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Use of Unithiol for Reducing Radiation Hazard of Renal Scintigraphy with Chlormerodrin ^{203}Hg

I. Estimation of the Urinary Excretion of ^{203}Hg

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The authors presented a method for reducing renal irradiation during ^{203}Hg Chlormerodrin scintigraphy. Renal excretion of ^{203}Hg was speeded up by Unithiol (U.S.S.R.) which was administered immediately after scintigraphy. The investigations concerned 9 patients who received i.m. 1 ampoule of Unithiol every 12 hours for 3 days. The activity of urine and per cent of excreted ^{203}Hg were measured. An average increase by 34.8% in urinary ^{203}Hg excretion was found after Unithiol administration in comparison to the control group of persons in whom the preparation was not applied.

The scintigraphic examination of the kidneys is generally performed with the use of Chlormerodrin, a mercury compound of diuretic action. The amount of mercury in Chlormerodrin doses used in renal scintigraphy is insignificant – 20 times smaller than that contained in its diuretic dose [14]. The harmful effect of the preparation labelled with mercury ^{203}Hg consists in renal irradiation due to its high energy of beta radiation – 208 KeV, and to its effective half life amounting to about 30 days. The kidneys receive a radiation dose of 23–57 rads [2, 7, 13]. Despite its high radiation properties, Chlormerodrin ^{203}Hg is still used in renal radiodiagnostics because it permits to make the best and most distinct renal scintigrams [3, 7, 13], and it was therefore recommended for general use by the United Nations Atomic Energy Commission [3]. Chlormerodrin ^{197}Hg used in certain centres of radiodiagnostics, produces – in comparison to Chlormerodrin ^{203}Hg – considerably lower gamma energy of the order of 77 KeV ray has a short $T_{1/2}$ amounting to 2.7 days. It is therefore applied less frequently especially when the isotope laboratories are a long way away from the production and distribution centres – in spite of the fact that the dose of ionizing radiation adsorbed by the kidneys after administration of Chlormerodrin ^{197}Hg is insignificant and averages 4.5–6.5 rads [2].

To reduce the degree of harmful radiation to which the patients are exposed during renal scintigraphy, the investigators of various countries have made attempts at elaborating a method of speeding up renal excretion of radioactive mercury. To this effect chelating agents were used, such as BAL, cysteamine, penicillamine thioglucolates, etc. These attempts, however, have not yielded the desired results [4, 5, 8, 9, 11].

In recent years reports have been published concerning Unithiol, a preparation used in industrial mercury poisonings [1, 5, 6, 10, 12]. It is produced in the U.S.S.R. in the form of ampoules containing an aqueous solution of a sodium salt of 2,3-dimercaptosulfopropanol acid.

BAL:

$$\begin{array}{l} CH_2-OH \\ | \\ CH-SH \\ | \\ CH_2-SH \end{array}$$

Unithiol:

$$\begin{array}{l} CH_2-SO_3Na \\ | \\ CH-SH \\ | \\ CH_2-SH \end{array}$$

The chemical structure of Unithiol resembles that of the generally known BAL, and – in a similar way – it speeds up the elimination of mercury from the body [5], but it is superior to BAL in many respects. The differences can be seen in Table 1.

Table 1

Differences in action between BAL and Unithiol

Properties of preparations	BAL	Unithiol
DL_{50} (for rats)	100 mg/kg	1000 mg/kg (10)
Tolerance dose	no data	300 mg/kg
Solubility in water	poor	very good
Recommended route of administration	intramuscular	intramuscular, subcutaneous, inhalation
Recommended dosage for one course of treatment for man	about 4300 mg	3600 mg

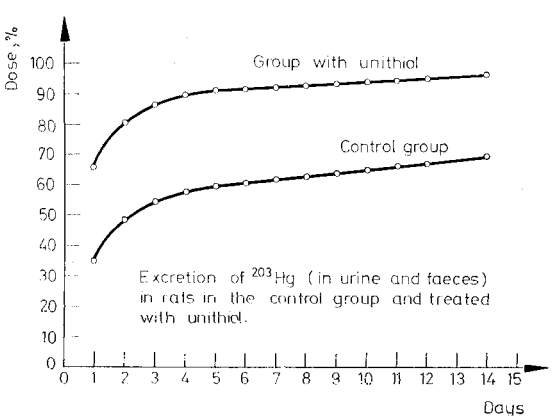

Fig. 1. Excretion of ^{203}Hg (in urine and faeces) in rats in the control group and in those treated with Unithiol

It was also found that the therapeutic doses of Unithiol as applied in man do not cause side effects, and that its toxic dose is 20 times higher than its therapeutic dose. 80% of the preparation is excreted in urine at 5–6 hours following its administration [10].

The above-mentioned advantages of Unithiol have been verified by the authors in experimental studies on rats. It became evident that Unithiol increased excretion of organic mercury compounds by 30%. This effect was already noted in the second 24-hour period of the experiment (Fig. 1). Mercury deposits in the kidneys of the animals which were given Unithiol were 13–21 times lower than in those of the control animals. The results of these investigations have been published in [13].

On the basis of the above observations, Unithiol was applied in patients in whom the scintigraphic kidney examinations were performed, as it became possible to lessen markedly renal irradiation in cases where the administration of Chlormerodrin ^{203}Hg was necessary.

Material and methods

The investigations involved 21 patients treated at the Department of Urology of the Medical Academy in Łódź, in whom renal scintigraphy had to be performed for diagnostic purposes. Exclusively patients with complete renal efficiency, as shown by the laboratory investigations of the blood (creatinine, urea and electrolyte levels, alkaline reserve) and by urography, were selected.

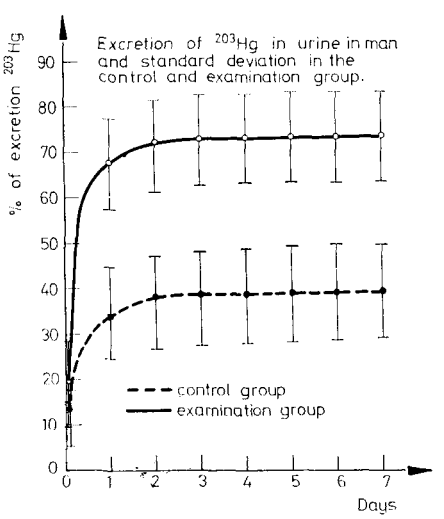

Fig. 2. Excretion of ^{203}Hg in urine in man and standard deviation in the control and the test group

Table 2

Total percentage of mercury ^{203}Hg excreted in urine after 7 days by patients from the test and control groups (the numbers of patients and of case histories are given next to the initials)

Chlormerodrin ^{203}Hg + Unithiol			Chlormerodrin ^{203}Hg	
Patient	Excreted mercury, %	Difference between excreted doses in relation to average values from group II, %	Patient	Excreted mercury, %
R.E.—3 4070/72	52.74	13.01	A.W.—9 5854/71	49.86
G.J.—4 5422/72	63.93	24.20	Ch.A.—10 7544/72	37.66
K.L.—5 5373/72	84.00	44.27	B.R.—12 3387/71	38.18
K.S.—6 5565/72	77.53	37.70	Z.E.—15 6880/72	39.02
M.A.—7 5380/72	73.85	34.13	R.A.—17 6721/72	25.37
Z.Z.—13 5675/72	81.81	42.08	Z.S.—18 6851/72	58.90
O.W.—14 5617/72	94.54	54.81	M.E.—20 5901/71	20.70
J.W.—16 6845/72	78.42	38.69	P.Z.—21 7805/71	22.49
G.M.—26 5494/72	63.86	23.13	B.W.—23 2107/71	62.18
			M.H.—25 5807/71	30.67
			S.K.—28 5265/72	24.21
			K.M.—29 3805/72	67.55
Average value	74.52	34.79	Average value	39.73

The subjects were divided into 2 groups:

I. The test group contained 9 patients who were given 5 ml Unithiol i.m. every 12 hours for 3 days after renal scintigraphy performed with Chlormerodrin ^{203}Hg.

II. The control group consisted of 12 patients who were not given Unithiol, but to whom Chlormerodrin ^{203}Hg was previously administered.

In both groups of patients urinary excretion of ^{203}Hg was estimated.

All the patients received intravenously at a given time 0.5 ml of Chlormerodrin ^{203}Hg of the activity of about 150 μCi contained in a "Record" syringe (used for inoculations with the BCG vaccine). For the investigations "Amersham" Chlormerodrin ^{203}Hg (England) of specific activity of 0.53 mCi/mg was chosen. Before its injection into the antecubital vein, the radionuclide activity in the syringe was

measured in c.p.m. in a special chamber of the authors' own invention. The chamber was placed above an "USB-2" scintillation meter of Polish make and connected to a "PT-67a" computer. After the injection of the radionuclide, the activity of the syringe was determined again. The difference between both these measurements stood for the activity of administered Chlormerodrin ^{203}Hg. For the estimation of the quantity and rate of ^{203}Hg excretion, the activity of urine was determined in beakers of 100 ml capacity in constant geometry. The measurements of the 24-hour collections of urine were made for 7 days by means of the same calculating outfit. On the examination day the activity of urine was also determined at 1 and 2 hours following radionuclide administration. The values obtained were compared with an experimental pattern which permitted to relate the activity measured in the syringe to the activity of urine in the beaker. The data obtained were calculated in per cent of excreted mercury and are presented in Table 2 and Fig. 2.

Results

Table 2 presents the quantities of excreted mercury ^{203}Hg in urine after administration of Chlormerodrin ^{203}Hg to the patients of the control group and of the test group (Chlormerodrin ^{203}Hg + Unithiol). It shows a rise in excreted mercury ^{203}Hg in each patient of the test group in comparison with average excretion of mercury in the control group.

The highest excretion of mercury was observed in patient O. W. (No. 14) whose urine contained 54.81 % more of mercury than the average for the control group, and the least difference of mercury urinary content amounting only to 13.01 % of the dose, was found in patient R. E. (No. 3).

The rate and quantity of urinary mercury ^{203}Hg excretion are presented in Figure 2. The curves rise gently and nearly asymptotically a straight line parallel to axis X – the curve of the control group to y = 39.7 %, and the curve of the test group to y = 74.5 %.

Figure 2 shows the curves of mercury ^{203}Hg excretion with errors calculated by the Student–Fischer method, the reliance level being 0.95. It was found that the differences between both curves are real, i.e. that the results obtained are not accidental, and that they are subsequent to the action of Unithiol.

Discussion

On the basis of the animal experimental studies and of the literature concerning the administration of Unithiol in mercury poisonings, an attempt has been made to check the influence of this preparation on the speeding up of the excretion of mercury (Chlormerodrin ^{203}Hg used in renal scintigraphy). The investigations have proved that Unithiol increases by 34.8 % the urinary excretion of ^{203}Hg

in man in comparison with the average values obtained in the control group. The results are compatible with the investigations performed in animals by M. Ogiński [12] who showed that also in rats the decrease of renal mercury content amounted to 30%.

It became evident that Unithiol is the only agent from among many of hitherto examined compounds which increases noticeably the excretion of Chlormerodrin ^{203}Hg introduced into the body. It reduces renal radiation to which the patient is exposed during renal scintigraphy.

Unithiol makes possible a repetition of renal scintigraphy in the same patient after a short period of time. The preparation is well tolerated by the patients and produces no side effects.

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