OVARIAN FOLLICULAR DYNAMICS AND DOMINANCE EFFECT IN SHEEP

A. Gonzalez-Bulnes and A. Veiga-Lopez
Departamento de Reproduccion Animal, INIA
Avda. Puerta de Hierro s/n, 28040-Madrid, Spain

Patterns of ovarian follicular development in sheep are characterised by the appearance of antral follicles that grow continuously until they ovulate or become atretic. Throughout reproductive life, different cohorts of follicles are recruited to resume growth and development in an FSH dependent process. The largest follicles in the cohort secrete high levels of inhibin A and oestradiol, causing decreased FSH concentrations. The drop in FSH levels causes the atresia of smaller follicles, whilst a dominant follicle avoids its own regression by shifting its dependence from FSH to LH. However, when LH concentrations remain low, large follicles become critically dependent on FSH without establishing dominance. There is a lack of dominance during the luteal phase of the ovine oestrous cycle, but after luteolysis, when secretion of LH is enhanced by increased secretion of oestradiol from preovulatory follicles, the effect of dominance becomes evident. The mechanism of dominance in sheep is different from that described for cows, in which the dominant follicle inhibits the growth of other follicles in the cohort and avoids the emergence of new follicles. In ewes, the preovulatory follicle inhibits the growth of other follicles present in the ovaries at time of emergence. The recruitment? of follicles, however, is decreased but not inhibited, although their subsequent growth is suppressed. Administration of exogenous FSH in sheep promotes the growth of small follicles to ovulatory sizes, but the presence of a dominant follicle at the start of FSH treatment decreases the number and viability of embryos recovered. This fact could be related to direct inhibitory effects from the dominant follicle at the ovarian level.

Key-words: Sheep, Follicle-dynamic, Follicle-dominance, Luteal-function.

Introduction

Transrectal ultrasonography has become an important tool for the study of ovarian structures in sheep from its first application in the early 1990's (Schrick et al., 1993). The use of ultrasound scanning has increased our knowledge of follicular and luteal function and, in fact, has triggered the revision of theories about patterns of follicular dynamics and existence and degree of follicular dominance. Our aim is to offer an overview of the current information about ovarian physiology and its influence on efficiency of reproductive technologies like oestrus synchronization, artificial insemination and embryo production.

Ovarian follicular dynamics

Patterns of follicular development in sheep are characterized by the appearance of antral follicles that grow continuously until they ovulate or become atretic (Scaramuzzi et al., 1993). Throughout reproductive life, different cohorts of follicles are recruited to resume growth and development in an FSH-dependent process (McNeilly et al., 1991). However, the different descriptions of patterns of follicular growth and development were controversial in early studies. Some authors described follicular growth as continuous and independent of the stage of the cycle (Hutchinson and Robertson, 1966; Schrick et al., 1993). Other studies were supportive of the notion of a wave-like pattern (Ravindra et al., 1994; Ginther et al., 1995). Currently, there is a general agreement that reconciles both viewpoints; the high variability in the number of follicles developing in each wave (the cohort of follicles) and the high variability in the number of cohorts developing in each oestrous cycle (Evans, 2003). In this way, follicles ≥5mm in diameter would exhibit a wave-like pattern while follicles smaller than 4mm would grow randomly (Ginther et al., 1995). Both patterns of growth are classified as primary and secondary follicular waves, respectively (Adams et al., 1999).

Effects of follicular dominance

The largest follicles in the cohort of each wave secrete high amounts of inhibin A and oestradiol, causing decreased FSH concentrations and the atresia of smaller follicles (Baird, 1983). The mechanism of dominance in sheep and goats is different from that reported for cows (Ginther et al., 1989), in which the dominant follicle inhibits the growth of other follicles in the cohort and prevents the emergence of new follicles (Fortune, 1994). In sheep, the preovulatory follicle inhibits the growth of other follicles present in the ovaries at time of emergence. The appearance of new growing follicles, however, is decreased but not inhibited, although their subsequent growth is finally suppressed (Gonzalez-Bulnes et al., 2001, 2004). The dominant follicle avoids its own regression by shifting its dependence from FSH to LH (Campbell et al., 1999). However, when LH concentrations remain low, large follicles become critically dependent on FSH without establishing dominance. This effect, induced by decreases of LH, explains the suppressive effects of progesterone from the corpus luteum on dominant follicles in sheep (Adams, 1999). There is a lack of dominance during the luteal phase of the ovine oestrous cycle, but after luteolysis, when secretion of LH is enhanced by an increased secretion of oestradiol from preovulatory follicles (Baird, 1983), the effect of dominance becomes evident (Lopez-Sebastian et al., 1997).

Effects of follicular status on yields of reproductive technologies

In Mediterranean countries, the use of reproductive technologies like artificial insemination or embryo production is associated to the use of oestrus synchronization with progestagens. Progestagen treatments cause alterations in patterns of follicular growth and dominance (Nöel et al., 1994; Leyva et al., 1998), although, at the same time, these changes are modified by the luteal environment at the time of insertion of the progestagen. The common practice is the insertion of progestagen sponges to a group of sheep without previous knowledge of the stage of the oestrous cycle of each female. There would be ewes with supra-luteal (progestagen from the sponge plus endogenous progesterone from the corpus luteum) and ewes with sub-luteal levels of progestagens (only progestagen from the sponge) dependent on the treatment. The activity and lifespan of large follicles is shortened when the sponge is applied in the presence of a corpus luteum and is lengthened in the absence of a corpus luteum (Leyva et al., 1998; Rubianes et al., 1996). Such persistence of dominant follicles can lead to the permanence of aged follicles; and the permanence of aged follicles in static or early atretic phase has been associated to lower fertility.

Follicular status also affects outputs in embryo production, either *in vivo* or *in vitro*. In both procedures, the number of oocytes/embryos may be increased by the administration of high dosages of exogenous gonadotrophins (mainly FSH) which stimulates the growth and development of ovarian follicles. Most of the studies on the effect of follicular status on embryo yields has been developed in protocols for *in vivo* embryo production. In such studies, despite of the source of hormones and the administration protocol, both ovulation rate and number of recovered embryos were related to the number of small (2-3 mm) gonadotrophin-responsive follicles present in the ovary at first FSH injection (Brebion and Cognie, 1989; Gonzalez-Bulnes et al., 2000). Administration of exogenous FSH stimulates the growth of small follicles until preovulatory stages and ovulation and rates of ovulation and embryo recovery are also related to the number of medium (4-5 mm) follicles at sponge withdrawal and to the number of large (≥ 6 mm) follicles at estrous behaviour (Gonzalez-Bulnes et al., 2000). However, some of these follicles may be immature or early atretic, as indicated by the lack of relationship between number of small follicles and number of viable embryos. In fact, the viability rate of embryos is related to the more limited category of follicles with 3 mm in size at first FSH dose. Follicles of 2 mm are related to a higher degeneration rate, indicating a compromised developmental competence (Veiga-Lopez et al., 2005) in agreement with a previous study showing that most of the ≥ 3 mm follicles are mature and functional, being the main source of inhibin A (Gonzalez-Bulnes et al., 2000). On the other hand, the presence of large dominant follicles (≥ 6 mm) at the time of a single superovulatory dose of eCG (Rubianes et al., 1995) or FSH (Lopez-Sebastian et al., 1999) decreases ovulation rate. In multiple dosage FSH protocols, although ovulation rate is not affected, both number and viability of recovered embryos are decreased in presence of dominant follicles (Gonzalez-Bulnes et al., 2002). Thereafter, more precise studies involving serial screening of the dynamics of dominant follicles have shown that inhibitory effects are markedly affected by the developmental stage of the follicular wave, with lower outputs in ewes bearing large follicles in a growing phase and smaller accompanying follicles (Veiga-Lopez, unpublished). The inhibitory effects of dominant follicles on embryo yields has commonly assumed to be exerted, although without direct evidences, through alterations on follicular and oocyte development during the superovulatory treatment that affects later embryo development. However, recent studies from our laboratory (Veiga-Lopez, unpublished) show that the beginning of oestrus behaviour, preovulatory LH surge and ovulation are affected by follicular status at start of the superovulatory treatment.

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