Effect of vanadium on serum cholesterol

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In vanadium workers over 40, Lewis[1] found that levels of serum cholesterol were significantly lower than in control subjects. Evidence of inhibition of cholesterol synthesis by vanadium compounds has been found in animals[2,3] and in healthy young men with a normal level of serum cholesterol.[4] Subsequent investigation suggested that vanadium was effective in lowering the level of cholesterol in patients with ischemic heart disease,[5] and it was decided to investigate this possibility further.

Material and methods

Twelve patients were treated with diammonium vanado-tartrate* for 6 months. The clinical data about the patients are summarized in Table I. All patients were on a diet restricted in fat, and all but 2 (Cases 2 and 5) had established ischemic heart disease and were on long-term anticoagulant therapy. Nine patients had persistent hypercholesterolemia (serum cholesterol above 340 mg. per 100 ml.); in 7 of these the condition was familial, and 6 had xanthomatosis tendinosum.

Samples of blood for the estimation of serum cholesterol[7] and paper electrophoresis[8] were taken on three occasions before vanadium was started, monthly during the period of administration, and for 2 months after the drug was stopped. Samples were taken 1 to 2 hours after a fat-free meal. In 9 patients a qualitative test for vanadium in the urine was performed.[9] Before and during administration of the drug the blood urea and hemoglobin were estimated, and the urine was tested for albumin.

Diammonium vanado-tartrate was given in doses of 25 mg. three times daily during the first 2 weeks; the daily dose was raised to 125 mg. during the following fortnight and was maintained for a further 5 months in 10 patients. In 2 patients the drug was stopped during the fifth month because of toxic gastrointestinal effects.

Results

Statistical analysis of the results showed that there was no significant effect on serum cholesterol during administration of vanadium (Table I). There were no changes in the lipoprotein pattern, blood urea, or hemoglobin, and no patient developed albuminuria.

Five patients had persistent upper abdominal pain, anorexia, nausea, and loss of weight. Symptoms improved in 3 when the dose was reduced, and in the other 2 (Cases 4 and 8) the drug was stopped after 4 months. Green tongue[10] appeared in 5 men, and one other developed pharyngitis with marginal ulceration of the tongue.

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*Although they considered it unlikely that vanadium would be of value in lowering the level of cholesterol,[6] the Pharmaceutical Division of I.C.I., Ltd., agreed to make a suitable preparation.

Table I. *Clinical and biochemical findings*

Case	Age and sex	Condition present	Serum cholesterol before therapy (mg./100 ml.)			Serum cholesterol after therapy (mg./100 ml.)				
						1 mo.	3 mo.	4 mo.	5 mo.	6 mo.
1.	40, M	Ischemic heart disease. Angina: xanthomatosis tendinosum	458	425	495	484	463	—	433	495
2.	37, M	Xanthomatosis tendinosum	285	285	319	294	335	321	282	342
3.	64, F	Ischemic heart disease. Angina: xanthomatosis tendinosum	—	647	655	667	600	619	583	619
4.	59, M	Ischemic heart disease. Myocardial infarction. Angina: xanthomatosis tendinosum	408	406	473	420	392	—	395	381
5.	23, M	Familial hypercholesterolemia	386	347	410	333	309	365	425	357
6.	63, F	Ischemic heart disease. Angina: xanthomatosis tendinosum	414	420	399	427	438	441	—	443
7.	36, M	Ischemic heart disease. Angina: xanthomatosis tendinosum	—	487	504	557	—	495	504	504
8.	58, M	Ischemic heart disease. Angina: xanthomatosis tendinosum	457	451	450	386	367	409	401	423
9.	55, M	Ischemic heart disease. Myocardial infarction. Angina	—	388	363	382	390	371	—	381
10.	39, M	Ischemic heart disease. Angina	310	227	229	246	271	252	—	304
11.	56, M	Ischemic heart disease. Angina	309	303	300	247	—	319	320	325
12.	61, F	Ischemic heart disease. Angina: hypertension	263	242	333	295	343	309	—	314

The negative results of this study are disappointing in view of the experience of other workers.[4,5] Curran[4] found a significant lowering of cholesterol only 6 weeks after vanadium was taken, but even in 3 of our patients who showed a slight reduction after 6 months (Cases 3, 4, and 8) no such trend was found early.

Vanadium was found in the urine of the 9 patients tested, which shows that the compound had been absorbed. However, no quantitative measurements were made, and it is possible that too little was absorbed to have a cholesterol-lowering effect.

Nine patients had hypercholesterolemia, and 6 of these had xanthomatosis tendinosum. It is possible that this type of patient has large stores of cholesterol which must be removed before reduction in serum cholesterol occurs. This might account for the fact that the results were different from those in Curran's normal people. There was no change in the size or shape of the xanthomata, which suggests that there was no mobilization of cholesterol from these sites.

The compound used in this study was the same as that described by Curran and his co-workers as diammonium oxy-tartrato vanadate.[6] Dimond[5] considered that vanadium should carry a valency of 5 to be effective, and that he had found the trivalent compound to be ineffective. Here, the tetravalent compound was used, as was the original vanadyl sulfate used by Curran on his liver slices.[2] Green[6] considered it unlikely that, once the compound was absorbed, it would matter whether it was tetravalent or pentavalent, and that it was possible that Dimond's trivalent compound was inadequately absorbed.

The clinical state of the patients remained unaltered except for one (Case 4) who developed cardiac infarction during the fourth month of observation.

Summary

Twelve patients were treated with oral vanadium for 6 months. Nine patients had hypercholesterolemia, and 7 of these had ischemic heart disease. Three patients had ischemic heart disease and normal serum cholesterol. No change in serum cho-

lesterol or lipoprotein patterns was found. The clinical course of the patients remained as would be expected for the natural history of the disease, and there was no alteration in the xanthomata. Toxic side effects occurred in 6 patients. In this limited study, therefore, we have found no evidence that diammonium vanadotartrate lowers serum cholesterol.

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