Beneficial Effects of Silymarin on Lipid Profile in Hyperlipidemic Patients: Placebo Controlled Clinical Trail

Corresponding Author:
Dr. Hayder M Alkuraishy,
Lecturer, Pharmacology, College of Medicine - Iraq

Submitting Author:
Dr. Hayder M Alkuraishy,
Lecturer, Pharmacology, College of Medicine - Iraq

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Author(s): Alkuraishy H M, Alwindy S

Abstract

The study was designed to evaluate the effect of silymarin alone on hyperlipidaemia within short interval (2 weeks) period on the lipid profile.

20 patients with hyperlipidaemia of various etiologies are involved in this study (13 males, 7 females) randomized into two groups, 10 patients received placebo and 10 patients received silymarin 600mg oral capsule once daily. The lipid profile was measured before the treatment and after two weeks of treatment with silymarin and placebo for comparison.

Results of this study showed that silymarin produce significant reduction in triglyceride, cholesterol, LDL, VLDL but significant elevation in HDL level. Therefore, silymarin can be used alone for effective treatment of different etiologies hyperlipidaemia.

Introduction

Hyperlipidaemia, is considered to happen when serum cholesterol and or triglycerides reach levels linked with an increased risk of ischemic heart disease (IHD). Hyperlipidaemia also embraces the terms hypercholesterolemia and hyperlipoproteinaemia. The term dyslipidaemia is used to cover both hyper and hypolipoproteinaemia (1).

The recognition of hypercholesterolemia as a risk factor for IHD has concerned much awareness, predominantly as to whether extensive broadcast should be undertaken (2). For every 1% increase in blood cholesterol levels, there is a 2% increase in the frequency of coronary heart disease, also, for every 1% decrease in high density lipoprotein cholesterol level (HDL–C), there is a 3% increase in coronary heart disease. Populations studies have revealed that total serum cholesterol level increases with age in males and females over the age of 20 year(3) but between the ages of 50–75 year the mean total cholesterol in women exceeds that of a similar age (4).

Cholesterol, triglycerides, and other lipids are transported in the body all the way through the blood stream in a spherical particles called lipoproteins which can be divided into (LDL) which accounts for 60–70% of total serum cholesterol, and (HDL) constitute 20–30% of total serum cholesterol, and (VLDL) comprising about 10–15%(5). The main two major clinical squealed of lipid profile disorders are acute pancreatitis and atherosclerosis (6).

The hyperlipidaemia description for 60% primary, 40% secondary (7). The most commonly adopted non – pharmacological treatment involve diet and exercise, also omega fatty acid, found in fish oil can induce profound lowering of triglyceride level.(7)

Ascorbic acid and ¿-tocopherol have up to that time been demonstrated to be potent inhibitor of LDL oxidation that were comparable to their physiologic serum level (8).

Silymarin is a combination of flavonolignans isolated from the ripe seed of medicinal plant silybum marianum (milk thistle), comprised mainly silybinin, silychristin, silydianin and taxifolin, the milk thistle usually standardized to contain 80% silymarin (9). The silymarin is closely associated with alteration of membrane lipid by interference with lipoprotein secretion and uptake (10). In rats, silymarin is able to partially antagonize the augment in total lipid produced in liver by CCI4 and probably to trigger fatty acid ¿-oxidation and lessen triglyceride synthesis in the liver(11). Silymarin reduces plasma level of cholesterol and LDL in hyperlipidaemic rat but not in normal rats, also in the experimental models of hepatic injury have shown that silymarin is talented to regularize the increase in plasma lipid after management of thioacetamide, also silymarin improve LDL binding to hepatocyte, which is an important factor for reduction of plasma LDL (12).

The aim of this study is to evaluate the short term effects within two weeks of silymarin on lipid profile in hyperlipidaemic patients.

Methods

This randomized clinical study was carried on 20 patients (13 males, 7 females) with age range of 35–71 years presented with hyperlipidaemia for 1–5 years. All patients were either newly or previously diagnosed with various types of hyperlipidaemia. Patients were
randomized into two groups and treated as follow:
Group A: include 10 patients (7 males and 3 females) treated with 600mg sugar as placebo in a form of opaque capsule for 2 weeks.
Group B: include 10 patients (6 males and 4 females) treated with 600mg silymarin once daily at evening as an oral capsule for 2 weeks (silymarin standardized powder from luna company in Egypt).
After overnight fasting, 10ml blood samples were collected by vein puncture at zero time and after 2 weeks, the serum was prepared after centrifugation.

Measurement of total serum cholesterol
Total serum cholesterol was measured according to Richmond method (1973)(13) based on enzymatic oxidation and hydrolysis.
The faint pink color measured by spectrophotometry at 500nm which is proportionally directed to cholesterol concentration.

Measurement of serum triglyceride (TG).
Lipase
TG measured by Fossati and Prencipe (1982)(14) by spectrophotometry at 500nm measured.

Measurement of serum LDL:
Using Friedwald formula (1972)(15)
LDL = (TC – HDL) – TG/5

Measurement of serum VLDL:
Using Burstein formula (1970)(16)
VLDL = TG/5

Measurement of HDL:
By Burstein method (17). The VLDL and LDL in the sample are precipitated by addition of phosphotungstic acid with Mg+, after the centrifugation the HDL separated from the cholesterol.
The results were expressed as mean ± SD, the significance of difference between the mean values was calculated using paired student's t-test. The P-value less that 0.05 was considered significant.

Results

The characteristics of present study showed in table (I). The effects of silymarin on different parameters of lipid profile have been showed in table (II) as it compared with effects of placebo at zero time and after 2 weeks
Table (II) showed that there is significant reduction (P < 0.05) in the levels of LDL and cholesterol after 2 weeks of therapy with silymarin compared with insignificant effects of placebo (P > 0.05) on both levels.
Regarding TG and VLDL there is significant reduction (P < 0.05) compared with placebo effects.
Silymarin lead to significant elevation in HDL from 32.30±3.368 to 44.40±5.816 (P < 0.05) compared with placebo effects that produce insignificant effects (P > 0.05).
Therefore, the placebo produces insignificant effects on lipid profile.

Discussion

It has been reported earlier that silymarin or its polyphenolic fraction amend the lipoprotein profile in animal model of dyslipidaemia (18).
For that reason, this clinical study was customary according to this biological activity and the very well known safety profile of this plan extort.
Table (II) showed that treatment with silymarin successfully improves the lipid profile markers in hyperlipidaemic patients during two weeks of treatment. It has been reported that bioflavonoids and lecithin produce anti-atherosclerotic activity in experimentally induced atherosclerosis in rabbits, mostly attributed to normalized lipid metabolism(19).
Administration of silymarin to rats with impaired lipid profile consequences in significant reduction in LDL, VLDL, triglyceride and cholesterol with elevation of HDL (20) this compatible with our result in table (II).Kercman (1998) reported that silymarin inhibit development of hypercholesterolemia in rats fed cholesterol-rich diet and compared this finding with that produced by probucol, related with an increase in HDL levels and decrease in liver contented of cholesterol (21). In addition, orally silymarin produced gentle increase in plasma HDL level without significant changes in total cholesterol level in the plasma of rat fed standard laboratory diet, but parentally administrated silymarin unsuccessful to reduce plasma cholesterol this may propose the interference of silymarin with absorption of cholesterol (22).
In clinical follow, it has been reported that treatment of patients having hyperlipidaemia exposed insignificant changes in cholesterol and HDL after treatment with silibinin but triglyceride and VLDL significantly decreased (23).
The mechanism of hypolipidemic effects of silymarin and other agents, like cholestyramin and ezetimibe, had been studies and compared in experimental animals, where both bind bile acid in the gut and limiting it synthesis from cholesterol or selective inhibition of intestinal absorption of cholesterol through blocking mucosal transport (24) are the mechanism that might be involved for the effect of silymarin.
Intracellular estrification of cholesterol, catalyzed by acyl-CoA enzyme, the silymarin slow down this enzyme and lead to hypocholestaolaemia and be due
to inhibition of HMG-CoA reductase enzyme, the silybinin and taxifolin, major components of silymarin, are found to decrease the cholesterol synthesis by liver in vitro (25). Consequently, silymarin may affect cholesterol level throughout dual mechanism by inhibition of synthesis and resin effect on cholesterol.

The effect of silymarin on triglyceride supported by that, silymarin partially antagonize the increase in liver content of triglyceride induced during exposure of rats to CCl4, also silymarin decrease VLDL synthesis, so decrease the availability of free VLDL secretion in the intestine (26).

Silymarin appears to act as an antioxidant not only because it acts as a scavenger of the free radicals that induce lipid peroxidation, but also because it influences enzyme systems associated with glutathione and superoxide dismutase. (27) Moreover, combination of silymarin and statin reduce lipid profile and elevate HDL after one month of treatment, this combination facilitate the reduction the dose of statin and so decrease the statin side effects, because most statin cause severe toxicities including myopathy and hepatotoxicity (28).

Therefore, silymarin short term effects produce significant effects on lipid profile in patients with hyperlipidaemia by different mechanism with little side effects and toxicities.

Conclusion(s)

The silymarin can be used alone effectively and safely in the treatment of hyperlipidaemia of different etiology, but large scale randomized clinical studies using different doses of silymarin are requisite to discover the dose – response relationship.

Acknowledgement(s)

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21. Kercman V, Skottova N, Walterova D. Silymarin inhibit the development of diet induced


Illustrations

Illustration 1

Table (I): The characteristics of study.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>20</td>
</tr>
<tr>
<td>Age</td>
<td>36 – 64 years</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
</tr>
<tr>
<td></td>
<td>Female</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>2 weeks</td>
</tr>
</tbody>
</table>
Illustration 2

Table (II): Comparison between placebo and silymarin effects before and after on the lipid profile.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo 600mg/day</th>
<th>Silymarin 600mg/day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>LDLP</td>
<td>264.20±28.44</td>
<td>263.40±1973</td>
</tr>
<tr>
<td>VLDL</td>
<td>71.30±4.398</td>
<td>69.80±3.225</td>
</tr>
<tr>
<td>HDL</td>
<td>42.60±2.875</td>
<td>42.20±2.936</td>
</tr>
<tr>
<td>TG</td>
<td>315.90±14.97</td>
<td>315.00±16.60</td>
</tr>
<tr>
<td>Ch</td>
<td>351.20±25.20</td>
<td>346.80±25.65</td>
</tr>
</tbody>
</table>
Illustration 3

Figure (I): Effects of placebo on lipid profile after 2 weeks of treatment.
Illustration 4

Figure (II): Effects of silymarin on lipid profile after 2 weeks.
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