

A NEW APPROACH FOR NON-SURGICAL STERILIZATION: TARGETING GONADAL SUPPORT CELLS

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The purpose of this study was to evaluate the effects of a non-surgical sterilization technique in rats. This technique consists of an antibody-guided, lipid-based nanoparticle that carries a cytotoxin. The nanocomplex is guided to specific cells in the gonads (female: granulosa/theca cells; male: Sertoli/Leydig cells) by the antibody for the anti-Mullerian II receptor (AMHII) and carries a cytotoxin to induce apoptosis in these specific cells. These cells are almost exclusively located in the gonads and are necessary for germ cells to develop, undergo meiosis, and survive. These cells also produce hormones that are needed for reproductive behavior. We hypothesize that destruction of these gonadal cells using the nanocomplex will lead to sterilization. Preliminary data in rats collected 24 hours after injection of the nanocomplex indicated that apoptosis was occurring in these gonadal cells, particularly in males. The goal of this pilot study was to expand the results of this promising work to determine the extent of damage in the gonads and impacts on the animals beyond 24 hours.

This study was conducted using sixteen adult Sprague-Dawley rats (8 males and 8 females) divided into two groups: one group injected IV into the tail vein with nanocomplex and the other group injected with sterile saline. Animals were housed for 4 weeks total and weighed twice a week. Females were assessed for estrous cyclicity during Weeks 3 and 4 of the experiment. At the end of the experiment, all animals were sacrificed by exposure to CO₂. Testes and uteruses were weighed, the epididymides were collected for semen evaluation, and gonads were preserved in 10% formaldehyde for histological processing. A low dose of antibody was used for this initial test (10 nmol in 0.5ml sterile saline).

Overall body weights, testicular weights and uterine weights were not significantly different when comparing experimental to control animals. There was an observable difference in epididymal sperm samples between the experimental and control males. All experimental males had many fewer sperm than controls, and the sperm exhibited limited motility. The female experimental animals exhibited a disruption in estrus cyclicity when vaginal smears were compared to control animals. Histological evaluation of gonadal tissue is ongoing, but preliminary results indicate disruption in normal gonadal architecture. Although limited in experimental days and numbers of animals, this pilot study indicates that the nanocomplex appears to negatively impact reproductive parameters in adult rats while not affecting observable health parameters.