Effects of Intermittent Hypobaric Hypoxia on Blood Lipid Concentrations in Male Coronary Heart Disease Patients

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ABSTRACT

Tin’kov, Aleksey N., Valeriy A. Aksenov. Effects of intermittent hypobaric hypoxia on blood lipid concentrations in male coronary heart disease patients. *High Alt Med Biol* 3:277–282, 2002.—The objective of the study was to evaluate the effects of intermittent hypobaric hypoxia (IHH) on plasma lipid concentrations of male coronary heart disease (CHD) patients. Forty-six male coronary patients were enrolled in the study. Thirty had a history of myocardial infarction and 16 had ischemic episodes documented by ergometer testing or Holter monitoring. The patients underwent acclimation to hypoxia by means of a protocol of intermittent exposure in a hypobaric chamber. Lipid profiles, including coefficient of atherogeneity (CA) by A.N. Klimov, were assessed at baseline, on completion of the study, and at 3-, 6-, and 10-month follow-ups. Total cholesterol decreased by 7% on completion of the IHH and by 9% at 3 months and persisted on that level to month 6. HDL levels increased by 12% at 3-month follow-up and remained significantly higher than baseline until month 6. LDL levels declined on completion of IHH, but the changes from baseline were most prominent at 3-month (13%) and 6-month (11%) follow-ups. Similar changes were found in levels of VLDL and TG. CA declined by 26% on treatment completion and by 37% at 3-month follow-up and increased to baseline at 10 months. No changes in lipid profiles were found in patients with CA < 3 (n = 22). In subjects with CA > 3 (n = 24), beneficial effects were more pronounced. IHH in CHD patients with abnormal lipid metabolism leads to favorable changes of plasma lipid patterns persisting to month 6 following IHH.

**Key words:** altitude; hypobaric chamber; acclimation to hypoxia; myocardial infarction; cholesterol; triglycerides

INTRODUCTION

Hypercholesterolemia is a major risk factor for coronary heart disease (CHD), and the benefits of lowering cholesterol in both primary and secondary prevention of CHD have been thoroughly established by a number of well-designed prospective, randomized, placebo-controlled multicenter trials (Frick et al., 1987; Scandinavian Simvastatin Survival Study Group, 1994; Shepherd et al., 1995; Sacks et al., 1996; Downs et al., 1998; Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group (1998)).

Pharmacologic treatment of dyslipidemias and therapeutic life-style changes have been well proved to prolong patient survival and reduce the incidence of cardiovascular events,
including myocardial infarction and cardiovascular deaths. However, some nonpharmacologic cholesterol-lowering interventions are not so well studied.

High altitude residence and migration to mountain regions are known to produce a beneficial effect on overall lipid patterns and reduce coronary heart disease event rates (de Mendoza et al., 1979; Aitbaev et al., 1990; Fujimoto et al., 1998; Dominguez Coello et al., 2000; Fiori et al., 2000). Various modalities of hypoxic training were also shown to produce favorable effect on lipid profiles (Topuria, 1975; Dudukalo et al., 1987; Mirrakhimov et al., 1991; Murataliev et al., 1991; Aleshin et al., 1993). Earlier we demonstrated a significant therapeutic effect of IHH in chronic stable angina patients of functional class I-III[2], but the metabolic effects of intermittent hypobaric hypoxia (IHH) in CHD patients have not been assessed.

The main objective of the present study was to evaluate effects of IHH on plasma lipid concentrations of CHD patients at baseline on completion of the study and at long-term follow-up.

METHODS

A total of 46 male coronary patients (mean age 48, age range 36 to 68) were enrolled in the study. The patients were eligible if they had a history of myocardial infarction more than 3 months before the study (30 patients) or ischemic episodes repeatedly documented by ergometer exercise testing or 24-h Holter monitoring (16 patients) and stable course of the disease. Lipid profiles were not taken into consideration during the patient selection. None of the subjects was taking lipid-lowering drugs. Pretreatment clinical assessment included a detailed physical examination and collection of baseline data. All participants gave informed consent.

The patients underwent acclimatization to hypoxia by means of a protocol of intermittent exposure in a hypobaric chamber. The protocol included 22 three-hour daily sessions in a hypobaric chamber, Ural-1, at a simulated altitude of 3500 m. All the subjects included in the study received their routine antianginal therapy. The patients were adapted starting from elevation to 1000 m at a rate of 3 to 5 m/s in the first day. The altitude was increased by daily 500-m stepwise ascent to 3500 m within 5 days.

Lipid profiles were assessed at baseline, on completion of the study, and at 3, 6, and 10 months of follow-up.

Measurements of plasma total cholesterol (TC) and triglycerides (TG) were made by means of the enzymatic method using Labsystems FP-900 analyzer (Finland). High-density lipoprotein (HDL) was determined in supernatants following precipitation of the other lipids by magnesium chloride. Low-density lipoprotein (LDL) was calculated using the Friedewald formula \[LDL \text{ mmol/L} = \text{TC-HDL}-(0, 45 \text{ TG})\].

The measurement quality control was performed with the use of two control serums, Leonorm U and Leonorm P (Lachema and Medlacor, St. Peterburg, Russia).

Coefficient of atherogenity (CA) by A. N. Klimov [(TC – HDL)/ HDL] (Klimov, 1977), which is thought to be an integral measure of plasma atherogenic potential and considered to be normal below 3 (Aleshin et al., 1997; Klimov, 1977), was calculated for every patient.

Statistical analysis was carried out in two steps: for the whole group and for two subgroups according to CA (≤3 and >3).

Group analysis and subgroup comparison were performed with the use of the ANOVA/ MANOVA module of STATISTICA package. The t-test was used to evaluate within-group and between-subgroup variations.

RESULTS

A total of 37 patients (80.4%) completed follow-up. As seen from our study results summarized in Table 1, on completion of the IHH treatment course the patients demonstrated 7% reduction of TC.

At 3-month follow-up a further decline of TC was noted, when it amounted to 9% reduction from baseline, which persisted to month 6. IHH resulted in significant increase of HDL levels. Their peak values of a 12% rise from baseline were noted at 3-month follow-up and remained significantly higher than baseline figures until month 6. Similarly, though, negative associa-
tion was observed in a lowering of LDL levels, which also declined on completion of IHH; but the changes from baseline were most prominent at 3-month (13%) and 6-month (11%) follow-ups.

IHH induced very similar changes in levels of VLDL and TG, which is easily explained by their close relationship. Their maximum reduction (14%) was marked on completion of the intervention and persisted to month 6, remaining significantly lower than baseline values.

Resulting from changes in the lipid profiles, CA differences were observed immediately after intervention and during follow-up. CA declined by 26% on completion of the treatment, but its reductions were greater at 3-month follow-up (37%). Later, CA figures steadily increased to their pretreatment values, and by month 10 they did not differ significantly from baseline.

In the second step of the statistical analysis, changes in the lipid profiles of patients with CA below 3 (22 subjects) were evaluated. No significant changes in any of the analyzed parameters were found either at the end of the intervention or during the follow-up period. Then changes in the lipid profiles of patients with CA above 3 (24 subjects) were analyzed. In this subgroup, IHH was associated with plasma lipid concentration changes similar to the whole study group, but beneficial metabolic effects of the treatment were more pronounced.

No subject had myocardial infarction during the study and follow-up.

Nine patients, who were lost to 10-month follow-up, did not complete the study for non-health reasons, and reexamining the statistics by excluding them from the beginning did not have any effect on the statistic results.

Figures 1 and 2 show diagrammatic summaries of changes in CA and plasma lipid concentrations in patients with higher (> 3) CA baseline values. As evidenced by Figure 2, CA decreased by more than one-third on completion of the treatment and at 3-month follow-up was 40% lower than the baseline value. At 6-month follow-up, CA was equal to its figures at the end of the treatment, and 10 months after intervention it was only 15% below baseline.

**DISCUSSION**

Our findings of plasma lipid concentration changes following IHHA were not unexpected. This effect of IHH was supported by earlier animal studies (Meerson et al., 1988) in which
IHH resulted in plasma TC concentration reduction due to its more intense oxidizing in the monoxygenase pathway of the cholesterol biosynthesis in hepatocytes, which was confirmed by elevation of 7-α-hydroxylase activity. As a result, hypoxic training increases plasma levels of primary bile acids (Gorbachenkov et al., 1994), one of the major cholesterol metabolites.

Reduction of TC following IHH is attributed to a decrease of its low-density fractions, LDL and VLDL (Kondrykinskaya et al., 1993). TG reduction is thought to be a secondary effect of VLDL decrease because of close relationships between these fractions.

In addition, intensified oxidizing of cholesterol leads to a reduction of its general pool in hepatocytes, which is associated with an increase in number of hepatocyte surface LDL receptors and more active capture of LDL and VLDL from the bloodstream.

Subgroup differences in lipid profile changes are believed to be due to the fact that cholesterol metabolism is affected by IHH only in patients with significantly abnormal values (Meerson et al., 1989).
CONCLUSIONS

1. IHH in CHD patients leads to a decrease of TC, LDL, VLDL, and TG and an increase of HDL plasma concentrations, resulting in lower values of AC.

2. Beneficial changes in CHD patient lipid patterns persist to month 6 following IHH.

3. The degree of changes in plasma lipid concentrations in CHD patients depends on their baseline values. Changes are most prominent in patients with CA above 3 and do not take place when CA is below 3.

4. The study data should be considered as preliminary because of the noncontrolled design of the study.

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