Medicinal Product Use Reglandin D-(+)- Cloprostenol, Synthetic Analogue of Prostaglandins F2α Natural Body in Fighting with Anestrus Lute (CL) in Cattle

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Abstract
The studies made by us are based on fundamental biological role of prostaglandin modulator of hormonal actions, influx nerve transmission and cellular ionic exchange. One of the main actions of PGF2α is luteolyse, a process that includes the secretion of progesterone and regression yellow body. PGF2α is a luteolic for almost species: cow, buffalo, sow, mare, sheep, rabbits, guinea pigs, hamsters and rats, except primates. At present it is considered that PGF2α have their specific receptors, which are fixed and through their model would enable guanidine monophosphate or cyclic GMP's Goldberg. The effect of ocitocic luteolic and pharmacodynamics basis of PGF2α, used in breeding biotechnologies and hormonal therapy. In medicine veterinary prostaglandines are used after 1973. Were injected with 2 ml Reglandin (150 mg D-(+)- cloprostenol) 24 women diagnosed with corpus luteum anestris and 22 females (87.5%) came in oestrus at a mean of 59 hours, and after an average interval of 70 hours.și were artificially inseminated (AI) a total of 20 female (83.33%).

Keywords: biotechnology pregnancy, luteolyse, parturition, prostaglandin.

1. Introduction
In organism the creation of prostaglandins takes place at the level of endoplasmic reticulum from endometrial, vesicular-seminal, lungs cells etc. Under the influence of A2 phospholipasis, the membrane phospholipids from cells are releasing the essential fat acids (EFA), especially linoleic and arahidonic. Under the PG - synthesis’s actions on arahidonic acid results peroxide compounds, recte endoperoxizi as PGG2 and PGH2 from which originates PGF2 α.

The structural modifications of synthesis PGF2α are inducing qualitative pharmacy-dynamic transformations such as - Cloprostenolul is 200 times more luteo-lytic in bovines, comparing with the natural prostaglandin [1, 2, 3, 4]. In veterinary medicine the prostaglandins are used after the year 1973 [3]. The half timing of endogen PG, respectively uterine luteolisina is extremely short, 1-3 minutes. For synthesis prostaglandins like Cloprostenol i.m. inoculated, the half timing is about 60 de minutes and is inactivated about 90% in liver, following one blood circuit and 10% is eliminated through lung and kidney [1].

The purpose of our researches was to retest medicinal product for veterinary use Reglandin in order to its reauthorization, a synthesis analog of natural prostaglandin F2α, which has as active
substance the Na salt of D-(+)- Cloprostenol, produced by The National Institute National for Research Development Chemistry Pharmaceutically (ICCF)-Bucharest and belongs to the prostaglandins class [2, 3], being registered and marketing by S.C. Zoovet Impex S.R.L.-Bucharest.

2. Materials and methods

The researches have been carried out in October - December 1999 in the elite farm of S.C. Agrimat S.A. Matca. It has been examined by ETR and eco-graphic 31 cows from din BNR race and in 24 cows was observed C.L. on one of the ovaries.

After carrying out clinical and eco-graphic exams which were correlated with data extracted from the reproduction files of the farm an experimental lot was constituted (LEV) from 24 cows in anestrus determined by the presence of luteal corpus.

It has been elaborated an individual file for each female (according to the annexed protocol), with the identification and reproduction data and before and after administering i.m. of 2 ml Reglandin – of the salt of Na of 0,150 mg D-(+)- Cloprostenol/cow, it have been monitored: the body temperature, the hard frequency, the respiratory frequency. Blood has been sampled before and after administrating Reglandin in vacutainers with EDTA in view of carrying out the blood exam in order to determine the following parameters: leucocytes, lymphocytes, monocytes, granulocytes, erythrocytes, hemoglobin, hematocrit, VEM, HEM, CHEM , thrombocytes, eosinophiles, and in vacationers with coagulating activator for blood biochemistry parameters: glucose, GPT, GOT, urea, creatinine, alkaline phosphatases, pancreatic amylase , estrogens and progesterone. After i.m injecting 2 ml/cow of REGLANDIN equivalent of 0,150mg Na salt of D -(+)- Cloprostenol, the lot was clinically followed: the local and general tolerance, the appearance of the eventual side effects, tachypnea, tachycardia, loss of appetite, sweating, temperature, the eventual side effects and the appearance and the moment of estrus noting the date and the hour.

The followed objectives were:
- The interval treatment - estrus;
- Percentage of cows entered in estrus and IA ;
- The hormonal dynamic;
- Side effects.

3. Results and discussion

Results recorded from all 24 cows determined by the presence anestrus CL, after 2 ml Reglandin - 0.150 mg sodium salt D (+) cloprostenol per cow, are shown in Table 1.

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**Table 1** Results recorded after 2 ml to 24 cows Reglandin CL

<table>
<thead>
<tr>
<th>No.</th>
<th>Serial No.</th>
<th>Breed BNR</th>
<th>The date of the last calving or abortion</th>
<th>Date and time E.T.R. or ultrasound</th>
<th>AI No./date</th>
<th>Date/hour of PGF2α i.m. administration Reglandin -2 ml</th>
<th>Estrus onset Date/hour</th>
<th>Interval from PGF2α administration to estrus onset h, m</th>
<th>Date and time AI administration h, m</th>
<th>PGF2α administration to estrus onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>5847</td>
<td>Av. 10.08.09</td>
<td>20.11.09 h11,38 E.T.R.-CL</td>
<td>I-14.10.09</td>
<td>20.11.09 h11,38 102 days p.p.</td>
<td>22.11.09 h12,30</td>
<td>h 49,30</td>
<td>22.11.09 h 15,35 Endometritis</td>
<td>32.35</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>5404</td>
<td>17.02.09</td>
<td>20.11.09 h11,41 E.T.R.-CL</td>
<td>II 03.10.09</td>
<td>20.11.09 h11,41 276 days p.p.</td>
<td>22.11.09 h19,30</td>
<td>h 56,11</td>
<td>22.11.09 h 15,30 h 8,10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>1091</td>
<td>15.08.09</td>
<td>17.11.09 h11,44 E.T.R.-CL</td>
<td>0</td>
<td>17.11.09 h11,44 97 days p.p.</td>
<td>22.11.09 h10,40</td>
<td>h 47,04</td>
<td>22.11.09 h 15,30 h 8,10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>5633</td>
<td>21.08.09</td>
<td>20.11.09 h11,47 E.T.R.-CL</td>
<td>I-25.10.09</td>
<td>20.11.09 h11,47 91 days p.p.</td>
<td>23.11.09 h5,00</td>
<td>h 65,13</td>
<td>23.11.09 h 8,15 h 68,28</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>5858</td>
<td>16.07.09</td>
<td>20.11.09 h11,50 E.T.R.-CL</td>
<td>I-10.09.09</td>
<td>20.11.09 h11,50 127 days p.p.</td>
<td>23.11.09 h10,50</td>
<td>h 71,00</td>
<td>23.11.09 h 15,30 h 8,10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>6028</td>
<td>26.11.08</td>
<td>20.11.09 h11,55 E.T.R.-CL</td>
<td>VI-17.09.09</td>
<td>20.11.09 h11,55 359 days p.p.</td>
<td>22.11.09 h10,90</td>
<td>h 37,54</td>
<td>23.11.09 h 15,40 h 43,33</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>8216</td>
<td>02.10.09</td>
<td>20.11.09 h14,56 E.T.R.-CL</td>
<td>0</td>
<td>20.11.09 h14,56 50 days p.p.</td>
<td>23.11.09 h6,10</td>
<td>h 62,14</td>
<td>23.11.09 h 8,40 h 64,44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>1064</td>
<td>06.07.09</td>
<td>20.11.09 h14,57 E.T.R.-CL</td>
<td>I-11.10.09</td>
<td>20.11.09 h14,57 137 days p.p.</td>
<td>23.11.09 h10,00</td>
<td>h 66,03</td>
<td>23.11.09 h 16,35 h 72,35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>3680</td>
<td>10.07.09</td>
<td>20.11.09 h14,59 E.T.R.-CL</td>
<td>I-12.10.09</td>
<td>20.11.09 h14,59 23.11.09 h7,12</td>
<td>23.11.09 h63,13</td>
<td>h 63,13</td>
<td>23.11.09 h 15,30 h 8,10</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Table 1 shows the following aspects:
1. Mean interval from birth to a Reglandin administration was 137.08 days with a minimum of 50 days and a maximum of 359 days;
2. After Reglandin injecting a total of 22 females (87.5%) came into estrus at a mean of 58.61 hours, with a minimum interval of 37 hours and 54 minutes and a maximum of 65 hours and 13 minutes;
4. After the second PGF2α 2 cows came into estrus was AI on 04/12/2009 (8201) and 1074 which A.I. fot on 12/15/2009;
5. Two -5858 and 3692 cows were in estrus although it endometritis was presented and were placed in treatment.

Results recorded from all 24 cows determined by the presence anestrus CL, after 2 ml Reglandin - 0.150 mg sodium salt D (+) cloprostenol per cow, shows the following aspects:
- Interval average from birth to a Reglandin administration was 137.08 days with a minimum of 50 days and a maximum of 359 days;
- After REGLANDIN injecting a total of 22 females (87.5%) came into estrus at a mean of 58.61 hours, with a minimum interval of 37 hours and 54 minutes and a maximum of 65 hours and 13 minutes;
- After the second PGF2α 2 cows came into estrus was IA on 04/12/2009 (8201) and 1074 which I.A. on 12/15/2009;
Two -5858 and 3692 cows in estrus although it was presented endometritis and were placed in treatment. For blood biochemical parameters, blood samples were taken before the administration of i.m. 2 ml of Reglandin after 24, 48, 72 and after 9 days of administration, the laboratory samples were processed in FMV Bucharest, and the dynamics of steroid hormones in figure 1.

The analysis of the figure 1 and table 2 shows that individual values of ovarian steroids progesterone (P4) and Estradiol, after 2 ml of the 24 cows Reglandin were within the normal physiological values. Mean progesterone (P4) in all 24 cows was before the injection of 2 ml Reglandin $X = 4.76$ ng / ml after 24 hours $x = 4.26$ ng / ml after 48 hours $X = 3.14$ ng / ml after 72 hours decreased to $X = 2.26$ ng / ml after 7 days and returned to a value of 4.37 ng / ml, compared with reference values from 1 - 15 ng / ml.

Mean estradiol (E) were injected before Reglandin $X = 3.94$ pg / ml after 24 hours $x = 4.63$ pg / ml after 48 hours at $X = 4.79$ pg / ml after 72 hours increased to $X = 5.18$ pg / ml, and after 7 days decreased the amount of 3.43 pg / ml, compared with reference values between 3-12 pg / ml.

As it is known the $\mathrm{F}_2\alpha$ prostaglandins do not have not only a luteolitic effect, they are also in the same time and the most powerful octocic known in clinic. Thoburn and Currie 1973 quoted by Knap, 1980 and V.Paraipan in 1982, considers that the contractile action appears due to the modulation excited by PGF2α on forming AMPc, which intervenes in cell permeability, hiper-polarizing the membrane and relaxing the fiber or depolarizing the membrane and contractile the myometrium fibers, with other words for growing is decreasing the forming of AMPc [5].

In 2003 Angela Maria Stoica et. al. [4] shows that the use of prostaglandins or synthetic analogical in the biology and pathology of reproduction in animals presents advantages of organizer, economic and sanitary veterinary order [6, 7]. Due to farmaco-dinamic, luteolitic and octocic the effect of prostaglandin $\mathrm{F}_2\alpha$ can be used in biotechnologies of reproduction [8] and in the pathology of reproduction in bovines so: inducing and synchronizing estrus; the therapy of persistent luteal corpus; the therapy of ovary cysts; inducing the abortion and starting the birth.

4. Conclusions

1. After a dose of 2 ml i.m. Reglandin, respectively sterile solution of sodium salt 0.150 mg D-(+) –Cloprostenol/cow, the average interval from calving to administrations was 137.08 days, with a minimum 50 days and a maximum of 359 days.

2. A total of 22 females (87.5%) came in to estrus at a mean of 59 hours, with a minimum interval of 37 hours and 54 minutes and a maximum of 65 hours and 13 minutes.


4. After the second PGF2α 2 cows came into estrus was IA on 04/12/2009 (8201) after 70 hours of fot IA 1074 12.15.2009-in after 72 hours.
5. Two cows, 5858 and 3692, although it was in estrus, showed endometritis and were placed in treatment.

6. The evaluation B.A. showed that the values of hematological parameters determined from the examination is within normal limits, with some exceptions. Where it can be concluded that the health of the cows studied was appropriate.

7. Mean progesterone (P4) in all 24 cows was before the injection of 2 ml Reglandinului X = 4.76 ng / ml after 24 hours x = 4.26 ng / ml after 48 hours at X = 3.14 ng / ml after 72 hours decreased to X = 2.26 ng / ml after 7 days and returned to a value of 4.37 ng / ml, compared with reference values ranging from 1 to 15 ng / ml.

8. Values mean estradiol (E) were injected before Reglandin X = 3.94 pg / ml after 24 hours x = 4.63 pg / ml after 48 hours at X = 4.79 pg / ml after 72 hours increased to X = 5.18 pg / ml, and after 7 days decreased the amount of 3.43 g/ml, compared with reference values between 3-12 pg/ml.

9. Lysis induced Reglandin C.L. the majority of treated cows, causing a decline in P4, triggering events and sexual clinic into estrus on average 58 hours of females. These sexual events overlapped with the values obtained by hormonal dosages, to overlap sexual events and sexual clinic into estrus on average 58 hours of females. These sexual events overlapped with the values obtained by hormonal dosages, to support this claim are emerging from individual file monitoring production and breeding farm removed from the computer.

10. La cows treated with 2 ml 0.150 mg Reglandin-sodium salt D (+) cloprostenol per cow, were not detected adverts reactions.

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