

# ADMINISTRATION OF A LONG TERM RELEASE GNRH SUPERAGONIST DURING THE CANINE POSTNATAL CRITICAL WINDOW

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The blockade of the pituitary-gonadal axis in the postnatal critical window has shown a negative impact on the development of the genital tract and subsequent reproductive function in several species. GnRH analogs have been used as endocrine disruptors during the critical postnatal time window in rodents, primates and felids. The objective of this study was to assess the efficiency and clinical safety of the early postnatal administration of a high dose of deslorelin acetate on canine puberty postponement. Secondly, sexual steroids and histological gonadal changes were also described. Twenty- four littermate, postnatal, mongrel dogs were randomly assigned to implants of deslorelin acetate (Suprelorin, Virbac, France) 18.8 mg SC (DESLO; n = 12) or placebo (PLACE; n = 12) within the first 24h after birth. The dogs were serially followed up (behavioral and libido observation, physical examination, vaginal cytology, spermograms, and testosterone [T] and estradiol-17 $\beta$  [E2] serum determinations) up to puberty when they were spayed/ castrated. After surgery the gonads were grossly and microscopically examined. At the time of writing, all PLACE (median 259 days) and 9/12 DESLO (median 574 days) dogs have already attained puberty ( $P < 0.01$ ) and the 3 non pubertal DESLO animals are 658 days old. Withers height ( $P > 0.1$ ) and body weight ( $P > 0.1$ ) did not differ throughout the trial. Both groups of dogs finished growing at similar age ( $P > 0.05$ ) independently of the pubertal status. No clinical side effect including the “flare up effect” appeared in any animal ( $P > 0.1$ ). At puberty, libido appeared normal in all the dogs ( $p > 0.1$ ) and all the bitches ovulated during estrous cycle ( $P > 0.1$ ). In the females that were mated, gestations were confirmed in 2/2 and 5/6 ( $P > 0.1$ ) of the DESLO and PLACE groups, respectively. In male dogs, serum T remained low ( $< 0.2$  ng/mL) up to weeks  $57.3 \pm 5.6$  and  $16.8 \pm 1.8$  in DESLO and PLACE groups, respectively ( $P < 0.05$ ). From those weeks on, T gradually began to increase up to puberty. In all the females, E2 concentrations remained low ( $< 5$  pg/mL) throughout the trial except in peripubertal and pubertal determinations in which the values were  $> 12$  pg/mL. The histomorphometrical study of the gonads revealed no differences for the ovaries ( $P > 0.1$ ) and a decrease in the germinal epithelium ( $P < 0.01$ ) and Sertoli cells ( $P < 0.05$ ). It was concluded that 18.8 mg of deslorelin acetate at the early neonatal period decreased sexual steroids postponing puberty without side effects.

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