From the Department of Biochemistry and Nutrition of the Polytechnic Institute, the Medical Department A and the Department of Surgery C of the University Hospital (Rigshospitalet), Copenhagen (Denmark)

Studies on human bile

V. Influence of cholestyramine treatment on the composition of bile in healthy subjects

By H. DAM, I. PRANGE, M. KROGH JENSEN, H. E. KALLEHAUGE and H. J. FENGER

With 12 tables

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Studies on the effects of the bile acid binding non-absorbable resin Cholestyramine in man have dealt mainly with the ability of this substance to lower serum cholesterol and to cause relief of pruritus through lowering of serum bile acids in jaundiced patients. The influence of cholestyramine treatment on gallstone disease in man or on the composition of human bladder bile does not seem to have been explored yet.

The experiments described in this paper were carried out in order to obtain an orientation as to how cholestyramine treatment may influence the composition of bile in healthy subjects, especially with respect to the molar percentages of each of the main bile acids in the total bile acids and the molar ratios between total bile acids and cholesterol, between lipid-soluble phosphorus and cholesterol, and between total bile acids and lipid-soluble phosphorus. This investigation forms a counterpart of the preceding study of the influence of dietary cholesterol on the composition of human bile (1).

Experimental

Seven healthy volunteer subjects, 20 to 23 years of age, received daily doses of cholestyramine through two consecutive periods of 3 weeks. Duodenal bile was collected, fasting after intravenous injection of cholecystokinin twice before beginning of the treatment and after 3 and 6 weeks of treatment. Simultaneously with the collection of duodenal bile, blood samples were taken for determination of serum total cholesterol.

The methods for collection and analysis of bile were as described in our previous studies (1, 2, 3).

Cholestyramine was given in the form of „Cuemid" from Merck Sharp & Dohme, Inc., West Point, Pa. According to the manufacturer's declaration, 4 g Cuemid contains 3.66 g cholestyramine resin (equivalent to 3.33 g anhydrous cholestyramine resin). Each volunteer subject received slightly lethan 400 mg Cuemid per kg body weight per day divided into 3 doses. The last dose in each period was given 17 hours before collection of the bile. No particular diet was prescribed during the treatment.

Results

The data determined before and after 3 and 6 weeks of treatment with cholestyramine are shown in tables 1–12[1]).

Table 1 shows dosage and serum cholesterol.

Table 2 shows the composition of the volunteer's duodenal bile with respect to pH, per cent Dry Matter, and the millimolar concentrations of Cholesterol (C), Lipid-soluble Phosphorus (P), and Total Bile Acids (TBA). As in our previous papers (1, 2, 3), TBA is taken as the sum of Glycocholic Acid (GC), Glycochenodeoxycholic Acid (GCD), Glycodeoxycholic Acid (GD), Taurocholic Acid (TC), and Taurochenodeoxycholic Acid plus Taurodeoxycholic Acid (TCD + TD).

Tables 3–7 show the molar percentages of GC, GCD, GD, TC and TCD + TD in TBA.

Tables 8–12 show the other molar ratios under discussion.

In the present experiments, the data obtained after 3 and 6 weeks of treatment are to be compared with mean values from two (blood or) bile samples, one taken 7 to 14 days before, and another taken immediately before beginning of the treatment.

In tables 1 and 3–12, a mean value for the whole group determined after 3 or 6 weeks of treatment is considered to indicate a significant change from the beginning of the treatment when its difference from the corresponding group mean value before treatment is greater than the difference between the first and second group mean values before treatment.

The main results were as follows:

Serum cholesterol (table 1) showed slight to moderate decrease in 6 out of the 7 cases after 3 weeks and in all cases after 6 weeks of treatment. The mean value of serum cholesterol was lower after 6 weeks than after 3 weeks.

The molar percentage of Glycocholic Acid in Total Bile Acids (100 GC/TBA, table 3) increased greatly in all cases. The mean value was higher after 6 weeks than after 3 weeks.

The molar percentage of Glycochenodeoxycholic Acid in Total Bile Acids (100 GCD/TBA, table 4) decreased in 5 out of the 7 cases after 3 weeks, and in all cases after 6 weeks. The mean value was lower after 6 weeks than after 3 weeks.

The molar percentage of Glycodeoxycholic Acid in Total Bile Acids (100 GD/TBA, table 5) was greatly decreased in all cases after 3 weeks, but only in 5 cases after 6 weeks. Of the two volunteers whose values for 100 GD/TBA were higher after 6 weeks than before treatment, AN, was particulary remarkable. He had the lowest values before treatment and after 3 weeks, but the value after 6 weeks was more than 5 times the mean value before treatment. In spite of this irregularity, the mean value for all the volunteers after 6 weeks was less than half of the mean value before treatment, although somewhat higher than the mean value after 3 weeks.

The molar percentage of Taurocholic Acid in Total Bile Acids (100 TC/TBA, table 6) was more or less reduced in 5 out of the 7 cases after 3 weeks, and in all the cases after 6 weeks. The mean value was lower after 6 weeks than after 3 weeks.

The molar percentage of Taurochenodeoxycholic Acid plus Taurodeoxycholic Acid in Total Bile Acids (100 (TCD + TD)/TBA, table 7) was more or less reduced in all cases after 3 weeks, but only in 6 out of the 7 cases after 6 weeks. The most

[1]) In the tables, figures in parentheses indicate per cent of the same volunteer's mean values before treatment.

irregular changes are exhibited by volunteer AN. His value for this percentage was particularly low before treatment. It was only slightly reduced after 3 weeks, and after 6 weeks it was 294 per cent of his mean value before treatment. For the other 6 volunteers, the mean value was slightly lower after 6 weeks than after 3 weeks.

As a consequence of the above-mentioned changes of the molar percentages of the different bile acids in the total bile acids, the ratio Glycine conjugation/Taurine conjugation (G/T, table 8) is slightly to markedly increased in all 7 cases after 3 weeks, and markedly increased in 6 out of the 7 cases after 6 weeks, the exception being AN whose ratio G/T decreased to 69 per cent of his initial mean value after 6 weeks. For several of the volunteers, the values of ratio G/T after 3 and 6 weeks markedly exceeded the highest values found among 42 untreated volunteers in our previous study (3).

Further, the molar ratio Dihydroxycholanoic Acids/Trihydroxycholanoic Acids (Di/Tri, table 9) decreased in 6 of the 7 cases after 3 weeks, and in all cases after 6 weeks. The decrease after 6 weeks was very marked except for volunter AN[1]. For several of the volunteers, the values of ratio Di/Tri after 3 and 6 weeks was markedly lower than the lowest value found among 42 untreated volunteers in our previous study (3).

The molar ratio Total Bile Acids/Cholesterol (TBA/C, table 10) was decreased in 5 out of the 7 cases after 3 weeks, and in 6 of the cases after 6 weeks. The exception after 6 weeks was AN.

The molar ratio Lipid-soluble Phosphorus/Cholesterol (P/C, table 11) was decreased in 5 cases after 3 weeks and in 6 cases after 6 weeks. The exception was not AN, whose different mode of reaction, apparently, was limited to the bile acids.

The molar ratio Total Bile Acids/Lipid-soluble Phosphorus (TBA/P, table 12), after 3 and 6 weeks, remained largely within the limits of variation before treatment.

Discussion

The interval of time from the last dose of cholestyramine to collection of the bile sample, and the fact that the samples were almost clear before centrifugation are believed to exclude the possibility that the results are due to adsorption of bile acids to cholestyramine present in the duodenum during collection of the bile. The changes in the composition of bile resulting from treatment with cholestyramine are, therefore, assumed to be consequences of the increased removal of bile acids from the body, and the ensuing increased synthesis of bile acids. According to Huff et al. (5), dihydroxycholanoic acids are more efficiently excreted bound to cholestyramine (in rats) than is cholic acid. The same circumstance may explain the marked decrease of the ratio Di/Tri observed in the present experiments. Conjugation of an increased amount of bile acids, apparently, is more easily obtained with glycine than with taurine, as shown by the increase of the ratio G/T.

The decrease of the mean values of the ratios TBA/C and P/C are unfavorable to the solubility of cholesterol. The decrease of the mean value of the ratio Di/Tri may be assumed to have the same effect since the dihydroxycholanoic acids are generally believed to be superior to cholic acid as solubilizers for cholesterol. According to NEIDERHISER and ROTH (6) and unpublished results from our laboratory, the glycine-

[1]) Decreased ratios Chenodeoxycholic Acid/Cholic Acid and Deoxycholic Acid/Total Bile Acids have been found by VAN DER LINDEN & NAKAYAMA (4) in hepatic bile of 8 cholelithiasis patients treated with cholestyramine during 8 to 14 days.

Table 1. Dosage and Serum Cholesterol

Initials	Sex	Volunteer's Age, years	Volunteer's Body weight	Cuemid g/day	Cuemid mg/kg day	Serum cholesterol[1] Samples before treatment 1st mg%	Samples before treatment 2nd[2] mg%	Mean value of 1st and 2nd sample mg%	3 weeks on treatment mg%	6 weeks on treatment mg%
EO	f	22	51	20	392	274[3]	303	288.5	252 (87.3)	236 (84.5)
TH	f	20	64	25	390	201[4]	176	188.5	163 (86.5)	185 (98.0)
AN	m	21	72	28	389	159[4]	149	154.0	156 (101.3)	122 (79.3)
SL	m	21	75	29	386	182[4]	172	177.0	163 (92.0)	154 (87.0)
KT	f	21	57	22	386	224[5]	232	228.0	184 (80.7)	168 (73.7)
JJ	f	23	58	22	380	185[4]	181	183.0	179 (97.8)	155 (84.7)
MJ	f	21	59	23	390	338[6]	339	338.5	256 (75.6)	259 (76.5)
Mean values for the whole group:						223.3	221.7	225.5 ± 0.8	193.0	183.9

[1] mg% = mg per 100 ml; figures in parenthesis represent per cent of the same volunteer's mean value before treatment.
[2] Second sample = sample taken immediately before treatment.
[3] Sample taken 8 days before treatment.
[4] Sample taken 7 days before treatment.
[5] Sample taken 14 days before treatment.
[6] Sample taken 12 days before treatment.

Table 2. pH, per cent of Dry Matter, and millimolarities of Cholesterol (C), Lipid-soluble Phosphorus (P), and Total Bile Acids (TBA)[1] in the bile samples before and during treatment with cholestyramine.

Volunteer	Sample	pH	Dry Matter % (w:v)	C mM	P mM	TBA mM
EO	8 days before treatment	7.9	5.9	4.0	10.6	47.8
EO	Immediately before treatment	7.4	5.9	4.8	13.4	45.5
EO	3 weeks on treatment	7.2	2.1	1.9	3.0	15.1
EO	6 weeks on treatment	7.3	5.0	5.3	9.1	22.2
TH	7 days before treatment	7.2	9.6	7.2	21.6	58.2
TH	Immediately before treatment	7.6	7.7	7.2	18.0	52.7
TH	3 weeks on treatment	7.5	7.3	6.8	16.1	40.7
TH	6 weeks on treatment	7.4	11.2	10.9	28.9	80.5
AN	7 days before treatment	7.0	4.5	2.9	9.5	27.3
AN	Immendiately before treatment	7.4	9.5	6.1	18.0	50.5
AN	3 weeks on treatment	7.3	10.5	7.7	22.4	73.1
AN	6 weeks on treatment	7.2	4.2	2.0	4.8	22.0
SL	7 days before treatment	7.4	4.4	3.7	8.2	43.4
SL	Immediately before treatment	7.1	6.4	5.7	16.0	31.4
SL	3 weeks on treatment	7.3	4.1	2.7	10.4	29.9
SL	6 weeks on treatment	7.5	10.6	9.7	28.3	68.9
KT	14 days before treatment	7.1	4.2	2.4	6.5	22.3
KT	Immediately before treatment	7.4	12.1	8.5	26.1	86.1
KT	3 weeks on treatment	7.5	10.0	7.0	20.1	77.3
KT	6 weeks on treatment	7.4	10.0	13.0	26.7	73.2
JJ	7 days before treatment	7.3	3.6	2.4	6.1	29.1
JJ	Immediately before treatment	6.8	2.7	1.3	3.5	10.3
JJ	3 weeks on treatment	7.2	5.0	3.9	7.9	25.9
JJ	6 weeks on treatment	7.5	5.0	5.3	11.9	29.6
MJ	12 days before treatment	7.8	9.3	10.3	26.2	62.0
MJ	Immediately before treatment	7.6	6.8	5.2	12.9	43.3
MJ	3 weeks on treatment	7.4	5.6	6.7	12.4	35.7
MJ	6 weeks on treatment	7.4	6.6	8.8	11.2	56.8

[1] TBA is considered equal to the sum of Glycocholic Acid (GC), Glycochenodeoxycholic Acid (GCD), Glycodeoxycholic Acid (GD), Taurocholic Acid (TC) and Taurochenodeoxycholic plus Taurodeoxycholic Acids (TCD + TD).

Table 3. Mol per cent Glycocholic Acid in Total Bile Acids (100 GC/TBA)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	21,0	16,8	18,9	24,7 (141)	43,4 (230)
TH	25,1	23,8	24,5	68,3 (280)	63,4 (258)
AN	43,2	36,3	39,8	69,6 (179)	51,8 (130)
SL	20,1	13,6	16,9	40,7 (246)	64,0 (379)
KT	27,2	33,4	30,3	69,7 (230)	79,0 (260)
JJ	17,7	31,2	24,5	51,6 (210)	60.6 (247)
MJ	35,1	33,1	34,1	62,4 (183)	62,7 (184)
	27,1	26,9	27,0 ± 0,1	55,3	60,7

Table 4. Mol per cent Glycochenodeoxycholic Acid in Total Bile Acids (100 GCD/TBA)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	15,0	27,8	21,4	40,4 (189)	8,8 (41)
TH	12,4	24,8	18,6	13,7 (74)	15,2 (82)
AN	36,3	42,9	39,6	16,9 (43)	8,9 (22)
SL	26,2	15,9	21,1	27,3 (130)	16,3 (77)
KT	27,3	20,3	23,8	7,7 (32)	6,8 (29)
JJ	28,0	17,6	22,8	10,5 (46)	10,1 (44)
MJ	14,0	11,1	12,6	6,0 (48)	6,6 (52)
	22,7	22,9	22,8 ± 0,1	17,5	10,4

Table 5. Mol per cent Glycodeoxycholic Acid in Total Bile Acids (100 GD/TBA)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	14,9	15,0	15,0	8,3 (55)	19,1 (127)
TH	37,8	29,6	33,7	7,2 (21)	7,5 (22)
AN	3,6	1,7	2,9	2,1 (72)	16,1 (555)
SL	32,7	33,3	33,0	5,4 (16)	5,1 (15)
KT	23,5	19,7	21,6	3,1 (14)	3,2 (15)
JJ	25,6	27,5	26,6	13,7 (52)	8,3 (31)
MJ	15,2	15,0	15,1	8,6 (57)	5,1 (34)
	21,9	20,3	21,1 ± 0,8	6,9	9,2

Table 6. Mol per cent Taurocholic Acid in Total Bile Acids (100 TC/TBA)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	21,6	14,2	17,9	10,4 (58)	6,3 (35)
TH	8,9	8,6	8,8	6,1 (69)	8,5 (97)
AN	10,1	14,9	12,5	6,3 (50)	7,0 (56)
SL	10,5	12,4	11,5	12,1 (105)	7,2 (63)
KT	10,5	14,7	12,6	12,0 (95)	7,6 (60)
JJ	9,6	14,5	12,1	12,9 (107)	9,4 (77)
MJ	17,9	26,3	22,1	18,3 (83)	20,2 (91)
	12,7	15,1	13,9 ± 1,2	11,2	9,5

Table 7. Mol per cent Taurochenodeoxycholic Acid + Taurodeoxycholic Acid in Total Bile Acids (100 (TCD + TD)/TBA)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	26,8	26,2	26,5	16,2 (61)	22,4 (85)
TH	15,8	13,2	14,5	4,7 (32)	5,4 (37)
AN	6,8	4,2	5,5	5,1 (93)	16,2 (294)
SL	10,5	24,9	17,7	14,5 (82)	7,4 (42)
KT	11,5	11,9	11,7	7,5 (64)	3,6 (31)
JJ	19,1	9,2	14,2	11,3 (80)	11,7 (82)
MJ	17,8	14,5	16,2	4,7 (29)	5,4 (33)
	15,5	14,9	15,2 ± 0,3	9,1	10,3

Table 8. Molar ratio Glycine-conjugation/Taurine-conjugation (Ratio G/T)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	1,05	1,48	1,27	2,76 (218)	2,48 (195)
TH	3,05	3,59	3,32	8,28 (249)	6,21 (187)
AN	4,94	4,58	4,76	7,74 (162)	3,30 (69)
SL	3,77	1,69	2,73	2,77 (102)	5,85 (211)
KT	3,55	2,77	3,16	4,13 (131)	8,01 (254)
JJ	2,48	3,21	2,85	3,12 (110)	3,73 (131)
MJ	1,80	1,45	1,63	3,35 (206)	2,90 (178)
	2,95	2,68	2,82 ± 0,14	4,59	4,64

Table 9. Molar ratio Dihydroxycholanoic Acids / Trihydroxycholanoic Acids (Ratio Di/Tri)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	1,33	2,23	1,78	1,85 (104)	1,01 (57)
TH	1,94	2,09	2,02	0,34 (17)	0,39 (19)
AN	0,77	0,71	0,74	0,32 (43)	0,70 (95)
SL	2,26	2,85	2,56	0,89 (35)	0,41 (16)
KT	1,65	1,08	1,37	0,22 (16)	0,16 (12)
JJ	2,66	1,19	1,93	0,55 (29)	0,43 (22)
MJ	0,88	0,68	0,78	0,24 (31)	0,21 (27)
	1,64	1,55	1,60 ± 0,05	0,63	0,47

Table 10. Molar ratio Total Bile Acids / Cholesterol (Ratio TBA/C)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	11,92	9,46	10,69	8,14 (76)	4,16 (39)
TH	8,04	7,36	7,70	6,08 (79)	7,39 (96)
AN	9,59	8,31	8,95	8,38 (94)	11,05 (124)
SL	11,67	5,52	8,59	11,23 (131)	7,08 (82)
KT	9,27	10,17	9,72	11,07 (114)	5,65 (58)
JJ	12,06	8,07	10,07	6,63 (66)	5,64 (56)
MJ	6,01	8,33	7,17	5,37 (75)	6,50 (91)
	8,17	9,79	8,98 ± 0,81	8,13	6,78

Table 11. Molar ratio Lipid-soluble Phosphorus / Cholesterol (Ratio P/C)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	2,08	2,79	2,44	1,61 (66)	1,70 (70)
TH	2,99	2,51	2,75	2,38 (87)	2,66 (97)
AN	3,35	2,96	3,16	2,57 (81)	2,39 (76)
SL	2,21	2,81	2,51	3,92 (156)	2,92 (116)
KT	2,71	3,08	2,89	2,89 (100)	2,06 (71)
JJ	2,53	2,72	2,63	2,02 (77)	2,26 (86)
MJ	2,53	2,50	2,51	1,86 (74)	1,28 (51)
	2,63	2,77	2,70 ± 0,07	2,46	2,18

Table 12. Molar ratio Total-Bile Acids / Lipid-soluble Phosphorus (Ratio TBA/P)

Volunteer	Before treatment			3 weeks on treatment	6 weeks on treatment
	1st sample	2nd sample	mean		
EO	4,49	3,39	3,94	5,02 (127)	2,44 (62)
TH	1,95	2,93	2,44	2,55 (104)	2,78 (117)
AN	2,87	2,81	2,84	3,26 (115)	4,63 (163)
SL	5,28	1,97	3,63	2,87 (79)	2,43 (67)
KT	3,42	3,30	3,36	3,84 (114)	2,74 (82)
JJ	4,78	2,97	3,88	3,29 (85)	2,49 (63)
MJ	2,37	3,33	2,85	5,37 (188)	5,08 (178)
	3,59	2,96	3,28 ± 0,32	3,74	3,23

conjugated bile acids are more efficient solubilizers for cholesterol than are the corresponding taurine-conjugated bile acids. Therefore, the increase of the ratio G/T may counteract the effect of the decrease of the ratio Di/Tri on the solubility of cholesterol to some extent. However, in human bile, the solubility of cholesterol, probably, is determined more by the lecithin than by the individual bile acids; further, it is not known how cholestyramine may affect biliary components not determined in the present study. Thus, an absolute prediction of the effect of cholestyramine on the solubility of cholesterol in human bile will require more data than those available at present.

We are not aware of direct observations of the influence of cholestyramine treatment on cholelithiasis in man.

In young hamsters reared on diets capable of producing gallstones in this species, addition of cholestyramine (3%) to the diet has been found to lessen the tendency to formation of cholesterol gallstones and to increase the tendency to formation of amorphous pigmented gallstones (7, 8).

In guinea pigs, receiving a diet causing drastic weight reduction, addition of cholestyramine (1%) to the diet has been found to produce decrease of the ratio between bile acids and cholesterol in the bladder bile, and appearance of a few small gallstones containing about 50% cholesterol (9).

Summary

Seven healthy young volunteers received daily doses of cholestyramine (ca. 0.4 g „Cuemid" per kg body weight) through two consecutive periods of 3 weeks.

Duodenal bile was collected, after injection of cholecystokinin, twice before and 3 and 6 weeks after beginning of the treatment. The bile samples were analyzed with respect to pH, dry matter, cholesterol, lipid-soluble phosphorus, glycocholic acid, glycochenodeoxycholic acid, glycodeoxycholic acid, taurocholic acid and taurochenodeoxycholic plus taurodeoxycholic acids. Simultaneously with the collection of bile, blood samples were taken for determination of serum total cholesterol.

Compared with the respective mean values before beginning of the treatment, the predominant changes were as follows:

Serum total cholesterol decreased.

In the bile, the molar ratio between dihydroxycholanoic acids, and trihydroxycholanoic acids decreased markedly, and the molar ratio between glycine-conjugation and taurine-

conjugation increased. These changes were due to drastic increase of the molar percentage of glycocholic acid and more or less pronounced decreases of the molar percentages of the other bile acids in the total bile acids. The mean values of the molar ratios between total bile acids and cholesterol and between lipid-soluble phosphorus and cholesterol were slightly to moderately decreased.

Thus, the results have not provided evidence for an increased solubility of cholesterol in the bile as a consequence of cholestyramine treatment, but rather point in the opposite direction, although further data are necessary before a decisive conclusion can be reached.

Zusammenfassung

Sieben gesunde junge Versuchspersonen erhielten tägliche Gaben von Cholestyramin (ungef. 0.4 g „Cuemid" pro kg. Körpergewicht) während zwei aufeinander folgenden Perioden von je drei Wochen.

Zweimal vor, und 3 und 6 Wochen nach dem Anfang der Dosierung wurde Duodenal-Galle, nach Injektion von Cholecystokinin, aufgesammelt.

Die Gallen wurden auf pH, Trockensubstanz, Cholesterin, Lipid-Phosphor, Glycocholsäure, Glycochenodesoxycholsäure, Glycodesoxycholsäure, Taurocholsäure und Taurochenodesoxycholsäure plus Taurodesoxycholsäure analysiert.

Gleichzeitig mit der Aufsammlung von Duodenal-Galle wurden Blutproben für Serum-Cholesterin-Bestimmung entnommen.

Die vorherrschenden Veränderungen waren, im Vergleich mit den bezüglichen Mittelwerten vor der Dosierung, die folgenden:

Mehr oder weniger ausgeprägte Abnahme des Gesamt-Cholesterins im Serum.

Markierte Abnahme des molaren Verhältnisses zwischen Dihydroxycholansäuren und Trihydroxycholansäuren, Zunahme des molaren Verhältnisses zwischen Glycin-Konjugation und Taurin-Konjugation. Diese Veränderungen waren auf reichliche Erhöhung des prozentualen Anteils der Glycocholsäure und mehr oder weniger ausgeprägte Erniedrigung der prozentualen Anteile der anderen Gallensäuren in den Gesamt-Gallensäuren zurückzuführen. Die Mittelwerte der Verhältnisse zwischen Gesamt-Gallensäuren und Cholesterin, und zwischen Lipid-Phosphor und Cholesterin waren leicht bis mäßig erniedrigt.

Die Versuche deuten somit nicht darauf, daß die Behandlung mit Cholestyramin eine Erhöhung der Löslichkeit des Cholesterins in der Galle herbeigeführt hat. Um den Einfluß der Behandlung auf die Lösbarkeit des Cholesterins endgültig beurteilen zu können sind weitere Daten erforderlich.

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Authors' address:
Prof. Dr. H. Dam et al.
Østervoldgade 10L II, DK-1350 Copenhagen K (Denmark)