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SIMULTANEOUS EFFECT OF CADMIUM AND MERCURY ON SOME BIOCHEMICAL PARAMETERS OF KIDNEY FUNCTION IN MALE RATS

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ABSTRACT

The present investigation has been undertaken to evaluate the alterations in kidney functions of male rats exposed to cadmium chloride (300 mg/L) and mercury chloride (40 mg/L) either alone or in combination in drinking water for 4 weeks. Results indicated a decrease in the body weight gain and an increase in kidney relative weight in all the treated rats as compared to control rats. We noted also an increase in serum creatinine concentration in cadmium group and no changes was signalized in the others treated groups, while serum urea concentration was increased in cadmium and combined treated rats and no change was observed in mercury treated rats. The comparison of combined treatment effect to individual treatment effect revealed that this effect is not additive.

Key words: Cadmium, Mercury, Kidney, Rat.

INTRODUCTION

Heavy metals have become one of toxic substances found in our environment[1]. In all heavy metals, cadmium and mercury are considered among the most important toxic metals. Cadmium is present in the environment as a result of industrial and agricultural practices[2]. Cadmium is listed among the hazardous chemicals because it can enter the food chain[3] and it has a long biological half-life (about 30 years) in humans[4,5]. Mercury (Hg) is a ubiquitous toxic metal that enters the environment as a result of natural and anthropogenic activities such as fossil fuel combustion, mining, volcanic eruption, dissolution and volatilization from rocks, soils and sediment, incineration of waste and industrial discharge[6]. Cadmium and mercury have a very strong ability to accumulate in the living organisms especially in the kidneys[7]. Several studies done in the past show that these two metals cause nephrotoxicity[8,9].

In real life, the human population is exposed to complex mixtures of contaminants. So, the experimental work with combination of contaminants is more relevant on the human exposure than the work with a single substance. However, for cadmium and mercury there is, to our knowledge, no information regarding the effect of simultaneous intoxication with these two metals on kidney functions. Therefore, the purpose of this experiment is the study of the combined effect of cadmium and mercury on kidney functions in the rat.

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EXPERIMENTAL

Materials and methods

Animals and treatment

Male Wistar rats (139 ± 13 g) purchased from Siphat (Ben arous, Tunisia) were used in this study. Animals were housed individually and food and water were provided ad libitum. After a period of at later 1 week acclimatizing, animals were divided into four groups:

(i) Control group (4 rats): Animals consumed distilled water as drinking water.

(ii) Cadmium group (4 rats): Animals consumed a solution of cadmium chloride (300 mg/L) as drinking water.

(iii) Mercury group (4 rats): Animals consumed a solution of mercury chloride (40 mg/L) as drinking water.

(iv) Cadmium-mercury group (4 rats): Animals consumed a solution of cadmium chloride (300 mg/L) and mercury chloride (40 mg/L) as drinking water.

Metal solutions were prepared in distilled water.

After 4 weeks of treatment, rats were weighed and then euthanized with exsanguinations by severing the brachial artery after anaesthetizing with ether. Blood was collected and centrifuged, and the serum was conserved at -80°C. The kidneys were removed quickly from animals, washed in ice-cold physiological saline and weighed.

Serum biochemical parameters

Serum creatinine and urea concentrations were determined by automat (Synchron CX9 PRO Beckman coulter).

Statistics

Data are expressed as means ± SD. The values were analyzed by Mann–Whitney non-parametric test. Differences at $p \leq 0.05$ were considered statistically significant.

RESULTS AND DISCUSSION

The body weight gain was decreased significantly ($p \leq 0.05$) in all the treated groups. In combined group, this parameter was comparable to that in cadmium group and significantly lower ($p \leq 0.05$) than that in mercury group. As shown in Table 1, the absolute kidney weight show a significantly decrease in cadmium group and a significant increase in mercury group, wherease no change was observed in combined metal treated group compared to control group. Compared to the individual treatment, the absolute kidney weight in combined metals group, was comparable to that in mercury group and significantly higher than that in cadmium group. Results presented in Table 1 also indicate that the relatve kidney weight show a significant increase in all the treated rats as compared to control rats. On the other hand, in combined metals group, this parameter was significantly higher than that in individual metal groups.

Renal function was evaluated by measuring serum creatinine and urea concentrations. As shown in Table 1, serum creatinine concentration was increased significantly ($p \leq 0.05$) in cadmium treated group, whereas no change was observed in mercury and combined metal exposed groups compared to control group.

In combined group, serum creatinine concentration was comparable to that in mercury group and significantly lower ($p \leq 0.01$) than that in cadmium group. On the other hand, serum urea concentration was increased in cadmium and combined metal groups, wherease no change was observed in mercury group compared to control group. Serum urea concentration in rats treated with the two metal was comparable to that in cadmium group and significantly highier than that in mercury group.

Our results indicate that the body weight gain of Cd-exposed rats and of Hg-exposed rats is significantly depressed. This is in agreement with previous studies[10,11] showing that these two metals affect growth development in rat. Our results also indicate that the decrease in body weight gain in animals receiving cadmium in combination with mercury was comparable to that observed in cadmium-exposed group and greater than that in mercury-exposed group. This means that the combined effect of cadmium and mercury is not additive.

In the present study, we have observed a significant decrease in kidney absolute weight in rats treated with $CdCl_2$. This is in agreement with previous works[8] showing that cadmium causes an atrophy of kidney. Althought this decrease in absolute weight, the relative weight of kidney show an increase. This may be explained by the decrease in the body weight gain caused by cadmium. In mercury-exposed rats kidney absolute and relative weights were significantly increased. Previous papers have reported alterations in kidney weights of animals exposed to this metal[12-15]. The increase of the kidney size and weight in Hg-exposed rats may be related to structural changes due primarily to an increase in proximal tubule volume[16]. In rats treated wih the two metals in combination, the kidney absolute and relative weights were greeter than those in cadmium-exposed group, wherease they are comparable to those in mercury group. So, we can suggest that the combined effect of these two metal is not additive.

Table 1: Effect of cadmium and mercury alone and in combination on body weight gain, absolute kidney weight, ratio of kidney weight to body weight, and serum creatinine and urea concentrations in male rats

Parameters	Groups			
	Control	Cd	Hg	Cd + Hg
Body weight gain (%)	78 ± 4	29 ± 9*	59 ± 7*	30 ± 2^{*b}
Absolute kidney weight (g)	1.57 ± 0.01	1.42 ± 0.02*	1.90 ± 0.09*	1.80 ± 0.11^{a}
Ratio of kidneys weight to body weight (%)	71.3± 0.7	79.8 ± 3.3*	83.5 ± 2.3*	94.8 ± 2.5^{*a}
Creatinine (U/L)	43.0 ± 0.6	48.0 ± 1.2*	42.0 ± 2.0	42.3 ± 1.4^{a}
Urea (U/L)	73.0 ± 0.3	81.8 ± 3.3*	66.5 ± 4.9	78.5 ± 0.9^{*b}

Data are means ± SE; $^{*}p \leq 0.05$ in comparison to control group; $^{a}p \leq 0.05$ in comparison to cadmium group; $^{b}p \leq 0.05$ in comparison to mercury group.

On the other hand, the levels of urea and creatinine in the serum are tested as indicators for kidney functions. Previous reports have showed that Cd induce an increase in these two markers[17]. In agreement with these studies, our results show in cadmium-exposed group an increase in creatinine and urea concentrations. This means that the kidney function was perturbed under the effect of cadmium. Whoever, in mercury-exposed rats no changes were observed in these two markers. This result may be related to the dose and the duration of the experiment used. In the combined metals treated group, the creatinine concentration was comparable to that in mercury group, and greeter than that in cadmium group, and the urea concentration were intermediate between those in the individual treatments. This means that there is not an additive effect between these two metals on kidney function.

It appears from the above results that there is not an additive effect between Cd an Hg on kidney function. This might due to the competition between the two metals for a single binding site. In fact previous studies[12,18] have showed that both metals inhibit hepatic δ-Aminolevulinate dehydratase (δ-ALA-D): a sulfhydryl-containing enzyme that catalyzes the asymmetric condensation of two δ-aminolevulinic acids (δ-ALA) molecules yielding porphobilinogen, a heme precursor[19]. Consequently, δ-ALA-D inhibition may perturb heme-dependent metabolic pathway[20] and can result in the accumulation of 5-aminolevulinic acid, which has some pro-oxidant activity[21-23]. Nogueira et al.[24] show that the prevailing mechanism for δ-ALA-D inhibition by cadmium and for mercury is likely related to the formation of stable mercaptides with d-ALA-D sulfhydryl groups. This means that there is probably a common point between the mechanisms of actions of these two metals in summary, this study provides added information on the consequences of simultaneous exposure to cadmium and inorganic mercury on the kidney function. From the above results, it is clear that the combined treatment effects are not additive.

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