Effects of Repeated HCG Administration on Serum Testosterone and Testicular Descent in Prepubertal Thoroughbred Colts With Cryptorchid Testicles

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Administration of human chorionic gonadotropin (HCG) to prepubertal Thoroughbred colts results in significant increases in serum testosterone concentrations. Colts with cryptorchid testicles have a reduced response in testosterone concentration compared to colts with descended testicles. Treatment with HCG facilitates descent of inguinally located testicles. Author's address: Large Animal Medicine and Surgery, College of Veterinary Medicine, University of Illinois, Urbana, IL 61802; e-mail: jpb@uvm.edu. © 2006 AAEP.

1. Introduction
Testicular descent in the normal equine colt occurs between 300 days of gestation and 10 days after birth.1 Cryptorchidism is a common developmental defect in boys2 and the horse,1,3 in which one or both testicles fail to descend into the scrotum. Normal descent in fetuses consists of transabdominal and inguinoscrotal phases. During the second or inguinoscrotal phase, the gubernaculum extends caudally into the scrotum and involutes after passage of the testis through the inguinal canal. The second phase of testicular descent is controlled mainly by androgens, affecting the gubernaculum either directly or through the genitofemoral nerve, modulating gubernaculum growth and differentiation.4

Human chorionic gonadotropin (HCG) is routinely used in prepubertal boys to facilitate testicular descent of inguinally retained testes.5 Repeated administration of HCG to mares has been shown to result in antibody production and decreased clinical responsiveness.5 While the endocrine response of mature stallions to HCG administration has been reported,1,3,6 little is known about the response in prepubertal colts. Previous work7 has shown that prepubertal Thoroughbred colts, with bilateral scrotal testes, were able to respond to HCG stimulation with increases in testosterone comparable with adult stallions. The goals of this study were to compare the endocrine response of prepubertal colts with descended or cryptorchid testicles to repeated HCG administration and determine whether HCG treatment influences testicular descent.

2. Materials and Methods
Sixteen Thoroughbred colts, 180–240 days of age, were included in the study. The location and volume of the testicles in all colts were determined by palpation and ultrasonography before inclusion in the study. To facilitate examination and ensure
accurate evaluation of testes location, the colts were tranquilized (xylazine, 100 mg; butorphanol, 5 mg; acepromazine, 10 mg, IV) before examination. Group 1 (n = 6) colts were noted to have both testicles readily identifiable in the scrotum. Group 2 (n = 10) had only one testicle identifiable by palpation and ultrasound in the scrotum. In eight of the colts, the retained testicle was noted, by ultrasonography, in the inguinal canal, proximal to the external inguinal ring. In the remaining two colts, the testicle could not be identified and was presumed to be intra-abdominal.

All colts received 2500 IU HCG IM two times weekly for 4 wk for a total of eight treatments. Once weekly, blood samples were collected for hormone analysis. Samples were collected immediately before each HCG treatment and at 1, 24, and 48 h after treatment. Serum testosterone and estradiol 17β concentrations were measured by radioimmunoassay (RIA) validated for the horse. Before initiation of treatment and 1 wk after the last treatment, colts were tranquilized, and the location and size of the testicles were determined by palpation and ultrasonography. Testicular volume was determined by ultrasonographic measurements using the following formula: Volume = 3.14 × D²/4 × L × 0.9³. Testosterone and estradiol concentrations and testicular volume were compared between treatment groups by Kruskal-Wallis one-way nonparametric analysis of variance (AOV). Significance was set at p < 0.05.

3. Results
Testosterone concentrations in all colts were below the level of detection of the assay before initiation of treatment (<9.163 pg/ml). All colts treated with HCG responded with significant increases in testosterone concentrations by 48 h after treatment (9.163 versus 111.2 pg/ml). Peak testosterone response to HCG treatment did not differ between the first treatment and the last treatments (111.2 pg/ml versus 234.4 pg/ml). Testosterone concentrations in the colts with one retained testicle were not significantly different from the response in colts with both testicles descended (132.5 versus 78.5 pg/ml; p = 0.20). Mean testicular volume did not differ (p = 0.30) in HCG-treated colts after treatment (16.4 versus 22.6 cm³). Estradiol concentrations in all colts were below the level of detection of the assay at all sampling times. In four of the eight (50%) colts in which one testicle was identified in the inguinal canal before initiation of treatment, the testicle was present in the scrotum after the last treatment. No change in testicle location was noted in the two colts with abdominal cryptorchid testicles.

4. Discussion
These results show that prepubertal colts are capable of responding to HCG stimulation with increased testosterone production comparable with adults. Testosterone response in colts with descended testicles was greater than that observed in colts with retained testicles, although this difference was not significant, possibly because of the limited number of animals in this study. Several previous studies have reported similar differences in response to HCG stimulation in cryptorchids. It has been proposed that the lower baseline and HCG stimulated testosterone concentrations reported in cryptorchids is attributable to the inguinal or intra-abdominal location, which results in degeneration of the interstitial cells. Evidence for Sertoli cell degeneration has been shown in older cryptorchid boys who exhibit low inhibin B levels. In contrast, boys who underwent orchiopexy or HCG treatment by 2 years of age had normal levels of inhibin B.

No decrease in response to HCG stimulation was observed with repeated administrations. While antibodies were likely developed as previously reported, the response by the Leydig cells was not effected. Treatment with HCG (2500 IU twice weekly) resulted in descensus of testes in four of eight inguinal cryptorchids treated. This is comparable with results observed in prepubertal boys undergoing similar treatment.

No control treatment group was included in this study. Anecdotal reports have suggested the spontaneous descent of testicles in colts after the normal peri-partum time period. While it is possible that delayed descent could and does occur spontaneously in certain individuals, such as colts with enlarged inguinal rings, this has not been supported by well-documented case reports. It is therefore unlikely that testicular descent would have occurred in 50% of the treated group without HCG administration.

The increase in testicular volume in HCG-treated colts offers a possible mechanism for the efficacy of HCG treatment for facilitation of testes descent reported in boys. Testosterone has also been shown to be necessary for the inguinoscrotal phase of testes migration modulating the involution of the gubernaculum. The HCG-induced testosterone increase could facilitate this process. Early surgical intervention in cryptorchid boys results in increased sperm production in adulthood. Additional studies are necessary to determine if early hormone intervention in prepubertal cryptorchid colts minimizes Sertoli cell degeneration and improves subsequent fertility.

References and Footnotes


*Sedazine 10%, Fort Dodge Animal Health, Fort Dodge, IA 50501.*

*Torbugesic, Fort Dodge Animal Health, Fort Dodge, IA 50501.*

*Promace, Fort Dodge Animal Health, Fort Dodge, IA 50501.*

*Chorulon, Intervet Inc., Millsboro, DE 19966.*

*Coat-A-Count testosterone, estradiol 17-β, DPC, Los Angeles, CA 90045.*