



ELSEVIER

Contents lists available at ScienceDirect

## Theriogenology

journal homepage: [www.theriojournal.com](http://www.theriojournal.com)

# Clinical use of deslorelin implants for the long-term contraception in prepubertal bitches: Effects on epiphyseal closure, body development, and time to puberty

D. Kaya<sup>a,\*</sup>, S. Schäfer-Somi<sup>b</sup>, B. Kurt<sup>c</sup>, M. Kuru<sup>a</sup>, S. Kaya<sup>a</sup>, C. Kaçar<sup>a</sup>,  
Ö. Aksoy<sup>c</sup>, S. Aslan<sup>d</sup>

<sup>a</sup> Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, University of Kafkas, Kars, Turkey

<sup>b</sup> Centre for Artificial Insemination and Embryo Transfer, University of Veterinary Medicine Vienna, Vienna, Austria

<sup>c</sup> Department of Surgery, Faculty of Veterinary Medicine, University of Kafkas, Kars, Turkey

<sup>d</sup> Department of Obstetrics and Gynecology, Faculty of Veterinary Medicine, University of Ankara, Ankara, Turkey

## ARTICLE INFO

### Article history:

Received 28 June 2014

Received in revised form 11 December 2014

Accepted 11 December 2014

### Keywords:

Body development

Deslorelin

Epiphyseal closure

Prepubertal bitch

## ABSTRACT

Long-acting GnRH agonists have been used both for canine estrus induction and prevention. The objective of the study was to investigate the use of a deslorelin implant as a long-term and reversible contraceptive in prepubertal bitches with special regard to the time of epiphyseal closure. Thirteen healthy, crossbreed, medium-sized prepubertal female dogs were used in this study. An implant containing 9.4 mg (G1, n = 5) and 4.7 mg (G2, n = 4) deslorelin acetate (Suprelorin) or a placebo (sodium chloride 0.9%; G3, n = 4) was inserted subcutaneously in the interscapular region. Estrus was monitored once daily by physical and sexual behavioral changes. Body development, vaginal cytology, and serum progesterone and estradiol 17 $\beta$  concentration were monitored weekly for the first 5 weeks, and then every 3 weeks throughout the treatment period. Radiographic examinations were performed monthly to determine the epiphyseal closure. Half of the deslorelin-treated bitches (G1: n = 2 and G2: n = 2) came into estrus during the 83-week observation period. All animals in the control group showed estrus between the 39th and 64th weeks of observation. Time to puberty averaged 82.7  $\pm$  8.9 and 61.9  $\pm$  9.7 weeks in the deslorelin-treated (G1 and G2) and the control bitches, respectively (P < 0.02). Both deslorelin implants (9.4 and 4.7 mg) can be used efficiently for the long-term prevention of estrus in prepubertal bitches; however, epiphyseal closure is clearly delayed which was without any clinical effect in the present study.

© 2015 Elsevier Inc. All rights reserved.

Part of the results of this paper have been presented as oral communication: "Postponement of puberty in bitches: effect of deslorelin on epiphyseal closure, hormonal status, and the genital tract" at the "17th Annual Conference of the European Society for Domestic Animal Reproduction, Bologna, Italy, 12 to 14th September 2013", and the abstract was published in *Reproduction in Domestic Animals*, 48 (Suppl. 1), 65, 2013.

\* Corresponding author. Tel.: +90 474 242 6807; fax: +90 474 242 6853.

E-mail address: [dygkaya@gmail.com](mailto:dygkaya@gmail.com) (D. Kaya).

## 1. Introduction

Gonadotropin-releasing hormone (GnRH) is a decapeptide hypothalamic hormone that acts on GnRH receptors in the pituitary. It is secreted in a pulsatile manner into the hypothalamo–hypophyseal portal system and has a short half-life of 2 to 5 minutes because of rapid cleavage by proteases. In the pituitary, GnRH stimulates production and secretion of both luteinizing hormone and follicle-stimulating hormone which in turn act on the gonads regulating steroid production, spermatogenesis, ovarian follicular development, and ovulation [1,2].

Prolonged administration of GnRH agonists leads to desensitization of the pituitary gland and effectively inhibits the pituitary–gonadal axis. In recent years, slow-release depot formulations of GnRH agonists have been developed for long-term fertility control of domestic animals. These products have a broad range of potential applications in domestic animal reproduction [2,3]. One of these products, a deslorelin implant, has been used both for suppression and induction of estrus in bitches [4–7].

A limited number of studies have been conducted on the efficacy of long-term release GnRH agonists to postpone puberty and its physiological effects on ovarian function and body development in female dogs [8–10]. In a recent study, Marino et al. [10] evaluated short- and long-term effects of repeated 4.7-mg deslorelin implant application on the genital tract and body development in prepubertal bitches.

It has been reported that hormonal changes after prepubertal gonadectomy cause delayed closure of growth plates in cats and dogs [11,12]. However, the effects of different dosages of deslorelin on the epiphyseal closure (EC) are not yet fully investigated. We hypothesized that prepubertal application of a GnRH agonist would cause comparable effects.

Therefore, the objective of this study was to investigate the deslorelin implant Suprelorin (9.4 and 4.7 mg) for use as a long-term, safe, and reversible contraceptive in prepubertal medium-sized bitches with special regard to the time of EC.

## 2. Materials and methods

### 2.1. Animals and treatments

The study was conducted at the Clinics of the Department of Veterinary Medicine, Kafkas University, Kars, Turkey, from 2011 to 2013. Thirteen healthy, crossbreed, medium-sized, prepubertal female dogs (age range, 4–5.1 months; body weight range, 6–15 kg) were used in the study. To provide a random distribution, dogs were distributed into groups according to the order they were brought to the clinic. The dogs were housed in indoor–outdoor runs and had a maximum daylight per day. They were fed with a standard commercial puppy food, and water was available *ad libitum*. For ease of applications, dogs were also identified with letter numbers (e.g., b1, b2, b3, b4, and henceforth). Only bitches that clearly proved to be prepubertal after gynecologic observation including vaginal cytology, estradiol 17 $\beta$  (E<sub>2</sub>), and progesterone (P<sub>4</sub>) measurement were used in the present study. After the first vaginal cytologic and blood sampling, an implant containing 9.4-mg (G1, n = 5) and 4.7 mg (G2, n = 4) deslorelin (Suprelorin; Virbac, France) or a placebo (sodium chloride 0.9%; G3, n = 4) was administered subcutaneously in the interscapular region by using a single use applicator. One of the treated bitches in G2 (b7) died in the 34th week of the treatment period for an unknown reason. Therefore, only the deslorelin concentrations of this dog were used in the statistical calculations. This study was reviewed and approved by the Animal Local

Ethics Committee (KAÜ-HADYEK; 2010/30) of the Faculty of Veterinary Medicine, Kafkas University, Turkey.

### 2.2. Clinical and radiographic observation, vaginal cytology, and blood sampling

After implant insertion, estrus was monitored once daily by physical (vulvar appearance and swelling, serosanguineous vaginal discharge) and sexual behavioral changes, until the occurrence of estrus. Body development (body weight [kg], height at withers [cm], size of vulva [cm], and humeral length [mm]) and vaginal cytology and serum P<sub>4</sub> and E<sub>2</sub> concentration were monitored weekly for the first 5 weeks, and then every third week throughout the treatment period. The size of vulva was measured with a metal Vernier caliper. For determination of height at withers, an assistant kept the dog in a standing position, and measurement was performed from the withers to the floor using a measuring tape. For standardization, the same person performed all body measurements. After the mean period of suppression (G1, 9.4 mg: up to 48 weeks; G2, 4.7 mg: up to 24 weeks), sampling period was shortened from 3 weeks to 2 weeks in each group. Furthermore, serum concentrations of deslorelin were monitored weekly for the first 4 weeks, and radiographic examinations were performed monthly throughout the treatment period to monitor EC. A portable X-ray device (Dynamic X-Ray; DRX 3-I, GM/094101, Ankara, Turkey) was used for radiographic examinations. Mediolateral radiographs of the right humerus were taken using a standardized direct radiographic technique (45–55 kV and 2.5 mAs X-Ray radiation doses with related to the size of the dog). Radiographic observation included measurements of humerus length and closure time of epiphyseal plate of the proximal humerus. The disappearance of the radiolucent line between the epiphysis and the metaphysis on the radiographic images was accepted as indicator for completion of the EC.

### 2.3. Hormone assays

The concentrations of P<sub>4</sub> (nmol/L) and E<sub>2</sub> (pmol/L) in peripheral blood serum samples were measured using “electrochemiluminescence immunoassay” with the fully automated Cobas Modular E170 Analyzer (Roche Diagnostics, Mannheim, Germany) in a special laboratory (Düzen Laboratories Group, Ankara, Turkey), as published by Agaoglu et al. [13]. Serum concentrations of deslorelin were measured by means of a commercially available Competitive Enzyme Immunoassay Kit (CEK 0100-06; AB Biolabs, Sovereign CT, USA) as recommended by the manufacturer. The assay is 100% specific for deslorelin. No cross-reactivity with physiological GnRH or the GnRH agonists triptorelin and goserelin was detectable. The assay sensitivity is 10 to 100,000 pg/mL. Photometric measurements were done with an ELx808 Absorbance Microplate Reader (BioTek Instruments, Inc., Winooski, VT, USA). Because of material restrictions, deslorelin resorption could only be analyzed during the first 4 weeks after implant insertion. Only in two dogs, this was possible until Days 49 and 70, respectively.

Download English Version:

<https://daneshyari.com/en/article/2094986>

Download Persian Version:

<https://daneshyari.com/article/2094986>

[Daneshyari.com](https://daneshyari.com)