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

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ANIMAL, DAIRY & VETERINARY SCIENCES
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

![Graph showing the changes in Progesterone and PGFM levels over days after ovulation.](Image)

- **Progesterone**
- **PGFM**

- Ovulation
- Days After 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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The Horse Magazine: March 2017
Estrus Suppression in the Performance Mare


The Horse Magazine: March 2017
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
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  - 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

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**Day 0**

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

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

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

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**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
Acknowledgements

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Supporting Slides
Pro- vs Anti-Luteolytic Functions of Oxytocin

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