Original Research Article

Hypercholesterolemia effectively managed with homeopathic medicine Guatteria gaumeri (Yumel): results from a clinical study in academic clinical set up in north India

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ABSTRACT

Background: Hypercholesterolaemia increases the risk of atherosclerosis, subsequently IHD. Herbal-homeopathic medicines are unexplored as lipid-lowering agents. This study presents safety and efficacy outcomes of homeopathic Guatteria gaumeri Q, in treatment of hypercholesterolaemia.

Methods: This was a homeopathic registry in real world population. A group of 29 subjects with mild to moderate hypercholesterolaemia with or without statin therapy were included in the study at a single centre in Udaipur, India. All subjects were given 10-15 drops of Guatteria gaumeri Q thrice in a day for 2 months and were followed fortnightly.

Results: The sample demographics were similar to typical Indian demographics (age 43±14 years, height 166.5cm, BMI 21kg/m²) having age 49±6 years, gender ratio 0.81 with 13 (45%) males and 16 (55%) females, height 157.07±26.18 cms and weight 71.5±11.78 Kg. The comorbidity included diabetes (44.83%), hypertension (68.97%), current smoking (44.83%) and CAD (31.03%). Thirteen (44.83%) subjects were taking statins for minimum 6 months. At baseline, mean TC, HDL, LDL, VLDL cholesterols and triglycerides were 223±25.8, 41.45±4.82, 150.9±25.97, 30.66±6.38 and 223±34.81 respectively. TC: HDL and LDL: HDL ratios were 5.44±0.82 and 3.69±0.77 respectively. At 2 months, TC reduced by 22.21 (9.96%), triglycerides, LDL and VLDL cholesterol demonstrated 39.55 (17.70%), 24.66 (16.34%) and 3.35 (10.91%) reduction respectively. HDL increased by 5.84 (14.09%). Proportion of population at risk defined as TC >200, LDL >120, VLDL >30, HDL <30 and triglycerides >200 was reduced by 17.24%, 31.04%, 13.79%, 100% and 31.03% respectively. (Baseline n=13). There were no ADRs in the study. Guatteria gaumeri was proved to be efficacious in treatment of hypercholesterolaemia.

Conclusions: Guatteria gumeri was observed to be efficacious in controlling hypercholesterolaemia. There was no significant effect of statin therapy prior to starting Guatteria gaumeri Q. No safety issues were reported in the study.

Keywords: Cholesterol lowering, Dyslipidemia, Guatteria gaumeri, Hypercholesterolaemia, Hyperlipidemia, High cholesterol, Lipid profile, Lipid lowering, Statins, Yumel

INTRODUCTION

Hypercholesterolaemia, a metabolic condition of increased circulating cholesterol in the blood is among the most commonly known risk factors of coronary heart disease, the leading killer of the world.1 Excess cholesterol has a tendency to deposit into various tissues especially, the adipose tissue. However, circulating cholesterols may also deposit in the arterial walls as fatty streaks and initiate atherosclerosis and subsequently
conditions like ischemic heart disease (IHD). In a continuous effort towards reducing morbidity and mortality risk associated with IHD, control on cholesterol, glycemia and blood pressure have key role. Hypercholesterolaemia imposes other risks such as cholelithiasis also.

Physiologically, cholesterol and triglycerides are required for several important processes. There are various types of cholesterol namely, chylomicrons, VLDL, IDL, LDL, and HDL, based upon enzyme that leads to its tissue level hydrolysis, particles size and nature of material in the core of the lipoprotein enveloped particle. Hydrolysis of cholesterol leads to release of free fatty acid which is required by the cell for its metabolic use or stored. Excess of fatty acids occurs due to excess intake of dietary fat, VLDL or excess endogenous synthesis of triglycerides (TG) in the liver. Excess of VLDL can be reduced to LDL cholesterol and all these excess cholesterols appears in the blood circulation, leading to hypercholesterolaemia. Among these, LDL cholesterol is the major part of total circulating blood cholesterol and is used for cell metabolism through LDL receptors in peripheral and hepatic cells. LDL cholesterol has similarity with plasminogen and is also used in peripheral cells in protection and development cell membrane and synthesis of hormones. Hence, LDL probably has an atherogenic property at higher concentration and imposes cardiovascular disease risk. These LDL particles may inhibit thrombolysis. Hence, the focus of lipid lowering treatment is majorly focused on LDL reduction.

The treatment includes the agent that tend to lower the blood cholesterol levels, such as statins and alpha asarone etc. Current conventional treatment of hypercholesterolaemia include dietary fat intake restriction and oral intake of many new molecules of statin group introduced by the allopathic system of medicine. Several herbal and homeopathic preparations have demonstrated efficacy in controlling cholesterol levels in the blood in mild to moderate hypercholesterolaemia. However, the use of these preparations is insufficiently explored.

Guatteria gaumeri, with its active principle alpha asarone has been used for maintaining normocholesterolaemia. This was a single arm, single centre, open label clinical study to evaluate the efficacy and safety of Guatteria gaumeri Yumel in treatment of mild to moderate Hypercholesterolaemia.

METHODS

The study was conducted in compliance with ICH GCP guidelines. Total 29 subjects were enrolled in the study and were followed up for 2 months. The subjects enrolled were given low fat diet, where the total dietary fat intake was restricted to 10 g/day. There was no restriction on carbohydrates and other dietary constituents. The concomitant medication including statin group fat lowering drugs were allowed if the patient was taking it regularly for more than 6 months and still had cholesterol levels in the range of inclusion in the study.

Assessment of lipids in the serum is an established method. The normal ranges of cholesterol are internationally accepted. Hence, the methodology to assess efficacy of the treatment was based upon the international conventions of the normal cholesterol range. Cholesterol levels were assessed at baseline and at 2 months after the start of treatment, with a hypothesis that there would be a normal cholesterol level at 2 months.

![Flow chart of study population](image)

**Figure 1: Flow chart of study population.**

The study included both males and female’s adults having mild to moderate hypercholesterolaemia defined as total cholesterol between 150 - 250 mg/dl or triglycerides 200 - 500 mg/dl or both. All enrolled patients were given Guatteria gaumeri Q, Mother tincture (B Jain Pharmaceuticals, Rajasthan, India, Introduced 2014) in 30 ml bottle with instruction to consume 10-15 drops thrice every day to consume the supplied medicine over 15 days. The medicine was prescribed with approximately 1 cup of water 30-60 minutes before the meals. At 15th day, the subject will be asked to bring the bottle and diary card back. The schedule continued for 3 visits. In the last visit the bottle and diary cards were collected back.

Total 33 subjects were screened in the study and 4 out of which did not meet the eligibility criteria. Hence, total 29 subjects were enrolled in the study and followed up for 2 months.

The primary efficacy variable was mean percent change in total cholesterol at 2 months from baseline. Secondary
endpoints included mean percent change in HDL, LDL, VLDL and triglycerides at 2 months from baseline and change in proportion of TC >200, HDL <30, LDL >120, VLDL >20 cholesterol and triglycerides >200 at 2 months from baseline.

**RESULTS**

The mean age of the population was 49±6 years, ranging from 38 to 57 years (p <0.001). There were 13 (45%) male subjects and 16 (55%) female subjects; hence, the Male:Female ratio was 0.81. The mean height was 157.07±26.18 cm and the weight was 71.5±11.78 Kgs (Table 1).

| Table 1: Demographics. |
|-------------------------|
| **Age (Years)** | **Mean (SD)** | **49±6** |
| Male | n (%) | 13 (45%) |
| Female | n (%) | 16 (55%) |
| Height (cm) | Mean (SD) | 157.07±26.18 |
| Weight (Kg) | Mean (SD) | 71.5±11.78 |
| BMI (Kg/sq meter) | Mean (SD) | 28.14±3.55 |
| Systolic BP (mm Hg) | Mean (SD) | 133.09±7.47 |
| Diastolic BP (mm Hg) | Mean (SD) | 81.62±2.66 |

Most of the population had minimum one risk modifier for complications of hypercholesterolaemia. These risk modifiers or comorbidity included, diabetes observed in 13 (44.83%), hypertension observed in 20 (68.97%), and coronary artery disease in 9 (31.03%) of the population. In the group, 13 (44.83%) patients were current smokers. The cohort had 13 (44.83%) patients who were taking any of the statin lipid lowering treatment for more than 6 months and still having a high cholesterol level (Table 2).

The mean total cholesterol at baseline was 223 and at 2 months was 200.79±21.57 mg/dl. There was a reduction by 22.21 mg/dl from the baseline which accounted for 9.96%. The mean LDL and VLDL Cholesterol at baseline was 150.9±25.97 and 30.66±6.58 respectively. At 2 months’s follow-up LDL cholesterol and LDL cholesterol were 126.24±21.62 mg/dl and 27.31±5.87 mg/dl respectively, leading to a difference of 24.66 mg/dl (16.34%) and 3.35 (10.91%) from baseline respectively.

The mean HDL Cholesterol at baseline was 41.45±4.82 and at 2 month’s follow-ups was 47.29±5.39 mg/dl demonstrated a mean increase of 5.84 mg/dl (14.09%). The mean triglycerides at baseline were 223.41±34.81 which decreased by 39.55 (17.70%) during the treatment and at 2 months the triglycerides were 183.86±28.93 mg/dl (Table 3). The figure 2 is comparative bar chart of Cholesterol at baseline versus 2 months.

| Table 2: Medical history. |
|-------------------------|
| **History of diabetes mellitus** |
| N | Percent |
| No | 16 | 55.17 |
| Yes | 13 | 44.83 |
| **History of hypertension** |
| N | Percent |
| No | 9 | 31.03 |
| Yes | 20 | 68.97 |
| **History of coronary artery disease** |
| N | Percent |
| No | 20 | 68.97 |
| Yes | 9 | 31.03 |
| **Family history of dyslipidemia related complex** |
| N | Percent |
| No | 14 | 48.28 |
| Yes | 15 | 51.72 |

The number at risk of hypercholesterolaemia was based upon the target international convention values for borderline risks. The total cholesterol and triglycerides above 200 mg/dl, HDL Cholesterol below 30 mg/dl, LDL and VLDL Cholesterol above 120 mg/dl and 30 mg/dl respectively, were considered to be above elevated risk. By these definitions 17 (58.62%) subjects were at elevated risk at 2 month’s follow-ups as compared with 22 (75.86%) patients at baseline demonstrating change of 17.24% (n=5). However, this number may not be considered as a sensitive parameter of efficacy, because it also includes the change in HDL cholesterol, which is supposed to elevate from the baseline at follow-up. As compared with 13 (44.83%) patients having HDL Cholesterol below 30 mg/dl at baseline, no subject had low HDL Cholesterol at 2 months, change demonstrated...
is 100%. In all 16 (55.17%) subjects had elevated LDL risk at 2 months as compared with 25 (86.21%) at baseline, a change of 31.04% was observed. The VLDL cholesterol above 30 mg/dl was observed in 7 (24.14%) at 2 months as compared with 11 (37.93%) patients at baseline, a change demonstrated was 13.79% (Table 4).

In this study, a group of 13 subjects was taking statin group medicines for cholesterol reduction and still had hypercholesterolaemia. Hence, the group was stratified with this criteria and cholesterol profile statistical analysis was performed. In this group mean cholesterol at baseline was 234±21.96 mg/dl as compared to 214±25.82 mg/dl of non-statin group.

Table 4: Change in proportion at risk from baseline.

|                       | Baseline | 2 months follow-up | Change | p-value |
|-----------------------|----------|---------------------|--------|---------|
| n                     | %        | n                   | %      |         |
| Total cholesterol > 200 | 22       | 75.86%              | 17     | 58.62%  | 17.24%  | p<0.001 |
| HDL < 30              | 13       | 44.83%              | 0      | 0.00%   | 100.00% | p<0.001 |
| LDL > 120             | 25       | 86.21%              | 16     | 55.17%  | 31.04%  | p<0.001 |
| VLDL > 30             | 11       | 37.93%              | 7      | 24.14%  | 13.79%  | p=0.142 |
| Triglycerides > 200   | 28       | 96.55%              | 9      | 31.03%  | 31.03%  | p<0.001 |

Table 5: Stratified comparison in cholesterol changes by statin consumption.

|                      | Statin group | Non-statin group |
|----------------------|--------------|------------------|
|                      | Baseline     | 2 months FU      | Change from baseline | Baseline     | 2 months FU | Change from baseline | p-value |
|                      | Value        | (Percentage) | Value | (Percentage) | Value | (Percentage) | Value | (Percentage) | RR |
| Total cholesterol    | Mean         | 234          | 193.56 | 17.24% | 20.50 | 9.58% | 0.92 |
|                      | SD           | 4.93        | 5.24 | 4.54 | 5.21 |
| HDL cholesterol      | Mean         | 40          | 45.38 | -5.38 | -1.46% | -1.06 | -14.22% | 1.06 |
|                      | SD           | 4.93        | 5.24 | 4.54 | 5.21 |
| LDL cholesterol      | Mean         | 162.69      | 136.15 | 26.54 | 16.31% | 141.31 | 118.19 | 23.13 | 16.36% | 1.00 |
|                      | SD           | 23.15       | 19.91 | 24.73 | 20.02 |
| VLDL cholesterol     | Mean         | 31.31       | 28.08 | 3.23 | 10.32% | 30.13 | 26.69 | 3.44 | 11.41% | 0.90 |
|                      | SD           | 7.16        | 6.13 | 6.25 | 5.78 |
| Triglycerides        | Mean         | 215.54      | 178.38 | 37.15 | 17.24% | 229.81 | 188.31 | 41.50 | 18.06% | 0.95 |
|                      | SD           | 36.08       | 31.09 | 33.51 | 27.24 |

At 2 months follow-up of the mean total cholesterol in statin consuming group was 209.62±19.82 as compared with 193.56±20.77 of the non-statin consuming group. The change from baseline was 24.38 mg/dl (10.42%) and 20.5 mg/dl (9.58%) respectively. (RR = 0.92) The HDL cholesterol in Statin group was 40±4.93 at baseline vs 42.63±4.54 in non-statin group. At 2 months, the LDL cholesterol in statin group was 45.38±5.24 mg/dl, with an increase of 5.38 mg/dl (13.46%) vs 48.69±5.21 mg/dl, with an increase of 6.06 mg/dl (14.22%) from the baseline (RR=1.06). The LDL cholesterol at baseline in statin group was 162.69±23.15 mg/dl vs 141.31±24.73 in non-statin group. At 2 month’s the LDL cholesterol was
136.15±19.91 mg/dl in statin group vs 118.19±20.02 mg/dl with a mean change of 26.54 (16.31%) and 23.125 (16.36%) in statin group and non-statin group respectively (RR=1). The mean triglycerides at baseline in statin group was 215.54±36.08 versus 229.81±33.51 in non-statin group. At 2 months, the triglycerides were 178.38±31.09 and 188.31±27.24 in statin and non-statin group respectively. The change in statin group from baseline was 17.24% and non-statin group was 18.06% (RR=0.95). All the Risk Ratios of the stratification were indicative of similarity of treatment in both groups (Table 5).

DISCUSSION

Guatteria gaumeri also known as Mosannona depressa is traditionally known Mexican herb for cholesterol control and treatment of gallbladder calculus. In hypercholesterolaemia, the line of treatment includes HMG-CoA reductase Inhibitors and ezetimibe. The HMG Co-A (3-Hydroxy-3-methylglutaryl-coenzyme A reductase is a significant enzyme required for cholesterol synthesis. HMG-CoA reductase inhibitors or commonly called statins are effective drugs that inhibit cholesterol synthesis. Various clinical trials conducted in hypercholesterolaemia with statins have demonstrated its efficacy to reduce serum cholesterol levels. A parallel group, randomized, placebo-controlled, double-blind, multicenter study compared cerivastatin a HMG-CoA reductase inhibitor with a placebo in 319 patients with hypercholesterolaemia. The study demonstrated that after 4 weeks treatment, LDL cholesterol reduced of approximately by 30%. Another study of in 26 patients with cholecystectomy in hypercholesterolemic subjects demonstrated 26% reduction in total cholesterol and 39% reduction in LDL cholesterol after Pravastatin therapy. The statin therapy is considered to be the most effective lipid lowering therapy.

Olsson AG et al reported that in a randomized, double-blind, multicenter trial conducted in 412 patients with hypercholesterolaemia, at 12 weeks rosuvastatin were associated with significantly greater LDL cholesterol reduction. The LDL cholesterol after 12 weeks was reduced by 46% in Rosuvastatin 5 mg arm, 50% in Rosuvastatin 10 mg arm and 39% in atorvastatin 10 mg arm. A significant proportion of population met the LDL cholesterol targets in both populations. However, Rhabdomyolysis, a rare muscle damage condition is suspected to be associated with its use. Therefore, certain herbal extracts or herbal preparations are capturing attention as the lipid lowering agents.

Rodríguez-Páez L et al published preclinical results demonstrating alpha-asarone, the active component of Guatteria gaumeri inhibits HMG-CoA Reductase in rats. The same study demonstrated significant changes in serum cholesterol in hypercholesterolemic rats when given in a dose of 80 mg/kg body wt. for 8 days. The human study data on use of Guatteria gaumeri is not available.

The current study was conducted to include 29 subjects of hypercholesterolaemia, which appears to be a statistically significant number for a first in human study. The outcomes of the study after 2 months of treatment and diet control look to be promising. The total cholesterol, LDL cholesterol, VLDL cholesterol and triglycerides show a considerable reduction. Unlike most of the studies in hypercholesterolaemia, HDL cholesterol increased in the study population. This change can be considered as an indication of physiological action of Guatteria, that it acts directly or indirectly on the particle size and helps normalizing the cholesterol levels than just lowering. Even if the number of subjects and length of follow-up was insufficient to significantly establish its property to maintain normocholesterolaemia, the HDL cholesterol increasing while other types of cholesterol decreasing can be considered as a sign of normalizing the cholesterol levels in the blood. Reduction of population at hypercholesterolaemia risk at 2 months was also a significant indicator of efficacy of the drug.

Limitations of this study, the subjects were screened for mild to moderate disease conditions. In the controlled conditions, the results are promising. However, the results may vary in the real-world conditions. Hence, revalidation of the outcome in larger, real world population will be important. The co-morbidities like diabetes, smoking, hypertension and coronary artery disease was present in group. Their medication was also reported. The drug interaction with all these medications could not be studied for two reasons. First, as it was a small group and was not designed to be focused on drug interaction. Second, in cases history of coronary artery disease treated with medicine, angioplasty and coronary artery bypass graft, the details of vasodilators and dual antiplatelet therapy was missing in the current medications.

In addition, all the subjects had restricted lipid intake, which started along with the treatment. Contribution of fat restriction on the lipid profile could not be substantiated because there was no placebo control. However, the results obtained include quite significant changes in the lipids which cannot be attributed to the diet control alone. Larger population controlled studies or real world study can add more information effect of diet and Guatteria gaumeri treatment independently.

The length of follow-up was insufficient to significantly establish its property to maintain normocholesterolaemia. The total cholesterol change was low, which included the change of HDL cholesterol. However, total non-HDL cholesterol change was significant despite the small number. This change of HDL cholesterol increasing while other types of cholesterol decreasing can be considered as a sign of normalizing the cholesterol levels in the blood.
CONCLUSION

Guatteria gumeri was observed to be efficacious in controlling hypercholesterolaemia. There was no significant effect of statin therapy before starting Guatteria gumeri. Q. No safety issues were reported in the study.

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