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Effects of an LHRH agonist analog upon sexual function in male dogs. Suppression, reversibility, and effect of testosterone replacement

B. H. Vickery, G. I. McRae, W. Briones, A. Worden, R. Seidenberg, B. D. Schanbacher and R. Falvo

Male beagle dogs were injected once daily with 10 micrograms/kg of [6-D-(2-naphthyl)alanine]-LHRH (D-Nal(2)6-LHRH), a potent LHRH agonist, for periods up to 42 days, with recovery periods up to 172 days. Blood samples collected at regular intervals were assayed for LH, FSH, and testosterone; total ejaculates were collected and analyzed weekly, and animals were sacrificed at various intervals for sex organ weights and histology. The first injection of D-Nal(2)6-LHRH caused an acute elevation in plasma levels of LH, FSH, and testosterone, measured at 2 and 4 hours after the injection. This acute response to injection was attenuated with each successive injection and by two weeks no elevation was seen, suggesting a down-regulation of pituitary response. Basal levels of LH and testosterone were maximally depressed by four days of treatment. Testis volume, duration of erection, ejaculate volume, sperm count, sperm motility and testis volume all declined during treatment, with sperm count significantly lowered by two weeks and ejaculation volume becoming zero by five weeks of treatment. Spermatogenesis, assessed histologically, was partially suppressed at ten days and completely suppressed by 38 days of treatment. All parameters returned to normal following cessation of treatment. Recovery time was longer for the dogs treated for 42 days than for those treated for ten days. When testosterone was supplemented during 42 days of agonist treatment, basal plasma testosterone levels were maintained at the low end of the normal range. Testosterone supplementation did not prevent pituitary down-regulation, suppression of spermatogenesis, or the decrease in testis and epididymis weights, but prevented the decline in duration of erection. Ejaculate volume and sperm count declined more slowly with combination treatment than with agonist alone. During the decline in sperm count sperm motility was maintained with combination treatment. Injection of hCG into control and agonist treated dogs resulted in similar percentage increases in plasma levels of testosterone, although peak levels were greater in control than in treated animals. The data suggest a pituitary desensitization with this LHRH agonist in the dog but only a minor role for testicular desensitization.

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