LETTER TO THE EDITOR

Dose Response Effects of Cadmium on Serum Sialic Acid Alpha-1 Acid Glycoprotein and Perchloric Acid-Soluble Protein Levels in Rats

Key words: Dose dependence—Cadmium—Serum—Sialic Acid—α₁-acid glycoprotein—Rats

Sialic acids are acyl derivatives of D-neuraminic acid which are involved in a variety of surface related vital cell functions of various tissues and occur as components of mucoproteins or lipopolysaccharides. Increased concentration of sialic acid and various sialoglycoconjugates in blood have been reported in malignancy and are considered useful as the biomarkers for staging prognosis and detection of early recurrence of cancer. In our previous studies, increased levels of serum sialic acid or its glycoconjugates were reported in animals intoxicated to certain metals like lead, zinc, mercury or manganese. Similarly, administration of cadmium has earlier been shown to elevate the levels of serum total sialic acid (TSA), perchloric acid (PCA)—soluble sialic acid (PSA), lipid bound sialic acid (LBSA) and free sialic acid (FSA). The purpose of the present study was to determine whether these changes are dose related. The dose dependence of sialic acid containing proteins like α₁-acid glycoprotein (α₁-AG) and PCA-soluble proteins is also studied.

Adult male Charles-Foster rats weighing 410–450 g were housed in a temperature controlled room (22 to 25°C) in groups of four. Staple diet and water were provided ad libitum. One group of rats was treated with saline (1 ml/kg, i.p.) which served as control and four other groups of rats were injected a single intraperitoneal dose of cadmium (II) chloride in saline at 0.5, 1, 2 or 3 gm/kg body weight. Forty-eight hours following injection of the challenge dose, rats were anaesthetized with ether and blood was withdrawn by cardiac puncture. Sera were separated in cold and stored at −20°C till the analysis was performed. TSA, PSA and FSA were estimated by modified thiobarbituric acid (TBA) assay of Skoza and Mohos using N-acetylneuraminic acid as a standard. To estimate TSA, serum samples were digested in sulphuric acid at 80°C (pH 1.6) for 1 h and the liberated sialic acid moieties were estimated by the TBA assay. PSA was estimated by diluting the aliquotes of PCA fractions with distilled water (final acid concentration; 0.05–0.1 N) followed by digestion and sialic acid analysis as described under TSA. PCA fractions were prepared by mixing sera with 1.5
volumes of 1N cold PCA followed by a centrifugation (6000 rpm, 15 min, 4°C) after 10 min. FSA was estimated by directly performing TBA assay on diluted sera without hydrolyzing them at 80°C.

For assaying LBSA, 100 μl of sera were treated with chloroform-methanol (2:1 V/V). The lipid extract was then partitioned with 0.5 ml cold distilled water and LBSA from the aqueous phase was precipitated with phosphotungstic acid and determined by resorcinol. α₁-AG was estimated according to the method of Winzler. Statistical evaluation of alterations from the controls were made by

Fig. 1. Changes in serum sialic acid levels with dose after a single i.p. injection of cadmium in rats. Data expressed as mean ± SD.

*** Significant at p<0.001
** p<0.01
* p<0.05
Student's t-test and the values were expressed as mean ± SD.

Figure 1 shows the data of serum levels of total sialic acid and their fractions at different dose levels of cadmium. It was observed that their levels were increased by cadmium treatment and were found to be dose related. At the highest administered dose of 3 mg/kg, the percentage changes in the levels of TSA, PSA, LBSA and FSA were 46, 326, 334 and 214 and at the lowest dose (0.5 mg/kg) respective values were 0.45, 92, 39 and 67 as compared to the control values.

Figure 2 and 3 show the results of serum α₁-AG and perchloric acid-soluble protein levels after cadmium exposure showing a dose related increase in their levels.

In cancer shedding or secretion of sialic acid or sialoglycoconjugates from the cell surface in the growth medium results in their increased levels in the blood. A similar mechanism might be expected for the observed changes since cell surface and membrane components are primary targets of the toxicants in the
surrounding medium of the tissues.

Of the parameters studied in the present study, the levels of PSA, FSA, \( \alpha_1 \)-AG and PCA-soluble proteins in serum changed significantly at all the dose levels used and thus appear to be more sensitive. Since \( \alpha_1 \)-AG and PCA-soluble proteins contain sialic acid, it can be concluded that serum sialic acid levels, particularly the PCA-soluble fraction, when considered with the exposure history might be useful for staging or monitoring the toxicity of cadmium.

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