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Novel TCPL delivery system: Inhibition of hypothalamic-pituitary gonadal hormones by sustained delivery of testosterone

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It is well documented that testosterone stimulates protein anabolism, muscular development, bone growth and increased metabolic rate. In addition, exogenous low levels of testosterone can inhibit the secretion of gonadotropins (LH and FSH) by the anterior pituitary. The objectives of this study were (A) to investigate the effect of sustained delivery of testosterone (T) on the testicular architecture by means of tricalcium phosphate-lysine (TCPL), and (B) to explore the effect of exogenously delivered T on the LH, FSH and endogenous T levels. . In this experiment adult male Sprague Dawley rats (250-300 g BW) were randomly divided into three equal groups (n=16). Rats in group I were implanted subcutaneously with T loaded TCPL implants (4-6 ng/ml). Rats in group II were implanted with sham TCPL capsules, and rats in group III served as intact unimplanted controls. Surgical aseptic techniques were performed according to standard laboratory procedures. At the end of 1, 2, 3 and 6 months post implantation, four animals from each group were sacrificed and the testes were collected, weighted, and embedded for histopathological evaluations. Blood samples were collected weekly and analyzed for T, LH and FSH by following standard lab protocols. The results of this study revealed the following: (1) remarkable reduction of testicular mass at the end of the two month phase, and continued for the duration of study in comparison to the sham and intact control; (2) cross sections obtained from group I animals have shown that the Leydig cells were decreased in size and number of organelle; (3) the epithelium of the seminiferous tubules decreased in height and cell number; (4) a significant decrease ($p<0.05$) in the number of secondary spermatocytes (70%) at the end of the 2 month phase, and azoospermia was observed at the 3-6 month phases in group I rats;(5) there were no significant differences in the number of spermatogonia between the three groups; and (6) remarkable suppression to LH, FSH and T levels at the end of the second week post implantation of T loaded TCPL and continued for the entire duration of the experiment. This study demonstrates that low sustained levels of exogenous T can impair spermatogenesis and inhibit LH, FSH and T levels ina rat model.

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