TREATMENT OF HYPERCHOLESTEROLEMIA WITH ALUMINUM NICOTINATE*†

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There is much evidence (1–4) suggesting that a high concentration of serum cholesterol is an important factor in the etiology of atherosclerosis. It remains to be demonstrated, however, that therapeutic reduction in the serum level of this lipid will decrease the rate of formation, or cause dissolution of atheromata in man. In order to carry out such investigations, procedures for sustained depression of high cholesterol levels by tolerable means must be available. Nicotinic acid administered in large doses has been found to be an effective method in both clinical (5–8) and animal (9) studies. One of the drawbacks to using this form of therapy, however, has been the occurrence of uncomfortable side effects. Flushing, pruritus, and gastric irritation have been troublesome, especially early in the course of treatment. For this reason, attempts have been made to modify the drug in such a way as to eliminate its side effects while retaining its cholesterol-lowering potency. The purpose of this report is to present the results of a clinical investigation of one such drug modification, aluminum nicotinate[1].

MATERIAL AND METHODS

Twenty-five patients with hypercholesterolemia, most of them with clinical manifestations of atherosclerosis, were studied on an out-patient basis. The group consisted of 12 females and 13 males. Patients were selected simply on the basis of demonstrated hypercholesterolemia and willingness to enter into an experimental situation requiring regular visits and serum cholesterol determinations.

Serum cholesterol concentration was determined by a modification of the method of Zak (10). "Baseline" specimens were obtained on three separate days before initiation of therapy. Thereafter, blood was obtained at monthly intervals, usually in conjunction with a personal interview, but occasionally through the mail.

Aluminum nicotinate (Nicalex) was administered in fractional doses three times daily after meals. Changes in dosage were recommended only at three-month intervals.

RESULTS

Effect on serum cholesterol level

Seven patients received, as aluminum nicotinate, 1.5 gm. of nicotinic acid per day for three months, and then 3.0 gm. per day for three months. Figure 1 illustrates the effect in each patient and the mean response of the group. The mean baseline value was 310 mg. per 100 ml. There was a fall to 303 mg. with

* Presented by title before the Spring Scientific Assembly of the Maryland and Washington, D. C., Chapters of the American Academy of General Practice, May 5–6, 1962, Washington, D. C.

† This work was supported in part by a grant from the Michigan Heart Association.

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[1] Kindly supplied as Nicalex by Walker Laboratories, Mount Vernon, N. Y.

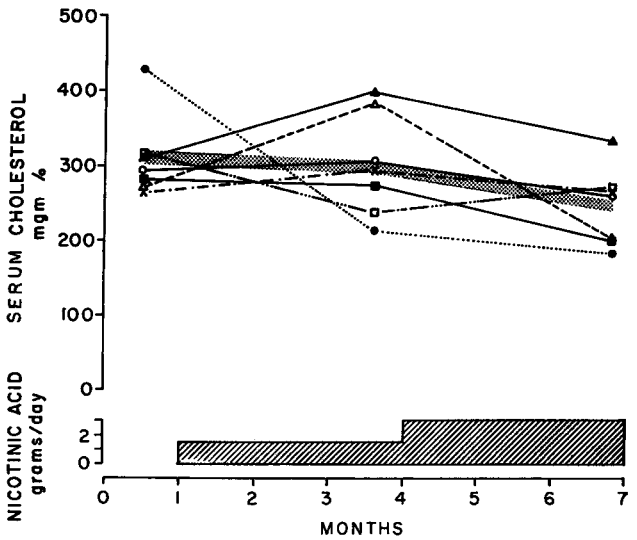

FIG. 1. Effect of aluminum nicotinate on the serum cholesterol level (mg./100 ml.) in 7 subjects. (Dosages in terms of nicotinic acid equivalents.)

TABLE 1

Serum Cholesterol Response to Aluminum Nicotinate*

Baseline Value	During Aluminum Nicotinate Therapy†	
	1.5 gm./day	3.0 gm./day
♀ 500		485
♂ 281	215	185
♂ 346		266
♂ 266	240	274
♂ 273	275	202
♂ 253		245
♂ 304	297	
♀ 283	251	
♂ 314	290	
♂ 311	297	269
♂ 315	387	206
♂ 428	401	338
♂ 295	309	265
♂ 234	217	

* Mg. per 100 ml. Each value is an average of 3 determinations.

† Dosage in terms of nicotonic acid equivalents.

the 1.5-gm. daily dosage and to 248 mg. with the 3.0-gm. dosage—a drop of 20 per cent from the pretreatment level. The decrease was statistically significant for the larger dosage ($t = 4.1$; $P < 0.01$) but not for the smaller dosage ($t = 1.11$; $P > 0.05$).

Table 1 contains the results for all patients who received aluminum nicotinate at a given dosage level for at least three months. In addition to the 7 patients who took the drug in both dosages, 4 patients took daily doses of 1.5 gm. only, and 3 patients took 3.0 gm. only. In the 11 patients studied with the 1.5-gm. dosage, the serum cholesterol level remained unchanged in 2, rose in 2, and fell in 7. In 3 of the 10 patients studied with the 3.0-gm. dosage, the cholesterol level remained unchanged; in the other 7 it fell.

Side effects

Almost all patients noted occasional flushing of the face while receiving aluminum nicotinate. With the larger dosage this tended to be more severe and prolonged, and frequently more generalized. Pruritus was extremely rare. Anorexia, nausea and vomiting occurred only rarely with the 1.5-gm. daily dosage, but was a problem to some of the women attempting to take 3.0 gm. daily. Intolerance to the drug altered the course of therapy in 10 women and 1 man; the difficulty was gastric in all but 1 patient in whom the problem was a dermatitis which appeared in the "blush" areas. In general, patients tended to complain less about flushing and nausea after a few weeks of therapy.

DISCUSSION

Our findings indicate that 3.0 gm. of nicotinic acid per day in the form of aluminum nicotinate will lower the serum cholesterol level impressively in most patients (7 of 10 in our study) who can tolerate this dosage. A dosage of 1.5 gm. per day is much better tolerated, but is less effective. The reduction in serum cholesterol concentration is similar to that obtained with comparable doses of unmodified nicotinic acid (7, 8).

Severe side effects necessitating interruption of treatment were limited almost to females. Only 1 woman out of 12 was able to maintain the higher dosage of 3.0 gm. per day for three months. In contrast, only 1 male out of 13 dropped out of the study because of intolerance. The reason for this sex difference in drug tolerance is not apparent, but it constitutes a limitation to the effective use of aluminum nicotinate in the management of hypercholesterolemia in women. On the other hand, the drug is unusually well tolerated by men and has a potency similar to that reported for unmodified nicotinic acid.

SUMMARY AND CONCLUSIONS

In 25 patients with hypercholesterolemia, aluminum nicotinate in a dosage of 3 gm. daily caused a drop of 20 per cent from the average pretreatment cholesterol level. When the drug was given in smaller amounts, the decrease in cholesterol concentration was not statistically significant.

Aluminum nicotinate is an effective blood cholesterol-lowering agent when administered in a dosage of 3.0 gm. daily.

Most women are unable to tolerate a dosage of this magnitude, primarily because of induced nausea, but the drug is well tolerated by men.

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