Effect of Thiazide Preparations on the Pancreas

The use of chlorothiazide has been widely extended since it was introduced in 1958 into practice as a diuretic and hypotensive preparation. Its primary effect is based on the inhibition of renal tubular sodium and chloride absorption which leads to the secondary effect of a raised water excretion. The advantage of chlorothiazide is that (1) if administered orally, it has the same effect as parenterally administered mercury preparations, (2) that even on long-term use it does not lose its effectiveness and (3) only very rarely it has a toxic effect. An undesirable effect observed after the administration of chlorothiazide is an impaired electrolyte balance, more frequently the consequence of an excessive therapeutic response than of toxic action. After its administration exfoliative dermatitis, purpura and jaundice were observed.

Hydrochlorothiazide, the dihydroderivative of chlorothiazide is ten times more effective than chlorothiazide. As a side-effect after two to three weeks treatment with hydrochlorothiazide pain in the epigastrium was observed and a raised uric acid blood level (G. Schwarz et al: J. amer. med. Ass. 170: 2057 [1963]). A very rare complication of long-term administration of chlorothiazide preparations is acute pancreatitis. Four cases of complications resulting from chlorothiazide treatment were described (Johnson and Cornish: J. amer. med. Ass. 170: 2054 [1959]) and one case as a complication after hydrochlorothiazide (Vykydal, J.: Cs. Gastroent. Výz. 20: 136 [1966]). All five patients were above 50 years, incl. three aged 78-81 years; all took chlorothiazide, 0.5–1.0 g, or 75 mg hydrochlorothiazide. None of the patients suffered from cholelithiasis and there was not an alcohol addict among them. In the course of treatment they developed an acute abdominal condition with epigastric pain, nausea and vomiting. One of Johnson’s patients suffered moreover from polyuria, polydipsia and a raised blood sugar level. Vykydal’s patient developed diabetes and died in a diabetic coma.

The development of impaired carbohydrate metabolism, even in the absence of concomitant pancreatitis, was also observed in rare instances during treatment with thiazide preparations. Kučera (Cas. lék. ces. 102: 1053 [1963]) described in four obese patients aged 57-64 years, treated for prolonged periods on account of cardiac insufficiency with chlorothiazide, the development of polyuria, polydipsia and glycosuria. The metabolic disorder manifested itself 2-5 weeks after the onset of treatment, in three instances it was severe, in one mild. The condition did not become normal even after chlorothiazide therapy was discontinued and the dietary carbohydrate intake was reduced. All patients had to be given relatively large amounts of insulin. Only in one patient the disorder improved gradually and insulin could be omitted, and later he could eat a free diet; the blood sugar curve also returned to normal. In the remaining three patients the disorder was permanent and insulin had to be administered permanently.

According to the experience of Saudan et al. (Praxis 50: 45 [1961]) there is no difference in the diabetogenic effect of chlorothiazide and hydrochlorothiazide. The size of the dose is immaterial. In rare instances deterioration of diabetes was observed in the course of treatment with thiazide...
preparations (Goldner et al.: New Engl. J. Med. 262: 403 [1960]). In most cases described, the
disorder of carbohydrate metabolism was temporary. Only in three of Kucera’s patients was it
permanent.
The cause of the development of acute pancreatitis and disorders
of the carbohydrate metabolism in the course of thiazide therapy is
so far not known. K. Herfort, Prague