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Vanadium intoxication in albino rat based on haematobiochemistry and behaviouristic changes

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ABSTRACT

Heavy metals are the source of substantial environmental and health problems. Vanadium pentaoxide (V_2O_5) is an environmental and industrial pollutant that affects body physiology via the food, drinking water and through the air. Toxicological study of V_2O_5, following acute (1day) and subacute (7, 14, 21 days) exposure, alter behaviour and serum biochemistry in Wistar rats in terms of significant increase in serum total proteins, serum total lipids, serum phospholipids along with a substantial increase in serum cholesterol, serum albumin, serum globulin and serum albumin-globulin ratio. The Spontaneous and delayed behavioural changes included scratching, thirst, lethargyness, shivering, tremor, piling, crowding and reduction in food intake under vanadium stress.

Key words: Vanadium pentaoxide, haematobiochemistry, behaviour, albino rat

INTRODUCTION

In this industrial age, the awareness of the potential danger posed by heavy metals to the ecosystem and in particular to human health has grown tremendously. Vanadium compounds have gained increasing interest because of their ubiquity in mammalian systems and selectivity in toxicological effects. Vanadium is widely distributed in environment (Aragon *et al*.,2005), is one of the essential trace element that is present in variety of food that we commonly eat like skim milk, lobster, vegetable oil, many vegetables, grains and cereals. In animals vanadium has been shown essential element in their diet (Badmaev *et al*.,1999) .The natural sources of vanadium include earth's crust, rocks, some iron ores and crude petroleum deposits. People are exposed to vanadium every day via the food, drinking water and through the air. Most of the vanadium oxides, get released into the air by burning fuels oil or coal and it can produce toxicity in an ecosystem. People get exposed to high levels of vanadium dust near an industry (ATSDR,1992).

The toxicity of vanadium depends on its physico-chemical state particularly on its valence state and solubility. Pentavalent V_2O_5 has been reported to be more than 5 times as toxic as trivalent V_2O_3. Inhalation exposure of vanadium compound leads to adverse effect in respiratory system (Ress *et al*.,2003; Worle *et al*.,2007), in blood parameters after oral or inhalation exposure (Scibior *et al*.,2006; Gonzalez-Villalva *et al*.,2006), in liver (Kobayashi *et al*.,2006; Saxena *et al*.,2010) besides neurological responses (Soaza and Garcia,2007).

In the present investigation an effort has been made to observe the impact of single and repeated vanadium exposure in Wistar albino rats with special reference to serum biochemistry.

MATERIALS AND METHODS

Animal: Randomly selected Wistar albino rats from inbred colony of almost equal size and weight (100±10g) were kept at temperature of 25±5ºc and relative humidity 60±5% and with a photoperiod 10 hrs/day. The rats were given standard laboratory feed obtained from Hindustan Antibiotic Ltd. India and water *ad libitum* throughout the experimentation.

Experimental design: Vanadium pentaoxide (V_2O_5) was used as a test compound obtained from Merck, India. The LD_{50} of V_2O_5 when given orally to rats was to be 69.6mg/kg b.wt,(Table-I) calculated by log-dose probit regression line method (Finney, 1971). To access the effect of V_2O_5, selected rats were divided into 4 experimental groups, one acute (1d) and three sub acute (7ds,14ds, 21ds) groups consisting 5 rats each. The control sets were run simultaneously for both the acute and sub acute experimental groups. The albino rats were given a sub lethal dose of V_2O_5 for acute (1d) treatment as 6.96mg/kg b.wt. and sub acute (7ds, 14ds, 21ds) treatments 0.99mg/kg b.wt., 0.49mg/kg b.wt. and 0.33mg/kg b.wt. respectively.

The albino rats were anaesthesized under diethyle ether, the blood samples were collected and centrifuged to separate serum for evaluating Serum total proteins, albumin,A/G ratio (Modified method of Biuret and Dumas, 1971) while serum globulin was determined by difference of total proteins and albumin. Serum total lipids (Fringe and Dunn, 1970) and Serum

cholesterol (Roeschlau, 1974), while serum phospholipids (Bartlett, 1959) for both control and experimental (acute and sub acute) sets. Spontaneous and delayed changes in behaviour were also observed after oral administration of V_2O_5 during the experiment.

Statistical analysis: Results were expressed as the mean values ± the standard error, and statistical differences between groups were assessed by student's t-test. Significance level was set at $P<0.05$, <0.01, <0.001.

RESULTS AND DISCUSSION

An increase in serum proteins, serum lipids, serum phospholipids, serum cholesterol, serum albumin, serum globulin and albumin-globulin ratio has been observed in acute (1 day) and sub acute (7, 14, 21 days) V_2O_5 treatment when compared to control sets of albino rats (Table-II).Vanadium pentaoxide (V_2O_5) revealed behavioural changes in both acutely and subacutely treated rats, included scratching, thirst, lethargyness, tremor, shivering, piling, crowding and reduction in food intake (Fig. 1)

The results in present study show increased serum total proteins, A/G ratio, serum total lipids, serum cholesterol, and serum phospholipids after vanadium intoxication. Absorbed vanadium is transported mainly in serum (Schroeder *et al*.,1963). Vanadium in blood is bound to serum protein transferrin and through albumin (Chasteen *et al*.,1986), it gets widely distributed in body tissues like liver, kidney, brain, muscles and bones. Therefore increased availability of serum proteins for vanadium binding causes elevation of serum total proteins including albumin. On the other hand, Vanadium pentaoxide has earlier been observed that after accumulation of V_2O_5 in liver,the hepatocytes are capable of producing macrophage inflammatory proteins (MIP-2) in response to V_2O_5 (Dong *et al*.,1998).This response is mediated by generation of reactive oxygen species (Thornton *et al*.,1990). These reactive oxygen species involved in stimulation of transcriptional activation factors which causes inflammation (Schreck *et al*.,1992; Remick and Villareti, 1996). Thus ROS involved in inflammation and stress responses through activation of transcriptional factor (Valko *et al*.,2005), which is probably responsible for synthesis of many harmful inflammatory proteins(MIP-2). It is also a clear evidence that increased level of vanadium binding proteins and inflammatory proteins in serum causes elevated total proteins in serum after vanadium intoxication. On the other hand after high dose of vanadium,it accumulates in various tissues such as liver, kidney, brain (Parker *et al*.,1980) is attributed to organ damage and alter the metabolism, due to which the detoxification mechanism of metals through glutathione conjugation gets reduced. Organs like liver ,kidney get necrotized in heavy metal exposition (Tandon *et al*.,1984)and due to this necrotization, synthesized cholesterol and lipids within tissue gets mobilized into the blood stream and causes increased concentration of cholesterol and lipids in serum.

In the present investigation after acute and subacute treatment with V_2O_5, enhancement in serum phospholipids is revealed. the prime target sites for xenobiotic toxicity are surface membrane possibly due to their exposed location and chemical reactivity. These metals interact with reactive biological entities to manifest their physiological, pathological, or pharmacological effects. The interaction of a chemical with either protein or lipid components of the cell membrane may substantially alter membrane structure and function (Upreti,1995).In acute toxicity studies, many of the adverse vanadium effects indicated initial membrane damage. It is well known that hydroxyl radicals (OH^-) are capable of membrane damage leading to a variety of pathologies (Halliwell and Gutteridge,1984) including lipid peroxidation. Vanadium has potent effect on biological systems and effective concentrations appear to exist normally *in situ.* Peroxidation of membrane phospholipid is implicated in a variety of pathological states and has been proposed as an index of cellular deterioration and causes rupture in plasma membrane, in turn membrane phospholipids get released out into circulation, probably the reason of increase in serum phospholipids. Administration of vanadium to adult rats resulted in behavioural alterations.The possible role of vanadium in behavioural changes is a known fact. Graded doses of vanadium have included remarkably high levels of lipid peroxides in discrete areas of rat brain (Haider *et al*.,1998) that lead various behavioural activities. Vanadium crosses the blood brain barrier and possibly alters biochemistry of brain of treated animals.CNS myelin could be a preferential target of vanadium , mediated lipid peroxidation in rats. The high metabolic activity as well as the high concentration of lipid of brain (myelin) increase the susceptibility of the nervous tissue to peroxidative

damage (Garcia *et al*.,2004) which causes behavioural alterations like scratching, thirst, lethargyness, tremor, shivering, piling, crowding and reduction in food intake. Decreased body weight has been observed during vanadium dosing (Saxena *et al*.,2010) due to reduction in food intake. It is thus evident that alteration in serum biochemical parameters and behavioural activities are suggestive of vanadium toxicity

CONCLUSION

Vanadium is one of the essential trace metal to maintain the metabolism of the body. However at higher concentration it can induce acute and subacute toxicity which causes serological alterations that can be a important tool for therapeutic approaches.

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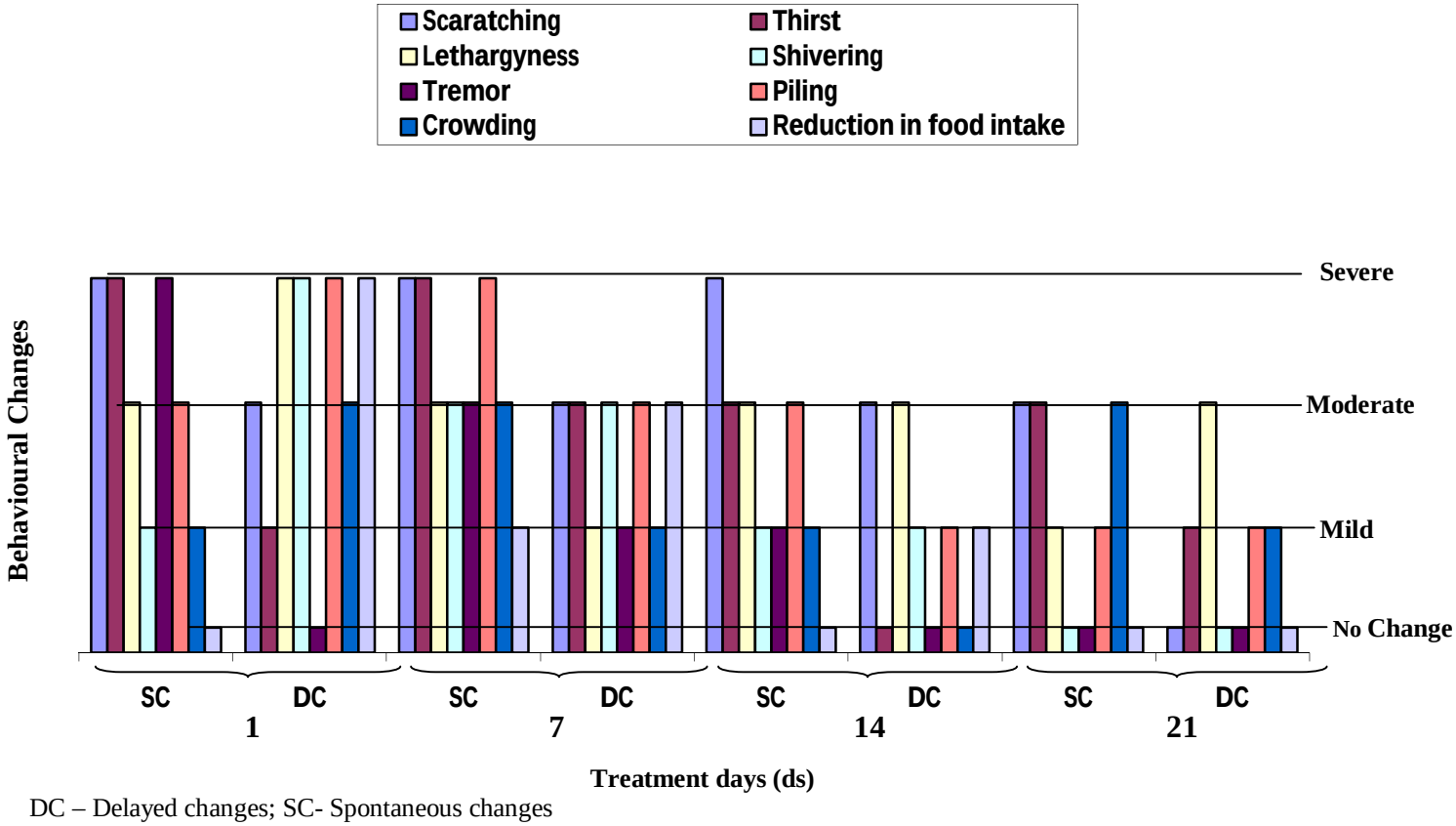
Fig. 1: Behavioural changes in albino rat after acute (1d) and sub-acute (7, 14 and 21 ds) Vanadium pentaoxide intoxication.



DC – Delayed changes; SC- Spontaneous changes

Experimental animal	Compound	Regression equation	LD_{50} (in mg/kg b.wt.)	Variance	Fiducial limits
Rattus norvegicus	Vanadium pentaoxide	Y=5.46+5.88 (m-1.92)	69.6	0.003	m_1=(+)1.845 m_2=(-)1.834

Table-I. LD_{50} value, variance and fiducial limits for vanadium pentaoxide against Albino rats (*Rattus norvegicus)*

Table-II. Vanadium pentaoxide induced acute (1d) and subcute (7, 14, 21ds) changes in serum biochemical parameters in wistar albino rats.

Index(unit)	Acute Studies		Sub acute Studies					
	1 day		7 days		14 days		21 days	
	Control	Treated	Control	Treated	Control	Treated	Control	Treated
Total proteins (g/100 ml)	6.00±1.01	6.33±0.99 (P>0.05)	5.81±1.48	7.42±0.49 (P<0.01)	6.93±2.41	8.00±1.21 (P<0.05)	7.11±1.55	8.30±2.54 (P<0.05)
Albumin (g/100 ml)	3.64±0.18	4.03±0.19 (P<0.05)	4.03±0.16	4.37±0.06 (P>0.05)	4.08±0.28	4.88±0.10 (P>0.05)	4.27±0.15	4.39±0.16 (P>0.05)
Globulin (g/100 ml)	3.71±0.12	4.00±0.20 (P>0.05)	4.10±0.19	4.11±0.15 (P>0.05)	4.21±0.20	4.74±0.33 (P>0.05)	3.60±0.10	4.41±0.22 (P<0.05)
A/G ratio	0.99±0.10	1.00±0.11 (P>0.05)	0.99±0.19	1.05±0.11 (P>0.05)	0.98±0.13	1.02±0.20 (P>0.05)	1.00±0.10	1.01±0.18 (P>0.05)
Total lipids (mg/100 ml)	505.20±28.99	567.70±3.15 (P<0.05)	676.00±18.91	677.08±37.55 (P>0.05)	676.00±13.86	708.33±24.42 (P<0.05)	687.00±31.33	739.58±13.77 (P<0.01)
Cholesterol (mg/dl)	174.66±4.80	177.33±7.42 (P>0.05)	176.00±10.6	182.66±5.81 (P>0.05)	176.00±8.32	188.00±6.11 (P>0.05)	185.00±5.81	205.10±9.61 (P<0.05)
Phospholipids (mg/ml)	3.46±0.99	4.86±1.10 (P<0.05)	3.45±0.89	5.26±1.05 (P<0.01)	3.47±1.01	5.42±0.98 (P<0.01)	3.43±0.56	5.74±1.12 (P<0.001)