Evaluation of a Proprietary Slow-Release Oxytocin Formulation on Corpus Luteum Function in Mares

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Mare Estrous Cycle

- 21 days
  - 1 week estrus (i.e., “heat”)
    - Follicular phase
    - Follicle- **Estrogen**
  - 2 weeks diestrus
    - Luteal phase
    - Corpus Luteum (CL)- **Progesterone**

- Uterus
  - Prostaglandin (PGF2α)
    - Measured as PGFM
  - Luteolysis
- Posterior Pituitary- **Oxytocin**
  - Role in luteolysis

Adapted from Neely, 1985
Mare Estrous Cycle

Images of Ultrasonographic Morphology

Follicle

Corpus Luteum

Equine Estrous Cycle

Progesterone

PGFM

Days After Ovulation

Ovulation

Ovulation

Adapted from Neely, 1985
Estrous Behavior (i.e., in heat)

Courtesy of Dr. Vanderwall

The Horse Magazine: March 2017
Estrous Behavior (i.e., in heat)

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Estrus Suppression in the Performance Mare
Methods of Estrus Suppression

• Administration of exogenous progesterone/progestins
  ▫ E.g., Oral Altrenogest

• Extending the functional span of the corpus luteum (CL)
  ▫ Intrauterine glass ball
  ▫ Oxytocin
Methods of Estrus Suppression

- Administration of exogenous progesterone/progestins
  - I.e. Oral Altrenogest
- Extending the functional span of the corpus luteum (CL)
  - Intrauterine glass ball
  - Oxytocin

Courtesy of Dr. Vanderwall
Oxytocin

- Released from the posterior pituitary gland
- Pulsatile nature
- Very short half-life
- Functions
  - Milk let-down
  - Stimulates uterine contractions
  - Oxytocin-Prostaglandin luteolytic pathway
- Therapeutic use to prolong CL function
  - 8-Day Protocol (1x daily: days 7-14)
  - Slow-release Oxytocin (SR-OT: two treatments)
Original Research

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Hypothesis

• A two-injection proprietary SR-OT protocol will deliver an appropriate amount of oxytocin for a sufficient duration of time to inhibit luteolysis

Objectives

• Determine if IM administration of 2,400 IU of SR-OT once on days 7 and 10 after ovulation would prolong CL function in treated mares compared to a non-treated control group
• Reduce number of injections from previous aqueous oxytocin methods
Ovulation
Detected via trans-rectal ultrasound/palpation

Collect Blood
3 times per week
Until day 50

Day 0

Day 7 SR-OT
2400 IU (1 CC)
Intramuscular
Day 10 SR-OT
2400 IU (1 CC)
Intramuscular

Groups
Control n=8 mares
SR-OT Treatment n=8 mares

Serum Progesterone concentration evaluated via chemiluminescent enzyme immunoassay (Immulite Progesterone)
Results

• 0/8 control mares with prolonged luteal function*

• 6/8 treated mares with prolonged luteal function*

• Prolonged luteal function defined as >1 ng/ml for over 30 days

• * Prolonged function compared with Fisher’s exact test; P < .01
Conclusions

- SR-OT administered on days 7 and 10 is an effective method of prolonging luteal function
- This proprietary SR-OT formulation provides a 75% reduction in number of treatments needed in previous aqueous oxytocin methods
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Supporting Slides
Pro- vs Anti-Luteolytic Functions of Oxytocin

Equine Estrous Cycle

Pro-Luteolytic
- Oxytocin after day 10
  - Binds to oxytocin receptor at endometrial epithelium
  - Stimulates secondary messengers associated with PGF2α synthesis
    - COX II
  - PGF2α circulates through the blood stream and targets the CL
  - CL undergoes luteolysis

Adapted from Neely, 1985
Pro- vs Anti-Luteolytic

Anti-Luteolytic

- Oxytocin administered **before day 10 and continued**
  - Binds to oxytocin receptor at endometrial epithelium
  - Lack of secondary messenger
  - Inhibits the upregulation of secondary messengers
    - Specifically COX II
  - No “spontaneous” luteolysis
  - CL has prolonged function
    - Up to 90 days

Adapted from Neely, 1985