Plasma Turbidity Changes and Electrocardiographic Alterations Induced by Alimentary Hyperlipemia in Anginal Patients before and after the Administration of Gastric Mucin

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The hyperlipemia induced by a fat meal in anginal patients is frequently associated with clinical and electrocardiographic changes suggesting transient coronary insufficiency. Gastric mucin administered to 10 anginal patients at the same time as a fat meal invariably prevented the hyperlipemia, evaluated as increase of plasma optical density, and in one half of the cases it reduced the magnitude of the electrocardiographic changes as compared with the changes found in control experiments. Gastric mucin therefore exerts a powerful antilipemic and clearing action. Its inhibitory effect on the electrocardiographic changes associated with alimentary hyperlipemia is less evident than that of heparin.

In a previous paper on plasma turbidity and electrocardiographic changes associated with alimentary hyperlipemia, we demonstrated that both the foregoing changes were inhibited when heparin was administered intravenously at the same time as the fat meal. We discussed in that paper the interpretation of this phenomenon and its possible relationship with the pathogenesis of postprandial angina and arterial atheroma.

Capraro and his associates, Cresseri, and Cantone, as a result of their researches on the biologic properties of hog gastric mucin extracts, recently clarified some points of considerable interest concerning the effect of such extracts on certain plasma conditions that many investigators believe to be related with atherogenesis or with frank atheromatous conditions.

A variety of biologic properties has been ascribed to the mucin compound prepared from hog gastric mucosa. Among such properties are the capacity to bind vitamin B₁₂ and thus render it undialyzable, and to act as growth factor for Lactobacillus bifidus, var. Penn, an antianemic action in mice, rats, and in human pernicious anemia, a protective effect (even when given by mouth) against alimentary and toxic liver steatosis in guinea pigs and rats, the capacity to enhance the plasma clearing power in the rabbit, and an antilipemic effect in rabbits and men. The 2 last-mentioned properties are of special interest and appear worthy of further investigation.

Because of the finding that in men and rabbits, gastric mucin administered by mouth increases the plasma clearing action on lipid substrates (emulsion of homogenized milk), the foregoing authors suspected that an acid

Fig. 1. Mean plasma turbidimetric curves after a fat meal consisting of 200 Gm. of milk cream (solid line) and after the same fat meal with the addition of 250 mg. of gastric mucin (broken line).
aminopolysaccharide, present in the gastric mucin preparation under study, might be responsible for this phenomenon, since it is known that an increase in the plasma clearing power may be obtained by the parenteral administration of sulfurated acid aminopolysaccharides (for example, heparin). They succeeded in isolating an acid aminopolysaccharide, composed essentially of d-glucuronic acid and d-glucosamine. Because of its physical and chemical properties, there is reason to believe that this substance is an acid aminopolysaccharide of the hyaluronic acid type, devoid of any appreciable anticoagulant effect, and active by mouth.

Cantone\textsuperscript{8} made a comparative study of the clearing effect of heparin and of that of the acid aminopolysaccharides contained in hog gastric mucosa, and concluded that the mechanism of the clearing effect exerted by the plasma of animals treated with gastric mucin is different from the mechanism underlying the clearing effect of heparinized plasma. Cantone concluded that the clearing factor acting in the rabbit after the administration of gastric mucin does not belong to the same enzymatic type as heparin. On the other hand, just as the heparin clearing effect is inhibited by protamine sulfate, also the gastric mucin clearing effect is inhibited in vivo by the administration of protamine sulfate.\textsuperscript{9}

In view of the interest aroused by heparin as a regulator of the chemio-physical state of plasma lipids, which many authors believe to be related to the problem of atherogenesis, we deemed it worthwhile to study the clearing effect of gastric mucin in human alimentary hyperlipemia, and to investigate whether

\begin{figure}
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\includegraphics[width=\textwidth]{figure2}
\caption{Reduction by effect of gastric mucin of the electrocardiographic changes associated with a fat meal. A. Electrocardiogram recorded before the test: optical density 65. B. Electrocardiogram recorded 3 hours after the fat meal without gastric mucin: optical density 75. C. Electrocardiogram recorded 3 hours after the fat meal with the addition of gastric mucin: optical density 60.}
\end{figure}
this substance was capable to prevent the electrocardiographic changes noted in certain anginal patients after a fat meal.

MATERIAL AND METHODS

A total of 10 patients was selected on the basis of the following criteria: long-standing and typical manifestations of effort angina; electrocardiographic signs of coronary artery insufficiency at rest; absence of any digestive complaint; development of electrocardiographic alterations after a fat meal.

The plasma lipemia was evaluated as plasma optical density, determined photometrically in the fasting state and at hourly intervals for 5 hours after a fat meal. The fat meal consisted of 200 Gm. of homogenized milk cream containing 40 per cent of fat.

The electrocardiogram was recorded at basal rest in the fasting patient and every hour for 5 hours after the fat meal.

The same procedure was adopted for another experiment, carried out on the same patients, who this time received 250 mg. of gastric mucin by mouth at the same time as the fat meal. Every precaution was taken to ensure that the exploring electrode was always placed exactly on the same points over the precordial region.

RESULTS

Alimentary Hyperlipemia with and without Gastric Mucin Administration (Fig. 1). The turbidimetric curve expressing the plasma hyperlipemia induced in 10 patients by a fat meal began to rise 1 hour after the meal, attained its peak during the third hour, and subsequently descended.

When 250 mg. of gastric mucin were given together with the fat meal, the contour of the turbidimetric curve was completely different. The optical density did not increase but instead decreased gradually; toward the end
of the second hour there was a mild elevation, which, however, never attained the pretest level.

At the end of the experiment (5 hours after the fat meal), the optical density of the untreated group was considerably higher than the initial value. In the treated patients, the plasma was much clearer than before the test. The administration of gastric mucin, therefore, not only inhibited the hyperlipemia associated with a fat meal, but in addition even reduced the plasma optical density existing before the experiment.

Electrocardiographic Changes with and without Gastric Mucin Administration. The electrocardiographic changes associated with the fat meal were as a rule of minor degree. They consisted of reduced amplitude, diphasism (+ or −), T-wave inversion of bifidity in one or more left precordial leads, and correspondingly in leads I and/or II and aV_L or in leads III and/or II and aV_P, depending on the electrical position; the T-wave changes were often associated with slight S-T abnormalities. The electrocardiographic alterations usually appeared 1½ hour after the fat meal; their incidence was highest during the third hour; in a few instances only they had cleared up completely by the end of the experiment (fifth hour). The findings are in perfect agreement with our previous results.1

When gastric mucin was given simultaneously with the fat meal, 5 of the 10 patients showed electrocardiographic changes of the same type and degree as the untreated patients. In the 5 remaining patients the changes either did not appear or were negligible. The results are shown in figures 2 and 3.*

Discussion

Our findings agree with the observations reported by Capraro and associates and by Cresseri concerning the antilipemic effect of gastric mucin in the rabbit and its clearing effect on homogenized lipid substrates.

In every one of our patients the plasma optical density not only failed to increase after the fat meal, but actually diminished steadily under the influence of gastric mucin. The clearing effect is similar to that of heparin: because of this similarity and of certain chemical affinities, it is likely that the antilipemic effect is due to the action of the hexuronic groups present in both heparin and gastric mucin. The latter, however, has the practical advantage of being active even by mouth.

With regard to the electrocardiographic changes induced by alimentary hyperlipemia in anginal patients, we were unable to demonstrate that gastric mucin invariably inhibits such changes. Actually, only 5 of the 10 patients showed an appreciable reduction in the severity and duration of the changes as compared with the group not receiving gastric mucin. It seems, therefore, that the inhibitory effect of gastric mucin on the electrocardiographic alterations associated with a fat meal is less evident than that of heparin.1,10 This may support the hypothesis that the action of heparin is not confined to its antilipemic and clearing effects, but may include other more complex actions, as several authors have suggested.

Summary

Hyperlipemia was induced in 10 anginal patients by a fat meal consisting of 200 Gm. of milk cream with a 40 per cent fat content. The plasma lipemia, determined photometrically as plasma optical density, was measured at hourly intervals. Electrocardiograms were recorded in the fasting state and at hourly intervals after the fat meal. The patients who showed electrocardiographic changes after the fat meal were again submitted to the same test but in addition received 250 mg. of gastric mucin at the same time as the fat meal. Gastric mucin invariably inhibited the alimentary hyperlipemia and in one half of the cases reduced the electrocardiographic changes associated with hyperlipemia.

Summario in Interlingua

Hyperlipemia esseva inducita in 10 patieñtes anginal per medio de un repasto grassee

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*Only the peripheral leads are shown because the chest leads are not more informative.
consistente de 200 g de crema de lacte con un contenido de 40 pro cento de grasa. Le lipemia del plasma es coniugata en intervallos de un hora per determinar fotometricamente le densitate optic del plasma. Electrocardiogrammas esseva obtenite in stato jejun e a intervallos de un hora post le ingestion del repasto grasae. Le patientes qui exhibiva alterationes electrocardiographic post le repasto grasae esseva resubmittite al mesme test, sed nunc illes recipeva additionalmente 250 mg de mucina gastric, administrate simultaneamente con le repasto de grasia. Mucina gastric inhibiva invariavilmente le hyperlipemia alimentari, e in un medidate del casos illo reduceva le alterationes electrocardiographic associate le hyperlipemia.

REFERENCES


Measurements of the cardiac output by the direct Fick principle utilizing cardiac catheterization in control subjects and patients with chronic congestive heart failure showed that exposure to a hot and humid environment increased the cardiac output, stroke volume of the ventricle, mechanical, and physiologic cardiac work, and tension upon the walls of the ventricles in both groups. There was less of an increase in the patients with congestive heart failure than in the control subjects. The increase in cardiac work and output was found to occur more as a result of a larger stroke volume than greater cardiac rate. The therapeutic implications of the observed stressful cardiac responses to a hot and humid environment are discussed.

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