Protection by Estrogenic Hormone against Nephrotoxicity Induced by Organic Mercury

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Summary. An organic mercurial compound, MEMC has been studied for its toxic effect on the renal tubuli in male rats. In view of the slight degree of the renal failure in subacute MEMC poisoning, for its demonstration urinary transaminase activity was chosen. The increase of GOT-GPT were accompanied by the presence of large numbers of disintegrated tubular epithel cells in urine. These phenomena could be protected by treatment with estrogenic hormone, whereas the acute toxicity could not.

Organomercurials are widely used as fungicides (Swensson, 1963). Depending on the radicals they include, they might cause characteristic central nervous system and renal damage: the methyl mercury compounds cause severe poisoning, contaminating the environment (Bidstrup, 1964; Friberg et al., 1971; Takeuchi et al., 1962; Barnes and Magos, 1958).

Observation carried at our laboratorium have shown that one of these compounds, methoxy-ethyl-mercury-chloride (MEMC) causes characteristic signs in the central nervous system, and affect conditioned reflex activity of rats (Lehotzky et al., 1968, 1972). In addition the toxicity of MEMC could not be protected either by dicaptol (BAL) nor by D-penicillamine and Rongalite-C (sodium-formaldehyde-sulphoxilate), while these antidotes proved to be effective against poisoning caused by HgCl₂ and some other organic mercury compounds (Swensson, 1967; Bordás and Lehotzky, 1968).

Renal tubular necrosis caused by HgCl₂ is accompanied by the increase of urinary glutamic-oxalacetic transaminase (UGOT) activity (Davies and Kennedy, 1967; Prescott and Ansari, 1969). According to the data of Harber (1965) and Selye (1944, 1970) the renal failure induced by HgCl₂ could be protected by estrogenic hormone on male rats.

In our present experiments we estimated the toxic effect on the renal tubuli of MEMC and possibility of its protection by estrogenic hormone.
We have applied the method suggested by Rosalki (1959), in addition with other tests (Balázs et al., 1962; Sharrat and Frazer, 1963; Rodin and Crowson, 1962) for estimating the slight tubular damage.

Methods

Compounds. Methoxy-ethyl-mercury-chloride (MEMC) in solution 1%, intraperitoneally (Berk Ltd., London). Estron acetate (10000 IE; 1 mg) intra musculare.

A. Acute Experiments

A total of 120 male rats weighing 180—200 g were used to estimate the acute i.p. LD_{50} according to the log probit method of Miller and Tainter; later estimates on influence of
1. 1000 and 2000 IE estrogenic hormone taken once simultaneously with MEMC;
2. 500 IE/daily for 4 days administered prior to MEMC on the value of acute LD_{50}.

B. Subacute Experiments

A total of 188 male rats, weighing 150—180 g were used, during the experiments they were fed a standard synthetic diet and allowed free access to water.

They were divided into 4 groups:

Group 1. 72 rats had been treated with 2 mg/kg/daily MEMC 6 times weekly, for 6 weeks. The dose corresponds to one fifth of the acute i.p. LD_{50} which was 9.4 ± 0.9 mg/kg.

Group 2. 60 rats were given 0.2 mg/kg/daily MEMC 6 times weekly, over 12 weeks.

Group 3. 28 rats were given 0.2 mg/kg/daily MEMC 6 times weekly, and 2000 IE estrogenic hormone once a week, for 10 weeks.

Group 4. 28 rats were given 0.2 mg/kg/daily MEMC, 6 times weekly, for 10 weeks (control of group 3).

Before and during the treatment the following investigations were performed once a week.

a) GOT and GPT were estimated by the method of Reitman and Frankel (1957) in urine collected for 16 hrs.

b) Epithelial cells counts in the unstained urinary sediment, using a Buerker-chamber.

c) Concentration test, by refractometric measurement of the specific gravity of urine collected for 6 hrs.

d) Dilution test, by measuring the specific gravity every hour after the administration of 2 ml top water per 100 g body weight through a stomach tube.

e) Estimation of GOT and GPT activity of the blood serum, being obtained by heart puncture.

During the experiments the animals' body weight were controlled, at the end they were killed and their parenchymatous organs were submitted to histological study.

Results

A. Acute Experiments

1. 1000 and 2000 IE estrogenic hormone had no effect on the acute toxicity, the LD_{50} value remained unchanged.