

Lipometabolic disturbances
Arteriosclerosis obliterans
Hyperlipoproteinemia

Vitamin C Therapy in Hyperlipoproteinemia

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Summary: Patients with HLP suffering from manifest arteriosclerosis obliterans of lower limbs were treated with a 1 g/die long-term vitamin C therapy (n = 63).

Only for serum cholesterol but not for serum triglycerides was a significant decrease observed. The best effect was achieved with type IIa, whereas type IIb and IV recorded only a significant cholesterol decrease and partially changed triglycerides.

The HDL-level in patients treated with vitamin C is increased. The hypothesis was discussed that ascorbic acid intervenes in the apolipoprotein synthesis.

Patients with lipometabolic disturbances represent a special risk group in our long-term examination of both development and prognosis of peripheral, coronary and extracerebral arteriosclerosis. In a group of 202 patients affected with angiographically proven arteriosclerosis obliterans and investigated in view of lipometabolic disturbances, one third had lipometabolic disturbances (Fig. 1).

On comparing patient groups with and without lipometabolic disturbances with respect to age, isolated or generalised manifestation of arteriosclerosis, obesity, diabetes mellitus, hypertension and gout, we observed that patients with lipometabolic disturbances showed a higher degree in the severity of arteriosclerosis than the control group; thus we found little manifestations of isolated arteriosclerosis but most often diabetes mellitus and gout (Fig. 2).

For a better understanding of the pathogenetic role of the given lipid disturbances and of their eventual consequences concerning differential therapeutics, we divided our patient groups by the terms of the HLP-classification according to Fredrickson (Fig. 3).

Type IIa and IV were most often observed. The patient group showing type IV was the most affected with generalised arteriosclerosis and risk factors listed above (Fig. 4). Based on these results and on our earlier study of the cholesterol-lowering effect of a high vitamin C dosage, we examined:

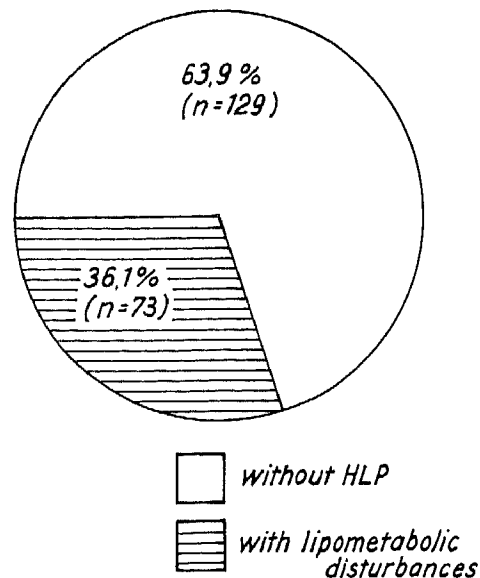


Fig. 1: Percentage of patients suffering from lipometabolic disturbances in a group of 202 patients affected with arteriosclerosis obliterans.

1. whether ascorbic acid would have an effect on HLP in manifest arteriosclerosis, and
2. for which HLP-types the best therapeutical effect could be found.

A group of 63 patients (10 women, 53 men) aged 35-73 (average 57.3 years) suffering from arteriosclerosis obliterans were treated daily for an average of 16.2 months (3-53 months) with 1.0 g ascorbic acid, without being subjected to a special diet.

In the whole group we observed a significant decrease in cholesterol, as shown in Fig. 5.

The initial cholesterol value was 329.6 mg/100 ml and attained during therapy 292.9 mg/100 ml. These values represent a significant decrease of 36.7 mg/100 ml.

We did not find any considerable improvement of triglyceride serum values in the whole group (Fig. 6). The triglyceride serum value during therapy (334.3) was only insignificantly lower than the 339.0 initial value. Figure 6 shows a decrease of certain individual triglyceride values. This fact prompted us to evaluate in which cases the ascorbic acid therapy would yield optimal results.

First, we studied the vitamin C effect in relationship with the cholesterol and triglyceride initial values. We found that the increase of the cholesterol-lowering effect depended on the initial values, but that the cholesterol serum level reached normal values only if the initial values did not exceed 300 mg/100 ml. When the

cholesterol level exceeded 400, vitamin C showed no effect in patients suffering from severe arteriosclerosis (Fig. 7).

There were made up groups showing triglyceride values up to 150, 151-250, 251-500, and triglyceride serum values over 500 mg/100 ml. We observed that vitamin C did not have any effect on the different triglyceride groups.

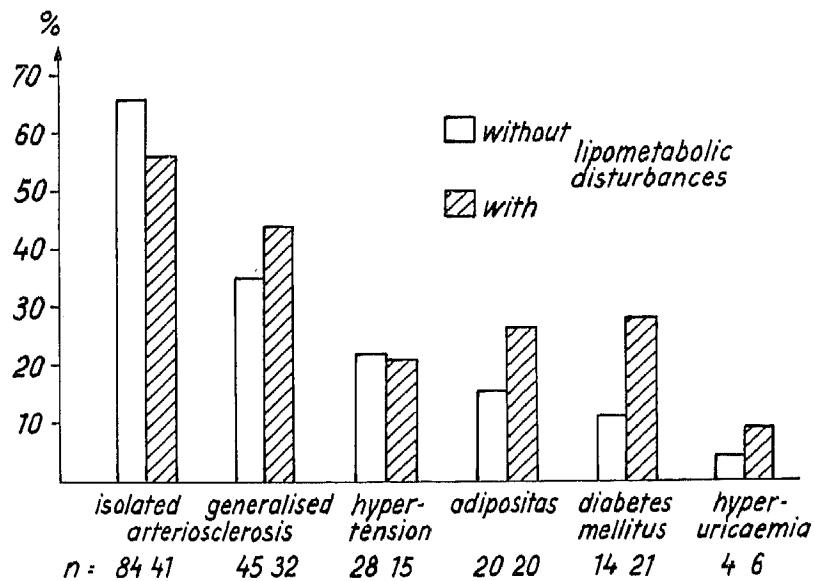


Fig. 2: Comparison of isolated and generalised manifestation of arteriosclerosis and risk factors in groups of patients with and without lipometabolic disturbances.

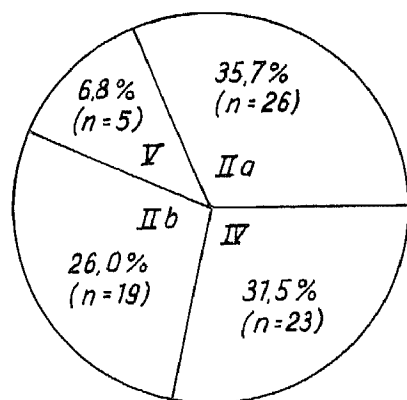


Fig. 3: Percentage of types IIa-V of HLP (Fredrickson) in a group of 73 patients suffering from arteriosclerosis obliterans and lipometabolic disturbances.

Therapy was interrupted with 18 cases. On discontinuing therapy, the cholesterol level of 15 patients rose up to the original one as is demonstrated for the whole group in Fig. 8.

This subdivision of groups with respect to initial levels was seemingly a too mechanical one. Based on the varying importance of the individual HLP-types for the development of arteriosclerosis, we decided to test the effect of vitamin C to the different HLP-types.

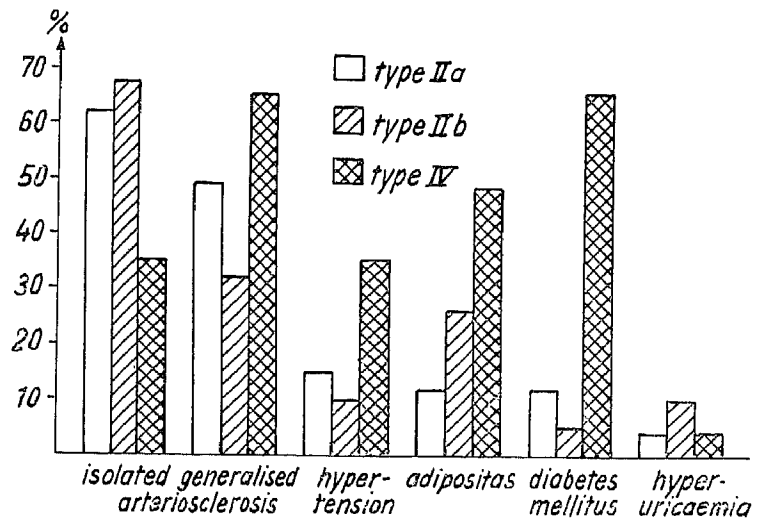


Fig. 4: Incidence of isolated and generalised manifestation of arteriosclerosis and risk factors according to the HLP-types IIa, IIb and IV.

We found a statistically significant decrease merely in the level of cholesterol and triglyceride in type IIa patients (Fig. 9).

The effect of vitamin C in lowering both cholesterol and triglyceride levels was also positive in type IIb patients (the triglyceride level although not being statistically significant). In type IV patients whom we have found to be the most aggressively reacting ones regarding arteriosclerotic development, the cholesterol level was also lower, while the triglyceride level was increased (statistically not significant). Our results show no effect in type V patients whose best number comprised merely 6.

The question arose how this positive effect of vitamin C could be explained. The role of the transport proteins and the enzymes responsible for the esterification of free cholesterol is well-known from recent studies about the role of lipometabolic disturbances in the pathogenesis of arteriosclerosis.

Therefore we took an interest in raising the question how the high-density

lipoproteins and lecithin-cholesterol-acyl transferase would react under a vitamin C hypervitaminosis in comparison to a normal group, a group of arteriosclerotic patients with untreated HLP and to a group of arteriosclerotic patients without HLP.

We observed that the group of patients treated with ascorbic acid showed the same amount of HDL as the healthy control group did. The HDL-level of the group of arteriosclerotic patients was significantly lower, regardless whether the patients also had HLP or not (Fig. 10).

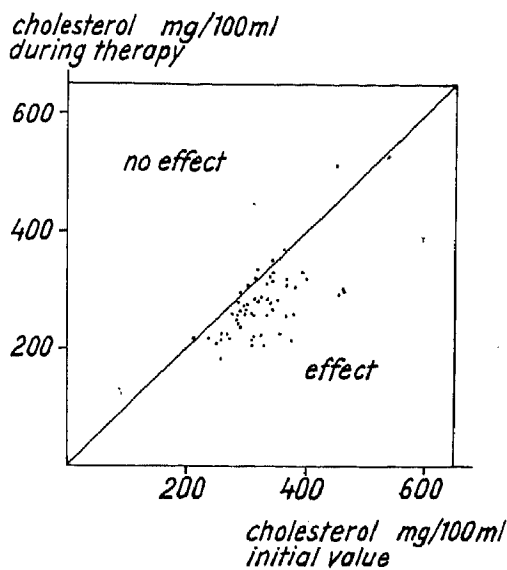


Fig. 5: Cholesterol-serum level before and during vitamin C therapy.

This observation prompted us to lay down the following two hypotheses:

1. The synthesis of apolipoproteins can be increased or its break-down postponed through vitamin C. This leads to an increase of the transport capacity of arteriosclerosis-producing agents (in this case of cholesterol) to the liver and possibly prevents a deposit in the blood vessels.

2. Compared with the normal control group, the HDL-level is significantly lower in patients suffering from arteriosclerosis even if there are no signs of HLP. This can possibly be explained as the second stage in the pathogenesis of arteriosclerosis, in which the body cannot react to an exposure of excess engendering an activation of metabolism. Furthermore, the transport capacity is diminished and the formation of cholesterol deposits in the blood vessels cannot be prevented.

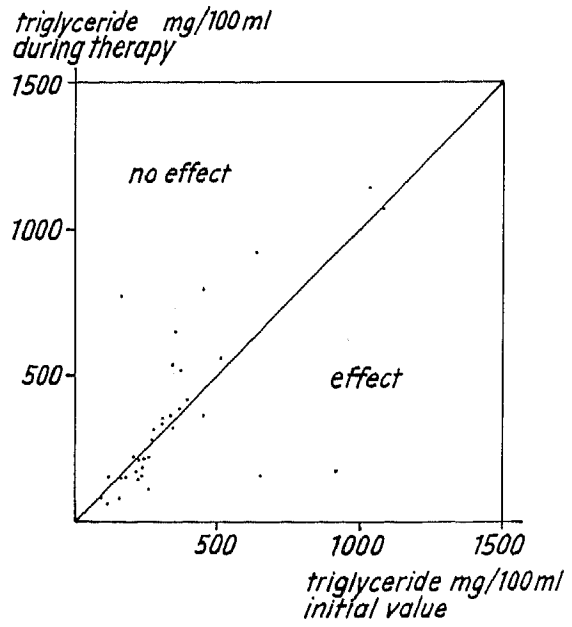


Fig. 6: Triglyceride-serum level before and during vitamin C therapy.

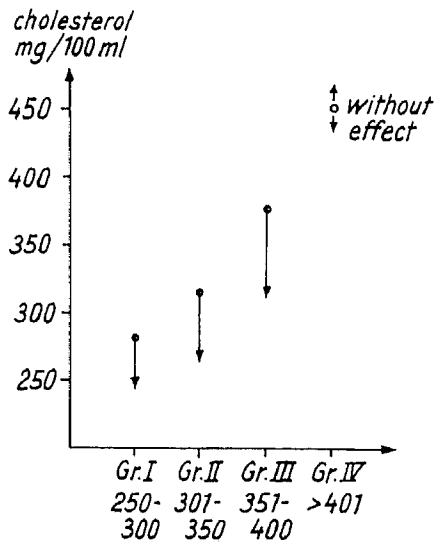


Fig. 7: Vitamin C effect in relationship to the cholesterol initial values.

We did not find any specific vitamin C effect regarding the activity of lecithin-cholesterol-acyl transferase, which is responsible for the esterification of free cholesterol and therefore comes into play as a prerequisite for further cholesterol metabolism. The HLP-level is the same as the one in the group of arteriosclerosis patients with HLP.

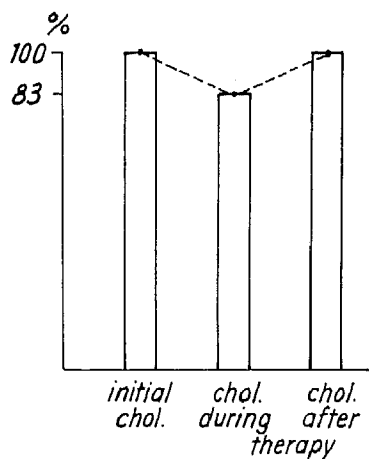


Fig. 8: 18 patients with interrupted vitamin C therapy. Comparison of individual cholesterol values (initially, during and after therapy).

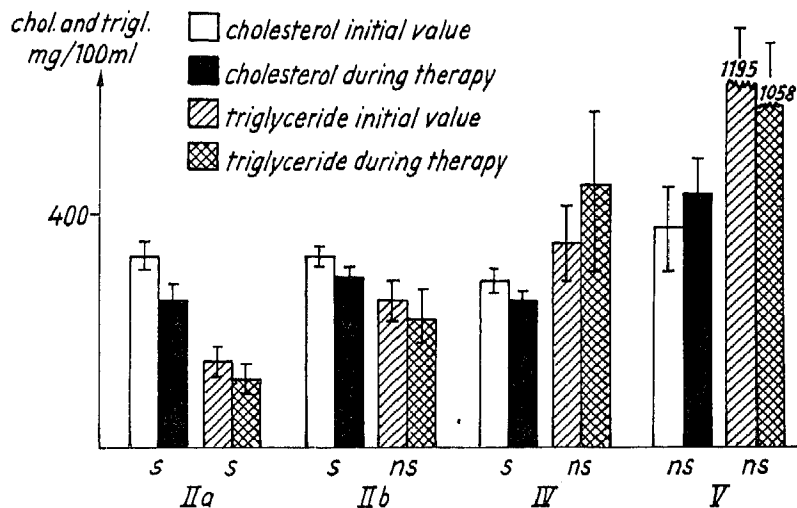


Fig. 9: The effect of vitamin C on cholesterol- and triglyceride levels in HLP-types II-V (Fredrickson).

It is interesting to note that the activity of lecithin-cholesterol-acyl transferase in arteriosclerotic patients without HLP is greater than in the normal group.

As a secondary finding we observed that a clofibrate therapy has no positive effect on the HDL-level. With 40 mg/100 ml it was similar to the one observed in the arteriosclerosis group.

In order to prevent potential sources of error in our examination we took the following steps:

- The whole of our results and control values concerning cholesterol and triglycerides are based on at least three measurements carried out with an interval of at least one month each.

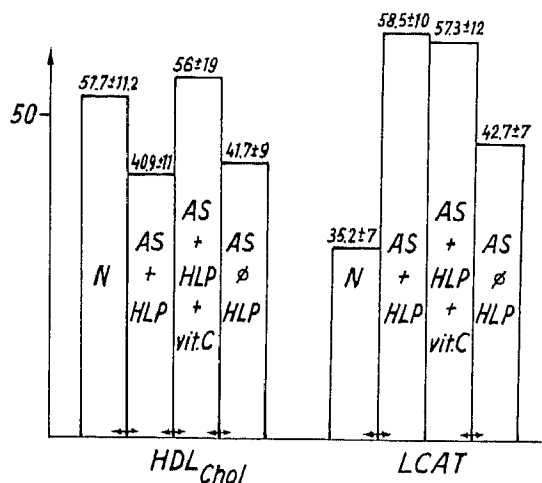


Fig. 10: Comparison of High Density Lipoprotein-Cholesterol (HDL_{Chol} mg/100 ml) and Lecithin-Cholesterol-Acetyltransferase (LCAT · $\mu\text{mol}^{-1} \cdot \text{h}^{-1}$) in groups of arteriosclerotic patients with untreated HLP (AS + HLP) and during vitamin C therapy to groups of arteriosclerotic patients without HLP (AS/HLP) and to a normal group (N).

- Additionally to comparing the groups (*t*-pair test) we examined even insignificant variations from the initial cholesterol value in the group of untreated HLP-patients.

- As seasonally adjusted variations of cholesterol were excluded, the cholesterol level was 295.1 mg/100 ml from November to March and 294.2 mg/100 ml from April to October. A comparison of the average levels in January (277.8) and in August (269.4) substantiates these results (Fig. 11).

- Potential errors with respect to the measurement conditions for cholesterol were ruled out by testing control-samples, in which ascorbic acid was added in

increasing concentrations to the test media. The cholesterol levels did not show any differences.

With the given doses we observed no side effects during the observation period.

Ascorbic acid had no effect on the long-term anticoagulant therapy. Forty-four of the patients underwent an anticoagulant therapy. A correction of the dosage of cumarine and indandione was not more often necessary during vitamin C therapy than before. There was no difference regarding hemorrhagic and thromboembolic complications in the groups having or not been given vitamin C.

Using a vitamin C dosage of 1 g daily we found no increase in the level neither of creatinine nor uric acid.

In conclusion we emphasize that

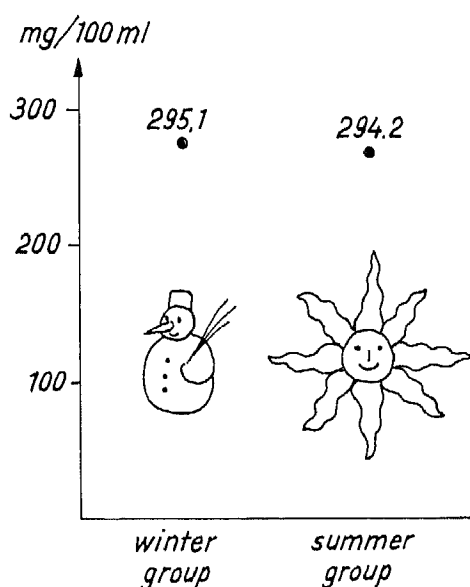


Fig. 11: Cholesterol-serum levels during winter (November-March) and summer (April-October) time (average values of 25 untreated HLP-patients with arteriosclerosis obliterans).

(1) A daily dosage of 1 g vitamin C is a suitable cholesterol-lowering agent in HLP types IIa, IIb and IV. The triglyceride-lowering effect is only significant in the one group that shows normal initial triglyceride levels. A seasonally adjusted dosage correction in view of our nutrition habits proves not necessary.

(2) One of the vitamin C mechanisms resides in engendering an increase of the serum transport capacity by simultaneously increasing the HDL-level.

(3) Further studies will be indispensable for determining the presumable role of ascorbic acid in both synthesis and breaking-down of apolipoproteins.

(4) Vitamin C therapy can be performed without any risk. There are no side-effects.

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