

Effect of an Intermediate Dose of Melengestrol Acetate (MGA) on Ovulation Inhibition in Ewes

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Abstract—The objective of this study was to evaluate the efficiency of an intermediate dose of MGA on the inhibition of ovulation. Twenty empty and cycling ewes were used, with a corporal condition of 3.2 ± 0.3 (scale 1-5), 40.18 ± 5.8 kg and 3.25 ± 0.6 years old. The intermediate dose consisted of 0.22 mg of MGA per ewe during 17 days. In the dosing period ovarian activity was observed by echography, to observe the effect on the inhibition of ovulation. It was found that the intermediate dose of 0.22 mg, had a suppressive effect on ovulation in 100% of the ewes, which was observed in follicular dynamics expressed in 2 and 3 follicular waves. Concluded that the intermediate dose of 0.22 mg of MGA is efficient in its main effect, the suppression of ovulation.

Index Terms—Intermediate dose, efficiency, ovarian activity, echography.

I. INTRODUCTION

Efficiency of a sheep production system is determined by numerous factors. Reproduction is undoubtedly one of the most important aspects, so that if the reproduction is handled properly, results are observed in the short to medium term on the productive performance of the flock [1].

Different techniques can be used to control reproduction. Such techniques included from the use of the male effect, photoperiod manipulation or use of various hormonal products, in order to affect reproductive endocrine function of the female and so facilitating the presence of estrus and ovulation. Among the different strategies used for this purpose this the use of melengestrol acetate (MGA), an synthetic progestational steroid of oral administration (estrus suppressor) which has been used for different purposes: among them is found, induction and synchronization of estrus [2]-[4], growth promoter and as anabolic in fattening bovine females [5], [6].

The use of MGA for induction and synchronization of estrus in ewes has been administered during periods lower than average life of a corpus luteum (12-14 days) generically called short treatments [7], [8], and over periods longer than the average of life the corpus luteum, denominated prolonged treatments [9], [10]. In both cases the MGA has been used without a clear criterion over thus dosing, so exist several doses in ewes ranging from 0.11 to 0.5 mg.

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The administration of MGA to control estrous cycle has been used in combination with estrogen and gonadotropins [11]-[13], also in combination with prostaglandins and their analogs as luteolytic agents [5], [3], [14]. Until now, attempts have been directed to the improvement in the fertility rate.

However, the fertilization rate in programs induction and synchronization of estrus in ewes when is used MGA vary widely, from 25 to 85% [15]; this variability may be related to the dose used, since doses high, inhibit production LH and affects development follicular [16], while dose low have an effect negative on the frequency of LH pulsatile same that can provoke a development of persistent dominant follicles [17].

Not exist research in ewes that explain efficiency of MGA on its effect inhibitor ovulation and neither about the appropriate dose to achieve this effect without affecting the normal development of follicular dynamics. The studies that exist are based on doses recommended by the manufacturer laboratory (doses for fattening), that in practicing has been as its suppressor of estrus; so studies are required to determine effective doses in suppressing ovulation but which in turn allow greater response on the percentage of fertility.

Therefore, the objective of this study was to evaluate if the intermediate dose of 0.22 mg of MGA is efficient in ovulation inhibition, without affecting the normal development of follicular dynamics.

II. MATERIAL AND METHODS

The study was conducted in the Ejido Agua Fria, in the municipality of Contepec, Michoacán, México; $19^{\circ}55'$ latitude north and $100^{\circ}11'$ latitude west, at an altitude of 2,490 masl, temperate climate with summer rains, rainfall of 1168.0 mm and temperatures ranging between 8.6 and 22.4°C [18].

During the month of July (full breeding season), 20 Dorper and Dorper-Pelibuey ewes were used, empty and cycling, with a corporal condition of 3.2 ± 0.3 (scale 1 to 5), 40.18 ± 5.8 kg live weight and 3.25 ± 0.6 years old. All the ewes were housed in the same pen of 72.0 m^2 , individually identified with an earring, dewormed and vitamin-enriched 30 days before the start of MGA dosing. All the ewes received the same handling and were fed with corn stover, oat grain, barley grain and water *ad libitum*.

At the beginning of the treatment, all ewes underwent a gynecological evaluation using an Ecograph in B mode (Draminski, Animal Profi model) provided with a sectorial transducer of 3.5 and 5.0 MHz rectally, to confirm that they

were empty and cycling.

The MGA dose used was of 0.22 mg and orally administered individually during 17 days. During this period of MGA administration, ovarian activity was observed using the Ecograph with a sectorial transducer of 7.0 MHz, transrectal ultrasound, to observe the effect over ovulation inhibition.

III. RESULTS AND DISCUSSION

After observing ovarian activity during the 17 days of the treatment, it was found that the dose of 0.22 mg had an inhibitory effect on ovulation in 100% of the 20 ewes, in which observing their ovarian activity during the treatment showed the development of 2 and 3 follicular waves without ovulation. This result indicates that the dose of 0.22 mg of MGA is effective to inhibit ovulation.

Even though there is no research that evaluates the dose of MGA on its function as inhibitor of ovulation in ewes, it is possible to compare the result with some studies where low and high doses of MGA have been used, considering that the response to the estrus manifestation and estrus synchronization depend on the efficiency of MGA on its principal function, the ovulation inhibition.

In MGA treatments in intrauterine insemination program, using a low dose of 0.125 mg MGA during 9 days, observed in 286 ewes that the response of estrus manifestation was 62% with a fertility rate of 41%, and when the same dose was administered during 12 days, observed that in 130 ewes the response to estrus manifestation was 89% with a fertility rate of 44% [19]. This suggests that the efficiency of the used dose on the response of estrus manifestation is associated to treatment duration, by the stage of the estrus cycle in the ewes [20] and perhaps, the low fertility observed is due to the fact that the inhibitory effect of ovulation could not be entirely efficient or it could have affected ovarian activity in some ewes, due to the fact that low doses of MGA have shown a negative effect on the pulsatile frequency of LH, can develop persistent dominant follicles [21].

When was used a low dose of 0.11 mg and an intermediate dose of 0.22 mg of MGA during 9 days to synchronize estrus in 37 ewes, finding that the percentage of estrus for ewes with the dose of 0.11 mg was of 67% and for the ewes with the dose of 0.22 mg was of 90%, which makes evident a greater efficiency of the intermediate dose [22]. This result coincides with the observed in this study when was evaluated the intermediate dose of 0.22 mg of MGA on ovulation inhibition.

In previous researches [23], administered a dose of 0.22 mg of MGA during 17 days to 20 hair ewes to evaluate its effect on follicular dynamics, observed that 85% of the ewes treated with MGA presented three follicular waves and 15% remaining two waves, none of them ovulated during treatment, which confirms the efficiency of the intermediate dose used in this study.

In other study [24], were used a high dose of 0.45 mg of MGA for 17 days in 20 ewes, evaluating its effect on the presentation of estrus and gestation rate, found that 100% of

the treated ewes showed estrus; however, gestation rate was 70%, which could be due to high doses of MGA, that has shown a suppressing effect to LH, affecting the selection and follicular development [25].

Using a dose of 0.25 mg of MGA for 9 days to evaluate its effect in the induction and synchronization of estrus in 78 ewes was observed that the rate of estrus about 70% within a period of 6 days after treatment [26]. In goats ($n = 35$), using the same dose of MGA but it for 10 days to evaluate its effect on the induction and synchronization of estrus and gestation rate, observed that 84% of the goats presented estrus and gestation rate of 58% [27]. In both investigations were used doses similar to those of this study, though the administration of the treatment was for a short period; possibly this affected the results due to the stage of the estrous cycle in which the ewes were at the beginning of experiment [20], in sheep is says that in females cycling the progestin administration must be long enough to allow that lyse of CL is of natural form and should be independent of the stage of estrous cycle in the which is realized. The prolonged use of a treatment would block ovulation when this is starting in follicular phase (pro-estrus and estrus), preventing the formation of a CL; if the treatment is starting in the meta-estrus, the formation of CL is altered shortening its half-life; and if the treatment started coinciding with di-estrus, the CL is degrades naturally without be affected by the treatment.

In a study made in goats for 12 days [28], was used a similar dose to this research to compare the relationship between estrus, surge of LH and ovulation; the last day of treatment was applied one dose of 75 mg PGF_{2a}, finding that after have treatment suspended all goats showed its estrus to 86.7 ± 3.9 h, and the interval between the LH preovulatory peak and ovulation was of 26.2 ± 1.1 h, maybe due to the duration of treatment (short) and stage of the estrous cycle of the ewes.

In another study, [15] evaluated the effects of melengestrol acetate and P.G. 600 on the fertility in ninety-nine Rambouillet ewes outside the natural breeding season, finding that after seven days of treatment at doses of 0.3 mg per day the pregnancy rate was 24%. Administering a dose of 0.4 mg of MGA during 12 days to 24 ewes to determine the response time of the LH surge and the fertility rate [29], didn't do any observations during the treatment but found that the average interval between the last dose of MGA and the LH surge was of 64.0 ± 12.6 h and the fertility rate was 45%. This result could have been to the high dose of MGA that inhibit ovulation, and at the same time suppress the secretion of LH and thus inhibit follicular development [30], affecting the rate of fertility. This indicates that high doses of MGA are not the most efficient for its use as a reproductive handling strategy in ewes. Similar results were found [31], when using a high dose of MGA (0.5 mg) during 10 days to evaluate its effect on estrus induction and fertility in 50 goats, finding a response of 73.5% of estrus with a fertility rate of 74%, result that can be explained similarly by the effect of the high dose of MGA on LH secretion and follicular development [21].

IV. CONCLUSION

It concluded that the intermediate dose of 0.22 mg of MGA is efficient in its main effect, the suppression of ovulation, without affecting the normal development of follicular dynamics in ewes; therefore represent an strategy for the reproduction control that can get better the response to induction and synchronization of estrus and fertility rate.

This study should be considered as a basis to future research aimed to studies on the precise doses of MGA in other species, above all by that its use was based on the doses recommended for suppression of estrus with purposes of fattening animals.

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A cooperating farmers of the state of Michoacán, Mexico. Product system Sheep.

REFERENCES

- [1] R. L. Alvarez and W. A. Ducoing, "Aspectos reproductivos del ganado ovino y caprino," *Universidad Nacional Autónoma de México, Facultad de Medicina Veterinaria y Zootecnia, Centro de Enseñanza Práctica e Investigación en Producción y Salud Animal*, Mexico, pp. 15-18.
- [2] T. Quispe, L. Zarco, J. Valencia, and A. Ortiz, "Estrus synchronization with melengestrol acetate in cyclic ewes. Insemination with fresh or frozen semen during the first or second estrus post treatment," *Theriogenology*, vol. 41, pp. 1385-1392, February, 1994.
- [3] C. A. Quezada, C. F. Pérez, R. L. Avendaño, and D. M. Hallford, "Comparación de dos protocolos de sincronización (MGA) del estro en vaquillas de carne con distintas calificaciones de tracto reproductivo," *Interciencia*, vol. 29, no. 11, pp. 638-642, Noviembre, 2004.
- [4] G. Perry, W. V. Welshorns, and M. F. B. Smith, "Basis of melengestrol acetate action as a progestin," *Domestic Animal Endocrinology*, vol. 2, no. 28, pp. 147-161, February 2005.
- [5] D. B. Imwalle, D. L. Fernandez, and K. K. Schillo, "Melengestrol acetate blocks the preovulatory surge of luteinizing hormone, the expression of behavioral estrus, and ovulation in beef heifers," *Journal of Animal Science*, vol. 80, pp. 1280-1288, 2002.
- [6] B. Schiffer, "Mobility of the growth promoters trembolone and melengestrol acetate in agricultural soil: column studies," *Science of the Total Environment*, vol. 326, pp. 225-237, 2004.
- [7] E. Rubianes, "Avances en el conocimiento de la fisiología ovárica de los pequeños rumiantes y su aplicación para el manejo reproductivo," *Actas de Fisiología*, vol. 6, pp. 93-103, 2000.
- [8] J. A. Farfán, J. A. Forero, N. A. Pardo, F. J. Tovar, J. E. Atuesta, and H. A. Grajales, "Efecto del tiempo de tratamiento con progestágenos sobre las características del celo sincronizado y su fertilidad en ovinos y caprinos bajo condiciones del trópico de altura colombiano," *Livestock Research for Rural Development*, vol. 21, no. 1, 2013.
- [9] E. Rubianes, A. Menchaca, and R. Ungerfeld, "Avances en las técnicas de sincronización de celos en ovinos y caprinos," *Cuarto Simposio Internacional de Reproducción Animal*, Uruguay, 2001.
- [10] R. Ungerfeld and E. Rubianes, "Short term primings with different progestogen intravaginal devices (MAP, FGA and CIDR) for eCG-estrous induction in anoestrus ewes," *Small Ruminant Research*, vol. 42, pp. 63-66, 2002.
- [11] P. M. Bartlewski, J. Aravindakshan, A. P. Beard, M. L. Nelson, A. M. Batista, S. J. Cook, and N. C. Rawlings, "Effects of medroxyprogesterone acetate (MAP) on ovarian antral follicle development, gonadotrophin secretion and response to ovulation induction with gonadotrophin-releasing hormone (GnRH) in seasonally anoestrous ewes," *Animal Reproduction Science*, vol. 81, pp. 63-75, October, 2004.
- [12] J. E. Stegner, F. N. Kojima, J. F. Bader, M. C. Lucy, M. R. Ellersieck, M. F. Smith, and D. J. Patterson, "Follicular dynamics and steroid profiles in cows during and after treatment with progestin-based protocols for synchronization of estrus," *Journal of Animal Science*, vol. 82, pp. 1022-1028, April, 2004.
- [13] O. G. S. Filho, D. J. Patterson, and J. L. M. Vasconcelos, "Development of estrous synchronization protocols using melengestrolacetate in *Bos indicus* cattle," *Journal of Animal Science*, vol. 87, pp. 1981-1990, March, 2009.
- [14] D. A. Mallory, D. J. Wilson, D. C. Busch, M. R. Ellersieck, M. F. Smith, and D. J. Patterson, "Comparison of long-term progestin-based estrus synchronization protocols in beef heifers," *Journal of Animal Science*, vol. 88, pp. 3568-3578, July, 2009.
- [15] E. J. Windorski, C. S. Schauer, A. K. Wurst, E. K. Inskeep, and J. S. Luther, "Effects of melengestrol acetate and P.G. 600 on fertility in Rambouillet ewes outside the natural breeding season," *Theriogenology*, vol. 70, pp. 227-232, April, 2008.
- [16] C. Viñoles, M. Forsberg, G. Banchemo, and E. Rubianes, "Effect of longterm and short-term progestagen treatment on follicular development and pregnancy rate in cyclic ewes," *Theriogenology*, vol. 55, no. 1, pp. 993-1004, March, 2001.
- [17] M. G. Colazo, R. J. Mapletoft, M. F. Martínez, and J. P. Kastelic, "El uso de tratamientos hormonales (MGA) para sincronizar el celo y la ovulación en vaquillonas," *Ciencia Veterinaria*, vol. 1, no. 9, pp. 4-16, Agosto, 2007.
- [18] Instituto Nacional para el Federalismo y el Desarrollo Municipal INAFED. (May 2013). [Online]. Available: <http://www.elocal.gob.mx/work/templates/enciclo/michoacan/mpios/16017hm>.
- [19] E. Emsen, D. C. Giménez, M. Kutluca, and F. Koycegiz, "Reproductive response of ewes synchronized with different lengths of MGA treatments in intrauterine insemination program," *Animal Reproduction Science*, vol. 126, pp. 57-60, April, 2011.
- [20] C. Galina and J. Valencia, *Reproducción de animales domésticos*, 2ª ed. Limusa, Mexico, 2006, pp. 458-462.
- [21] S. K. Johnson, R. A. Dailey, E. K. Inskeep, and P. E. Lewis, "Effect of peripheral concentrations of progesterone on follicular growth and fertility in ewes," *Domestic Animal Endocrinology*, vol. 13, pp. 69-79, 1996.
- [22] Q. T. Quispe, Q. L. Zarco, and H. A. Ortiz, "Sincronización de estros en ovejas mediante un tratamiento cortó con acetato de melengestrol (MGA) combinado con cipionato de estradiol (ECP)," *Revista Veterinaria México*, vol. 1, no. 26, pp. 23-28, Octubre, 1995.
- [23] R. G. Salas, M. J. A. Rojo, P. R. Garcidueñas, P. J. P. Flores, P. M. Perea, and E. J. L. Villavicencio, "Effect of Prolonged Treatment with Melengestrol Acetate (MGA) on the Persistence or Non-Persistence of Ovarian Follicles in Ewes," *International Journal of Bioscience, Biochemistry and Bioinformatics*, vol. 3, no. 4, pp. 298-240, July, 2013.
- [24] G. Salas, F. Mata, M. Perea, R. Garcidueñas, E. Gutierrez, A. Caratachea, and J. P. Flores, "Estrus Grouping in Sheep Treated with Melengestrol Acetate (MGA)," *Journal of Agricultural Science and Technology*, vol. 1, pp. 1295-1296, December, 2011.
- [25] C. R. García, R. S. Rangel, R. D. L. Rodríguez, and J. A. M. Apodaca, "Aplicación de progesterona al final de un protocolo de sincronización en ovejas criollas," *XIX Reunión Internacional Sobre Producción de Carne y Leche en Climas Cálidos*, Mexicali, Baja California, México, Octubre 8-9, 2009.
- [26] D. C. A. Gimenez, E. Emsen, F. Koycegiz, B. Emsen, M. Yaprak, and M. Kutluca, "Synchronization of estrus in fat tailed sheep using melengestrol acetate (MGA) in the breeding season," *Journal of Applied Animal Research*, vol. 28, pp. 25-27, November, 2005.
- [27] D. J. Jackson, C. M. Fletcher, D. H. Keisler, and N. C. Whittle, "Effect of melengestrol acetate (MGA) treatment or temporary kid removal on reproductive efficiency in meat goats," *Small Ruminant Research*, vol. 66, pp. 253-257, September, 2006.
- [28] A. L. E. Martínez, C. J. Hernández, P. E. González, M. G. Perera, and J. Valencia, "Serum LH peak and ovulation following synchronized estrus in goats," *Small Ruminant Research*, vol. 69, no. 1-3, pp. 124-128, 2007.
- [29] F. Castonguay, G. Leduc, and Goulet, "Use of melengestrol for estrus synchronization in an artificial insemination program in ewe," *Journal of Animal Science*, vol. 80, no. 1, pp. 268-269, 2002.
- [30] S. A. López, D. B. A. González, M. J. Santiago, and B. A. Gómez, "Dinámica folicular en pequeños rumiantes," *Ponencias. Departamento de Reproducción Animal*, INIA, Madrid, España. pp. 65-77, 2002.
- [31] J. N. Valenzuela, C. J. Hernández, M. C. Murcia, and M. R. Rodríguez, "Efecto del benzoato de estradiol en la presentación del pico preovulatorio de LH, momento de ovulación y fertilidad en cabras sincronizadas con acetato de melengestrol (MGA)," *Agrociencia*, vol. 38, no. 6, pp. 603-611, Octubre, 2004.



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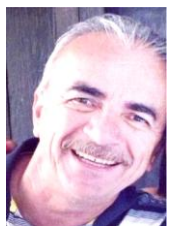
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