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Research Article

EFFECTS OF MEDICAL NUTRITION THERAPY ON PLASMA LIPOPROTEINS OF TYPE II DYSLIPIDEMIC PATIENTS: A SHORT-TERM PILOT STUDY

SUBHRANIL SAHA*[1], MALAY MUNDLE[2], SHUBHAMOY GHOSH[3] & MUNMUN KOLEY[1]

Mahesh Bhattacharyya Homeopathic Medical College & Hospital, Government of West Bengal
Drainage Canal Road, Doomurjola, Howrah 711104, West Bengal, India
Email: drsubhranilsaha@hotmail.com

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ABSTRACT

Background: Hyperlipidemia, being frequently associated with diabetes mellitus, hypertension and coronary artery disease represents a continuing crisis of epidemic proportions, leading cause of death every year and a major public health challenge to the population. Despite development of several therapeutic strategies, patients' compliance remains poor due to high cost of medicines. The study aims at exploring the clinically desirable impact of nutrition intervention on serum lipoprotein profile of dyslipidemic patients.

Objective: To investigate the efficacy of medical nutrition therapy (MNT) in bringing changes in lipoprotein profile and symptom score of type II dyslipidemic patients.

Methods: A single arm, experimental, interventional, prospective, non-randomized, short-term, before and after comparison pilot study without control has been carried out on 30 participants suffering from Frederickson's type II (a, b) hyperlipidemia. 33 out of 49 patients with hyperlipidemic lipoprotein profile were selected after screening by the eligibility criteria; all 33 were enrolled and were allocated to MNT. MNT comprised of restricting fat to 15-20% of total calories, reducing saturated fat and cholesterol intake and increasing consumption of monounsaturated fatty acids and polyunsaturated fatty acids etc. Two were drop-outs and one was incomplete (irregular); 30 were regular. Outcome measures were assessed and analyzed after 2 months.

Results: After 2 months, reduction in low density lipoprotein cholesterol (175.43±8.49 *vs* 166.3±9.02), total cholesterol (265.6±15.12 *vs* 256.63±17.56), total cholesterol : high density lipoprotein cholesterol (6.78±1.57 *vs* 6.39±1.15), triglyceride (333.77±84.67 *vs* 316±79.76) and symptom score (8.5±3.38 *vs* 7.5±3.17) - all were statistically significant (P<0.001). No adverse effects or complications were observed. Conclusion: The data suggest that medical nutrition therapy may be a useful measure without any adverse events for the patients suffering from hyperlipidemia. However, randomized controlled trials with larger sample size and longer duration should be undertaken for confirmatory conclusion.

Keywords: Hyperlipidemia, lipoproteins, therapeutic lifestyle change diet

INTRODUCTION

Hyperlipidemia, the commonest form of dyslipidemia, is a condition of abnormally elevated levels of any or all lipids and/or lipoproteins in the blood [1,2]. Hyperlipidemia and cardiovascular disease represents a continuing crisis of epidemic proportions and leading cause of death with numerous individuals dying from stroke and heart disease each year [3-5]. According to the most recent statistics, if all forms of major cardiovascular diseases (CVD) were eliminated, life expectancy would rise almost 7 years [3-5]. Compared to the general population in the United States, prevalence of coronary heart diseases (CHD) in Asian Indians is approximately 4 times higher. The rates are similar among vegetarians and non-vegetarians [6-10].

Primary hyperlipidemia is usually due to genetic causes (mutation in receptor protein) [2,9], while secondary/acquired hyperlipidemia arises due to other underlying causes - diabetes, hypothyroidism, renal failure, nephrotic syndrome, alcohol, some rare endocrine and metabolic disorders and drugs (diuretics, beta blockers, estrogens etc.) [9]. Fredrickson's Type IIa hyperlipidemia is characterized by familial hypercholesterolemia, deficiency of low-density lipoprotein cholesterol (LDLc) receptors, increased LDLc in blood; and manifest by ischemic heart disease, xanthelasma, corneal arcus and tendon xanthomas [2]. Fredrickson's Type IIb hyperlipidemia is familial combined hyperlipidemia with decreased LDLc receptors and increased ApoLipoproteinB, raised LDLc and very low-density lipoprotein cholesterol (VLDLc) due to overproduction of substrates, including triglycerides and acetyl co-enzyme A and decreased clearance of LDLc [2].

The leading cause of death of diabetics is CHD, developing on the basis of accelerated arteriosclerosis from lipid disorder, a modifiable risk factor for cardiovascular disorders [2]. The role of dyslipidemia as a causal factor in vascular disease associated with diabetes mellitus was previously downplayed, because total cholesterol was frequently normal or minimally elevated. However, diabetic dyslipidemia is characterized by elevated triglyceride and LDLc, and lowered high-density lipoprotein cholesterol (HDLc) – called 'lipid triad' [11-19]. Their treatment by diet and drugs is of uttermost importance [20]. The issue of whether a monounsaturated diet is preferable to a high carbohydrate diet remains controversial. Short-term studies show that high carbohydrate diet has been associated with higher triglyceride levels and lower HDLc levels than a higher fat diet [21-29].

Because a basic principle of prevention is that risk reduction therapy must be adjusted to a patient's absolute risk, the first step is to assess risk status, including cholesterol levels, blood pressure, family history, smoking status, diabetes, sex, and age, in every adult, beginning at age 20 [4,5]. Healthy lifestyle changes should be promoted to reduce CVD risk [4,5]. Lipid management should be beyond LDLc lowering, including aggressive treatment of elevated triglycerides. Even borderline-high triglyceride levels should be treated with diet and exercise; for higher triglyceride levels, medication is often indicated as well. [4,30]

A large, parallel, randomized controlled trial is needed to investigate the effectiveness of cholesterol lowering diet and other dietary interventions for fat [26]. Though a very low fat diet remains the first line of therapy in the treatment of severe hypertriglyceridemia, reduction in saturated fat, not total fat, is required to reduce serum total cholesterol and LDLc levels [31,32]. A study reveals that restriction of fat intake to <10% of daily energy produces, though not proportional, increasing benefit on cardiovascular risk factors in hyperlipidemic subjects [33]. But the impact of nutrition intervention on serum cholesterol levels has been found less than clinically desirable. These are difficult to implement in usual practice settings, which are not typically designed to manage long-term programs for behavioral changes [34]. This study tries to explore whether only dietary management without drugs can suffice and to what extent its implementation is feasible in low to moderate risk dyslipidemic patients.

Objectives

Primary Objective – To assess the efficacy of MNT in bringing changes in lipoprotein profile of type II dyslipidemic patients; Secondary Objective – To detect changes in symptom score of the dyslipidemic patients following dietary intervention (as per the symptom scoring scale of dyslipidemia; (table 1)

Table 1: Symptom scoring scale of dyslipidemia type ii (a, b)

SCORES & SYMPTOMS	0	1	2	3
Chest Pain	Not at all	Occasional	2-3 times per day	More than 3 times/day
Palpitation	Not at all	Occasional	2-3 times per day	More than 3 times/day
Breathlessness	Not at all	Occasional	Exertional	Paroxysmal nocturnal
Perspiration	Nothing significant	Slightly high	Moderately high	Profuse / drenching
Fatigability	Not at all	Occasional	Present, but not disturbing work	Disturbing routine work

SCORES & SIGNS	0	1	2
Xanthelesma	Absent	Started to develop	Well developed
Corneal arcus	Absent	Started to develop	Well developed
Tendon xanthomas	Absent	Palpable, but not visible	Visible and palpable

0-3: Not significant; 4-9: Mild; 10-15: Moderate; 16-21: Severe

TABLE 2: BASELINE DATA

BASELINE DEMOGRAPHIC CHARACTERISTICS	
Age	
1. 20-35 years	4 (13.33%)
2. 36-50 years	9 (30%)
3. 51-65 years	17 (56.67%)
M : F	17 : 13
Weight (kg)	61.93±4.72
Height (cm)	161.04±7.26
BMI	23.94±1.89
Waist – Hip Ratio	0.92±0.13
Married : Unmarried	24 : 6
Urban : Rural	28 : 2
Risk Factors	
1. Stress	23 (76.67%)
2. Sedentary habits	14 (46.67%)
3. Rich food	21 (70%)
4. Smoking	12 (40%)
5. Alcohol	5 (16.67%)
BASELINE CLINICAL CHARACTERISTICS	
Symptom Score	
1. Not significant	1 (3.33%)
2. Mild	18 (60%)
3. Moderate	10 (33.33%)
4. Severe	1 (3.33%)
Co-morbid Conditions	
1. Hypertension	17 (56.67%)
2. Hyperglycemia	11 (36.67%)
Concomitant Disease(s)	
1. Osteoarthritis	7 (23.33%)
2. Acid Peptic Disorder	5 (16.67%)
3. Irritable Bowel Syndrome	4 (13.33%)
4. Piles	3 (10%)
5. COPD/Br. Asthma	2 (6.67%)
6. PCOD	2 (6.67%)
7. Migraine	2 (6.67%)
8. Miscellaneous	14 (46.67%)
BASELINE PATHOLOGICAL-BIOCHEMICAL DATA & ECG, CHEST X-RAY FINDINGS	
Hemoglobin%	13.29±1.13
Total WBC Count	8368.17±1129.47
ESR	21.3±5.69
Fasting Sugar & PP Sugar	109.1±20.83 & 150.47±18.43
Blood Urea & Serum Creatinine	27.16±6.9 & 1.14±0.26
Albuminuria, Hematuria, pus cells in urine	Absent
ECG – Ischemic Heart Disease	5 (16.67%)

CXR – Normal	All (100%)

Materials & Methods

A single arm, experimental, interventional, prospective, non-randomized, short-term, before and after comparison pilot study without control was carried out on 30 hyperlipidemic patients at Mahesh Bhattacharyya Homeopathic Medical College & Hospital, Government of West Bengal; Drainage Canal Road, Doomurjala, Howrah – 711104, West Bengal, India; Ph (033) 26774449, Email: principalmbhmch@gmail.com, from April, 2012 to June 2012. The study protocol was completely in accordance with the Helsinki declaration on human experimentation and Good Clinical Practice (GCP) [35,36]. Clearance was obtained from the ethical committee of the institution. Consequently, before recruitment, each participant was explained verbally about the study with the help of Patient Information Sheet and thereafter a written consent was obtained from them. However, they were free to withdraw from the study at any point of time.

Sample size was determined using computer software of Creative Research System's sample size calculator (http://www.surveysystem.com/sscalc.htm). Considering confidence level 95%, confidence interval 5 and exact prevalence of Frederickson's type II dyslipidemia in the population being unknown, recommended sample size was 384. But as the trial was a short-term pilot study, sample size was chosen as about 8% (n=33) of the sampled population. Samples were chosen randomly from the population undergoing lipoprotein profile testing in the hospital and found to be hyperlipidemic. These patients were recruited in the trial after obtaining their written informed consent

Out of 49 hyperlipidemic patients selected, 33 were enrolled after screening by eligibility criteria and all of them were allocated to medical nutrition therapy (MNT). After 2 months of dietary intervention, two were drop-outs, one was incomplete (irregular), and 30 patients were regular. Outcome measures were assessed and analyzed after 2 months. A structured, specially designed case record sheet, a symptom scoring scale (table 1) and observational checklist for each patient was used to collect and keep record of the data. Data was extracted from the reports directly and independently in the end and were subjected to statistical analysis.

Inclusion criteria included age between 20 and 65 years, both sexes and patients having type $II_{a,b}$ dyslipidemia, i.e. familial hypercholesterolemia (type IIa – LDLc elevated, total cholesterol greatly increased, but triglyceride normal) and familial combined hyperlipidemia (type IIb – LDLc and VLDLc elevated, total cholesterol greatly increased and also triglyceride increased); commoner occurrence than other varieties; i.e. 1 in 100-500; with LDLc 130-189 mg/dl and/or total cholesterol : HDLc = 4.5 – 11 and/or triglyceride 150-499 mg/dl (average to moderate risk patients)

Exclusion criteria included dyslipidemia type I, III, IV and V (rare occurrence), LDLc <100-129 mg/dl (optimal to near optimal range) and ≥190 mg/dl (high risk patients), blood cholesterol : HDLc = 3.3 - 4.4 (low risk patients) and more than 11.0 (high risk patients); triglyceride <150 mg/dl (normal) and ≥500 mg/dl (very high; high risk patients), any kind of continuous drug therapy including oral contraceptive pills, presence of severe concomitant disease(s) demanding drug intervention, stage II hypertension (BP $^{\geq 160}/_{\geq 100}$ mm of Hg), malignant hypertension (BP $>^{200}/_{140}$ mm of Hg) and isolated systolic hypertension (BP $^{\geq 140}/_{<90}$ mm of Hg), failure of vital organs (e.g. heart, lungs, liver, kidney etc.), pregnancy, breast feeding and likelihood of pregnancy.

The intervention model was the 'Therapeutic Lifestyle Change (TLC) diet' [26] consisting of carbohydrate 60-70% of total calories, protein 1 gm/kg body weight; saturated fat less than 7% of total calories, polyunsaturated fat up to 10% of total calories, monounsaturated fat up to 20% of total calories, cholesterol less than 200 gm/day, fiber 20-30 gm/day, viscous/soluble fibers 10-25 gm/day, total calories to balance energy intake and expenditure to maintain desirable body weight and/or to prevent weight gain. The only exception was that total fat was reduced further from 25-35% to 15-20% of total calories to obtain optimum possible benefits, but not beyond that to ensure compliance and to prevent endogenous production of lipoproteins. To reduce visible saturated fat and cholesterol intake and to maintain monounsaturated fatty acids (MUFA) : polyunsaturated fatty acids (PUFA) = 2:1 in cooking oil, blending of groundnut oil (MUFA content 50%) and mustard oil (PUFA content 10%) in 2:5 ratio was advised. Avoiding whole milk, whole egg, red meat etc. and consuming defatted (double toned) milk, egg-white, lean meat etc. were some of the instructions given. Additional supplementation of PUFA in the form of eicosapentanoic acid (EPA) 180 mg and docosahexanoic acid (DHA) 120 mg daily was advised. One multi-vitamin tablet providing daily requirement of all essential vitamins were included along with the diet. Trans-fatty acids (LDLc-raising fat) were kept as low as possible. Carbohydrates were derived predominantly from foods rich in complex carbohydrates including grains, especially whole grains, fruits, and vegetables. Viscous fiber intake (goal 10-25 gm/day) was increased by emphasizing certain foods like husk, cereal grains, fruits, vegetables, dried beans, peas, and legumes. Daily energy expenditure included at least moderate physical activity (contributing approximately 200 Kcal per day). Additional modifications (e.g. total calorie reduction, salt restriction etc.) were done accordingly as per need of the patients.

The end points were reduction in LDLc level, improvement in total cholesterol : HDLc ratio, reduction in triglyceride level and reduction in symptom score.

Consequent study variable was clinical improvement in signs and symptoms as per the scoring scale. Independent variables were age, gender, occupation, height, weight, body mass index, waist-hip ratio, family history, risk factors (including stress, sedentary habit, rich food, smoking, alcoholism), life-style modifications, e.g. regular exercises etc.

Result

Baseline data shows that dyslipidemia was mostly prevalent in the age group of 51-65 years (n=17; 56.67%). As risk factors, stress, rich food and sedentary lifestyles were present in 23 (76.67%), 21 (70%) and 14 (46.67%) participants respectively. Symptom severity among the participants was less marked and mild in most of the cases, i.e. n=18 (60%). Hypertension and hyperglycemia were present in 17 (56.67%) and 11 (36.67%) participants respectively. Among concomitant diseases, osteoarthritis was prevalent (7; 23.33%), either alone or in combination with other diseases, in most of the cases. No specific baseline pathological and/or biochemical abnormalities were detected. ECG revealed ischemic heart disease in 5 cases (16.67%). Chest x-ray detected no specific abnormalities.

After 2 months of dietary intervention, LDLc and total cholesterol : HDLc, each was lowered in 25 (83.33%) cases; symptom score was reduced in 19 (63.33%) cases. (Table 3, Chart 1)

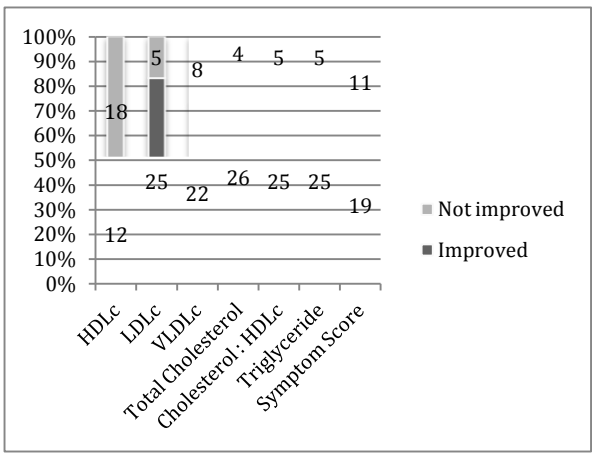

chart 1: bar diagram showing changes in lipoprotein profile & symptom score after mnt

TABLE 3: Changes in lipoprotein profile & Symptom score after mnt

SERIAL NO.	OUTCOMES AFTER INTERVENTION	IMPROVED; n (%)	NOT IMPROVED; n (%)
1	HDLc	12 (40%)	18 (60%)
2	LDLc	25 (83.33%)	5 (16.67%)
3	VLDLc	22 (73.33%)	8 (26.67%)
4	Total Cholesterol	26 (86.67%)	4 (13.33%)
5	Total Cholesterol : HDLc	25 (83.33%)	5 (16.67%)
6	Triglyceride	25 (83.33%)	5 (16.67%)
7	Symptom Score	19 (63.33%)	11 (36.67%)

Paired *t*-test comparing before and after HDLc levels (41.3±10.01 *vs* 41.73±9.38; t_{29}=1.6; P<0.1) was statistically non-significant. But paired *t*-test comparing before and after LDLc (175.43±8.49 *vs* 166.3±9.02; t_{29}=7.25; P<0.001), VLDLc (50.7±6.20 *vs* 48.6±6.48; t_{29}=6.18; P<0.001), total cholesterol (265.6±15.12 *vs* 256.63±17.56; t_{29}=7.2; P<0.001), total cholesterol / HDLc ratio (6.78±1.57 *vs* 6.39±1.15; t_{29}=5.25; P<0.001), triglyceride (333.77±84.67 *vs* 316±79.76; t_{29}=7.56; P<0.001) and symptom score (8.5±3.38 *vs* 7.5±3.17; t_{29}=4.35; P<0.001) showed statistically significant results. (Table 4)

Table 4: Before & after comparison of laboratory parameters & paired t-test

OUTCOME MEASURES	BEFORE INTERVENTION	AFTER INTERVENTION	t_{29} (*P* VALUE) & STATISTICAL SIGNIFICANCE
HDLc	41.3±10.01	41.73±9.38	1.6 (P<0.1); *ns*
LDLc	175.43±8.49	166.3±9.02	7.25 (P<0.001); *s*
VLDLc	50.7±6.20	48.6±6.48	6.18 (P<0.001); *s*
Total Cholesterol	265.6±15.12	256.63±17.56	7.2 (P<0.001); *s*
Total Cholesterol : HDLc	6.78±1.57	6.39±1.15	5.25; (P<0.001); *s*
Triglyceride	333.77±84.67	316±79.76	7.56 (P<0.001); *s*
Symptom Score	8.5±3.38	7.5±3.17	4.35 (P<0.001); *s*

Discussion

Although reductions in LDLc, VLDLc, total cholesterol, total cholesterol : HDLc as well as symptom score showed statistically significant results, no significant improvement was observed in HDLc profile. However, it will not be wise to conclude; rather studies of similar design with larger sample size and longer duration with IPD approach should be replicated and randomized controlled trials (RCTs) with placebo control, active control and MNT as adjunctive therapy should be undertaken to reach a definite conclusion.

Summary & Conclusion

A single arm, non-randomized, before and after comparison pilot study without control was carried out involving 30 participants suffering from Frederickson's type II (a, b) hyperlipidemia to investigate the efficacy of MNT in bringing changes in lipoprotein profile and symptom score. The MNT comprised of fat restriction up to 15-20% of total calories, reduction of saturated fat and cholesterol intake and increase in consumption of MUFA, PUFA, dietary fibers etc. Outcome measures were assessed and analyzed after 2 months. Reduction in LDLc, total cholesterol, total cholesterol / HDLc, triglyceride and symptom score - all were statistically significant. No adverse effects or complications were observed. The data suggest that MNT may be a useful measure for the patients suffering from hyperlipidemia.

Trial Identifiers

1. Clinical Trials Registry of India Number: "CTRI/2012/08/002901" (Date – August 22, 2012)
2. Universal Trial Number: "U1111-1130-7238" (Date – May 11, 2012)
3. Protocol Identification Number: "256/MBHMCH/CH/Adm/11/12" (Date – April 2, 2012)

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