Serum Cholesterol Esterifying Activity in Kwashiorkor

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ABSTRACT

Serum lipid levels were determined in 30 children with kwashiorkor and in 30 healthy children of comparable age. The serum concentrations of unesterified and esterified cholesterol, albumin and the cholesterol esterifying activity (CEA) were also measured in children with kwashiorkor before treatment and after recovery. All serum lipid fractions were significantly lower in kwashiorkor than in the normal children. After treatment and recovery, serum lipid levels were comparable to those observed in normal children. There was also a significant increase in serum cholesterol esterifying activity (CEA) following recovery from kwashiorkor.

Introduction

Kwashiorkor is a disease of protein—calorie malnutrition which is characterized by such clinical features as edema, growth retardation, dyspigmentation of hair and scaly skin. Disturbed lipid metabolism with hypolipidemia is a well recognized feature of severe kwashiorkor and a low concentration of cholesterol ester is a distinct feature of the hypocholesterolemia.

In normal sera, the enzyme lecithin cholesteryl acyl transferase (LCAT) catalyzes the synthesis of a major portion of cholesterol esters. The concentration of cholesterol esters depend upon the overall cholesterol esterifying activity of serum.

This study investigated the concentration of serum lipids and cholesterol fractions in the sera of patients with kwashiorkor and also examined the association between net CEA and the concentrations of esterified cholesterol, unesterified cholesterol and albumin. The assay used in the present study does not absolutely measure LCAT enzymatic activity. However, the absolute change in unesterified cholesterol fraction determined at the end of an incubation period of five hours at 37°, provides a good assessment of the rate of cholesterol ester
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Materials and Methods

The subjects were 30 healthy children ages one to four years with no symptoms of disease and 30 patients of similar age group with severe kwashiorkor diagnosed by clinical and laboratory findings. Only children with hemoglobin genotype AA were admitted to the study. Fasting blood samples were collected from healthy children and sick patients at the start of the study and again from the kwashiorkor children after recovery. The blood samples were iced immediately after drawing, were allowed to clot and were centrifuged at 4°. Serum was separated immediately into three aliquots and was frozen. Analysis was carried out on the day following blood collection.

The concentration of serum total cholesterol was determined by the method of Parekh and Jung. The same procedure was carried out in the determination of free cholesterol isolated from serum on the basis of a modification of the method of Leffler and McDougald. Serum cholesterol esterifying activity was determined by the procedure described by Jones et al and expressed as ΔF which is the difference in the concentration of unesterified cholesterol in mg per dl before and after incubation of serum for five hours at 37°.

Results

The mean concentrations of serum lipids in normal children and children suffering from kwashiorkor are given in Table I. The children with severe kwashiorkor had significantly lower levels of serum cholesterol, phospholipids and triglycerides when compared to normal children of similar age groups. After treatment and recovery, serum lipids in the kwashiorkor group were comparable to those in normal children.

In Table II are compared the means of total, unesterified and esterified cholesterol, percent of esterified cholesterol, ΔF and the albumin concentrations in the kwashiorkor children before treatment and after recovery. Patients with severe kwashiorkor had much lower levels of esterified cholesterol, percent of esterified cholesterol, ΔF and albumin than were found in the recovery group. There was no significant difference in the unesterified cholesterol concentration. There was no significant correlation between ΔF and serum albumin, whereas the con-

| TABLE I |
| Mean Concentrations of Serum Lipids in 30 Normal and 30 Kwashiorkor Children |
| Total Cholesterol mg per dl | Phospholipids mg per dl | Triglycerides mg per dl |
| Mean ± S.D. | Mean ± S.D. | Mean ± S.D. |
| Normals | 130 ± 11 | 168 ± 19 | 76 ± 10 |
| Kwashiorkor before treatment | 65 ± 5* | 129* ± 11 | 57* ± 7 |
| Kwashiorkor after recovery | 141 ± 12 | 171 ± 16 | 80 ± 13 |

*Value significantly different from value in normals and from value after recovery.

| TABLE II |
| Serum Concentrations of Cholesterol and Fractions Percent of Cholesterol Esters, ΔF and Albumin in 30 Kwashiorkor Children Before and After Treatment |
| Total Cholesterol mg per dl | Unesterified mg per dl | Esterified mg per dl | Percent of Esters | ΔF mg per dl | Albumin g per dl |
| Mean ± S.D. | Mean ± S.D. | Mean ± S.D. | Mean ± S.D. | Mean ± S.D. |
| Before treatment | 65 ± 5 | 45 ± 4 | 20 ± 2.0 | 31 ± 4 | 4.6 ± 0.6 | 1.6 ± 0.25 |
| After treatment | 141 ± 15 | 44 ± 6 | 97 ± 3 | 69 ± 3 | 9.9 ± 1.1 | 3.6 ± 0.9 |
| P value | <0.001 | NS | <0.001 | <0.001 | <0.001 | <0.001 |
centrations of esterified cholesterol and percent of esterified cholesterol correlated with ΔF.

Discussion

The hypolipidemia observed in patients with kwashiorkor in this study agrees with previous reports. Recovery from kwashiorkor was accompanied by significant increases in all serum lipid levels and also in the serum esterified cholesterol fraction. Dean and Schwartz suggested that one of the early effects of correct and successful treatment of kwashiorkor may be the release of fat and cholesterol from stores in tissues, especially the liver. This suggestion was later corroborated by several other investigations. Thus, it seems that a block in the release of hepatic lipoproteins to plasma is the primary mechanism in the finding of hypolipidemia in kwashiorkor. This impairment of hepatic lipoprotein release is also the cause of the fatty liver usually observed in patients with the disease.

In the present study, ΔF was much lower in the patients at the start of the investigation than after recovery. The increase in ΔF following recovery was accompanied by a dramatic rise in serum esterified cholesterol concentration and in the percent esters. The mechanisms that underlie the observed changes can only be properly explained when more is known about factors affecting the synthesis and secretion of LCAT. However, there is good evidence implicating LCAT in a specific component of plasma where it plays an important role in formation of plasma cholesteryl esters. It has been reported that the liver is a site of LCAT synthesis and that decreases in LCAT activities have been observed in patients with liver disease.

It is conceivable that the low ΔF observed in kwashiorkor may be secondary to a reduced hepatic synthesis and release of LCAT. The massive hepatic fatty infiltration that accompanies severe kwashiorkor would undoubtedly lead to an impairment in the normal function of the liver. The observation that ΔF correlates positively with serum cholesteryl esters and percent esters also supports the concept that CEA is important in the formation of serum cholesteryl esters and that decreased CEA is a principal mechanism for the decreased cholesteryl esters observed in kwashiorkor.

The physiological significance of the LCAT reaction has not been fully determined. It has, however, been demonstrated that in human subjects, the LCAT reaction is the principal source of plasma cholesteryl esters. In a study in which human plasma lipoprotein fractions were separately incubated with purified LCAT for 24 hours, it was shown that the decrease in unesterified cholesterol was greatest in the high density lipoprotein fraction, much less in the low density lipoprotein fraction and insignificant in the very low density fraction. This finding suggests a preferential action of LCAT on high-density lipoprotein.

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References