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INCREASE IN SKIN SURFACE LIPIDS DURING NUTRITIONAL REHABILITATION OF MALE ALCOHOLICS*

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ABSTRACT

Skin surface lipid production was studied in a group of chronic alcoholics during a period when alcohol was replaced by a balanced diet. All subjects studied had abnormal liver function tests at the start and these returned to normal during the study. A statistically significant increase in skin surface lipid production occurred during the period of observation. Although several explanations are available, the reason for this increase is unknown.

A spontaneous increase in skin surface lipids was an unexpected observation made during a previous investigation. Many explanations for this increase were initially entertained but one common denominator appeared as the group increased in number. All were alcoholics with evidence of liver disease. In order to further evaluate this possibility, a larger group of alcoholics with liver disease was studied. The group was large enough to apply statistical analysis to the results. This paper deals with our findings and outlines possible explanations for our observation.

MATERIAL AND METHODS

Fifteen adult male patients on the dermatology service of the Cleveland V.A. Hospital were studied. A certain number of beds were set aside for this project to which minor skin problems could be admitted and the patients followed for a prolonged period of time.

Ten of the subjects were chronic alcoholics. A history of chronic excessive alcohol consumption was obtained from either the patient or a member of his family. The severity of the alcoholism in each case was sufficient to impair steady employment. All subjects had been drinking up to the time of admission. Besides the history of alcoholism, each subject had hepatomegaly and one or more abnormal liver function tests at the start of the study. Prospective subjects were excluded if there was reason to suspect another type of hepatic disease. Also excluded were those unable to cooperate with the skin surface lipid collections. The latter included those with Korsakoff's psychosis, alcoholic chronic brain syndrome and hepatic coma.

The control group consisted of five subjects in whom there was no history suggestive of alcoholism. Liver function tests were normal for members of this group. The alcoholic and control groups were studied concurrently.

Prospective subjects were excluded from either group for the following reasons: 1) dermatologic problems which required topical treatment of the face, scalp, or neck, 2) systemic medications known to alter cutaneous or blood lipids or, 3) dermatitis of the sample area. Systemic drugs withheld during the study period were corticosteroids, sex hormones, antibiotics, insulin, oral hypoglycemic agents, aspirin, heparin, cholestyramine resin and stimulants or antagonists of the autonomic nervous system. Aspirin was used prior to the study by members of both the alcoholic and control groups. Local dermatologic therapy in other areas of the body included corticosteroids without occlusion and saline or silver nitrate compresses. All subjects received a regular house diet and used Ivory® soap for washing. The environment was air conditioned during the summer months.

Skin surface total lipid production was determined as follows: a 36.4 cm^2 area on the cheek was washed three times with 20 ml of reagent grade acetone introduced into a glass cylinder held against the skin. Three hours later the central 27.4 cm^2 of the larger area was washed three times with 15 ml of reagent grade acetone. These latter washings were passed through lipid-free filter paper, evaporated into micro weighing bottles, desiccated over $CaCl_2$ and olive oil and then weighed to constant weight. Baseline collections were done at the time of admission and consisted of two collections done on consecutive days. The baseline value was taken as the mean of these two collections. Patient availability determined whether follow-up collections were done each week or every other week. Frequently two collections were done on the same subject during the same week. In such cases the value for that week was taken as the mean of the individual values. Occasionally a sample was lost due to a laboratory accident.

Liver function tests were done on the day of admission. Except for bromsulphalein (BSP) retention they were repeated periodically until normal. All liver function tests returned to normal values by the time of discharge. Besides the BSP, the tests of hepatic function included serum glu-

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tamic oxalacetic transaminase (SGOT), alkaline phosphatase, total bilirubin, and albumin. Forty-five minute BSP tests were done according to the procedure outlined by Sherlock (1). The other tests were done by the autoanalyzer.

RESULTS

Initial liver function tests for each subject in the alcoholic group are outlined in Table I. Normal values for each test in our laboratory are also included. All liver tests in the control group were normal.

Baseline and weekly skin surface total lipid production rates for the five control subjects are outlined in Table II. The mean of the weekly collections for each subject is also presented in this table as well as the percent change of this mean from the baseline value. The percent change in the five control subjects varied from 0 to 4%.

Baseline and weekly lipid production rates for the ten alcoholic subjects are outlined in Table II. Mean and percent change of the mean from baseline values are presented as in the control group. All ten subjects showed an increase in surface lipid production and the percent increase varied from 10% to 105%. The average percent increase for the alcoholic group was 37%. Application of a t test to the difference between each subject's baseline and mean follow up value gave an overall p value of $<.001$ for the entire group. The increase in surface lipid production was therefore statistically significant.

Although the mean baseline lipid production rate in the alcoholic group (4.8 mg/27.4 cm^2/3 hr) was less than that observed in the control group (5.4 mg/27.4 cm/3 hr), the large individual variation in lipid production rates and the small size of the two groups does not allow statistical evaluation of this difference.

TABLE I

Initial liver function tests for each subject in the alcoholic group

	BSP % Retention	SGOT Units	Alk. Phos. King-Armstrong Units	Albumin Gm %	Bilirubin Total Mg %
Normal Subject	<5	<25	4–12	3.5–5.0	0.3–1.0
#1	—	35	12	3.4	1.1
2	12	20	13	4.0	1.0
3	15	15	15	4.7	0.6
4	—	55	11	3.8	0.5
5	10	20	13	4.3	0.6
6	8.5	20	15	2.6	0.6
7	21	60	10	3.2	0.8
8	31	35	11	4.0	1.6
9	32	105	13	3.9	1.1
10	22	40	11	2.7	0.7

DISCUSSION

This study demonstrates an increase in skin surface lipid production upon withdrawal of alcohol from a group of alcoholics. Concomitant with the alcohol withdrawal was the institution of a balanced diet. Another variable during the period of increased surface lipid production was the return of hepatic function tests to normal values. How the increase in surface lipid production is related to alcohol, diet, hepatic function, or other factors cannot be determined from this study.

TABLE II

	Baseline	Weeks						Mean	% Change
		1	2	3	4	5	6		
Control subject									
#1	5.1	—	5.0	5.4				5.2	+2
2	4.5	4.2	4.8	5.0				4.7	+4
3	5.2	5.4	5.8	5.7	5.0	4.5	4.6	5.2	0
4	5.4	5.1	6.0	5.2	6.1			5.6	+4
5	7.0	7.6	6.5					7.0	0

Baseline and weekly skin surface total lipid production rates (mg./27.4 cm^2/3 hr.) for the five control subjects. The mean of each subject's weekly values and the % change of this mean from their baseline is presented.

TABLE III

	Baseline	Weeks						Mean	% Change
		1	2	3	4	5	6		
Subject									
*1	3.1		4.9	5.6	5.8	7.2	8.4	6.4	+105%
2	4.5		5.5	6.3	6.9	9.3		7.0	+55%
3	4.1	4.0	5.2	5.6	6.1	8.8	7.0	6.1	+49%
4	4.4		6.7	5.9	5.3			6.0	+36%
5	4.3		5.1		L	6.1	5.6	5.6	+30%
6	2.8	3.2	3.4	4.1		L		3.6	+29%
7	6.7		6.3	10.3	8.1	8.0	7.2	8.0	+20%
8	7.1		7.8	10.0	7.8			8.5	+20%
9	7.9		L	8.8		9.5	8.9	9.1	+15%
10	2.9	3.5	3.1	3.1	L		3.3	3.2	+10%

Baseline and weekly skin surface total lipid production rates (mg./27.4 cm^2/3 hr.) for the ten alcoholic patients. The mean of each subject's weekly values and the % change of this mean from their baseline is presented. L is sample lost.

Several features of an alcoholic with liver diseases may have some relationship to our finding. These include alterations in systemic lipid metabolism, nutritional deficiencies, direct toxicity of ethanol and sex hormone imbalences. Systemic lipid alterations in alcoholics are well documented and are reflected in changes in serum lipids as well as the development of a fatty liver (2). Blood alcohol levels above 200 mg% are associated with an elevation of blood free fatty acids as much as sixfold. Blood triglyceride increases with alcohol administration until intoxicating levels are reached and then the triglycerides return to normal values (3). Whether these changes have any relationship to skin surface lipid changes is unknown since little is understood about the relationship of systemic and cutaneous lipid metabolism.

The frequency and severity of nutritional deficiencies in alcoholics is well known (4). Not only do poor dietary patterns contribute to this deficiency, but malabsorption has recently been found to exist in many alcoholics (5). Little is known about the influence of nutrition on skin surface lipid production. Rothman (6) reviewed the work of Serrati (7) which showed diets excessive in either carbohydrate or fat produced an increase in skin lipid production. This work reported in 1938 has not been repeated nor are studies available on the opposite situation: the influence of nutritional deprivation on skin surface lipid production.

It is difficult to differentiate a primary toxic effect of alcohol from the many other manifestations of alcoholism, but recent investigations have supported the concept of a direct toxic effect for ethanol on the myocardium and liver. An ever increasing number of studies has led to the recognition of cardiomyopathy in well nourished alcoholics in whom peripheral neuritis and pellagra are absent and in whom thiamine produces little or no improvement (8, 9, 10). Cardiac muscle damage following acute ingestion of large amounts of alcohol has been reviewed by Ferrano (11). Isselbacher and Greenberger (2) and Lieber and Schmid (12) feel a number of the effects of ethanol on the liver appear to be direct. If such a direct toxic effect exists for skin and its appendages is unknown.

Sex hormone imbalances are suggested by the clinical appearance of some male chronic alcoholics. Gynecomastia (13), female pubic escutcheon (14), palmar erythema (15), spider angiomas, and testicular atrophy (16) are frequent clinical findings. Indirect evidence supports the idea that estrogen activity in the body is increased (17). Liver disease patients have been studied with respect to urinary recovery of endogenous and exogenous estrogens (17, 18, 19, 20), blood estrone (21) and blood estriol binding (22), yet the physiologic basis for the feminizing changes is not known (22).

With respect to the findings reported in this study, alterations in androgen metabolism with

liver diseases may be more important than estrogen alterations. This is because sebaceous gland function appears to be under androgen influence (23) and these glands are a major source of skin surface lipids. Although systemic estrogens suppress skin surface lipid production by suppressing sebaceous activity, it is felt this is done indirectly by lowering blood androgen rather than by a direct action on the sebaceous glands (24).

Androgen activity can be low in liver disease. Urinary 17 ketosteroid and urinary androgen measured by bioassay are both low in liver disease (25). The rate of removal of exogenous testosterone from plasma is normal in these patients (26). Recently it has been shown that blood testosterone is low in some male cirrhotics (27). Over half of these men had plasma testosterone concentrations in the range of orchiectomized men, although individual values ranged from normal to essentially complete absence of testosterone. Secondary hypogonadism rather than a primary testicular abnormality was suggested by low gonadotropin levels. It was postulated the low testosterone was due to high estrogen levels, since exogenous estrogens produced a marked fall in blood testosterone.

Besides liver disease, a second reason exists for possible low androgen activity in the subjects reported in this study. Animal experiments have shown poor nutrition is associated with decreased androgenic activity of the testes (28) and decreased urinary testosterone (29). Recently the same urinary findings were shown to exist in men whose malnutrition was either psychogenic or medical in origin (30).

Further investigation is needed to determine if one or more of the above explanations account for the changes reported in this study.

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