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Spermatotoxic Effects of Nickel in Mice

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Nickel is an essential trace element. The industrial application of nickel has broad spectrum. Primarily it is used in alloys. The other uses are in electroplating, welding, flame cutting, flame spraying and mold making. Nickel is also used in the manufacture of artificial jewelry, coinage, cutlery, cooking utensils and dental or surgical prostheses (Toxicological Profile For Nickel, 1997). Nickel has been reported to leach out from the utensils, used during cooking and storage of food. Human exposure to nickel may occur in industrial environment or through food chain. The nickel is being absorbed through oral, dermal, and inhalation routes as well. Nickel play some important role in biological system such as enzyme activity, harmonal control and also in RNA, DNA and protein stucture or function (EHC, 1991)

The dietary requirement of nickel is 50-80 ng/g of diet (Nielsen, 1976). Higher quantity of nickel is known to be injurious for human health. It causes allergy, cancer, non malignant respiratory tract disorders and iatrogenic nickel poisoining. Nickel hypersensitivity also causes asthma, conjunctivitis, inflamatory reactions. In acute exposure symptoms, adrenal insufficiency, hyperglycemia, hepatic toxicity and renal damage, may also develop. Nickel crosses the placental barrier, effecting directly the developing embryo or foetus in experimental animals (Sunderman et al, 1978a). Its effects on various aspects of reproduction have been described (EHC, 1991). Animal studies may include that nickel reaches the testis, seminal vesicle and prostate gland (EHC, 1991), and there is similar report of adverse effect on sperm (Sobti and Gill, 1989). Its action in the

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mice on sperm motility, morphology and count, are important parameters for the evaluation of male fertility, have now been studied. The spermatotoxic effects of nickel evaluated in young growing mice.

MATERIALS AND METHODS

Nickel sulphate and nickel chloride of AR grade were procured from E-Merck. Other chemicals were of the highest purity available.

Young (25±5g) male mice from the Animal Breeding Facility, Industrial Toxicology Research Centre, Lucknow were fed pelleted diet (Lipton India) and water *ad libitum*, and were maintained under standard conditions. Fourty eight male mice were divided in two main groups, consisting of twenty four animals in each main group. Further each main group were divided in four sub groups II, III and IV sub group recieved nickel sulphate or nickel chloride 5, 10 or 20 mg/kg b wt/d, orally 5d/wk for 35 days, in 0.2 mL distilled water. Group I in both the sub group recieved only 0.2 mL distilled water served as vehicle control.

Body weight was recorded at initiation and completion of the experiment. The mice were fasted over night and were killed by cervical dislocation on the 36^{th} day of experiment. Testes, epididymides, seminal vesicles and prostate glands were quickly removed and weighed.

Epididymal sperm were obtained by mincing epididymis with normal saline and filtering through mesh. Sperm were counted using a Neubauer Chamber (Freund and Carol, 1964). Sperm motility was assayed microscopically within 5 min at 37°C and is expressed as percent motile forms (Adelman 1936). Morphological abnormalities were enumerated under light microscope (Hemavathi and Rahiman, 1993).

Students ‘t’ test was used, $P<0.05$ was regarded as significant (Fischer, 1950).

RESULTS AND DISCCUSSION

No overt toxicity or mortality was observed. Dose related effects, on body weight gain were observed at 10 and 20 mg/kg b wt. The effects

were more pronounced at the dose level of 20 mg/kg b wt, no change were found at the 5 mg/kg b wt. The absolute and relative weights of testes, epididymides, seminal vesicles and prostate gland were significantly decreased at 20 mg/kg b wt (data not shown).

Dose dependent changes in sperm motility and count were observed at 10 and 20 mg/kg groups. The mice recieving nickel sulphate at 10 mg/kg and 20 mg/kg dose level had a 15.1% and 26.4% motility and 12.5% and 25% epididymal sperm count. But the animals exposed to nickel chloride showed higher values i.e. 24.4% and 42.9% motility and 25% and 37.0% epididymal sperm count at 10 and 20 mg dose level (Table 1).

There was a significant dose related and salt specific increase in, abnormal sperm. In mice abnormal sperm were 24.4% at 10 mg/kg dose and 28.0% at 20 mg/kg exposed to nickel sulphate solution. Similar is the case with nickel chloride, 29.1% at 10 mg/kg and 34.6% at 20 mg/kg dose level (Fig 1). The abnormalities were in head, neck and tail region of the sperm i.e. banana and detached head were found, acrosome may be up or down, may be absent. Curved neck and curved, bent, round, loop and folded tail were seen at both the higher doses of each nickel species (Fig 2).

The experiment involved prolonged treatment of animals and oral administration of nickel in distilled water, both these factors are able to enhance toxicity. The decrease in body weight gain may be due to a direct effect of heavy metal on somatic cells or to an indirect influence through the genotoxic effects (EHC 1991).

Our observations are consistent with those of Dieter et al (1988) who also observed decrease in body weight gain of mice dosed with nickel. The decrease in absolute organ weight with no significant effect on relative weight in mice (20 mg/kg) is probably due to the greater reduction in their body weight gain.

Table 1. Effect of nickel on motility and total epididymal sperm count in mice treated with nickel chloride and nickel sulphate for 35 days.

	Motile sperm (%)		Sperm count epididymis (10^7)	
Group	$NiSO_4$ treated	$NiCl_2$ treated	$NiSO_4$ treated	$NiCl_2$ treated
I	88.3±2.11	86.0±2.39	8.0±0.32	8.0±0.17
II	85.8±2.3(2.8%)	85.10±1.29(1.2%)	8.5±0.31(6.2%)	8.2±0.08(2.5%)
III	75.0±4.91(15.1%)*	65.0±1.29(24.4%)*	7.0±0.24(12.5%)	6.0±0.07(25%)*
IV	65.0±4.8(26.4%)*	49.1±1.35(42.9%)*	6.0±0.21(25%)*	5.0±.05(37.5%)*

*P<0.05, Mean±S.E.M. of 6 mice per group.

Group I - Controls, Group II - Mice treated with Nickel (sulphate/ chloride) at 5 mg/kg b.wt. dose level., Group III - Mice treated with Nickel (sulphate/chloride) 10 mg/kg b wt. dose level, Group IV - Mice treated with Nickel (sulphate/chloride) 20 mg/kg b wt dose level.

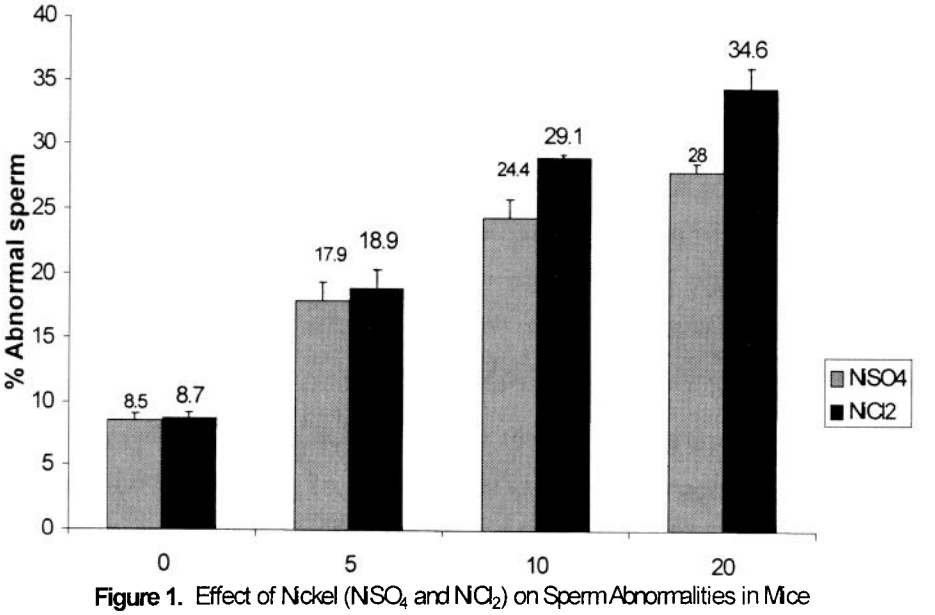

Figure 1. Effect of Nickel ($NiSO_4$ and $NiCl_2$) on Sperm Abnormalities in Mice

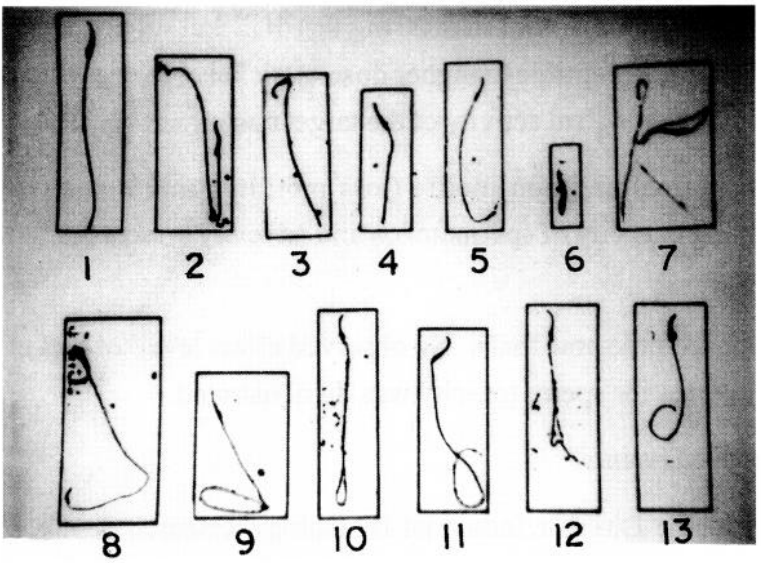

Figure 2. Sperm shape abnormality

1. Normal sperm 2.Acrosome up 3.Acrosome down 4. Acrosome absent 5. Banana head 6. Detached head 7. Curved neck 8. Bent neck 9. Bent tail 10. Round tail 11. loop tail 12. Folded tail 13. Signet tail.

The reduction in epididymal sperm count may be due to an adverse effect of nickel on spermatogenesis as has been reported for phthalates (Parmar et al, 1995). Krasovskii (1979) and Chawdhury (1984) also observed reduced sperm count and loss in sperm motility in rat due to lead exposure. Sperm morphology also has an important relationship to sperm motility and the reduced motility observed here been due to the morphological abberations (Kasker, 1994) or to other mechanisms (Wyrobeck,1975). The loss in number of motile sperm may be due to greater number of abnormal sperm. The abnormal sperm may establish inverse relation to the motility of spermatozoa.

Our observations are similar to those reported by Sobti and Gill (1989) who observed significantly larger sperm with abnormal shaped heads in mice exposed to nickel. We have doccumented a more marked spermatotoxic action at higher doses (10 & 20 mg/kg) of nickel chloride

compare to higher doses (10 & 20 mg/kg) of nickel sulphate. The animals may be more suceptible to higher dose of nickel chloride because of the greater physiological activity of the target tissue (salt specific toxicity).

The abnormal and non motile (less motility) sperm may reduce the fertilizing capacity of spermatozoa and adversly affects the fertilization of ovum.

It is important to note that a 'No observed effect level' of nickel 5 mg/kg b wt in mice for sperm toxicity was demonstrated.

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