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Induction and synchronization of oestrus in sheep and goats

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ABSTRACT

Different methods for oestrus induction and synchronization in domestic small ruminants have been developed. Seasonality and female's status are important factors for choosing the most appropriate treatment. In the case of females during breeding season, prostaglandins can be used since functional corpus luteum must be present in the ovaries, while during non-breeding season females should be treated with progesterone-based treatments, accompanied by equine chorionic gonadotrophin (eCG), releasing hormones and other compounds. Significant spread of oestrus synchronization during and after the breeding season has been achieved by the use of intravaginal sponges impregnated with synthetic analogues of progesterone. However, the effect of hormonal drugs on the female reproductive system may manifest differently depending on the initial functional state of reproductive organs and the hormonal status, and negative consequences can be observed when drugs are wrongly administered. In addition, insufficient knowledge about the patterns of change in the reactivity of the nervous sexual centers and the corresponding reactions of the body to the administration of hormones reduces their effectiveness, which limits the widespread use. In general, the induction and synchronization of oestrus in small ruminants is an currently important direction of scientific research and an urgent problem of sheep and goat breeding, but the proposed methods require further improvement by reducing the costand increasing biosecurity and predictability of the result.

Keywords: small ruminants, reproductive function, stimulation, oestrus

INTRODUCTION

The use of biotechnological methods in reproduction management should serve to maximize the reproductive potential of animals. The implementation of these methods requires a profound knowledge about the biological reproductive patterns and, in order to obtain good results, their application should be carried out in animals with optimal health and physical condition (Holtz, 2005; Alexander et al., 2010; Gama and Bressan, 2011; Aksenova et al., 2012; Ajbazov and Seitov, 2013; Skljarov et al., 2015; Choudhary et al., 2016).

Synchronization of oestrus cycles allows for grouping at the beginning of oestrus and then at the time of artificial insemination (AI). By stimulating the ovulation process, fertility could be also improved and between-parturition interval will be reduced in females showing heats during early lactation. After parturition, a refractory period occurs in many breeds of sheep and goats, and the stage of sexual excitation is manifested only with the onset of autumn, when daylight shortens (Ajbazov and Aksenova, 2007; Erohin, 2011; Koshevoj et al., 2011; Aksenova et al., 2012; Delgadillo et al., 2015; Dardente et al., 2016; Luo and Sun, 2018; Đuričić et al., 2019; Ungerfeld, 2019).

To optimise the management of the reproductive function in small ruminant, a number of zootechnical and organizational measures, and biotechnological processes (i.e. the induction and synchronization of oestrus and ovulation, the induction of superovulation, artificial insemination or embryo transfer) are nowadays implemented (Anel et al., 2006; Rahman et al., 2008; Amridis and Cseh, 2012; Arrebola et al., 2012; Ordin and Plahotnjuk, 2012; Gordon, 2017; Özalp et al., 2017; Sharan and Grymak, 2017; Fedorenko et al., 2017; Fonseca et al., 2018).

The basis for the methods of regulation of reproductive functions is The use of hormonal drugs forms the basis for the methods which regulate reproductive functions. However, while applying drugs, it should be borne in mind that their effects on the female reproductive system can manifest in different ways, depending on the initial functional state of reproductive organs and the hormonal status of the organism. Incorrect administration of the drug, without taking into account indications, may have negative effects Sharan and Topurko, 2007; Abecia et al., 2011; Karynbaev and Akynbekova, 2013; Tihona et al., 2013; Menlikulova et al., 2014; Erohin and Pridanova, 2015; Skljarov and Koshevoj, 2016; Ramos and Silva, 2018).

The purpose of the work is to analyze the direction of research on induction and synchronization of oestrus cycle in sheep and goats.

ANALYSIS OF LITERATURE DATA ON THE INDUCTION AND SYNCHRONIZATION OF OESTRUS IN SHEEP AND GOATS

To date, various hormonal treatments have been developed to influence the sexual cycle of sheep and goats. The choice of scheme and method of regulation depend on breeding season and time of the year. For example, prostaglandins are used during the breeding season, when females have functional corpus luteum in the ovaries. Other hormones for oestrus stimulation schemes are used outside the breeding season. In this case, progesterone, equine chorionic gonadotrophin (eCG), releasing hormones and other compounds are commonly used. In reference to small ruminants, intravaginal sponges impregnated with synthetic progesterone analogues are widely used. These are more active in comparison with natural hormones in low doses (Gungor et al., 2007; Erohin, 2011; Arrebola et al., 2012; Khanthusaeng et al., 2013; Grymak, 2014; Zarazaga et al., 2014; Erohin and Pridanova, 2015; Knights and Singh–Knights, 2016; Omontese et al., 2016; Erarslan and Karaca, 2017; Budevich et al., 2018; Chaudhary et al., 2018; Dogruer et al., 2019; Biehl et al., 2019; Sun et al., 2019).

Inducing oestrus behaviour during non–breeding season

During the non–breeding season (spring and summer), as well as in animals that do not show oestrus signs for 20 days or more since the beginning of the breeding season or remain non–pregnant after the first mount/insemination, it is necessary to stimulate the sexual behaviour and to promote gestation as soon as possible.

The oestrus cycle induction during summer or spring offers the additional chance to treat young sheep and goats that suffered abortion or lost lambs/kitts shortly after birth. Another goal is to shorten intervals between parturition in order to get three lambs/kitts in 2 years or two per a year.

In order to induce oestrus in small ruminants during the non-breeding season, the administration of progestagen is the choice method and it provokes the prolongation of the luteal phase in these animals. As a result they are synchronized and, after the cessation of hormonal treatment, the animals simultaneously come into oestrus. (Ajbazov et al., 2006; Aksenova et al., 2012).

In order to synchronize the oestrus in sheep, the use of gestagens in intravaginal devices is additionally combined with administration of gonadotropins. Menlikulova et al. (2014) found that the use of eCG on Ordabasin sheep breed promoted the increment of heat duration in the first cycle after treatment and 87.8–97.2% of females showing oestrus signs were artificially inseminated. However, only about 10.9% of animals were in oestrus in the next cycle after the use of the mentioned gonadotropin.

In the first, second and third days after the application of eCG in fat–tailed sheep (3.5 years), the percentage of inseminated animals was 67.9%, 29.5% and 2.6%, respectively. And it was observed that in older females (3.5 to 5.5 years), the proportion of fertilized animals on the first day rose from 67.9 to 77.9% (Menlikulova et al., 2014).

Progesterone is intramuscularly injected in sheep and goats at a dose of 30 mg (3 ml of 1% oil solution) 3–4 times at intervals of 48 hours. Two days after the last injection, a dose of 1200 IU eCG is administered. Two days later, animals are treated again with progesterone twice a day for 8 days. Animals who did not show heat on day 16th can be re–treated with eCG (but no progesterone) and continue to inseminate them as they enter in oestrus for the next 8 days. In Karakul sheep, using this scheme, 80% of the treated ewe showed heat, with fertility around 40%, and in individual flocks – up to 56%. In Romanov sheep treated during the summer season, effective three–fold injections of progesterone at an interval of 72 hours in a dose of 35 mg followed by eCG in a dose of 700 IU administered in two days after the treatment with progesterone. If, after such treatment, the sheep did not come to heat, then after 15 days, the introduction of eCG is repeated. In such treatment, 34% of the ewe comes from the first injection of eCG and 45% after the second injection. Fertility at first insemination reached 53%, with 2.45 lambs per birth (Shubin, 1987).

Synthetic progestagens (megestrol acetate, dimol, amol, etc.) can be administered orally or intravaginally. The oral route is the least labor–intensive. The drug is mixed with salt and then it is added to the feed, or it can be dissolving with ethyl alcohol and then it is pulverized and mixed with the feed. This treatment should be administered every day for 8–10 days, but this administration route does not guarantee the total consumption of the required dose in all the treated animals.

The intravaginal devices for progestagen supplementation are more frequently used in small ruminants. A fine porous sponge with alcohol or propylene glycol solution of the progestagenic preparation can be introduced for around 10–14 days. In this method, sponges are impregnated with at a rate progestagen (100–500 mg), megastrol acetate (30 mg), kronolon (30 mg), dimol (10–15 mg) and others. A silk thread in the length of 15–20 cm is pre–stitched to the sponge and it is left 2–3 cm out of the vulva in order to easily remove the sponge from the vagina. When the sponge is withdrawn, 700–1200 IU eCG will be subcutaneously administered. After 48 hours, females show heat signs and they can be inseminated. Females which do not show heat signs after the first eCG injection will be treated again 16 days later, but the management of animals as a block makes difficult and impractical to repeat the treatment for an individual or a small–groups. The effectiveness of hormone stimulation of sexual cycles in sheep and goats at the beginning of the non–breeding season is much lower than at the end of it. In lactating females, the effectiveness of heat stimulation and fertility is lower than in non-lactating animals. It is not recommended to induce heat in small ruminants earlier than a month after parturition, as the result of insufficient involution of the uterus is conducing to very low fertility (10–35%).

Currently, advanced methods for progestagen administration are used by introducing polyurethane sponges or silicone elastic devices impregnated with a certain amount of progesterone or its synthetic analogues. Usually, fluorogestone acetate or medroxyprogesterone acetate are used for these purposes, and different trade names are used for these intravaginal devices (sponges or spirals): «Chronogest», «Veramix», «Ovakron», «Syncrite», «CIDR–G» (Powell et al., 1996; Romano, 1998a; Wieldeus, 1999; Kausar et al., 2009). These intravaginal devices are introduced for a period from 9 to 19 days, usually in combination with eCG, which is administered during or 48 hours before withdrawal of the devices. Oestrus synchronization occurs in 90% of animals within 24–48 h after removing sponges or spirals (Erohin, 2011).

The fertility after oestrus synchronization depends on the specie, breed, treatment and method of insemination. A comparative study about the use of polyurethane sponges containing 15, 30, 45 or 60 mg medroxyprogesterone acetate for Corriedale sheep breed during the non-breeding season did not reveal differences depending on the dose in the number of ovulated sheep (96.8%) (Iglesias et al., 1997).

In order to clarify the relationship between the maintaining progestagen devices in the vagina and fertility, different studies were conducted. Fertility after the insertion of polyurethane sponges containing 60 mg medroxyprogesterone acetate for 1, 2, 3, 6 and 12 days was 12.5%, 20%, 50%, 75% and 68.8%, respectively (Ungerfeld and Rubianes, 1999). These studies have shown that maintaining these intravaginal devices for 6 days contributes to the achievement of high fertility, as in the traditional introduction of sponges for 12 days. Another study comparing the effectiveness of three different intravaginal progestagen-releasing devices (polyurethane sponges impregnated with fluorogestone acetate or medroxyprogesterone acetate, and silicone spiral with progesterone) maintained for 6 days inside the sheep during seasonal an oestrus showed almost the same results for oestrus induction (91.5%, 94.1% and 95.9%) and fertilization (67.4%, 62.5% and 59.6%) (Menchaca and Rubianes, 2004).

In France, the most common method for synchronizing oestrus in sheep and goats is the use of intravaginal sponges containing 45 mg of fluorogestone acetate for a period of 11 days. Then, 48 hours prior to the removal of the sponge, the animals are given 400–600 IU eCG and 50 µg of cloprostenol (a synthetic analogue of prostaglandin F2α) administered once. After that, one–time artificial insemination of females by cooled or frozen semen is carried out 43–45 h after removing the sponge without revealing signs of heat (Corteel et al., 1988).

The efficiency of various doses of eCG (300, 450, and 600 IU) after the insertion of intravaginal polyurethane sponges containing 40 mg fluorogestone acetate for 14 days showed a significantly higher fertility (81.2%–84.3%) than in control group (57.5%), which did not receive eCG. However, when prolificacy was analysed, the best results were obtained when 450 IU (155%) and 600 IU (177%) were used, which confirms the greater effectiveness of these dosages (Zaiem et al., 1996).

A comparative study analysed the effect of introducing tampons with progestogen into the vagina of goats on the percentage of animals that showed signs of oestrus and their fertility (Baril et al., 1993). Results showed that maintaining a 45 mg fluorogestone acetate sponge for 11 days and the subsequent administration of 400 IU eCG and 50 µg cloprostenol at 48 hours prior to the withdrawal, contributed to the expression of oestrus in 81–98% of animals and a fertility rate of 62–65%.

It has been reported that the use of PG–600 drug offers good results for oestrus stimulation in sheep, since this product contains 400 IU eCG and 200 IU human chorionic gonadotrophin (HCG), in contrast with a unique dose of eCG (Safranski et al., 1992; Morrical et al., 1995; Windorski et al., 2008).

Also, studies were conducted on the effectiveness of the use of gonadotropic release hormone (GnRH) instead of eCG in Merino sheep involved in a treatment based on intravaginal sponges with medroxyprogesterone acetate. GnRH in a dose of 100 µg was injected 12 hours after the removal of the sponge. As a result, there was a reduction in the timing of the onset of oestrus and higher heat incidence was observed (Jabbour and Evans, 1991).

The possibility of improving the efficacy for oestrus stimulation in sheep using intravaginal gestagen–containing sponges was investigated by additional treatment with melatonin implants. Laliotis et al (1998) described the use of subcutaneous melatonin implants (Regulin, 18 mg) in sheep for 35 days prior to the sponge's insertion. The sheep were then inseminated 48 or 60 h after the sponge was withdrawn. In the melatonin group, fertility increased in females in the second oestrus after treatment (60.4% versus 32.6% in control group) and their prolificacy increased by 0.17 lambs. The positive effect of additional melatonin treatment in combination with gestagen and eCG was also noted in studies about oestrus stimulation during anestrus period in Awassi sheep breed (Kridli et al., 2006). Researchers found that melatonin exerts a positive effect when it is jointly used with progestagens and eCG schemes to stimulate oestrus, but the use of melatonin without other drugs was ineffective for these purposes (Stellflug et al., 1994; Kridli et al., 2006).

In New Zealand, elastic silicone spirals impregnated with progesterone, which have the trade name CIDR–S and SIDR–G, were developed to stimulate oestrus in cattle (Ainsworth and Downey, 1986). Currently, they are widely used in sheep breeding (but they arenot approved for goats) and the effectiveness is comparable with intravaginal sponges based on synthetic progestogens (Carlson et al., 1989; Hamra et al., 1989).

In America, for oestrus induction in cattle, an ear implant containing 6 mg of norgestomet (commercially called Syncromate–B) is used. For sheep and goats, a half or a third of this implant has been used (Mellado and Valdes, 1997). This implant is inserted in the sheep for 9–14 days and additionally eCG or prostaglandin are administered 2 days before or during the device withdrawal. The onset of the oestrus after such treatment is noted in 62–100% of animals, depending on the season, breed and dose (Freitas et al., 1996; Gonzales–Reyna et al., 1999).

Malahova and Novopashina (2011) on the basis of the conducted research in goats concluded that the use of pessaries with progestogen for a period of 16 days requires the administration of eCG on the day of pessaries' removal, which will significantly reduce the cost of labour for animal treatment. When reducing the period of treatment with progestagens up to 14 days, eCG should be administered 24 hours after the removal of pessaries. The authors found that the time of injection of eCG at the removal of pessaries for 16 days did not significantly affect the effectiveness of the hormonal treatment. The number of goats in heat when eCG was administered immediately after the removal of pessaries or 24 hours later was 83.3 and 80.0%, respectively. However, the injection of eCG at the same time as the removal of pessaries can significantly reduce the cost of labor for animal treatment. By reducing the treatment period to 14 days, the extension of the time between the removal of pessaries and the administration of gonadotropin up to 24 hours increased the stimulatory effect by 3.3%.

However, the use of progestogens by the administration of intravaginal polyurethane sponges or silicone elastic spirals is quite expensive, so the devices do not always have the appropriate permission, and preparations – the appropriate registration (Erohin and Pridanova, 2015).

A progestagenic preparation based on pregnadien acetate (DAP) has been tested. This substance is an intermediate for the synthesis of acetate megestrol, as well as chlorsuprululin. It turned out that pregnadien acetate possesses high gestagenic activity, but in the same doses in sheep is less effective than megestrol acetate. Chlorsuprululin, even in very small doses (0.001 mg), in combination with eCG, causes heat in a significant number of sheep (72%). It is believed that pregnadien acetate and megestrol acetate are relatively long delayed in the body, have a blocking effect on the hypothalamic–pituitary system and reduce the reactivity of ovaries in sheep to the eCG effect (Bekeova et al. 1991).

The use of a new drug, such as diazetate of mepregenol (MPD), was most effective in the 8–day regimen (0.5–1 mg per day per head + 1200 IU eCG), which provides ovulation during refractory period in 88% of cases, and polyovulation in 50% of sheep. A good result for oestrus synchronization in sheep (79–80%) was obtained with subcutaneous single administration of 150–250 mg of 17–hydroxyprogesterone–capronate (17–COP) in a solution of cottonseed oil and 5% benzyl benzoate. The additional administration of eCG (1200 IU) before the onset of the theoretical beginning of synchronized heat (34 days after 17–COP treatment) increases the effect of synchronization to 4–5 days in 85% of animals (Prokofiev, 1977).

Megestrol acetate is fed at a rate of 5 mg per head per day for 8 days. Then, 48 hours after the last dose, animals are subcutaneously treated with 1000–1200 IU eCG. After 36 hours animals are monitored twice a day for 5 days and females in heat are inseminated. Those sheep that did not show oestrus signs received a new eCG dose 15 days later. This protocol reaches an insemination rate of 30–50% for the first cycle and 60–70% for two cycles.

Ukrainian researchers have developed a method for sexual behaviour stimulation in sheep. The scheme involves the i.m. administration of 1.5% progesterone oil solution (2 ml per treatment) on day 1, 3 and 5, in combination with a dose of 500 IU eCG at the beginning of treatment and 125 µg PGF2α on day 10. Progesterone induces the sensitization of the nerve centers of the hypothalamus, which prepares the body for the next stimulating action of gonadotropins. Prostaglandin stimulates the proliferative and secretory processes in the mucous membrane of the uterus and ovaries and promotes the resorption of luteal tissue in the ovaries, which favours the presence of sexual behaviour signs and ovulation. Results obtained in Karakul sheep breed showed high–grade sexual heat signs in 90% of treated animals, while only 20% showed heat signs in the control group. This study reported 89% and 119% for kidding and prolificacy rates, respectively (Turinskij et al., 1997).

Working with sheep, Chekunkova (2016) developed and compared 2 schemes for heat stimulation during spring, i.e. out of the breeding season. In the first scheme, the group of ewes (n=30) was injected intramuscularly with 600 mg progesterone (Progestemag) and a vitamine-mineral complex (8 ml Gabivit–Se). After 7 days, 500 IU eCG (Folimag, s.c.) and a i.m. vitamine-mineral complex (8 ml Gabivit–Se) were also administered. In the second scheme, ewes (n=30) were initially subcutaneously treated with 500 IU eCG (Folimag, s.c.) with 0,75 mg selenium and 75mg vitamin E (1.5 ml E–selenium) intramuscularly. Then, after 7 days, animals received 600 mg progesterone (4 ml Progestemag) (i.m.), 3 ml analogue GnRH (Surfagon) with 0,75 mg selenium and 75 mg vitamin E (1.5 ml E–selenium). The first scheme resulted in a total of 83.3% of pregnant ewes, of which 36% had two lambs. After the application of the second scheme, pregnancy was confirmed in 86.6% of animals, with 46% having two lambs.

Topurko (2005) recommends the use of surfagon (a GnRH analogue) in a dose of 15 µg (i.m.) in combination with biologically active substances (inosin 250 mg, unitiol 20 µg, insolvit 3 ml, dimethylsulfoxide 10% 2 ml), which makes it possible to increase the prolificacy (up to 1.75–1.86 lambs) with a simultaneous increase in the birth weight at 39.5–50.7%. The joint use of GnRH and biologically active substances during the breeding season increases the fertilization of sheep breeds of Merino precoce and their crossbreeds (1/2 and 3/4 of Sufolk) by 11.1–19.7%, and the lambing rate by 42.0–50.0%.

Sharan et al. (2012) considered the application of different methods for stimulation of sexual heat and schemes of introduction of a complex of biologically active substances in different sheep breeds. The general scheme of sexual heat stimulation was similar for all experimental animals, in conjunction with vitamin supplements and the administration of vaginal sponges with progesterone for 14 days. Animals in the control group were given 500 IU eCG (Sergon, Bioveta, a.s., Czech Republic), while animals involved in the experimental groups received 350 IU Sergon with a complex of biologically active substances (inosine 250 mg, unitiol 10 µg, insolvit 3 ml, dimethylsulfoxide–10% 2 ml); one experimental group was treated with GnRH analogue (10 µg luliberin acetate; surfagon) and saline was used in the other experimental group. Authors showed that the use of their improved scheme gives positive results in all studied genotypes and provides a high level of fertilization. The use of a complex of biologically active substances and an analogue GnRH when the eCG dose was 30% reduced, increases the fertility of sheep breeds.

Hashemi et al. (2006) conducted a trial to investigate the efficiency of synchronization using different progesterone treatments during the non–breeding season. Ewes received oil progesterone, intravaginal progesterone (CIDR) or intravaginal medroxyprogesterone acetate for 12 days, with eCG at the intravaginal devices withdrawal. The interval from the cessation of treatment to the onset of oestrus was significantly ($p < 0.05$) longer in the progesterone in oil group, compared to CIDR and medroxyprogesterone acetate sponge groups (51.4 ± 10, 30.1 ± 7.6 and 29.6 ± 5.6 h, respectively). The oestrus response after intravaginal progesterone administration was higher than in oil progesterone parenteral (93.3%

for CIDR, 100% for medroxyprogesterone acetate sponge and 80% for the oil progesterone). The duration of the induced oestrus period did not significantly differ between the treatment groups. The mentioned study concluded that oestrus synchronization using CIDR and medroxyprogesterone acetate sponge followed by eCG (i.m.) is superior under local conditions for fixed-time AI in Karakul ewes outside the natural breeding season.

Topurco (2005), in order to stimulate the oestrus induction in sheep during non–breeding season, recommends the usage of intramuscular injection of a complex of biologically active substances (eCG – 350 IO, unitiol – 10 µg, inosin – 250 mg, insolvit – 3 ml, dimethyl sulfoxide 10% – 2 ml) associated to scheme based on progesterone vaginal sponges. Furthermore, to increase the prolificacy, authors recommended additional injections of gonadolybirin (10 µg). Influenced by the supplementation with eCG and a complex of biologically active substances outside the sexual season in sheep, the number of preovulatory follicles increased by 19.1–31.8%, while the number of corpus luteum decreased by 1.5–2 times. Injection of eCG in combination with biologically active substances during the anestral season enhances metabolic processes in reproductive organs of the sheep of the Merino precoce breed and their crossbreeds, which manifests itself by increasing the content of soluble proteins, phosphorus of nucleic acids, SH–groups, glycogen and alanine aminotransferase activity, and aspartate aminotransferase (10.1–34.1%) in ovarian and uterine tissues. Fertility increased in Merino precoce sheep and their crossbreed (1/2 and 3/4 of Sulfok) by 6.6–20.8%, the yield of lambs by 18.5–27.0%, and in combination with GnRH increases the number of lambs by 24.5–33.0%.

Of particular interest is the biological method to stimulate oestrus in sheep during the non–breeding season by multisensorial contact with mature rams, that is called "ram/buck effect" (Perkins, Fitzgerald, 1994; Romano, 1998b; Ungerfeld, 2008). The oestrus stimulation in ewes and goats appears as a consequence of a change in the pulsation frequency of the GnRH and an increase in the tonic secretion of the luteinizing hormone (LH). The first ovulation occurs 2–3 days after the introduction of males jointly with females, but it often runs without the manifestation of the heat signs ("quiet heat") and is accompanied by low fertility in ewes. It should be noted that goats usually have oestrus signs in the first ovulation and fertility is not so compromised. The second ovulation occurs on average of 5 days after the first, accompanied by the usual signs of an oestrus and the normal duration of the luteal phase. The stimulating effect due to the introduction of males depends on their sexual maturity, sexual activity and body weight. In the complex response of females, this multifactorial stimulus involves olfactory, tactile and visual receptors. The smell effect is due to the presence of specific pheromone in male's wool. The main limiting factor for using this biological method is the reduced fertility of the sheep in the first cycle and the reduction of the synchronizing effect in subsequent cycles. A reduction in the viability of the corpus luteum after induced ovulation is due to several causes. The treatment of females with 20 mg of progesterone during the introduction of rams into herds reduces the number of shortened sexual cycles and increases the rate of ovulation (Lassoued et al., 1995). In addition, it has been shown that in females with low live weight, the response to the introduction of males into the herd was significantly weaker compared to animals of medium to high live weight. French scientists have found that in order to increase the efficiency of this method in small ruminants, it could be interesting to artificially extend the light period during the two previous months (Pellicer–Rubio et al., 2007). Using this scheme for oestrus stimulation outside of the breeding season, it was possible to cause ovulation in 99% of females. It should be highlighted that this biological method for oestrus stimulation in sheep has significant interest in the possibility of excluding hormonal treatments.

Oestrus synchronization during breeding season

For heat synchronization, progestogens or prostaglandin are used in order to inseminate sheep and goats in the short term (5–6 days) and to plan lambing in only 8–10 days.

The use of gestagen preparations

Offers an enhanced fertility in sheep, and the treatment is more effective if it is combined with the proper organization of grazing, timely weaning of lambs from the females and preparation of animals for artificial insemination.

The essential difference between the induction of synchronous heat in the refractory and breeding seasons is that gonadotropin (usually eCG) become unnecessary during the positive reproductive season after the end of treatment of animals by progestagenes. The exception is the Karakul sheep, in which oestrus synchronization can be combined with hormonal stimulation of multiple fertility.

In Karakul sheep, heat synchronization during the breeding seasons can be carried out using oral megestrol acetate in the ration for 10 days in a dose of 5 mg per sheep per day. Then, 18 days after the last dose, animals receive 1000 IU eCG (s.c.) and 24 hours later, they are monitored for heat during 6 days, selecting those showing heat signs. For females that are not in heat, eCG is administered 15 days later and they are again monitored for 6 days in order to do artificial insemination when they show oestrus signs. On the contrary in fine–wool and meat–wool breeds multiple births are undesirable. Then, the proposed protocol in based in megestrol acetate in the diet for 8 days (5 mg/animal/day) or in intravaginal pessaries for 14 days (30 mg/animal) (Moroz, 2012). On day 16 after stopping the use of progestogen, animals are checked for oestrus signs and, if positive, artificial insemination is carried out. If this protocol is used in Karakul sheep, 2 days after the last megestrol acetate feeding or the sponge removal, 1000–1200 IU of eCG are injected. 36 hours after the injection of eCG the heat detection (and insemination if positive) is carried out during 5 days. In sheep showing no heat signs, after 15 days a doses of eCG is repeated. Fertility of sheep and goats after the first insemination in synchronized heat is somewhat lower (by 10–15%) than in spontaneous (Zhurbenko, 1983).

Experiments conducted in Merino sheep breed showed no significant differences for fertility after laparoscopic insemination using frozen sperm 12 hours after the beginning of heat signs (62.9%) or in time–fixed insemination at 60 hours after the removal of intravaginal sponges (59.1%) (Moses et al., 1997).

The use of prostaglandins

The corpus luteum of the sheep are sensitive to the luteolytic action of prostaglandins between the 4th and 14th day, and in the goats between the 4th and 16th day of the sexual cycle.

Oestrus synchronization with prostaglandin in small ruminants is only recommended for the breeding season. The traditional treatment with prostaglandin F2α (PGF2α) consists of two–fold administration of the drug at intervals of 9 to 14 days (Duran Hontou, 1993). The use of this scheme leads to the onset of oestrus after the second treatment with prostaglandin in most of animals, but the onset of the oestrus can occur over 4 days. The administration of prostaglandin two times at intervals of 7 days promotes a more synchronously stroke of the oestrus in sheep. However, this method is a less effective way of synchronizing oestrus in the cattle (Nuti et al., 1992; Greyling and Van Niekerk, 1991; Wildeus, 1999). Despite the fact that signs of oestrus in animals after the second injection of prostaglandin cloprostenol or dinoprost occur in 46–72 h, their fertility significantly decreases in the first cycle after stimulation, due to which this technique does not find a wide practical application.

In cycling sheep from the 3rd day of the cycle, good results are obtained by intramuscular administration of 2 mg of the synthetic PGF2α analogue. After the drug is introduced, the heat occurs within 24–50 hours (87%). And in case of double processing (after 7 days), without determining the cycle stage, the heat detection reaches 82% of sheep.

In Australia, two–time intramuscular injections of the synthetic PGF2α (ICI–80996), regardless of the stage of the sexual cycle, are practiced for ovulation in sheep. Ovulation occurs in sheep 73 hours after the second injection.

In Karakul sheep, the use of prostaglandin makes it possible to cause abortion to obtain valuable raw materials – Karakul (fur, made from the skins of premature lambs). In some part of sheep it makes possible to get two falls per year. It has been established that prostaglandins possess gonadotropic effects, as well as affect the fertilization after artificial insemination in animals.

Ajbazov et al. (2006) studied the comparative effectiveness of different PGF2α preparations for the purpose of heat synchronization and the effectiveness of this method was substantiated for shortening the periods of insemination. The authors note the high synergistic effect of aniprost drug, after which 100% of treated animals showed heat. At the introduction of the drug enzaprost, this figure was lower by 3.3%, and for estrofan and clathroprostin the percentages were reduced 6.0 and 6.75% respectively. The highest fertility of the female was obtained in the group of animals treated with the aniprost drug, while in animals treated with enzaprost, estrofan and clathroprostin the percentages were lower by 20.3%, 26.7% and 28.3%, respectively. The duration of pregnancy of the experimental goats was within the limits of the physiological norm and amounted to an average of 151 days (with a limit of 143–154 days). The parturitions occurred in a range of 9 days in the experimental group. During this period, 77.9% of processed goats gave birth. On the basis of the obtained data it was established that synchronization of oestrus in goats based on different prostaglandin preparations allows to reduce the periods of insemination and parturition by 2,5 times, while preserving physiological functions related to reproduction at a high level.

The commonly accepted scheme of double administration of PGF2α with a 11–day interval

Yellow bodies in sheep regress between the 4th and 14th days, and in goats – between the 4th and 16th days of the sexual cycle. It is generally accepted scheme of double administration of prostaglandin F-2α with an 11-day interval, applicable for sheep and goats. The selection of females in heat and their insemination is carried out after the second injection of prostaglandin. A single injection of PGF2α in females at different time of their sexual cycle causes heat in 65% of animals within 3–5 days. Those animals that do not show heat after the first PGF2α received a second dose 10–11 days later, providing heat in 80–90% of the treated animals. The second injection of PGF2α coincides with the phase of corpus luteum sensitivity to the drug in all animals, and heat occurs in 48–72 h. In this case, one cannot re–sample females in heat, and inseminate them in the programmed time – between 68 and 80 hours (on average 72 hours) after the second PGF2α (Ajbazov et al., 2013).

Malahova et al. (2003), analyzing the efficiency of different prostaglandin preparations for oestrus synchronization in goats, noted that 87.5% of animals showed heat signs after the dinoprost administration. When administering cloprostenol or aniprost, this figure was lower by 12.5% and estrophane by 7.5%. The results of this experiment indicate that the synchronization of heat in goats with different prostaglandin preparations allows the insemination of 79.4% of animals after the first administration of drugs.

A number of schemes of stimulation of sexual activity of sheep and goats during the breeding season are proposed:

- Prostaglandin treatment (Romano, Alkar, & Amstalden, 2017; Souza-Fabjan, et al. 2018);
- Oral administration of gestagen drugs (Omontese et al., 2016; Salas-Razo, 2016; Biradar, 2019);
- Using of intravaginal sponges or CIDR with progestogens, followed by or without parenteral administration of gonadotropins and prostaglandins (Cosentino, 2019; Dursun, 2019; Yu, Wang & Bai, 2019);
- Using of subcutaneous progestogen implant implants with (or without) gonadotropins and prostaglandins (Dogan, Nur & Dogan, 2018; Bragança et al., 2019; Júnior et al., 2019).

To compare the effectiveness of the methods and the development of an effective scheme for heat synchronization in goats a series of experiments were performed by Ajbazov et al. (2004, 2006, 2007, 2012, 2013). As a result, it was found that heat synchronization can effectively be carried out in goats with both progestogens and prostaglandins. Among prostaglandins, the most effective was aniprost, while among progestogens, water–soluble mepregenolacetate was choice (Ajbazov et al., 2006). However, European rules prohibit the use of parenteral progesterone for oestrus synchronization in small ruminants and, it could be recommended the use of intravaginal devices, moreover when results published with the mentioned devices offer similar results and give us the possibility to work under European standards.

By Motlomelo et al. (2002), the efficiency of medroxyprogesterone acetate, fluorogestone acetate sponges and controlled internal drug release (CIDR) devices for oestrus synchronization in goats was evaluated during the natural breeding season. The three progestagen treatments did not show significant differences in oestrus response (around 97%) and duration (33.3±13.4 h) of the induced oestrus period. Time to the onset of oestrus was significantly shorter in the CIDR group (27.2±0.4 h), when compared to fluorogestone acetate the (30.9±0.4 h) and medroxyprogesterone acetate (32.2±0.5 h) groups. The overall serum progesterone concentrations in the CIDR group were higher ($P<0.05$) between days 4 and 16 of treatment, compared to the medroxyprogesterone acetate and fluorogestone acetate groups. No significant difference was observed for pregnancy rate at 40 days after AI (52, 60 and 47% for CIDR, medroxyprogesterone acetate and fluorogestone acetate groups, respectively). Results indicate that the use of medroxyprogesterone acetate, fluorogestone acetate and CIDR intravaginal progestagen treatments are equally efficient for oestrus synchronization in goats.

Injection of biologically active substances with a GnRH analogue during the sexual season (and with eCG in the refractory period) leads to an increase in the concentration of progesterone and a decrease in the concentration of oestradiol–17β in the blood of sheep at the 5th day of the sexual cycle. At the same time, there is an increase in metabolic processes in the sheep organism of the Merino precoce breed and their crossbreed (1/2 and 3/4 Suffolk), which is manifested by the increase in total cholesterol, total protein, transaminase activity, glucose and pentose in the blood. Under the influence of an injection of an analogue of GnRH and biologically active substances in the tissues of the uterus and ovaries of sheep, an increase in metabolic processes in the genital organs was reported (Topurko, 2005).

Erohin and Pridanova (2015) carried out comparative experiments about oestrus synchronization in Zaanen goats in different seasons of the year with the help of intramuscular administration of progesterone, eCG and an analogue of PGF2α. The best results on fertility of the females were obtained during their complex treatment during the reproduction season with the studied drugs compared with the separate use of prostaglandin. The combined use of progesterone and eCG outside the breeding season contributed to effective stimulation of the oestrus, but the effectiveness of insemination of goats was significantly lower than in the reproduction season.

A more effective method of synchronizing oestrus in goats during the reproductive season is the intramuscular administration of 25 mg of progesterone to females for 5 days and a single injection of prostaglandin magometrophane in a dose of 0.5 ml and 500 IU of gonadotrophin in serum foal mares within 24 hours after that. Within 72 hours after treatment symptoms of an oestrus were noted in 78.5% of females, and fertility was 63.6%.

It was established that one– or two–fold intramuscular administration of prostaglandin with a dose of 0.5 mg in the breeding season provided a high synchronization effect, but the fertility of the goats was lower in comparison with the group where progesterone and gonadotrophin were used in the serum foal mares (Erohin and Pridanova, 2015).

CONCLUSIONS

The existing biotechnological methods and techniques based on detailed knowledge of reproduction biology allow to significantly improve the efficiency of the use of genetic resources of high–value animals, increase the extent of their participation in the reproduction of sheep and goats.

Different methods of oestrus induction and synchronization in sheep and goats have been developed up to the current day. The choice depends on the season of reproduction and the time of year. Prostaglandins are used during the breeding season in the presence of functional corpus luteum in the ovaries, while progestagen–based preparations recommended for non-breeding season. Then, progesterone, exogenous gonadotropins, releasing hormones and other compounds are used for this proposal. Significant spread for the synchronization of the oestrus during and after the breeding season became the use of intravaginal sponges, soaked with synthetic analogues of progesterone.

However, insufficient study of the laws of change in the reactivity of the nerve sexual centres and the corresponding reactions of the body to the administration of hormones reduces their effectiveness, which limits the widespread use of it in the production. Thus, in the case of artificial stimulation of reproductive function during the relative sexual rest of animals, heat tends to be manifested in most treated females, and their fertility is low – about 50–60%. In general, the fertility of sheep and goats after the first insemination in synchronized heat is somewhat lower (by 10–15%) than that of spontaneous heat.

Thus, the induction and synchronization of sexual behaviour in sheep and goats is an important area of scientific research and an urgent problem of sheep and goat breeding, but the proposed methods require further improvement by reducing the costand increasing biosecurity and predictability of the result.

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