Evaluation of lipid profile for psoriatic patients treated by cyclosporine and biological treatment

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Abstract

Background: Psoriasis is a common disease with the population prevalence ranging from 2% to 3%. Its prevalence in the population is affected by genetic, environmental, Psoriasis is associated with an atherogenic lipid profile but longitudinal changes in lipids around disease onset are unknown. Because of the wide range of comorbid conditions associated with psoriasis, comprehensive screening and treatment must be implemented to most effectively manage psoriasis patients. The purpose of our study is to examine the effect of type of treatment on serum lipid profiles for psoriatic patients.

Methods: We compared changes in lipid profiles in a psoriatic patient never treated incident 20 patients with 5 psoriatic patient treated by cyclosporine and 5 psoriatic patient treated by biological treatment (infliximab) all lipid measures index date were abstracted. Random-effects models adjusting for age, sex and calendar year were used to examine trends in lipid profiles.

Result: Decrease LDL and increase HDL level with biological treatment, but no effect of cyclosporine on lipid profile.

Conclusions: This study results showed a good effect of biological treatment on lipid profile.

Introduction

Psoriasis is a common disease affecting, as presumed, approximately 120–180 million people worldwide (1). The most characteristic lesions consist of red, scaly, sharply demarcated, indurate plaques, present particularly over extensor surfaces and scalp. The disease is enormously variable in duration, periodicity of flares and extent that may affect any part of the skin surface (2).

Different clinical types of psoriasis have been reported, and the commonest one is psoriasis vulgarism; which can affects 80%-90% of psoriatic patients. The size of psoriatic lesions (plaques) was varied from small spots to large scaly patchy lesions, with multiple shapes and appearance (3). Psoriasis has been shown to be associated with a higher incidence of myocardial infarction, stroke, and cardiovascular mortality (4). In moderate to severe psoriasis, a significantly deteriorated lipid profile was observed compared to healthy controls, with higher values of low-density lipoprotein, triglycerides and significantly decreased HDL level. Recent studies clearly demonstrated that inflammation impairs reverse
cholesterol transfer in vivo(5), lipid metabolism disorders may play a role in psoriasis pathogenesis (6).

Treatment of psoriasis depends on the type and severity of the disease. Typically, topical therapies are used to treat mild and localized psoriasis. Topical treatments are the foundation for mild to moderate psoriasis. However, this approach can decrease the number and thickness of the plaque lesions, and reduce the percentage of body surface involved. In general, pharmacological treatment should start with the use of topical corticosteroids(7). Classified as a calcineurin inhibitor, cyclosporine is as effective for psoriasis as methotrexate (8). Systemic retinoid (derivatives of vitamin A) are utilized for patients with severe psoriasis(9). Biologic agents are important treatment options for moderate to severe plaque type psoriasis(10).

Cyclosporine acts by inhibiting T-cell activation and therefore produces an immunosuppressive response(11). Cyclosporine should be administered consistently at the same time of day. The solution can be mixed with milk or orange juice, but not grapefruit juice due to cytochrome reactions. The most common and serious adverse effects include hypertension and nephrotoxicity(12).

The available biologics for psoriasis have excellent short-term and long-term efficacy and favorable tolerability. Biologic therapies available for the treatment of psoriasis include etanercept, infliximab, adalimumab, and ustekinumab. The FDA approved secukinumab, an additional biologic agent, in January 2015. Network meta-analyses evaluating etanercept, infliximab, adalimumab, and ustekinumab support the designation of infliximab as the most effective of these biologic agents for psoriasis(13).

There is a concern that all TNF-alpha inhibitors have the potential to activate latent infections such as tuberculosis, and increased rates of infection have been seen in patients with rheumatoid arthritis treated with etanercept, infliximab, and adalimumab. In addition, risk for herpes zoster may be increased in patients receiving biologic therapy in combination with methotrexate (14).

Materials and Methods
This is a hospital-based, case control study included one hundred twenty psoriatic patients admitted in the Department of Dermatology of Rezgary Hospital. through the period from March 2015, till the September 2015. in this study there is fifty patient who were afflicted with psoriasis Twenty of these new case psoriatic Patient never used any treatment before selected as a control group, five patents treated by cyclosporine , And five patients treated by biological treatment . Exclusion criteria were: diabetes, obesity(body mass index higher than 30Kg/m2), family history of hyperlipidemia, renal and liver failure,
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Hypothyroidism, taking systemic drugs especially lipids lowering agents, smoking and drinking spirits (alcoholic beverages) in order to eliminate damaging factors on serum lipids level of the patients.

Most participants were selected from Iraq and some of these Syrian they usually had breakfast and lunch at work with a similar diet. Subjects who had high-fat foods at dinner were excluded. After explaining the purpose of the study and obtaining consent letter, data were recorded on questionnaires for each patient. After a 14 h fasting period, 5 mL venous blood was taken in sterile syringe in the morning from all cases and submitted to the laboratory. Serum levels of total cholesterol, triglyceride, LDL, and HDL were measured by the using of enzymatic colorimetric method, using cholesterol enzymatic biolabo kit (maizy, France). The severity of psoriasis was evaluated based on the standard criteria of psoriasis.

**The result**

Compared Lipids Profile between cyclosporine treated group and Control group:

The mean differences of total serum cholesterol (TC), triglycerides (TG), high density lipoprotein (HDL) and low density lipoprotein (LDL) among patients which treatment by cyclosporin with control subjects. There were TC (159217±52 mg/dl), TG (50±12 mg/dl), HDL (52±8 mg/dl) and LDL (164.04 ± 49.63 mg/dl) among patients while the mean serum concentrations of TC (169.25 ±36.32 /dl), TG (73.15±32.52mg/dl), HDL (50.75±7.72mg/dl) and LDL (103.87±36.38mg/dl) for control group, the P value of TC is 0.111 that is mean no significant mean differences of TC and P value of TG is 0.019 significant mean of TG . P value of HDL is 0.843 that is no significant mean differences of HDL. P value of LDL is 0.122 that is no significant LDL, as shown in able (1). And we see no significant correlations of duration of treatment with total cholesterol in cyclosporine treated group (R: 0.00) as shown in figure (1), but negative correlations of duration of treatment with triglyceride in cyclosporine treated group (R: 0.557) as shown in figure (2).

Compared Lipids Profile between biologic treated group and Control group:

The mean differences of total serum (TC), (TG), (HDL) and (LDL) among patients which treatment by biological treatment with control subjects. There were TC (166±18 mg/dl), TG (141.8 ±65.6 mg/dl), HDL (70 ± 5 mg/dl) and LDL (68.44 ± 17.40 mg/dl) among patients while the mean serum concentrations of TC (169.25 ±36.32 /dl), TG (73.15±32.52mg/dl), HDL (50.75±7.72mg/dl) and LDL (103.87±36.38mg/dl) for control group, the P value of TC is 0.805 that is mean no significant mean differences of TC and P value of TG is 0.078 no significant mean of TG . P value of HDL is 0.0000 that is highest significant mean differences of HDL. P value
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of LDL is 0.007 that is significant LDL. As shown in Table (2). So we found positive significant duration of treatment with total cholesterol in biological treated group. (R: 0.599) as seen in figure (3), but negative significant correlations of duration of treatment with triglyceride in biological treated group (R: 0.469) as shown in figure (4).

Discussion

The Abnormality of lipids can often be recognized at the early stage of the psoriasis and some time at onset of the disease. This fact gives us an idea about genetic predisposition or determination of lipid dys-regulation or abnormalities. Other pro-atherogenic lipid abnormalities in psoriatic patients indicated a high serum concentrations of total cholesterol had been reported. Study by (Aysun Toker, A 2009) concerning with total serum cholesterol concentrations in patients with psoriasis, showed that the results varies from normal, low or some time elevated values had been reported(15)

Many studies through the past time demonstrates disturbed lipid metabolism in psoriatic patients and shows clear changes in the compositions of lipid components (lipid profile) in their serum. These abnormalities in plasma lipid in psoriatic patients may have a major role in the initiation and proceeding of atherosclerotic process in many inflammatory conditions including psoriasis. Study by (Bernard FX, 2012) revealed that psoriasis is associated with atherogenic dyslipidemia with elevated plasma concentrations of total cholesterol, triglycerides, low density lipoprotein (LDL), very low density lipoprotein (VLDL) and decreased serum levels of high density lipoprotein (HDL) (16).

A number of drugs that were frequently used to treat psoriasis, such as cyclosporine and retinoids, are well known to adversely affect serum lipid levels and could contribute to the differences between studies(17).

The Effect of cyclosporine treatment on lipid profile:

The present study there was no significant change in the level of serum lipids was showed in serum of psoriatic patients on cyclosporine treatment in compared to control group as shown in table (1) (TC) (p. value is 0.111), (TG) (p. value is 0.132), (HDL) (p. value is 0.290) and (LDL) (p. value is 0.083).

Our finding disagreed with study by (Delia Colombo 2012) Hyper triglyceridaemia (>750 mg/dL) occurs in approximately 15% of cyclosporine treated patients, and hyper cholesteroloma in <3%, hyperlipidaemia should be actively managed in cyclosporine-treated patients with psoriasis. If cyclosporine therapy is continued, the initial intervention is a lipid lowering diet. If this is unsuccessful, the cyclosporine dosage should be reduced, or
treatment with a lipid-lowering agent started. Fluvastatin was shown to be well tolerated in association with cyclosporine (18).

Low dose cyclosporine as used in the treatment of psoriasis does not significantly affect the lipid profile. Drugs that have an unfavorable effect on lipid profile include retinoids and cyclosporine. Cyclosporine has also been linked to hypertriglyceridemia, although the mechanism of this association is unclear. Eighty percent of plasma cyclosporine is bound to VLDL, and cyclosporine is hypothesized to either increase hepatic output of VLDL or interfere with the clearance of VLDL.(19)

No change in (TG) figure (1) (R= 0.311). But increase (TC) by time when use this treatment for long time as seen in figure (2) (R= 0.000). But this result disagree with (Morales JM 2009) he found Patient survival at 5 years were analyzed by average fasting total cholesterol (<or=200 or >200 mg/dL) and triglyceride (<or=240 or >240 mg/dL) subgroups. At 5 years, total, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) cholesterol and triglyceride values were similar between the groups. Statins (approximately 80% of patients of both groups) were most effective to lower cholesterol (approximately 50 mg/dL; P < .001; both groups), and fibrates (approximately 25% of patients of both groups) were most effective to decrease triglycerides (approximately 100 mg/dL; P < .001; both groups)(20).

The Effect of biological treatment on lipid profile:

The present study demonstrated increase (HDL) as seen in table (2) (p. value is 0.000) and decrease (LDL) level in psoriatic patients use biological treatment in compared to control psoriasis patient group as shown in table(2) (p. value is 0.007).

Our finding agreed with study reported by (Bacchetti T, Campanati A, 2013) who foundTreatment with the anti-TNF drugs etanercept, infliximab, and adalimumab has been shown to reduce the levels of inflammatory markers (CRP) and lipid peroxidation products while increasing serum antioxidant capacity. These effects are associated with an increase in the level of paraoxonase, an antioxidant enzyme and anti-inflammatory enzyme associated with HDL. HDL levels also increased after treatment. (21) Anti-TNF drugs have also been found to induce structural changes in the High density lipoprotein (HDL) protein composition. During inflammation, the HDL protein composition changes so that it is unable to protect low density lipoprotein (LDL) from oxidation. Anti-TNF drugs were found to restore HDL’s protein composition back to an atheroprotective state in patients with rheumatoid arthritis.(22)
However, other studies have found no favorable change in lipid profiles of psoriasis patients with TNF inhibitors (23).

On the other hand there was no significant change in the level of (TC) and (TG) compared with long term of use biological treatment as seen in table (2) (TC) (p. value is 0.805) (R= 0.214)in figure (3). And (TG) (P. value is 0.359) (R= 0.202) in figure (4).

The result of our study disagreed with study reported by (Yannick A 2005) who found increase in TC that treatment with infliximab is associated with increased concentrations of both (TC), (HDL), its multiple effects, TNF-a has the capacity to induce dyslipoproteinemia and insulin resistance Therefore, one would expect a decrease in (LDL), an increase in (HDL) and a decrease in TG level after anti-TNF-a therapy(24).

Conclusions
Regarding to the results of this study, we can conclude the following:

1. This study indicates that psoriasis is associated with increased serum lipid profile levels and type of treatment .The association between lipid profile level and type of treatment very importantbecause lipid profile levels regarded as key players in initiation, proceeding and maintenance of atherosclerosis and ultimately, in psoriasis pathogenesis.

2. This study results showed a good effect of biological treatment on lipid profile.

Reference
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18. Delia Colombo,Antonino Di Pietro; Systemic Cyclosporin in the Treatment of Psoriasis, NI Nordin - qmro.qmul.ac.uk 2012


Table (1): Mean levels of lipid profile of cyclosporine treated group in comparison to controls group:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cyclosporine</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. deviation</td>
<td>Mean</td>
</tr>
<tr>
<td>Total cholesterol mg/dl</td>
<td>207</td>
<td>52</td>
<td>169.25</td>
</tr>
<tr>
<td>Triglyceride mg/dl</td>
<td>50</td>
<td>12</td>
<td>73.15</td>
</tr>
<tr>
<td>HDL mg/dl</td>
<td>52</td>
<td>8</td>
<td>50.75</td>
</tr>
<tr>
<td>LDL mg/dl</td>
<td>164.04</td>
<td>49.63</td>
<td>103.87</td>
</tr>
</tbody>
</table>

Table (2): Mean levels of lipid profile of biological treated in comparison to control group:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Biological treatment</th>
<th>Control</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. deviation</td>
<td>Mean</td>
</tr>
<tr>
<td>Total cholesterol mg/dl</td>
<td>166</td>
<td>18</td>
<td>169.25</td>
</tr>
<tr>
<td>Triglyceride mg/dl</td>
<td>141.8</td>
<td>65.6</td>
<td>73.15</td>
</tr>
<tr>
<td>HDL mg/dl</td>
<td>70</td>
<td>5</td>
<td>50.75</td>
</tr>
<tr>
<td>LDL mg/dl</td>
<td>68.44</td>
<td>17.40</td>
<td>103.87</td>
</tr>
</tbody>
</table>

Figure (1): no significant correlations of duration of treatment with total cholesterol in cyclosporine treated group (R:0.00)
Figure (2): negative correlations of duration of treatment with triglyceride in cyclosporine treated group (R: 0.557)

Figure (3): positive significant duration of treatment with total cholesterol in biological treated group. (R: 0.599)

Figure (4): negative significant correlations of duration of treatment with triglyceride in biological treated group (R: 0.469)
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