Journal of Andrology, Vol 13, Issue 1 65-74, Copyright © 1992 by The American Society of Andrology

JOURNAL ARTICLE

Effects of subchronic treatment with cis-platinum on testicular function, fertility, pregnancy outcome, and progeny

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Cis-platinum-based chemotherapy is known to impair spermatogenesis, but the effects of paternal cis-platinum treatment on the progeny are unknown. To study this effect, sexually mature male Sprague-Dawley rats were administered intraperitoneal injections of saline or cis-platinum (0.5 mg/kg per day) for 9 weeks. Every week, one set of control and treated animals was mated with females in proestrus. Nineteen days later, the females were subjected to laparotomy, and the numbers of corpora lutea, resorptions, and normal and abnormal fetuses were noted. In conjunction, the effects of treatment on the hypothalamo-pituitary-gonadal axis of the treated males were evaluated. Cis-platinum-treated animals failed to grow; the weights of the reproductive organs and the sperm counts declined from week 2 onward, and sperm motility was reduced throughout the testing period. Circulating and intratesticular levels of testosterone declined from week 3 of treatment and follicle-stimulating hormone levels were not affected. Serum levels of luteinizing hormone declined from week 3 and were not detectable from week 6 onward. However, the pituitary response to gonadotropin-releasing hormone was intact in all treated groups. There was no significant decrease in fertility, but a prominent increase in pre- and postimplantation losses of fetuses after cis-platinum treatment was observed. There was also a decrease in the male-to-female ratio of the offspring. A small but significant number of malformed and growth-retarded fetuses was also found among the offspring of cis-platinum-treated males. These results suggest that subchronic treatment with low doses of cis-platinum may affect progeny; such effects are seen in addition to the apparent alteration in a number of measures of reproductive function of treated males.

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