New Method for the Determination of Bile Acid Turnover
Using $^{75}$Se-Homocholic Acid Taurine

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Abstract. The introduction of $^{75}$Se-homocholic acid taurine ($^{75}$SeHCAT) greatly facilitates the investigation of diarrhoea of unknown origin. By using gamma-labelled bile acids, daily faecal bile acid loss can be measured in total collected stools, thus circumventing laborious mixing and sampling. The $^{75}$SeHCAT method proved to be reliable for the determination of bile acid turnover, giving results identical to the established turnover method using $^{14}$C-taurocholic acid. The new method however, is simpler and faster.

Introduction

Bile acids (dihydroxy bile acids in particular) are known to decrease reabsorption of water in the colon. Therefore in the analysis of diarrhoea, estimation of bile acid loss from the enterohepatic circulation plays an important role. Chemical quantitation of bile acid concentration in faeces is cumbersome and prone to errors. The introduction of $^{14}$C-taurocholate as a bile acid marker (Lindstedt 1957) was a major step forward, though the method is tedious and time-consuming. With the recent introduction of a gamma-labelled bile acid derivative (see Fig. 1 for structural formulas), a fast and reliable method for determination of faecal bile acid loss has become available (Boyd 1981). The reliability and application of this new method for measuring bile acid turnover is shown by direct comparison with the established method using $^{14}$C-TCA.

Materials and Methods

Turnover of $^{14}$C-taurocholate was studied according to the method of Lindstedt (1957). Stools were collected for 5 days after the administration of about 200 KBq ($5\mu$Ci) $^{14}$C-taurocholate ($^{14}$C-TCA) (specific activity about 2 GBq/mmoll) in a 200-ml liquid test meal containing: 12 g glucose, 12 g maize oil and 21 g skimmed milk.

One gram samples of homogenized 24-h stool collections were precisely weighed and combusted in a tube-oven. Carbon dioxide evolved was trapped in phenethylamine, the radioactivity of an aliquot of which was counted in a liquid scintillation counter (variation coefficient for duplicate determinations was 3.5%).

Appropriate standards were included to check the efficiency of combustion and counting. Daily excretion is expressed as the fraction of the administered dose. Elimination of bile acids from a pool follows first order kinetics; turnover is expressed as half-time (in days) of elimination of the administered dose of $^{14}$C-taurocholate (Lindstedt 1957). For $^{75}$Se-homocholic acid taurine a similar procedure was followed; after administration of 370 KBq ($10\mu$Ci) $^{75}$SeHCAT (specific activity 4.81 GBq/mmoll) (Amersham Radiochemical Centre; We appreciated very much receiving this compound as a gift from Dr. J. Midgley, Amersham Radiochemical Centre, item code nr. SCQ 3415) in the same liquid standard meal, stools were collected for 5 days. Entire 24-h portions were counted for $^{75}$Se-activity with a collimated 2-inch NaI crystal in a selected standard geometry. Effect of faecal weight under these counting conditions was negligible: for the range 50–850 g faeces the variation coefficient was 2.2%.

Appropriate standards were included to assure reproducibility of measurements. Variation coefficient of measurements was be-
Results

Daily excretion of both tracers, expressed as percentage of the administered dose showed an excellent correlation ($P < 0.01$, paired $t$-test). The regression line was as follows: ($^{75}$SeHCAT) = 1.0 ($^{14}$C-TCA) + 0.2; $r = 0.97$ (Fig. 3). Both tracers exhibited identical physiological behaviour as far as resorption and excretion phenomena are concerned. For 16 patients half-times of bile acid elimination were compared (Fig. 4). No significant deviation from the line of identity was found ($P > 0.2$, paired $t$-test). The regression line was: ($^{75}$SeHCAT) = 0.86 ($^{14}$C-TCA) + 0.54; $r = 0.93$.

Discussion

In the investigation of the cause of diarrhoea, bile acid loss from the enterohepatic circulation is a factor of major importance. Initially, determination of bile acids in faeces was hampered by the lack of adequate techniques. A breakthrough was the introduction of $^{14}$C-labelled bile acids by Lindstedt (1957). Although the results with this method using $^{14}$C-TCA are excellent, it is laborious and special technical facilities are needed. This has prevented its widespread use in gastroenterology. The introduction of commercially available $^{75}$SeHCAT overcomes