Tranquilization Affects Intrauterine Pressure in Mares Administered Oxytocin

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The tranquilization of mares with xylazine prior to treatment with uterine lavage and oxytocin is preferred over tranquilization with acepromazine, since xylazine increases uterine contraction time. Mares with a delay in uterine clearance exhibit an enhanced response to α agonists and α antagonists, possibly because of a denervation hypersensitivity. Authors’ addresses: Dept. of Physiology, Animal Reproduction and Biotechnology Laboratory, Colorado State University, Fort Collins, CO 80523 (De Lille) and Dept. of Large Animal Clinical Sciences, College of Veterinary Medicine, University of Florida, Gainesville, FL 32610 (all other authors). © 1998 AAEP.

1. Introduction

A treatment consisting of the administration of oxytocin and uterine lavage is commonly performed after breeding in mares that accumulate intrauterine fluid in response to insemination. Fractious mares requiring treatment frequently require tranquilization with either xylazine or acepromazine. Both drugs may interfere with uterine clearance because they bind to α adrenoreceptors. Xylazine, an α agonist, causes a tetanic increase in intrauterine pressure during estrus in cattle and increases myometrial activity in mares during diestrus. In contrast, acepromazine, an α1 blocker, suppresses myometrial activity in the mare during diestrus.

Damage to autonomic nerves in an organ results in enhanced responsiveness to α- and β-adrenergic agonists and is referred to as denervation hypersensitivity or supersensitivity. During pregnancy the weight of the fetus may stretch the broad ligaments and damage the nerves contained within the ligament. Damage to nerves that innervate the myometrium may contribute to the phenomenon of decreased myoelectrical activity seen in mares with delayed uterine clearance after intrauterine bacterial challenge. As a way to test the hypothesis that mares with delayed uterine clearance (DUC) experience denervation hypersensitivity, the effects of xylazine, an α agonist, and acepromazine, an α1 blocker, on intrauterine pressure (IUP) and their interaction with oxytocin were evaluated in reproductively normal mares and mares that exhibited a delay in uterine clearance after breeding.

2. Materials and Methods

Eight mares, four that were reproductively normal and four that exhibited DUC, were used. Criteria for normalcy included no history of persistent uterine infection, a normal reproductive examination, <3 neutrophils per high-power field (400×) on uterine cytology, and no bacteria isolated from the uterus. Normal mares had either a grade 1 or grade 2 uterine biopsy score according to the system of
Kenney and cleared >50% of a radiocolloid infused into the uterus within 2 h. Mares that exhibited DUC had a history of endometritis and fluid accumulation after breeding, a grade 2 or grade 3 biopsy score, and cleared <30% of the radiocolloid within 2 h.

Changes in IUP were measured in each mare for three 100-min sessions by using a Millar microtip catheter placed in the uterine lumen during estrus. The protocol consisted of 10 min of baseline recording followed by the administration of xylazine 0.5 mg/kg, acepromazine 0.05 mg/kg, or 0.9% saline 0.005 ml/kg IV (as a control) and the measurement of IUP for 30 min. Ten IU of oxytocin were then administered intravenously and the IUP was recorded for an additional 60 min. Data were recorded on a physiograph and digital records were stored in a computer. Data were analyzed by using the general linear method of SAS.a

3. Results
An analysis of variance detected a treatment by group interaction (p < 0.0001). Xylazine and oxytocin caused an increase in IUP in both groups, whereas acepromazine and the saline solution did not. Xylazine caused a tetanic increase in IUP that lasted for 11.16 ± 0.97 min (mean ± SEM) in both groups. Oxytocin increased the IUP in a wavelike pattern for 18.5 ± 1.69 min in normal and 20.1 ± 1.67 min in DUC mares. Oxytocin priming of oxytocin in normal mares increased the number of IUP waves from 5 ± 0.46 (control) to 6.92 ± 0.46 (p = 0.008) and decreased the length of the first IUP wave from 7.64 ± 0.81 min (control) to 4.77 ± 0.81 min (p < 0.05). In contrast, oxytocin priming of oxytocin in DUC mares increased the length of the first oxytocin-induced IUP wave from 8.28 ± 0.82 (control) to 10.3 ± 0.85 min (p < 0.05). Mares with DUC contracted their uteri for a longer time than normal mares after xylazine priming (23.95 ± 1.77 min and 15.79 ± 1.69 min, respectively; p < 0.0001). However, both groups had a similar number of contractions (6.92 ± 0.46). Acepromazine had no effect on the oxytocin-induced IUP wave pattern in normal mares, but in DUC mares it decreased the number of IUP waves from 6.41 ± 0.46 (control) to 4.73 ± 0.48 (p < 0.01) and increased the length of the first oxytocin-induced IUP wave from 8.34 ± 0.81 min (control) to 12.5 ± 0.85 min (p < 0.05).

4. Discussion
Myometrial contractility is under hormonal, neuronal, and myogenic control. The stimulation or inhibition of one system most likely interacts positively or negatively with the other. The equine uterus contains both α- and β-adrenergic receptors. The uterine response to adrenergic stimulation depends on the existing hormonal influence. In the estrogen-primed uterus, α adrenoceptors predominate and are excitatory. In the progesterone-primed uterus, β adrenoceptors predominate and are inhibitory. Xylazine, an α-adrenoceptor agonist, caused a tetanic increase in IUP that enhanced the effects of oxytocin in both normal mares and DUC mares. Clinically, combining xylazine with oxytocin may increase the expulsion of inflammatory products postbreeding and aid in fluid recovery after uterine lavage. The administration of xylazine alone may facilitate attempts to crush a twin as it increases uterine tone and intrauterine pressure.

Acepromazine blocks α adrenoceptors, thereby allowing circulating catecholamines to relax the uterus. In this study, acepromazine did not affect the IUP of normal mares, nor did it cause appreciable changes in IUP following oxytocin administration. In DUC mares, however, acepromazine decreased the number of IUP waves when it was administered with oxytocin. Clinically, it may hamper uterine emptying if it is given with oxytocin.

When α-adrenergic drugs were combined with oxytocin, the two groups responded differently, possibly because of a denervation hypersensitivity. The cause of denervation hypersensitivity is only partially known. When a nerve is damaged, neurotransmitters are no longer released at the synapses. This results in an upregulation of receptors in the postsynaptic membranes of effector cells. If a hormone or drug (α or β agonist or antagonist) is then injected into the circulating blood, the effector reaction is vastly enhanced. Hormones upregulate neural systems and induce distinct morphological changes in the effector organ. We found no differences in IUP responses when a single drug was administered. When xylazine or acepromazine was combined with oxytocin, DUC mares overresponded compared with reproducitively normal mares. The overresponse of DUC mares may be due to oxytocin’s upregulating effector cells and amplifying the denervation hypersensitivity response. In conclusion, the xylazine priming of oxytocin prolonged uterine contractions in DUC mares, whereas the acepromazine priming of oxytocin decreased the number of IUP waves. We recommend that fractious mares be tranquilized with xylazine prior to treatment with uterine lavage and oxytocin since xylazine increases uterine contraction time.

The Dorothy Havemeyer Foundation supported this study.

References and Footnotes

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