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SciVerse ScienceDirect

Theriogenology 78 (2012) 842–847

Theriogenology

www.theriojournal.com

Control of the estrous cycle in guinea-pig (*Cavia porcellus*)

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Received 31 January 2012; received in revised form 22 March 2012; accepted 24 March 2012

Abstract

The aim of this work was to look for a simple method to obtain synchronized ovulation in guinea pigs under farming conditions while respecting animal welfare. The luteolytic activity of three different prostaglandins F2alpha (PGF2α) analogs (D-cloprostenol, D,L-cloprostenol and luprostiol) and a daily treatment with oral progestagen (altrenogest) was tested successively at different stages of the estrous cycle on the same group of females during a period of 8 mo. The estrous cycle length was not modified by the administration of PGF2α analogs, whatever the stage of the estrous cycle when the treatment was initiated. Our results led us to reject the use of PGF2α analog to induce practical synchronization of the estrus in this species. In females (n = 29), given 15 days with altrenogest (0.1 mL po once a day), ovulation occurred 4.43 ± 0.13 days after the end of the treatment. Altrenogest treatment was followed by mating. No negative impacts of the treatment on the pregnancy rates, delivery rates and litter sizes were observed. This standard method of guinea-pig estrus synchronization is less stressful for the animals compared to techniques using progesterone tubing.

Keywords: Estrus; Synchronization; Guinea Pig; Altrenogest; Prostaglandin-F2α

1. Introduction

The guinea-pig (*Cavia porcellus*), together with the camelids and the dog, was domesticated in the Andes [1] where it still plays an important role in highland societies as a source of protein for many low income indigenous people [2]. Peru is the country with the highest population and consumption of guinea pigs. About 16, 500 tons of meat are produced there every year, out of a constant population of about 22 million animals raised essentially upon family production systems [3]. In this part of the world, guinea pigs are also involved in many folklore traditions, exchanged as gifts and used in traditional medicine to diagnose diseases [4]. The conservation of native genetic diversity is a longterm issue.

The guinea-pig has also been used commonly since the late 18th century as a laboratory animal [5]. It played a major role in the establishment of the germ theory in the late 19th century, in particular through the studies of Robert Koch on tuberculosis [6]. Despite its important role in laboratory animal science, the use of guinea pigs has decreased significantly since the middle of the 20th century, mostly because mice and rats have replaced them. In 2007, guinea pigs represented only

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http://dx.doi.org/10.1016/j.theriogenology.2012.03.034

2% of the total number of laboratory animals [7]. Nonetheless, the guinea-pig is still a reference model for very specific research, because its immune system possesses an antigen-macrophage interaction similar to that of the human [8,9]. The relatively long gestation period (68 days), compared to other rodents with mature central system at birth, makes it a very relevant model for teratology studies. This characteristic is particularly interesting for the study of deleterious factors which act differentially with respect to the stage of pregnancy, as do many noxious agents in man [10]. The most common strains used in scientific research are outbred animals, such as the albino short-haired Duncan-Hartley guinea pig. Inbred strains are also available, Strain 2 and Strain 13 being the most commonly used. New strains for specific purposes are regularly established [11].

The establishment of an embryo cryobank will permit the preservation of the genetic pool of both scientifically valuable strains and native guinea pigs. It is also an interesting strategy to reduce maintenance costs related to livestock.

To produce guinea-pig embryos and to set up the technique of embryo transfer, it is first necessary to control the female estrous cycle. Controlling the heat period is required to obtain embryos at morula or early blastocyst stage and to prepare synchronous recipients for embryo transfer. In the present work we sought estrus synchronization through two approaches. One was to block ovulation using a progestagen treatment, and another was to induce estrus with a PGF2α analog treatment.

A treatment to synchronize ovulation under laboratory conditions was proposed using a subcutaneous implant filled with crystalline progesterone over a 4 wk period[12]. The withdrawal of the implant induces ovulation within 5 d. This treatment is difficult to set up in farming conditions and presents ethical problems regarding the use of general anesthesia to insert a large implant (1.0 cm long and 0.4 cm i.d.).

Most of the work to discover the luteolytic factor in guinea pigs was carried out in the late 1960s and early 1970s. Blatchley and Donovan [13] established that exogenous PGF2α was luteolytic in hysterectomized guinea pigs. Poyser [14] indicated that guinea-pig uteri are probably the major source of this luteolytic factor. Further results [15] identified PGF2α as the uterine luteolytic hormone in guinea-pig since the treatment of females during their cycles with indomethacin (blocker of PGF2α synthesis) lengthened their estrous cycles. In 1976, Blatchley and Donovan indicated that the response of the corpus luteum to treatment with PGF2α changes during the estrous cycle. Treatment with PGF2α over Days 4–6 or 6–8 of the cycle temporarily depressed progesterone release without shortening the life of the corpus luteum. When the drug was administered over Days 8–10, 10–12 or 12–14, the depression in progesterone was not followed by any recovery (Day 1 is the day on which maximum cornification was seen in smears) [16]. In hysterectomized guinea pigs, the corpus luteum responds to the luteolytic action of $PGF_{2\alpha}$ only after Day 9 of the estrous cycle (Day 0 is the first day when the vaginal membrane is fully perforated) [17].

The aim of this work was to look for a simple method to obtain synchronized ovulation in guinea-pigs under farming conditions while respecting animal welfare. We tested the luteolytic activity of three different PGF2α analogs (D-cloprostenol, D,L-cloprostenol and luprostiol) currently used for mammal synchronization and we tested the oral administration of a progestagen (altrenogest) as it is used in sows and mares [18,19]. These treatments were administered to guinea pigs at different stages of their estrous cycle.

2. Materials and methods

2.1. Animals

Forty-four multiparous female guinea pigs with normal cycles, aged between 18 and 24 mo, from the Maria-Marcela Farm (Puente Piedra-Peru), weighing from 1.0 to 1.5 kg, were used in this study. Females were housed under farming conditions and were fed on commercial pellets (vitamin C enriched) and tap water *ad libitum*. To determine the day of ovulation, the colony was checked twice a day for vaginal opening. As perforation of at least half the vaginal membrane was observed, vaginal smears were made at 12-h intervals to determine the day of ovulation (Day 0), judged by the first leukocytic smear following a cornified smear [20]. The natural length of the estrous cycle in the guinea pigs used in this study was 16.17 ± 0.21 d (observed on 83 cycles).

2.2. Treatments

In this study, four treatments to control the heat period of the guinea-pig were tested. First, three treatments with injections of PGF2α analogs had been performed to clarify their capacity of luteolysis (D-cloprostenol; D,L-cloprostenol and luprostiol), and last, a daily treatment with oral progestagen (altrenogest) was