Kathmandu University Medical Journal (2005), Vol. 3, No. 4, Issue 12, 411-414

Original Article

Effectiveness of nicotinic acid and bezafibrate alone and in combination for reducing serum triglyceride level

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Abstract
Objective: To study the effectiveness of nicotinic acid and Bezafibrate alone and in combination for reducing triglyceride level.
Design: It was a randomised, prospective, longitudinal study.
Setting: Patients attending a private clinic, and medical department of Kathmandu Medical College, Sinamangal.
Methods: This study included 83 consecutive patients, 19 females and 64 males with hypertriglyceridaemia (defined as serum triglyceride >200mg/dl) attending the department of medicine, Kathmandu Medical College, Sinamangal and private clinic.
Main outcome measures: Statistically significant reduction of serum triglyceride level.
Result: 51 out of 83 patients completed the study in which Nicotinic acid alone reduced the serum trygleceride level from 320.62 ± 104.23 to 182.55 ± 46.21, which is a reduction of 138.07 ± 85.69 (P. value = 001). Bezafibrate when given alone also reduced triglyceride level significantly from 345.25 ± 181.03 to 203.30±93.59 which is a reduction of 141.95 ± 121.130 (P value= .001). When a combination of both drugs was given the reduction of 472.73±247.53 (P value =.002) was achieved.
Conclusions: Nicotinic acid is a very effective drug in reducing serum triglyceride level and its effectiveness is similar to Bezafibrate. There is no added benefit of giving a combination of nicotinic acid and Bezafibrate in reducing serum triglyceride level.

Keywords: Hypertriglyceridaemia, Nicotinic acid, Bezafibrate.
Abbreviations: TG= Triglyceride, TC = Total cholesterol, HDL= High density lipoprotein, LDL= Low density lipoprotein NCEP-ATP III= National Cholesterol Education Programme-Adult Treatment panel 111

The prevalence of coronary artery disease is on the increase even in developing country like Nepal. Out of the different risk factors, dyslipidaemia is one of the important modifiable risk factor. Both low HDL cholesterol and high triglyceride are independent risk factors for coronary artery disease.

Hypertriglyceridaemia is more common in Nepalese population. In one of the study by DB Karki et al, the incidence of hypertriglyceridaemia has been found as high as 70% in the Nepalese population[1].

The NCEP-ATP III has identified triglyceride level of less than 150mg/dl as optimal and recommends treatment for TG level of 200mg/dl and high[2]. Treatment of hypertriglyceridaemia with nicotinic acid is a logical choice. Niacin blocks fatty acid reflux from adipose tissue. It also suppresses hepatic assembly and release of very low-density lipoprotein. This latter effect reduces TG levels and decreases the number of small, dense LDL particles. Niacin may also block a HDL holoparticle catabolic receptor responsible for intra-hepatic degradation of HDL, thereby increasing the effective half life of HDL concentration[3]. Niacin is the most potent drug currently available to raise HDL-C level[4]. Despite this rationale use, high doses of nicotinic acid has been discouraged in diabetic patients because of the reports of increased fasting blood glucose levels during therapy[5].

Materials and methods

This study included 83 consecutive patients, 19 females and 64 males with hypertriglyceridaemia (defined as serum triglyceride >200mg/dl) attending the department of medicine, Kathmandu Medical College, Sinamangal and Temple of Healing, old Baneshwor, out of which 51 patients completed the study. Rest of the patients were lost to follow up. The inclusion criteria were age more than 18 years, no previous hypolipaemic treatment and increased TG level defined as TG>200mg/dl.

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Patients with clinically significant history of psychiatric illness, liver disease, gout, peptic ulcer, pregnant and lactating women were excluded from the study. Diabetic patients were not excluded from the study because the dose of nicotinic acid used was only 1125mg/day.

The patients were randomised into three groups and they were treated for 8 weeks, either with Nicotinic acid (1125mg/day n=20), or Bezafibrate (400mg/day n=20) or a combination of Nicotinic acid and Bezafibrate (Nicotinic acid 1125mg/day + Bezafibrate 400mg/day n=11).

Lipid profile assessment was done at the beginning of the study and after 8 weeks of treatment. Lipid profile assessment was done by End point method and measured in Micolab 2000 analyser. Statistical analysis was done using SPSS 11.5 version software system.

Results

Table 1: Demographic characteristics and base line values of measured parameters.

	Nicotinic acid group	Bezafibrate group	Combination group
	20	20	11
Sex M/F	14/6	14/6	7/4
BMI (M±SD)	25.04 ± 2.22	25.63±4.07	25.04±2.22
T. cholesterol (M±SD)	220.74±31.66	206.4±31.72	212.27±34.55
LDL (M±SD)	109.29±29.44	87.26±32.66	70.69±29.59
HDL (M±SD)	43.35±11.15	47.45±9.55	40.46±8.24
Triglyceride (M±SD)	320.62±104.23	345.25±181.04	472.73±247.53
Diabetes mellitus (no of patients)	2	7	0
Hypertension (No of patients)	10	18	5

Table 2: Effectiveness of Nicotinic acid.

	Before Treatment M ± SD	After Treatment M ± SD	Difference	P. Value
TC	220.74 ± 31.67	171.45 ± 32.19	49.29 ± 37.47	.001
LDL	109 ± 29.44	94.25 ± 26.87	15.03 ± 35.92	.077
HDL	43.35 ± 11.15	49.95 ± 17.5	-6.61 ± 15.72	.076
TG	320.62 ± 104.23	182.55 ± 46.21	138.07 ± 85.69	.001

Nicotine acid treatment decreased TC, LDL, & TG but significant reduction was seen only in TC & TG. HDL level was also increased but it was not statistically significant

Table 3: Effectiveness of Bezafibrate

	Before Treatment M ± SD	After Treatment M ± SD	Difference M ± SD	P. Value
TC	206.40 ± 31.72	180.40 ± 30.722	26 ± 36.38	.005
LDL	87.26 ± 32.66	96.70 ± 34.31	9.44 ± 34.95	.242
HDL	47.45 ± 9.55	50.40 ± 25.42	2.95 ± 29.95	.665
TG	345.25 ± 181.04	203.30 ± 93.59	141.95 ± 121.135	.001

Bezafibrate significantly lowered TC and TG level. However the increase in LDL & HDL level was not significant.

Table 4: Effectiveness of combination of Nicotinic acid and Bezafibrate

	Before Treatment M ± SD	After Treatment M ± SD	Difference M ± SD	P Value
TC	212.72 ± 33.35	167.18 + 36.24	45.09 + 33.13	.001
LDL	70.09 ± 29.59	78.73 + 32.34	8.64 + 25.86	.294
HDL	40.45 ± 8.24	57.00 + 18.65	-16.55 + 21.139	.027
TG	477.73 ± 247.53	177.54 + 71.89	300.19 + 232.98	.002

Combination of both drugs significantly lowered TC & TG level. It also significantly increased the level of HDL.

A total of 83 patients were included in the study of which 51 completed the study. The rest were lost to follow up. The reduction of triglyceride level was statically significant in all the three groups. Nicotinic acid reduced Triglyceride level from a mean value 320.62+104.23 to 182.55 ± 46.21 which is a reduction of 135.07 ± 85.69 (P value = .001) Bezafibrate also significantly reduced triglyceride level from 345.25 ± 181.04 to 203.30 ± 93.59 which is a reduction of 141.95 ± 121.13 (P value =.001). When a combination of both drugs were given the reduction was 295.18 ± 232.98 (P =.002).

The reduction of total cholesterol was statistically significant in all the three groups. In the Nicotinic acid group the reduction was 44.29 ± 37.47 (P value=.001), in the combination group the reduction was 45.09 ± 33.11 (P value=.001) and in the Bezafibrate group the reduction was 26 ± 36.38 (P value=.005). Increase in the level of HDL cholesterol was found in all the three groups but was statistically significant only in the combination group. The increase in HDL in the combination group was 16.55 ± 21.14 (P=.027).

Nicotinic acid also reduced serum LDL cholesterol level from 109 ± 29.44 to 94.25 ± 26.87 but the reduction was not statistically significant. In the Bezafibrate group and in the combination group there was an increase in the level of LDL cholesterol but was not statistically significant. In the Bezafibrate group there was an increase of LDL level from 87.26 ± 32.66 to 96.70 ± 34.31 (P value= .242) and in the combination group the level of LDL cholesterol increase was from 70.09 ± 29.59 to 78.73 ± 32.34 (P value=.294).

Discussion

Hypertriglyceridaemia and low HDL level are risk factors for CAD. In one study hypertriglyceridaemia was found in 70% of Nepalese population [1]. The Veterans Affair HDL Intervention Trial (VA-HIT) group has found triglyceride level of >200mg% in 33% of 8500 patients [6]. The coronary drug project was the first trial to study the effect of niacin on cardiovascular end points [7]. Niacin has been found to reduce the incidence of nonfatal MI by 26% and cerebrovascular events by 24%. In Stockholm Ischaemic Heart disease secondary prevention study, combination therapy with immediate release niacin and clofibrate reduced levels of TC by 13% and TG by 19%. Total mortality and CHD mortality were significantly reduced by 26% and 36% respectively with combination therapy [8]. Cutaneous flushing and itching can be troublesome side effects requiring its discontinuation. Aspirin (325mg) taken 30 minutes to 1 hour before the first niacin dose of the day decreases the severity of flushing [9].

In addition to flushing and hepatotoxicity, use of niacin has been associated with nausea, vomiting, diarrhoea, abdominal pain, activation of peptic ulcer disease, hyperuricemia, gout, hyperglycemia and acanthosis nigricans [10]. In one study done by Morgan JM et al [11] and Capuzzi DM et al [12] a dose of 1000 mg niacin daily reduced triglyceride level by 21%, LDL by 6% & raised HDL by 17% from the base line. In our study nicotinic acid in a dose of 1125mg /day reduced triglyceride level by 43.03%, LDL by 13.79% and increased HDL by 15.48% from base line, which is comparable to the previous study.

Conclusions

Nicotinic acid is a very effective drug to reduce serum triglyceride level. Its effectiveness was similar to Bezafibrate. There was no added advantage of combining these two drugs. Nicotinic acid also significantly lowered total Cholesterol level when given alone or in combination with Bezafibrate. There was an increase in the level of HDL cholesterol in all the groups, but the increase was statistically significant only in the combination group. As the cost of the nicotinic acid is much less compared to fibrate and it is equally effective in reducing triglyceride level, use of nicotinic acid is recommended to patients with hypertriglyceridaemia

Acknowledgement
We thank Dr Nimesh Bhattarai, Ms Pratiksha Thapa, Mrs Kalpana Joshi and Mr Subendra Maharjan for their help in preparing this article.

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