Bull. Environm. Contam. Toxicol. 27, 55-58 (1981)

Urinary Enzymes as Indicators of Kidney Damage by Methylmercury Exposure

Y. Tsuzuki

Department of Legal Medicine, Aichi Medical University, Nagakute, Aichi-gun, Aichi 480-11, Japan

Methylmercury (MeHg) is considered a hazardous environmental pollutant because this compound damages the nervous system (Okuda et al. 1978). In addition to this action, many investigations have reported histopathological changes in fatty degeneration and necrosis of the proximal convoluted tubule of the kidney after exposure to MeHg (KLEIN et al. 1973; CHANG & SPRECHER 1976). MAGOS (1979) described mercury concentrations in kidney greater than in other tissues after chronic exposure to MeHg.

STROO & HOOK (1977) reported that chronic exposure to MeHg caused a decrease in the excretion of β-galactosidase and acid phosphatase in rats, but did not affect the excretion of alkaline phosphatase.

The object of this work was to study the nephrotoxic effects of MeHg exposure in rats. To elucidate the mechanisms for the development of renal damage, the activities of alkaline phosphatase, lactate dehydrogenase, muramidase, glutamate dehydrogenase, and acid phosphatase were determined in kidney and urine.

MATERIALS AND METHODS

Wistar male rats weighing 200-220 g were used. Animals were provided food and ad libitum. Rats were orally administered 2 mg/kg of MeHg for 11 days. Control rats were administered 2 mg/kg physiological saline solution. All assays were conducted at 30°C under optimal condition in a automatic recording spectrophotometer with a constant temperature cell housing. Activities of alkaline phosphatase, lactate dehydrogenase, muramidase, glutamate dehydrogenase, and acid phosphatase in the kidney and urine were determined according to the methods of WRIGHT et al. (1972); LEATHWOOD et al.(1972); PLUMMER & NGAHA (1977); and WRIGHT et al. (1972), respectively. Total mercury in the kidney was measured using the method of DENITZ et al. (1973).

RESULTS

Table 1 gives the changes in the amount of mercury and enzymatic activities in the kidneys of rats following the administration of 2 mg/kg of MeHg. The amount of mercury in the kidneys exposed to MeHg was found to be 62 ± 9 μg/g wet weight

0007-4861/81/0027-0055 $01.00

of tissue. The activities of alkaline phosphatase, lactate dehydrogenase, and muramidase in the kidneys were depressed by MeHg, while the activity of acid phosphatase was considerably increased. The activity of kidney glutamate dehydrogenase was unchanged following MeHg exposure.

The changes in enzymatic activities in the urine of rats orally administered 2 mg/kg of MeHg are shown in Table 2. MeHg exposure increased the activities of alkaline phosphatase, lactate dehydrogenase, muramidase, and glutamate dehydrogenase in the urine by 21, 13, 14, and 35 %, respectively, while the activity of acid phosphatase in urine was decreased.

Table 1. Changes in Amount of Mercury and Enzymatic Activities in Rat Kidney Foiiowing the Administration of 2 mg/kg Methylmercury

Parameter	Control	Treated
Mercury (μg/g)	0.15 ± 0.02	62 ± 9
Alkaline phosphatase (μmoles/min/g)	4.7 ± 0.9	4.0 ± 0.6 (85 %)
Lactate dehydrogenase (μmoles/min/g)	70 ± 7	53 ± 4 (75 %)
Muramidase (μg/min/g)	17 ± 3	14 ± 2 (85 %)
Glutamate dehydrogenase (μmoles/min/g)	1.4 ± 0.3	1.4 ± 0.2 (99 %)
Acid phosphatase (μmoles/min/g)	3.1 ± 0.4	4.5 ± 0.7 (145 %)

The results are expressed as the mean of six ± S. D.

DISCUSSION

The concentration of Hg in the kidney (62 ± 9 μg/g) was similar to that reported by KLEIN et al. (1973) under similar conditions.

Recently, MAGOS (1979) reported that the concentration of mercury in the kidneys of rats dosed orally with 8 mg/kg of MeHg for 5 days was found to be 84 ± 2 μg/g of tissue.

The decrease in kidney lactate dehydrogenase and muramidase activities (Table 1) corresponded in time with the increased excretion of these enzymes into the urine (Table 2). The lower activity of kidney alkaline phosphatase after MeHg exposure

could be explained on the basis of the observed loss of the tubular borders. The brush borders are the richest sourse of alkaline phosphatase in the kidney. The loss of lactate dehydrogenase activity in the kidney have been reported following renal damage by MeHg exposure (STROO & HOOK 1977). However, the decrease in kidney alkaline phosphatase activity to 85 % of the control value did not lead to an increased excretion of this enzyme into the urine, while a comparable decrease in the kidney

Table 2. Changes in Enzymatic Activities in the Urine of Rats Orally Administered with 2 mg/kg of Methylmercury

Parameter	Control	Treated
Alkaline phosphatase (nmoles/min excreated/h)	17.0 ± 9.5	20.7 ± 9.9 (120 %)
Lactate dehydrogenase (nmoles/min excreated/h)	5.7 ± 1.0	6.4 ± 1.1 (110 %)
Muramidase (µg/min excreted/h)	1.10 ± 0.06	1.25 ± 0.10 (110 %)
Glutamate dehydrogenase (nmoles/min excreted/h)	1.00 ± 0.04	1.35 ± 0.10 (140 %)
Acid phosphatase (nmoles/min excreted/h)	15.5 ± 7.5	12.7 ± 4.3 (81 %)

Six rats were used in the experiment and the results are given as the mean value ± S. D.

lactate dehydrogenase activity to 75 % of the control value occured at the same time as an increase in the urinary lactate dehydrogenase activity occured. An explanation for the low excretion of alkaline phosphatase could be the presence of a non-dialysable phosphatase inhibitor complex in the urine (WILKINSON 1968).

As described in Table 1, the activity of kidney glutamate dehydrogenase was unchanged following MeHg exposure in spite of some increase in the urinary glutamate dehydrogenase activity (Table 2). This could be explained on the basis of a small loss of this enzyme from the kidney into the urine indicating the occurrence of mitochondria damage following by a turnover of glutamate dehydrogenase to maintain the overall activity in the kidney (PLUMMER & NGAHA 1977).

As described above, the changes in the enzyme activity in the kidney was extremely small, while those in the urine were

quite considerable. Urine enzyme measurements would seem therefore to be more useful in detecting kidney damage. The increase in lactate dehydrogenase activity in the urine (Table 2) suggests an early membrane permeability change in the cells of the kidney. The lysosomal enzyme was affected by the MeHg and possibly stabilized (STROO & HOOK 1977). Of all the enzymes examined, the assay of urinary lactate dehydrogenase provides the most sensitive means for detecting renal damage by MeHg exposure.

From these results, the data suggests that MeHg at relatively low exposure alters lysosomal and mitochondria function. It also suggests that MeHg exposure had little protective effect.

REFERENCES

CHANG, L. W., and J. A. SPRECHER: Environ. Res. 11, 392(1976).

DENITZ, F. D., J. L. SELL, D. BRISTOL: J. Assoc. Off. Anal. Chem. 56, 378(1973).

KLEIN, R., S. P. HERMAN, B. C. BULLOCK, F. A. TALLEY: Arch. Pathol. 96, 83(1973).

LEATHWOOD, P. D., M. K. GILFORD, D. T. PLUMMER: Enzymologia 42, 285(1972).

MAGOS, L.: Factors affecting the neurotoxicity of mercury and mercurials, eds. L. MANZO, N. LERY, Y. LACASSE, and L. ROCHE, Oxford·New York·Toronto·Sydney·Paris·Frankfurt: Pergamon. p. 17(1979).

OKUDA, J., Y. TSUZUKI, T. YAMADA: Jap. J. Legal Med. 32, 51 (1978).

PLUMMER, D. T., and O. NGAHA: Urinary enzymes as an index of kidney damage by toxic compounds, ed. J. -P. FILLASTRE, New York·Paris·Barcelona·Milan: Masson. p. 175(1977).

STROO, W. E., and J. B. HOOK: Toxicol. Appl. Pharmacol. 42, 399(1977).

WILKINSON, L. H.: Enzymes in urine and kidney, ed. U. C. DUBACH, Berne: Hans Huber. p. 209(1968).

WRIGHT, P. J., P.D. LEATHWOOD, D. T. PLUMMER: Enzymologia 42, 317(1972).

WRIGHT, P. J., P. D. LEATHWOOD, D. T. PLUMMER: Enzymologia 42, 459(1972).

Accepted April 14, 1981