CHAPTER 1

Introduction

Canine overpopulation has become a considerable problem in many countries all over the world. Throughout cities and countryside worldwide, packs of roaming dogs present serious public health problems, including rabies in some countries. World Health Organisation (WHO) statistics report about 50,000 deaths annually worldwide from rabies, and more people die each year from dog bites than from rabies (Mechler, 2002). Most of the research concerned with this problem has been directed towards developing a contraceptive for use in the bitches (Simmons and Hamner, 1973; Van Os, 1982; Fieni et al., 1997). Sterilization, usually meaning surgical gonadectomy, has long been considered as one of the principles of means to control canine populations along with pet owner's education and legislation (New, 2002). In dogs, surgical contraception including castration and vasectomy are both safe, effective and proven procedures (Pineda, 1986), however surgery and associated anesthesia always carries some risk. Castration is generally performed as the method to control canine population; however, castration is not a practical proposition in large stray dog populations, because of the time required per procedure and the increased risk of carrying this out in the field. The method of chemically blocking the spermatozoal excurrent duct system by the intratesticular administration of sclerosing agents (Pineda and Hepler, 1981), termed chemical vasectomy, produces a severe inflammatory reaction, and the ethics of such treatments is questionable.

As this is a world health problem, methods that are economical, easily performed and safe need to be developed. To achieve this, a better understanding of male fertility with regard to endocrinology together with spermatogenesis is required. In mammals, spermatogenesis is testosterone dependent (Sharpe, 1987) and testosterone is under the control of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), the regulation of which are influenced by the gonadal steroids, peptides such as inhibin, and ultimately GnRH. The gonadotrophins LH and FSH act on the Leydig cells and the

Sertoli cells, respectively. In the dogs, FSH stimulates spermatogenesis indirectly by an action upon the Sertoli cells, and LH stimulates the Leydig cells to produce testosterone (England, 1998). Within the testis, LH binds to membrane receptors on the Leydig cells and stimulates them to convert cholesterol to testosterone. High local concentrations of testosterone within the testis are considered essential for normal spermatogenesis to occur both in men (Sharpe, 1994) and animals (Cunningham, 2002). The subsequent mechanisms associated with the testosterone required in production of spermatozoa are locally controlled (Sharpe, 1983). The testosterone released gains access to the seminiferous tublues by diffusion across the blood-testis barrier. The Sertoli cells require a proportion of this testosterone for spermatogenesis, while the remainder becomes attached to the available androgen-binding protein, which transports it to the epididymis where it is involved in providing the environment necessary for maturation and storage of spermatozoa. On the basis of negative feedback mechanism, it should be possible to suppress gonadotrophin secretion and as a consequence block spermatogenesis. The production of spermatozoa and androgens are closed linked and it is difficult to suppress spermatogenesis without simultaneous suppression of androgen release, which may influence libido and male-like behavior. Suppression of testosterone production by the Leydig cells could be a suitable method of male contraception.

The use of androgens alone may be useful to suppress spermatogenesis, since testosterone inhibits hypophyseal LH secretion so that ultimately intratesticular androgen concentrations decline, whereas peripheral testosterone concentrations remain high, owing to the exogenous androgen (England, 1997). Testosterone was first administered to men with the aim of suppressing spermatogenesis in 1950 (Heller et al., 1950 cited by England, 1997). In man, many studies have been done with regard to the response of suppressing spermatogenesis by testosterone (Nieschlag et al., 1978; Schulte-Behrbuhl and Nieschlag, 1980). However, androgen treatment regimen is not practical in clinical use due to the frequency of hormone administration ,and its effect on antifertility in dogs is unacceptable (Taha, 1980).

Progestogens are used for their anti-androgenic effects, which inhibit the release of gonadotrophins. Progestogens administered to dogs at the same dose as used routinely in bitches to control estrous cycle have no effect upon testicle size, semen quality or libido (Wright, 1979). High doses of progestogens produce a rapid and significant decrease in sperm motility, morphology and sperm output, but it is not sufficient to render the animal infertile. The effect of progestogens is probably mediated by action upon the epididymis, since semen quality declined rapidly; morphological changes are the result of more secondary sperm abnormalities, and there is no suppression of plasma LH concentration (England, 1997). The dogs appears to differ from other species in the sensitivity of pituitary-hypothalamic axis to progestogen feedback, since gonadotrophin suppression does not occur even when high doses of progestogens are used and there are no significant effects on libido (England, 1997). It can be concluded that progestogens alone are not suitable for contraception in the male dogs (Hewitt, 1998). Although, combinations of progestogens and androgens may provide a clinically useful method of reversible contraception in the dogs, the glucocorticoid agonist effect of progestogens ,particularly long-term treatment or use of high doses, may result in a iatrogenic Cushing's syndrome and diabetes mellitus (Selman et al., 1997)

Recently, many researches have been explored for development into an efficient, long-acting, non-surgical contraceptive for dogs and cats. These included Zona pellucida vaccine (Frayer-Hosken et al., 2000), vaccine against GnRH (Hwang et al., 2002), Zinc gluconate intratesticular injection (Wang, 2002) and also GnRH agonist implants (Trigg, 2002).

Aims of this study

1. To investigate the effects of GnRH agonist deslorelin on semen characteristics, serum testosterone concentrations, testicular size and prostate gland in dogs.
2. To evaluate the possibility of subcutaneous deslorelin implantation to control male fertility in dogs.
3. To determine how subcutaneous deslorelin implantation affect prostatic volume.

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