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Osteoporotic risk and physeal closure in prepubertal ovariohysterectomized cats

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ABSTRACT

We aimed to examine the early effects of prepubertal ovariohysterectomy (P-OHE) on bone loss and proximal physeal closure in cats. Fourteen kittens randomly underwent P-OHE or sham operations (S-OP) at three months (mo) of age and were allocated to group I and group II. Each mo between four and nine mo of age, dual-energy X-ray absorptiometry (DEXA) scans were performed to determine the total body bone mineral density (BMD) and bone mineral content (BMC). Proximal radial physeal closure and radial length were determined by radiography. Bone-specific alkaline phosphatase (BAP), carboxy-terminal collagen teleopeptide (CTX), 17-β estradiol, progesterone, calcium (Ca) and phosphorus (P) were measured in the serum samples. No significant differences were observed between the groups in terms of BMD, BMC, BAP, BAP/CTX, P, progesterone and body weight (BW) (between 4 and 9 mo) and for Ca (between 5 and 9 mo) and for CTX levels (between 4 and 8 mo). The 17-β estradiol was significantly higher at 6, 8 and 9 mo of age in the S-OP group due to puberty ($P = 0.02$, $P = 0.03$ and $P = 0.02$ respectively). Although there was a significant difference ($P = 0.0002$) between the P-OHE and S-OP groups in terms of the proximal radial physeal closure times (7.43 ± 0.20 mo and 6.14 ± 0.14 mo, respectively), no significant difference was observed for the mean radius length (10.59 ± 0.10 cm and 10.06 ± 0.27 cm, respectively) at the last evaluation time. In conclusion, prepubertal ovariohysterectomized cats do not have any osteoporotic risks until nine mo of age and exhibit a delayed physeal closure time without a change in radius length.

1. Introduction

The uncontrolled rapidly increasing population of cats and dogs has been a substantial problem in some countries for many years. Neutering of cats and dogs at an early age (6–14 weeks old) has been widely applied in recent years to reduce pet overpopulation and prevent the unwanted signs of oestrous (Joyce and Yates, 2011; Olson et al., 2001).

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The results of previous studies (Howe, 1997; Olson et al., 2001) on the "early age neutering of cats" have showed that the anaesthetic and surgical procedures are apparently safe, the surgery duration is decreased and the recovery is faster. However, concerns have been raised regarding the potential risks of prepubertal gonadectomy (Howe, 1997; Howe et al., 2000; Root et al., 1997; Salmeri et al., 1991; Spain et al., 2004; Stubbs et al., 1996).

The timing of the growth plate (physeal) closure of long bones is controlled partly by gonadal hormones. Gonadectomy at any age prior to physeal closure delays that closure (Root et al., 1997; Salmeri et al., 1991; Stubbs et al., 1996), and this extended growth period may result in greater final radial/ulnar length (Root et al., 1997; Salmeri et al., 1991).

Osteoporosis (bone loss) is characterized by an imbalance between bone formation by osteoblasts and bone resorption by osteoclasts that results in bone loss. Osteoporotic bone is believed to be less mineralized than healthy bone due to this imbalance following oestrogen deficiency. Ovariectomized animals, including mice, rats (Inada et al., 2011; Muhammad et al., 2012), ewes (Brennan et al., 2011; Johnson et al., 1997; Turner et al., 1995) and beagle dogs (Faugere et al., 1990; Malluche et al., 1986) exhibited marked bone loss with increased bone resorption and thus these animals have been typical experimental models for investigating postmenopausal osteoporosis due to oestrogen deficiency in women. The time frame in which osteoporotic changes can be expected after ovariectomy in rats (Muhammad et al., 2012), ewes (Brennan et al., 2011; Johnson et al., 1997; Turner et al., 1995) and beagle dogs (Faugere et al., 1990; Malluche et al., 1986) are 4 weeks, 3–12 mo and 1–4 mo respectively.

The dual-energy X-ray absorptiometry (DEXA) technique is known as the gold standard for the diagnosis of osteoporosis and allows rapid, noninvasive, relatively inexpensive, precise measurement of total body bone mineral density (BMD) and bone mineral content (BMC) or BMD and BMC in specific body regions (Franck and Munz, 2000; Grier et al., 1996). On the other hand, serum and/or urine biochemical/molecular markers that indicate osteoblastic and osteoclastic activity have been widely used in the diagnosis and monitoring of osteoporosis in humans for many years. They can also be used in combination with DEXA to improve the diagnosis. Bone specific alkaline phosphatase (BAP), a marker of bone formation, and carboxy-terminal collagen telopeptide (CTX), a marker of bone resorption, are the two most commonly measured of these biomarkers (Garnero, 2009; Seibel, 2000). DeLaurier et al. (2004) evaluated a number of biochemical assays which originally developed for use in humans for their ability to measure indicators of bone cell activity in serum and urine of normal cats. Serum BAP measured by Enzyme-linked immunosorbent assay (ELISA) was found to be appropriate for cats but although CTX measured by auto-analysis method was defined as a rapid and an easier way to use than the ELISAs, CTX concentrations measured automatically did not show a significant relationship with age (DeLaurier et al., 2004).

The purpose of this study was to examine the early effects of prepubertal ovariohysterectomy (P-OHE) on bone loss and proximal physeal closure in cats. To the best of our knowledge the osteoporotic risks in prepubertal neutered cats have not yet been investigated utilizing DEXA and serum markers of bone turnover.

2. Materials and methods

2.1. Animals and study design

Fourteen kittens at three months (mo) of age were enrolled in the study. Ethics approval for the study was obtained from the local Ethics Committee (number: 2013/37). All animals were vaccinated against infectious diseases (Felocell® CVR, Zoetis, US., Leukocell® 2, Zoetis, US., Fel-O-Vax® FIV, Zoetis, US., Defensor® 3, Zoetis, US) and administered an antiparasitic (Caniverm 175 mg oral tablet, Bioveta, Ankara, Turkey). The kittens were housed and allowed to exercise in an indoor facility, and toys and scratching pads were provided. They were offered dry food (Hill's Kitten, Hill's Pet Nutrition Inc., USA) twice daily according to the recommendations of the cat food company, and water was available ad libitum from an automatic system.

Kittens were randomly allocated into one of two groups: the group I animals underwent P-OHE ($n = 7$) and the group II animals underwent a sham operation (S-OP) ($n = 7$). P-OHE and S-OP were performed with the animals at three mo of age. The cats were observed during the anaesthetic and post-operative period.

Every mo between four mo and nine mo of age, total body DEXA scans were performed; serum samples were collected, and radiographs were taken. Body weight (BW) was also recorded. Total body BMD and BMC were measured using DEXA, and BAP, CTX, estradiol 17-β, progesterone, calcium (Ca) and phosphorus (P) were measured in the collected serum samples; proximal radial physeal closure and radial length were evaluated by radiography.

2.2. Anaesthesia and surgical procedures

The last daily meal was given to the kittens at 8–10 p.m., the night before the surgeries (8–10 a.m.). Uneaten food was left in the cage for 4 h. The relatively short time of fastening food was required because of their minimal hepatic glycogen stores. An intravenous catheter was placed in each animal for fluid administration with 5% dextrose and balanced electrolyte solution (Polifleks®, Polifarma, Turkey) and vascular access was also obtained in case of emergency. After a subcutaneous (SC) injection of atropine sulphate (Atropine®, 0.2%, Vetaş, Turkey) (0.02 mg/kg), induction of anaesthesia was performed with an intramuscular (IM) injection of medetomidine hydrochloride (Domitor®, Pfizer, USA) (80 μg/kg) and ketamine hydrochloride (Alfamine®, 10%, Alfasan, Holland) (7.5 mg/kg). The kittens were intubated, maintained on isoflurane (Forane®, Baxter, USA) and oxygen, and monitored (GT9000F, MVM, Turkey) during the surgery. Surgeries were performed using standard techniques.

2.3. DEXA procedure

The total body scans were performed at the Faculty of Medicine using a dual energy X-ray absorptiometer and