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Evaluation of Role of Add on Anti Hyperglycaemic Drugs Metformin and Pioglitazone in Patients of Psoriasis with Metabolic Syndrome

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ABSTRACT

Background: Psoriasis is a chronic non communicable autoimmune cutaneous disorder characterised by abnormal patches of skin. Psoriasis in recent times is known to be associated with systemic manifestations. People suffering from this disorder are at an increased risk of developing metabolic syndrome. An additional anti inflammatory and anti proliferative role of anti hyperglycaemic drugs such as metformin and pioglitazone has been explored to improve the symptomatology and quality of life of psoriatic patients with metabolic syndrome.
Material and Methods: 50 psoriatic patients (mild to moderate severity) with metabolic syndrome were randomized into 3 groups to receive topical clobetasone 3% alone as standard therapy (ST) (Group 1), metformin 500 mg once daily in addition to ST (Group 2) and pioglitazone 15 mg once daily as add on therapy to ST (Group 3) for 12 weeks. Primary efficacy assessment was done using change in Psoriasis Assessment Severity Index (PASI) and change in quality of life was assessed using Dermatological Life Quality Index (DLQI). The secondary outcomes were number of patients achieving PASI 50, 75 and improvement in parameters of metabolic syndrome.
Results: All the treatments significantly reduced the PASI score, maximum being at 12 weeks. Standard therapy reduced the PASI score from 9.39 ± 0.65 to 5.90 ± 0.55 ($p < 0.0001$), metformin from 9.46 ± 0.45 to 3.91 ± 0.57 ($p < 0.0001$) and pioglitazone from 9.61 ± 0.57 to 5.83 ± 0.44 ($p < 0.0001$). Add on treatment with metformin and pioglitazone caused an additional reduction in PASI score as compared to ST alone. Metformin was also found to be significantly superior to pioglitazone therapy in reducing this score. 9 patients achieved PASI 50 and 3 patients achieved PASI 75 with metformin, 4 patients achieved PASI 50 with pioglitazone and 2 patients achieved PASI 50 and 1 patient achieved PASI 75 with ST alone. Both metformin and pioglitazone caused a significant improvement in parameters of metabolic syndrome. Add on treatment caused a significant improvement in QoL, metformin being superior to pioglitazone.
Conclusions: Add on therapy with metformin and pioglitazone to ST showed a better clinical improvement in signs and symptoms of the disease (PASI) as well as quality of life (DLQI) with a good safety profile. Metformin was found to be superior to pioglitazone and both the drugs can be a useful add on therapy for better therapeutic outcome.

Keywords: Psoriasis Assessment Severity index, Dermatological Life Quality index, Metabolic Syndrome

INTRODUCTION

Psoriasis is a chronic inflammatory disorder of skin that is characterised by abnormal patches of skin that are dry, itchy and scaly. These patches have predilection for nails, scalp, genitalia, extensor surface and lumbosacral region. The disease tends to show bimodal distribution of age with its first onset at an early age of 16-22 years (early onset) and second onset between the

age of 57-60 years (late onset).[1] Although the exact etiology of psoriasis remains unknown but in recent years it has been more so classified as an autoimmune disorder with systemic manifestations. Several other factors that are also implicated in occurrence of psoriasis include suburns, trauma, systemic drugs and stress etc.[2,3] But since it considered to be a systemic disease, it has been more found to be associated to various co morbid illnesses like cardiovascular diseases and an increased risk of occurrence of metabolic syndrome which comprises of diabetes mellitus, deranged lipid profile, altered waist hip ratio and occurrence of hypertension. The incidence of these co morbid illnesses is more found in patients with late onset psoriasis.[4]

Currently there is no cure available for this disease and till yet the treatment of psoriasis primarily aims to control the symptomatology of the disease. A wide range of topical and systemic therapeutic options are available in the market and there usage depends upon the clinical severity of disease at the time of presentation. Out of all the available options, topical agents are most commonly used for mild disease, phototherapy for moderate disease and systemic agents for severe disease. Corticosteroids due to their anti inflammatory properties have gained primary status in treatment of mild to moderate disease.[5]

Since the therapy with topical corticosteroids do not completely attenuate the underlying cause of the disease, attention needs to be focussed on several other additional treatment options which might completely cure or modify this disease progression and prevent relapses by more potent suppression of its inflammatory and proliferative pathways. The newer therapeutic targets should also aim to improve the other systemic manifestations associated with this disease such as metabolic derangements.

Recently there have been studies which evaluated the potential role of several oral anti hyperglycaemic groups of drugs in treatment of psoriasis more so with metformin and pioglitazone. These drugs besides improving the parameters of metabolic syndrome have also shown anti inflammatory and anti proliferative properties in such patients.[6] Metformin inhibits the NF-κB signalling pathway in the human vascular endothelial cell there by significantly decreasing the mRNA and protein levels of tumour necrosis factor-α (TNFα), interleukin (IL)-6, IL-8, and IL-1β induced by TNFα whereas pioglitazones by activation of peroxisome proliferator activated receptor-ϒ (PPAR-ϒ) results in reduced inflammation as well as proliferations of human keratinocytes.[7,8] Further metformin has also shown to ameliorate hepatic toxicity associated with systemic therapies. These additional benefits of metformin and pioglitazone in psoriasis have been particularly demonstrated in patients with metabolic syndrome and reduced glucose tolerance. Therefore these drugs can serve as an add on therapy to standard treatment regimen in management of psoriasis.

A randomized, placebo controlled clinical trial (Topical treatment Cohort) was conducted by Singh S and Bhansali A[9] in which patients were randomized to receive placebo (empty gelatine capsules), pioglitazone (30 mg once daily) and metformin (1000 mg once daily) treatment in addition to topical coal tar/calcineurin derivative as standard treatment. The study was conducted over a period of 12 weeks and efficacy was assessed by means of PASI score. After 12 weeks of treatment add on drugs caused a greater reduction in mean PASI score and metformin was found to cause greater reduction in PASI score out of all the treatments.

Singh S and Bhansali A[10] also conducted a systemic treatment cohort study to evaluate the role of metformin in psoriatic patients with MS. It was a randomized, placebo controlled study with metformin 1000 mg as add on drug to systemic methotrexate and folic acid.

However metformin in comparison to placebo failed to achieve the statistical significant proportions in reducing the PASI scores.

With view of such conflicting reports this study was carried out to evaluate the potential role of metformin in reducing the clinical severity and improving QoL of psoriatic disease in patients with and without metabolic syndrome.

MATERIALS AND METHODS

Study Design, population and treatments

The study was a prospective, controlled, randomized, parallel group, open label, comparative clinical study carried out by the Department of Pharmacology and Dermatology, Pt. BD Sharma PGIMS, Rohtak, a tertiary care institute in the state of Haryana, India. The study was approved by the Institutional ethics Committee of the institute.

Eighty eight patients of either gender aged between 18-75 years of age suffering from chronic stable plaque psoriasis were initially screened for clinical severity (mild-moderate) as per predefined inclusion and exclusion criteria. The clinical severity of the disease was determined by PASI score with a score of equal to or less than 11. They were further screened for presence or absence of metabolic syndrome as per SAM-NCEP criteria. Metabolic syndrome was defined as presence of three or more criteria of South Asian Modified National Cholesterol Education programme (SAM-NCEP).[11] HDL cholesterol <40 mg/dl (1.03 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in women, fasting blood glucose ≥ 100 mg/dl (5.6 mmol/l) or previously diagnosed with type 2 diabetes, blood pressure ≥ 130/85 mmHg or on antihypertensive medication and central obesity (defined as waist circumference ≥ 90 cm in men and 80 cm in women according to the ethnic criteria for Asians), triglyceride ≥150 mg/dl (1.7 mmol/l). All those patients who did not meet the above criteria of MS were excluded from the study. Also those patients who have received systemic therapy in the past or were suffering from erythrodermic, generalized pustular psoriasis or an unstable form of plaque psoriasis of severe type were excluded from the study. Pregnant or lactating females at the time of study or patients who had a history of acute serious or psychiatric illnesses, chronic kidney/liver diseases or history of allergy to any of the study medications and not willing to give informed consent were also excluded from the study.

All the eligible patients were randomized to their respective treatment groups by simple randomization technique to receive either standard treatment alone (ST) (Group 1) or Metformin plus ST (Group 2) or Pioglitazone plus ST (Group 3). Standard treatment (ST) included topical 0.05% betamethasone dipropionate which was applied twice daily whereas study treatment included an oral therapy with tablet metformin 500 mg in Group 2 or tablet pioglitazone 15 mg in Group 3 which was taken once daily in addition to ST. The treatment was given for a period of 12 weeks.

Efficacy Assessment:

The efficacy assessment of the study was done using primary and secondary end points. The primary end points comprised of change in Psoriasis Area and Severity Index score and change in Dermatological Life Quality Index score. The secondary end points comprised of number of patients achieving PASI 50, 75 and change in parameters of metabolic syndrome.

Primary end Point:

Psoriasis Area and Severity Index (PASI) score [12]:

PASI score is a composite score formed by the combination of individual scores of area of coverage of the plaque and its appearance (Erythema, scaling and Induration). This score is used to measure the clinical severity of disease and is currently the most widely accepted tool by the physicians worldwide. The score ranges from 0 (no disease) to 72 (maximal disease). Efficacy assessment using this score was

done at baseline and then at the subsequent visits at the end of 4th, 8th and 12th week post treatment. The mean change in PASI score was calculated.

Dermatological Life Quality Index (DLQI) Score [13]:

It is a simple set of questions that is used to assess the change in quality of life of a patient suffering from skin diseases. It is a set of 10 questions that covers six domain of a patients regarding symptoms and feelings, leisure, daily activity, work and school, personal relationship and treatment satisfaction. The response to each question ranges from 3 (very much affected) to 0 (not affected). Thus the overall range of a questionnaire extends from 0-30, indicating better QoL of patient having least score. The DLQI score was calculated before the onset of treatment and then after the 12 weeks of therapy. Efficacy assessment using this parameter was done by mean change in composite DLQI score.

Secondary End Points:

PASI 50/75:

The overall response to a treatment is measured using number of patients effectively achieving PASI 50/75. PASI 50 is said to be achieved when patients achieve 50 percent reduction in their baseline PASI score post treatment. Similarly PASI 75 is said to be achieved when patients achieve 50 percent reduction in their baseline PASI score post treatment. After a follow up period of 12 weeks, number of patients achieving PASI 50 and PASI 75 was recorded

Metabolic syndrome:

The parameters of metabolic syndrome comprising of obesity, hypertension, triglycerides level, HDL level and fasting blood glucose level were assessed in all patients of psoriasis with metabolic syndrome. These were recorded at baseline followed by subsequent visits at 4th, 8th and 12th week to estimate the change in these parameters from baseline after 12 weeks of therapy.

Statistical Analysis:

The values of all continuous variables (e.g. PASI, DLQI scores in each group) were expressed as mean ± standard error of mean (SEM). Paired 't' test was used to assess intra-group outcome comparison for changes within PASI score, DLQI score and individual parameters of metabolic syndrome at 12 weeks from baseline. Independent 't' test was used for inter-group analysis between 2 groups at week 12 for comparing changes in PASI score, DLQI score and individual parameters of metabolic syndrome. P-value of less than 0.05 was considered as statistically significant.

RESULTS

A total of 77 patients with symptoms of psoriasis and having metabolic syndrome were screened as per pre defined inclusion and exclusion criteria. Out of this 27 patients were not eligible for the study due willing to participate in the study. The remaining 50 patients were randomized into their respective treatment groups via simple randomization technique. Distribution of patients in their respective groups is summarized in figure 1

There was no significant difference in the baseline characteristics of control and study group patients with respect to disease and parameters of metabolic syndrome. (Table 1)

Psoriasis Area and Severity Index (PASI):

In Group 1, receiving standard treatment alone, the baseline score was 9.39 ± 0.65 which reduced to 8.11 ± 0.69 at 4 weeks, 7.07 ± 0.67 at 8 weeks and 5.90 ± 0.55 at 12 weeks and this decrease was statistically significant when compared to baseline at 4, 8 and 12 weeks. (Table 2)

Similarly in Group 2, receiving metformin as add on therapy the baseline score was 9.46 ± 0.45 which reduced to 7.43 ± 0.56 at 4 weeks, 5.90 ± 0.52 at 8 weeks and 3.91 ± 0.57 at 12 weeks and this decrease was statistically significant when compared to baseline at 4, 8 and 12 weeks. (Table 2)

The same was observed in Group 3 receiving pioglitazone as add on therapy, where the baseline score was 9.61 ± 0.57 which reduced to 8.5 ± 0.53, 6.4 ± 0.51 and 4.97 ± 0.44 at 4, 8 and 12 weeks respectively. The reduction in PASI score was statistically significant when compared to baseline. (Table 2)

The maximum percentage reduction in PASI score was seen at 12 weeks as 37.16 % in Group 1, 58.67 % in Group 2 and 48.28 % in Group 3 respectively

On intragroup analysis there was clinically and statistically significant decrease in the mean PASI score in all the three treatment groups. The improvement was seen as early as week 4 which further continued as seen on week 8 and it was maximum at week 12. This decrease in score in all the treatment groups is indicative that all the treatments were significantly effective in improving the psoriatic symptoms. (Table 2)

Fig 1: Flow chart for distribution of patients

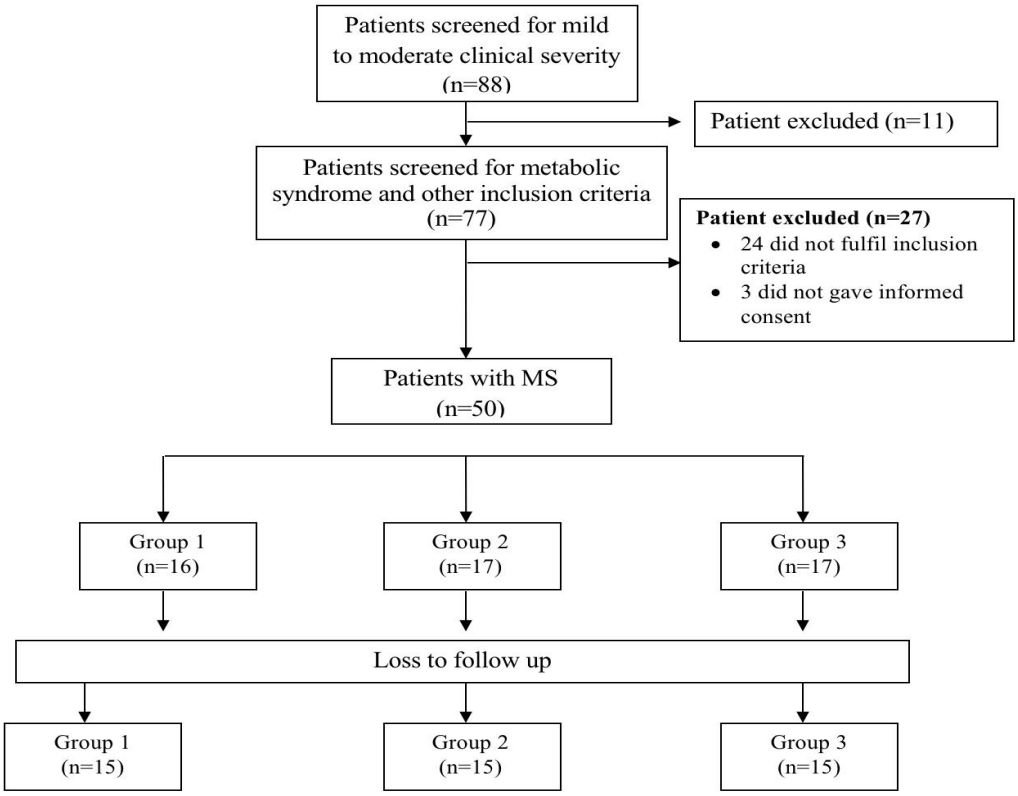

Table 1: Baseline characteristics of Study Population

Time	Standard Therapy (ST) alone (0.05% Betamethasone Dipropionate)	Metformin Plus ST	Pioglitazone plus ST	p Value (Inter Group)
	Mean ± SEM (%)	Mean ± SEM (%)	Mean ± SEM (%)	
Age(years)	52.57 ± 2.44	54.1 ± 1.97	53 ± 3.1	NS
Gender Male Female	 12 2	 11 5	 12 4	NS
PASI	9.39 ± 0.65	9.46 ± 0.45	9.61 ± 0.57	NS
DLQI	17.92 ± 0.73	18.43 ± 0.77	18.62 ± 0.53	NS
WC (cm)	97.92 ± 1.29	98.56 ± 1.02	97.25 ± 1.70	NS
SBP (mm Hg)	151 ± 4.09	153.38 ± 3.52	152.38 ± 3.13	NS
DBP (mm Hg)	91.14 ± 2.13	93.87 ± 1.95	94.37 ± 1.87	NS
TG (mg/dl)	171.71 ± 3.47	171.3 ± 4.305	170 ± 4.32	NS
HDL level (mg/dl)	37.78 ± 0.57	37.31 ± 0.637	37.81 ± 0.82	NS
FBG (mg/dl)	117.42 ± 8.15	119.93 ± 6.51	118.313 ± 8.51	NS

Table 2: Comparison of composite Psoriasis Area and Severity Index (PASI) in patients with metabolic syndrome

Time	Standard Therapy (ST) alone (0.05% Betamethasone Dipropionate)	Metformin Plus ST	Pioglitazone plus ST	p Value (Inter Group)
Baseline	9.39 ± 0.65	9.46 ± 0.45	9.61 ± 0.57	0.969 [(a)] 0.929 [(b)] 0.802 [(c)] 0.943 [(d)]
Week 4	8.11 ± 0.69[#]	7.43 ± 0.56[#]	8.5 ± 0.53[#]	0.434 [(a)] 0.454 [(b)] 0.659 [(c)] 0.329 [(d)]
Week 8	7.07 ± 0.67[#]	5.90 ± 0.52[#]	6.4 ± 0.51[#]	0.130 [(a)] 0.049 [(b)] 0.425 [(c)] 0.725 [(d)]
Week 12	5.90 ± 0.55[#]	3.91 ± 0.57[#]	4.97 ± 0.44[#]	0.130 [(a)] 0.030 [(b)] 0.154 [(c)] 0.054 [(d)]
PASI (Intra Group)	<0.0001	<0.0001	<0.0001	

a : Inter group comparison of PASI score carried out by One way ANOVA
b : Metformin with standard treatment compared to standard treatment alone
c : Pioglitazone with standard treatment compared to standard treatment alone
d : Metformin with standard treatment compared to Pioglitazone with standard treatment alone
: Statistically significant (p <0.05)

Table 3: Comparison of composite Dermatological Life Quality Index (DLQI) in patients with metabolic syndrome

Time	ST alone	Metformin plus ST	Pioglitazone plus ST	p Value (InterGroup)
Baseline	17.92 ± 0.73	18.43 ± 0.77	18.62 ± 0.53	0.770 [(a)] 0.640 [(b)] 0.445 [(c)] 0.844 [(d)]
Week 12	14.21 ± 0.71[#]	10.87 ± 0.69 [#]	13.43 ± 0.56 [#]	0.002 [(a)] 0.002 [(b)] 0.397 [(c)] 0.008 [(d)]
p Value (Intragroup)	<0.0001	<0.0001	<0.0001	

a : Inter group comparison of PASI score carried out by One way ANOVA
b : Metformin with standard treatment compared to standard treatment alone
c : Pioglitazone with standard treatment compared to standard treatment alone
d : Metformin with standard treatment compared to Pioglitazone with standard treatment alone
: Statistically significant (p <0.05)

Intergroup analysis:

On simultaneous intergroup analysis (table-2) at the end of 4, 8 and 12 weeks after treatment there was no statistically significant difference in reduction of PASI between the treatments

On comparing, add on therapy with metformin to standard treatment alone, the PASI score was reduced more with metformin as add on therapy and this difference was statistically significant from week 8 onwards (p value 0.049) and continued till week 12(p value 0.030)

Similarly on comparing, add on therapy with pioglitazone to standard treatment alone, the PASI score was reduced more with pioglitazone as add on therapy. However it did not attain the statistically significant proportions. (p value 0.154)

On comparing metformin and pioglitazone as add on therapies to each other, therapy with metformin was found to be almost statistically superior to pioglitazone by the end of 12 weeks (p value 0.054).

Overall, it can be concluded from above observations on PASI score that standard therapy alone, add on treatments with metformin and pioglitazone all are effective treatment in reducing the PASI score. Both metformin and pioglitazone when given as add on therapy caused a more reduction in PASI score and where found to be significant statistically when compared to standard treatment alone.

Table 4: Changes in parameters of metabolic syndrome

Treatment	Standard Treatment alone (0.05% Betamethasone Dipropionate)		Group 3 Metformin plus ST		Group 4 Pioglitazone as add on to Standard Treatment		p Value (Inter group)
Parameter	Mean change	pValue[a]	Mean change	pValue[a]	Mean change	p Value[a]	
WC (cm)	0.214 ± 0.914	0.818	-2.938 ± 0.81	0.01[f]	-2.250 ± 0.75	0.009 [f]	0.937 [b] 0.001 [c] 0.002 [d] 0.949 [e]
SBP (mm Hg)	1.857 ± 2.395	0.452	-4.875 ± 1.87	0.12	-4.625 ± 1.85	0.025 [f]	0.827 [b] 0.001 [c] 0.001 [d] 0.956 [e]
DBP (mm Hg)	0.286 ± 1.68	0.868	-4.25 ± 1.88	0.23	-4.25 ± 1.23	0.010 [f]	0.963 [b] 0.001 [c] 0.001 [d] 0.989 [e]
TG (mg/dl)	1.429 ± 2.825	0.630	-9.30 ± 3.21	0.04 [f]	-9.25 ± 0.37	0.001 [f]	0.982 [b] 0.001 [c] 0.001 [d] 0.965 [e]
HDL (mg/dl)	-2.0 ± 1.44	0.104	4.31 ± 0.794	0.003 [f]	3.75 ± 1.07	0.003 [f]	0.941 [b] 0.001 [c] 0.001 [d] 0.889 [e]
FBG (mg/dl)	-8.07 ± 3.67	0.47	-9.31 ± 2.79	0.027 [f]	-12.25 ± 3.19	0.002 [f]	0.654 [b] 0.001 [c] 0.001 [d] 0.412 [e]

WC- Waist circumference; SBP- Systolic Blood Pressure; DBP- Diastolic Blood Pressure; TG- Triglyceride levels; HDL- High Density Lipoprotein; FBG- Fasting Blood Glucose

[a] Intra-group comparison for WC, SBP, TG, HDL, FBG

[b] Inter-group comparison for individual parameters between all the groups carried out by One way ANOVA,

[c] Inter group comparison between the metformin as add on to standard treatment vs standard treatment alone

[d] Inter group comparison between the pioglitazone as add on to standard treatment vs standard treatment alone.

[e] Inter group comparison between the metformin as add on to standard treatment vs pioglitazone as add on to standard treatment.

[f] Statistically significant result compared to baseline.

Table 5: Reported Adverse Drug reactions

ADVERSE EVENT	Standard treatment alone (0.05% Betamethasone Dipropionate)	Group 2 Metformin plus ST	Group 2 Pioglitazone plus ST
	n = 15	n = 15	n = 15
	Number of patients (%)		
Any adverse event	3/14 (35%)	5/16	3/16
Gastritis	-	2/16	
Hypopigmentation of skin	1/16		
Exacerbation of plaque	2/16		
Abdominal pain	-	1/16	1/16
Myalgia	-	1/16	
Nausea	-		1/16
Vomiting	-	-	-
Diarrhoea	-	1/16	1/16

Dermatological Life Quality Index:

There was an improvement in composite DLQI in Group 1, when the score at week 12 was compared with the baseline score. The improvement was found to be statistically significant (p value <0.05). There was an additional reduction in composite DLQI score with add on treatment in both the Groups 2 and 3 which was found to be statistically significant (p value <0.05). These observations indicate that all are effective treatments. The values are shown in Table 3

On simultaneous intergroup analysis at week 12, there was statistical significant reduction of composite DLQI score between the treatments. Metformin and pioglitazone as add on therapy caused additional reductions in composite DLQI score when compared to standard therapy alone. However the reduction was found to be statistically significant only with comparison of metformin as add on therapy to standard treatment alone. Also metformin was found to be significantly superior to pioglitazone in improving overall quality of life. The values are shown in Table 3.

So in patients of psoriasis with metabolic syndrome all the treatments were effective in improving the QOL. Add on treatments with metformin and pioglitazone further provided additional benefit in improving the QOL but metformin was much superior to pioglitazone in improving these beneficial outcomes.

Number of Patients achieving PASI 50/75:

In psoriatic patients with metabolic syndrome who received standard treatment alone, two patients achieved PASI 50 and 1 patient achieved PASI 75. But there was an increase in number of patients who achieved PASI 50 (9 out of 15) and PASI 75 (3 out of 15), amongst the patients who received metformin as add on. In patients receiving pioglitazone as add on, only four patients achieved PASI 50 (4 out of 15) and none of them achieved PASI 75

Parameters of metabolic syndrome:

All the parameters of metabolic syndrome were significantly improved with metformin and pioglitazone as add on drug after 12 weeks of therapy. Metformin and pioglitazone were found to be significantly superior to standard therapy alone in improving these parameters. However metformin and pioglitazone were found to be comparable with respect to each other. (Table 4)

Safety Evaluation:

The most commonly reported adverse drug reactions with standard treatment alone were exacerbations and hypopigmentation and with metformin as add on drug the most common ADRs were myalgia, abdominal pain, gastritis and diarrhoea. With pioglitazone as add on drug abdominal pain, nausea and diarrhoea were the most common ADRs. (Table 5)

All the ADRs were of mild severity and none of the patient discontinued the study medication due to any ADRs in any of the groups. All the ADRs were evaluated for causality assessment and categorized as possible using WHO UMC scale[14].

DISCUSSION

PASI score which was the main primary outcome to assess the clinical improvement of psoriatic disease was significantly improved with all the study treatments. Add on therapy with both metformin and pioglitazone caused an additional improvement in PASI score. Metformin was found to be significantly superior to standard therapy alone as well as to add on therapy with pioglitazone. The study drugs metformin and pioglitazone were used in the lowest approved dose from therapeutic window of these drugs. This probably is the reason that pioglitazone produced a similar response as compared to standard therapy alone and also that the response could be much more with the use of higher dose of both the drugs from the approved therapeutic window. The possible reasons for these submaximal benefits of add on therapy could be attributed to the usage of lowest possible approved dose of therapeutic window of these drugs, keeping in mind the safety of patients and also since it was an add on therapy. The cause of the additional benefit by study drugs could be attributed to the fact that besides improving parameters of metabolic syndrome, these drugs are known to possess additional anti inflammatory and anti proliferative properties. Metformin inhibits the NF-κB signalling pathway in the human vascular endothelial cell there by significantly decreasing the mRNA and protein levels of tumour necrosis factor-α (TNFα), interleukin (IL)-6, IL-8, and IL-1β whereas pioglitazone acts through PPAR receptors which are known to be expressed and regulates proliferation of keratinocyte cells[7,8]. Further by improving the condition of metabolic syndrome, they are known to reduce systemic inflammation. The results in accordance to a study conducted by Singh S and Bhansali A[9] where 23, 16 and 21 patients who were randomized to receive placebo (empty gelatine capsules), pioglitazone (30 mg once daily) and metformin (1000 mg once daily) treatment in addition to topical coal tar/calcineurin

derivative as standard treatment. After 12 weeks of treatment there was statistically significant reduction in PASI score in both metformin and pioglitazone group as compared to placebo and the greater reduction in mean PASI score was seen in those patients who received metformin as add on drug.

Add on therapies also caused significant improvement in QoL of psoriatic patients with metabolic syndrome when compared to Standard therapy alone. Metformin was also found to be significantly superior to pioglitazone. Improvement in QoL could be much more with the usage of higher dose of both the drugs. The improvement could be expected due to an additional anti inflammatory action resulting in reduced redness, scaling and induration of skin with additional improvement in parameters of metabolic syndrome. Similar findings were observed in a study by Lajevardi et al[15] for pioglitazone and Xuan et al[16] for metformin, where significant improvement was noticed by these add on drugs. PASI 50 and PASI 75 which were the secondary outcome measures were also significantly improved with these add on drugs. Expectedly both metformin and pioglitazone caused a significant improvement in parameters of metabolic syndrome which is well established.

The safety of both the add on drugs is already known and same was observed in study which is in line with the known safety profile. On causality assessment the ADRs were categorised as possible and none of the patients discontinued the study treatment due to any ADRs in any of the groups.

CONCLUSION

The observation of study clearly indicate that the psoriatic patients can derive an additional benefit with the use of add on therapies with metformin and pioglitazone and that benefit could further improve with higher doses used from therapeutic window of 2 drugs. Also both add on therapies can cause an improvement in overall QoL of psoriatic patients. Further clinical studies with these add on drugs using a higher dose and all grades of psoriasis may make the issue clear regarding the use of these drugs to give an additional benefit with good safety in psoriatic patients.

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