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Dietary Glycine and Taurine on Bile Acid Conjugation in Man.*† Bile Acids and Steroids 75. (24741).

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Common bile acids occurring in human bile, *i.e.*, cholic, chenodeoxycholic and deoxycholic acids, are conjugated with glycine and taurine(1), glycine conjugates normally predominating. Thus, in 21 healthy medical students, a mean value of 3.2 was obtained for the ratio of glycine to taurine conjugates,§ and no free bile acids could be found. Bergström and Gloor(2), studying conjugation of cholic acid in homogenates of human livers, found that addition of 3 moles of taurine/mole of cholic acid caused pronounced increase in the proportion of taurine conjugates formed. Glycine did not have such a marked effect. These findings have been confirmed by Ekdahl(3). In our investigation, the *in vivo* effect of taurine and glycine has been studied.

Materials and methods. Two female and 9 male medical students were used. They were told to retain their ordinary diet, eat regularly, and to avoid excesses of alcohol intake during experiment. Taurine‖ (Eastman, puriss.), or glycine (Merck, for medical use) was given them with their meals 3 times a day for 5 days. Three other females with stones in roentgenologically normally functioning gallbladder were given taurine 3 times a day for 3 weeks. One subject (A.K.) had cancer in the deep bile ducts causing obstructive jaundice. Therefore, a T-tube had been inserted into the common duct so that one leg passed above the obstruction. After some weeks drainage was closed so that bile passed into the duodenum. The drainage had been closed for some weeks and the patient was at home with no jaundice when our experiment was done. Taurine was given 3 times a day for 5 days. Before and during taurine feeding, bile samples were taken through the drainage, which was opened for about one hour at noon every day. The samples were kept in refrigerator and frozen and stored at –16°C as soon as possible. In the other subjects, duodenal contents were collected through a polyvinyl tubing(4) which was introduced through the nose. Samples were taken at a level of 70-80 cm from the nose and the subjects were fasting on day of collection. Samples were immediately frozen at –16°C. Bile acids were analyzed according to Sjövall(5). Glycocholic, taurocholic, glycochenodeoxycholic and glycodeoxycholic acids were determined separately, whereas taurochenodeoxycholic and taurodeoxycholic acids were determined together.

Results. Fig. 1 shows the effect of orally administered taurine on conjugation of bile acids in the patient with a "circulating bile fistula." Prior to taurine feeding, glycine conjugated bile acids constituted between 65 and 75% of total bile acids. The day after administration of 3 g of taurine, equal amounts of glycine and taurine conjugates were found. Taurine was given 5 days and dose was increased by 3 g every day. On sixth day 96% of bile acids were taurine conjugated. Traces of free bile acids were found

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in some samples. Neither conjugated nor free deoxycholic acid could be found. This might indicate that bile acids in this patient did not take part to a normal extent in the enterohepatic circulation, since deoxycholic acid is formed by bacterial action on cholic acid during this circulation(6-8). The ratio between cholic and chenodeoxycholic acids did not change significantly during the experimental period (Fig. 1).

Because of the striking effect of taurine on conjugation of bile acids in the patient described above, the effect of giving glycine and taurine to healthy persons was investigated. Various amounts of the amino acids were given for 5 days and bile acids in duodenal contents were determined before and after administration. The results are shown in Fig.

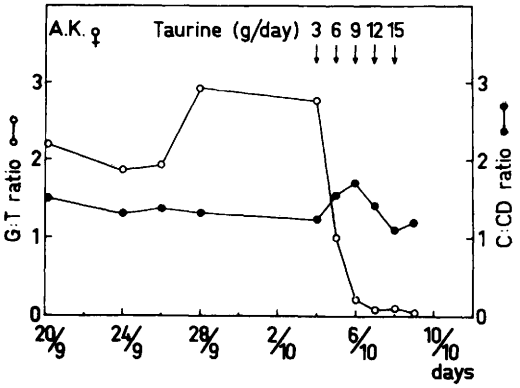

FIG. 1. Changes in ratio between glycine and taurine conjugated bile acids (G:T) after administration of taurine to patient A.K. who had a "circulating bile fistula." Ratio of cholic to chenodeoxycholic acids is fairly constant (C:CD).

2. Twenty-one g of glycine/day did not change the state of conjugation of bile acids. In a case not illustrated in the Figure, 2 g of glycine were given every second hour for 3 days, except at night when 6 g were given in the evening and in the morning. No change in ratio between glycine and taurine conjugates was observed. In contrast to results obtained with glycine, 0.5 g of taurine 3 times a day gave a pronounced increase in the proportion of taurine conjugated bile acids. This proportion tended to increase further when larger amounts of taurine were given. Five to 7 days after last administration of taurine, the proportion between glycine and taurine

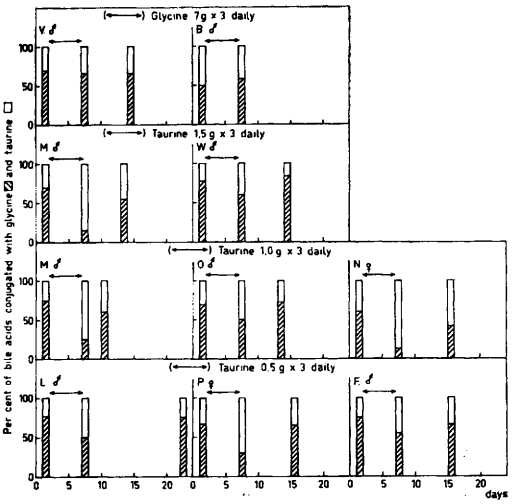

FIG. 2. Proportions between glycine and taurine conjugated bile acids before and after feeding of various amounts of taurine or glycine to healthy subjects.

conjugates had usually returned to starting value.

To test the effect of prolonged taurine administration, 3 patients were given 3 g of taurine daily for 3 weeks. All patients had stones in the gallbladder. The proportion of taurine conjugates was increased at end of experimental period (Fig. 3).

The proportions between cholic, chenodeoxycholic and deoxycholic acids were variable in different samples from the same subjects, as is also the case when no taurine is given.

When labelled taurine is administered to rats, most of it is excreted in urine though it can also be found in bile conjugated with cholic acid(9). After intravenous injection, the taurine is rapidly taken up from blood by various organs(10). Bile acids are normally conjugated almost exclusively with taurine in the rat, and *in vitro* experiments have shown that cholic acid is preferably conjugated with taurine even in the presence of excess glycine

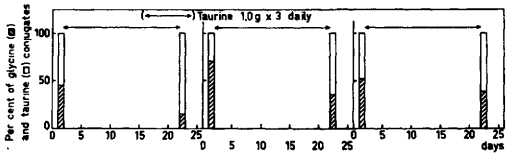

FIG. 3. Proportions between glycine and taurine conjugated bile acids before and after feeding of 3 g of taurine daily for 3 wk to patients with gallstones.

(11). It is reasonable to assume that in our investigation the taurine given was partly used for conjugation of bile acids.

The marked influence of taurine administration on the ratio between glycine and taurine conjugated bile acids in man, might have some bearing on the findings of Ekdahl(12), that homogenates of human livers under certain pathological conditions conjugate cholic acid with taurine in a higher proportion than normally. This is, for example, the case in hepatitis where Walshe(13), among other semiquantitative findings, noted increased urinary excretion of taurine as compared with glycine.

Even when given in large amounts, glycine did not affect the ratio between glycine and taurine conjugated bile acids. This is in agreement with the *in vitro* findings(2,3). However, it appears that addition of glycine to a homogenate of pathological human liver, conjugating mainly with taurine, causes an increase in glycine conjugation(13). It would, therefore, be of interest to give glycine to patients having mainly taurine conjugated bile acids.

The results might also have some bearing on the finding that newborn children conjugate bile acids mainly with taurine, though during days after birth the proportion of glycine conjugates rapidly increases.¶ Semiquantitative measurements of urinary excretion of amino acids in newborn children(14) indicate a relative decrease of taurine excretion as compared with glycine during the first days after birth. According to Durande and Colombo(15), sucklings show a decreased capacity for hippuric acid synthesis which can be increased by administration of glycine.

Since taurine is formed from cysteine, it appears likely that the diet should influence conjugation of bile acids. Datta and Harris (cited by Westall(16)) found an increased urinary excretion of taurine in cats given fish diet exclusively.

Summary. Taurine and glycine were given to human subjects and the bile acids studied. Taurine (0.5 g x 3 daily) markedly increased the proportion of taurine conjugated bile acids, whereas glycine (7 g x 3 daily) did not change the bile acid pattern of the normal subject. The findings have been discussed in relation to conjugation of bile acids under normal and pathological conditions.

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