16. Mahajan VK. Psoriasis treatment: Unconventional and non-standard modalities in the era of biologics. World J Dermatol 2016;5:17-51.
17. Ahmad GKA, Choudhary AM, Kondker L, Khan MSI. Comparative safety of topical Calcipotriol (0.005%) versus topical Corticosteroid (Betamethasone 0.1%) in plaque type Psoriasis. J Pak Assoc Dermatologists 2013;23:394-400.
18. Oh J, Teoh H and Leiter LA. Should C-reactive protein be a target of therapy? Diabetes Care 2011; 34(2):55-60.
19. Philippine Dermatological Society. Efficacy of Atorvastatin as adjunctive treatment for chronic plaque type Psoriasis. Updated on 2015; https://clinicaltrials .gov/ct2/ show/ NCT02432040.
20. Ni C and Chiu MW. Psoriasis and comorbidities: links and risks. Clin Cosmetic Invest Dermatol 2014; 7:119-132
21. Mattei PL, Corey KC and Kimball AB. Psoriasis area severity index (PASI) and the dermatology life quality index (DLQI): The correlation between disease severity and psychological burden in patients treated with biological therapies. J Eur Acad Dermatol Venereol 2014; 28(3):333-7.
22. Newman C, Tsai J, Szarek M,Luo D and Gibson E. Comparative safety of Atorvastatin 80 mg versus 10 mg derived from analysis of 49 completed trials in 14,236 patients. Am J Cardiol 2006; 97(1):61-7.
23. Aslam S, Khurshid K, Asad F, Rani Z and Pal SS. Efficacy and safety of Simvastatin in chronic plaque Psoriasis. J Pak Assoc Dermatologists 2013; 23(3):310-314.