Effect of Acepromazine, Detomidine, and Xylazine on Myometrial Activity in the Mare

Hugh M. Gibbs III and Mats H.T. Troedsson

Department of Reproduction, School of Veterinary Medicine
University of California, Davis, California 95616

ABSTRACT

Effects of acepromazine, detomidine, and xylazine on myometrial activity were investigated through use of electromyography (EMG). Four pairs of electrodes were surgically implanted in the myometrium of five normally cycling mares. Each electrode was passed through the abdominal wall of the left flank, tunneled s.c., exteriorized near the withers, and attached to a Grass (Quincy, MA) polygraph. Acepromazine (0.05 mg/kg), detomidine (0.015 mg/kg), and xylazine (0.5 mg/kg) were each administered i.v., and effects on myometrial activity were recorded. Myometrial activity was analyzed for the duration and frequency of activity bursts, the intensity of electrical activity, and the percentage of time that activity was present. Results were expressed as means ± SEM. Significance was set at p < 0.05. Prior to treatment, 1 h of baseline recordings and 30 min of recordings after administration of i.v. saline were carried out. Statistical analysis was performed through use of a split-plot analysis of variance. After administration of acepromazine, myometrial activity was suppressed for 90 min (13.4 ± 3.6% post-treatment vs. 31.6 ± 8.2% pretreatment). Myometrial activity was increased for 60 min after detomidine administration (70.9 ± 5.7% post-treatment vs. 23.8 ± 6.1% pretreatment) and 30 min after xylazine administration (59.4 ± 7.8% post-treatment vs. 35.0 ± 3.6% pretreatment). It was concluded that acepromazine, detomidine, and xylazine all significantly affect myometrial activity, and this could be important in a number of clinical situations.

INTRODUCTION

It is a common practice to sedate mares to aid in restraint and to facilitate the performance of various examinations or procedures involving the uterus. Acepromazine (an α-adrenergic receptor antagonist) and detomidine and xylazine (α-adrenergic receptor agonists) are used alone or in combination for this purpose [Geiser, 1990]. Little is known about the effects of these drugs on the activity of the myometrium. Myometrial activity and uterine tone are significant from both a diagnostic and therapeutic standpoint, and it is therefore important to consider effects on myometrial activity should one choose to administer a sedative to a mare. We hypothesized that acepromazine would suppress myometrial activity via its α-adrenergic receptor antagonist mechanism of action and that detomidine and xylazine, in contrast, would stimulate myometrial activity. The purpose of this study was to measure the myoelectrical effects of acepromazine, detomidine, and xylazine on the myometrium.

MATERIALS AND METHODS

Mares

Five healthy mares (Arabian, Standardbred, or Quarter horse breed) were used in this study. They were all confirmed to be normally cyclic and had no history of fertility problems. The mares were fed alfalfa hay and housed in stalls. During recordings, the mares were kept in stocks. The stage of the estrous cycle was determined by transrectal ultrasonographic (5-MHz linear-array transducer) examinations of the reproductive tract every other day for detection of ovarian follicles and the presence of a CL, and also by teasing the mares with a stallion. Diestrus was confirmed by determining concentrations of progesterone in blood samples obtained at each recording session. All handling, treatment, and procedures were conducted in accordance with the NIH guide for the care and use of laboratory animals and approved by the animal care and use committee at the University of California, Davis.

Collection of Blood Samples

In conjunction with each recording session, 10 ml of venous blood was withdrawn from the
jugular vein in a vacutainer system (Becton, Dickinson and Co., Rutherford, NJ) containing sodium heparin as an anticoagulant. The samples were centrifuged at 400 × g for 10 min, and plasma was removed and stored at -20°C until analyzed for progesterone.

**Hormone Analysis**

Plasma progesterone concentration was determined through use of a solid phase microtiter plate enzyme immunoassay as described by Munro and Stabenfeldt [1984] and Troedsson et al. [1993a, 1993b]. The mean intraassay coefficients of variation for pools of high, medium, and low progesterone concentration were 4.9, 6.2, and 10.5%, respectively. The sensitivity of the progesterone assay was < 0.1 ng/ml.

**Myometrial Electrode Implantation**

Four pairs of bipolar electrodes were surgically implanted into the myometrium of each mare as previously described by Troedsson et al. [1993a]. The uterus was exposed via a ventral midline laparotomy performed under general anesthesia induced by 100 mg/kg gufensin (Rhone-Poulenc, Collegeville, PA) and 2 mg/kg thymyalal (Surtial; Parke-Davis, Morris Plains, NJ) i.v. and maintained with halothane (Halocarbon Laboratories, N. Augusta, SC). Three pairs of electrodes (44-gauge multi-strand stainless steel Teflon-coated wire) were implanted into the myometrium of the left uterine horn, and one pair was implanted in the uterine body. Electrodes within a pair were implanted approximately 1 cm apart. This technique allowed exposure of the electrodes to both the longitudinal and circular layers of the myometrium. The recorded activity therefore represented the combined activity of the two myometrial layers. Each electrode, covered by a Teflon tube, was passed through the abdominal wall of the left flank, tunneled s.c., exteriorized near the withers, fixed in place, and capped.

**Electromyographic (EMG) Recordings**

After implantation and recovery from surgery, the mares were allowed to rest for at least 1 wk to allow the uterus to stabilize. Myoelectrical activity was monitored by a Grass Instr. (Quincy, MA) polygraph with each electrode joined to the appropriate lead of the polygraph. EMG signals were amplified through Grass DC preamplifiers, and the signals were transcribed to a Grass polygraph at a chart speed of 10 mm/min and at an amplitude of 100 μV/cm. Signal filters were set at 10 and 35 Hz [Haluska et al., 1987].

All recordings were carried out during a single diestrus. Treatments tested were 0.05 mg/kg acepromazine i.v., 0.015 mg/kg detomidine i.v., and 0.5 mg/kg xylazine i.v.; these dosages were within the range recommended for standing chemical restraint [Geiser, 1990]. The order of treatments was randomized in each mare. All treatment recordings were preceded by 1 h of baseline recordings and 30 min of recordings following treatment with isotonic saline solution i.v. Recordings continued until visual stabilization of myoelectrical activity occurred. At the end of each recording, 20 IU of oxytocin was administered i.v. as a control for myometrial activity. The response to oxytocin administration was marked and therefore was considered to be an accurate positive control for electrical myometrial activity.

All recordings were manually transformed to a digitized form, and myometrial electrical activity was analyzed as previously described by Troedsson et al. [1993a]. Total electrical activity was expressed as the percentage of time any electrical activity was recorded. The characteristics of myoelectrical activity analyzed were frequency, duration, and intensity. Frequency was defined as the number of activity bursts per 30 min, with each burst consisting of at least 10 electrical activity spikes per minute and separated from other bursts by at least 1 min. Duration was defined as the time (minutes) that elapsed from the start to the end of a burst. Intensity was measured as the number of spikes per minute. It was coded as 0 = quiescence (< 10 spikes per minute), 1 = low (11–15 spikes per minute), 2 = intermediate (16–20 spikes per minute), 3 = high (> 20 spikes per minute). Total intensity was analyzed as the degree of registered electrical activity, including periods of quiescence, divided by the total time of registration.

**Statistical Analysis**

Myometrial electrical activity was calculated as the mean of recordings from each pair of electrodes in the myometrium. The difference for each response variable between the average of the replicate of the pretreatment period and the treatment period was examined by a split-plot ANOVA with the mare used as a blocking variable. The treatments were detomidine, xylazine, acepromazine, and saline solution. All
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comparisons of interest were performed using contrast and proper error term. Results were expressed as means ± SEM; significance was set at p < 0.05.

RESULTS

The mean concentration of plasma progesterone was 7.4 ng/ml (range: 5.9–10.8 ng/ml), confirming that all mares were in diestrus at the time of the experiment.

Intravenous injections of saline solution did not affect the myoelectrical activity. Myoelectrical activity in the uterus was increased for 60 min after the administration of 0.015 mg/kg detomidine i.v. (p < 0.005) and for 30 min after the administration of 0.05 mg/kg xylazine i.v. (p < 0.05; Fig. 1). After the administration of 0.5 mg/kg acepromazine i.v., myoelectrical activity was significantly suppressed for 90 min (p < 0.05; Fig. 1). The mean total activity was higher for treatment with detomidine compared to acepromazine (p < 0.005) and higher for xylazine than for acepromazine (p < 0.03; Fig. 1). Detomidine was not different from xylazine treatment in its effect on mean total activity.

Detomidine treatment resulted in increased duration of myoelectrical bursts of uterine activity (p < 0.01) without affecting the frequency of bursts (Table 1). In addition, the intensity of activity bursts was increased following administration of detomidine (p < 0.05). Xylazine treatment resulted in a decrease in the number of myoelectrical activity bursts (p < 0.05), which increased in duration (p < 0.03). A tendency toward an increase in intensity was observed after treatment with xylazine (p < 0.1; Table 1). Administration of acepromazine did not affect the frequency of activity bursts but tended to shorten the duration of bursts (p < 0.1; Table 1). The intensity of the myoelectrical uterine activity was decreased after treatment with acepromazine (p < 0.005; Table 1).
TABLE 1. Myoelectrical activity of the uterus prior to and following treatment with detomidine (60 min of recordings), xylazine (30 min of recordings), and acepromazine (90 min of recordings) shown as mean ± SD.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Before treatment</th>
<th>Detomidine</th>
<th>Before treatment</th>
<th>Xylazine</th>
<th>Before treatment</th>
<th>Acepromazine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total activity (%)</td>
<td>23.8 ± 6.1</td>
<td>70.9 ± 5.7 *</td>
<td>35.0 ± 3.6</td>
<td>59.4 ± 7.8 *</td>
<td>31.6 ± 8.2</td>
<td>13.4 ± 3.6 *</td>
</tr>
<tr>
<td>Frequency (burst/min)</td>
<td>1.9 ± 0.5</td>
<td>1.4 ± 0.2</td>
<td>3.5 ± 0.5</td>
<td>1.5 ± 0.2 *</td>
<td>1.9 ± 0.4</td>
<td>1.3 ± 0.3</td>
</tr>
<tr>
<td>Duration (min)</td>
<td>3.9 ± 1.2</td>
<td>13.0 ± 2.7 *</td>
<td>4.4 ± 0.9</td>
<td>15.1 ± 2.8 *</td>
<td>4.9 ± 1.5</td>
<td>2.6 ± 0.9 *</td>
</tr>
<tr>
<td>Intensity (1-3)</td>
<td>1.3 ± 0.1</td>
<td>1.7 ± 0.1 *</td>
<td>1.3 ± 0.1</td>
<td>1.7 ± 0.2 *</td>
<td>1.3 ± 0.07</td>
<td>1.1 ± 0.03 *</td>
</tr>
</tbody>
</table>

* p < 0.01; * p < 0.05; ° p < 0.1.

**DISCUSSION**

EMG measures changes in action potentials over the membrane of the muscle cells in the range of the recording electrodes. A close relationship between electrical and mechanical activity has been demonstrated in the myometrium [Toutaine et al., 1983]. In the present study, the term myoelectrical activity was used to describe the recorded EMG activity rather than uterine contractions.

EMG activity of the equine uterus has been described during the estrous cycle [Taverne et al., 1979; Jones et al., 1991; Troedsson et al., 1993a], during late pregnancy and parturition [Haluska et al., 1987], and following intrauterine bacterial inoculation [Troedsson et al., 1993b]. The effect of detomidine on myoelectrical activity of the uterus has also been investigated in pregnant mares [Jedruch et al., 1989], but little is known about myoelectrical activity following treatment with detomidine, xylazine, and acepromazine in cycling non-pregnant mares.

Acepromazine, which acts as an α-adrenergic receptor antagonist [Booth, 1988], was found to suppress the myoelectrical activity in the uterus for 90 min. Detomidine and xylazine act as α-adrenergic receptor agonists [LeBlanc, 1991] with a stimulatory effect on smooth muscle. These drugs were found to increase myoelectrical activity. In contrast, Jedruch et al. [1989] found a decrease in myoelectrical activity in the uterus of mares treated with 0.020 mg/kg detomidine i.v. during the last trimester of pregnancy. In our study, a dose of 0.015 mg/kg detomidine i.v. resulted in increased activity for 60 min. In both experiments, mares had elevated plasma progesterone at the time of detomidine administration. It is possible that other factors influence the effect of detomidine on myoelectrical activity in pregnant mares.

Further studies that compare myoelectrical activity in the uterus in nonpregnant and pregnant mares during different stages of gestation are needed to clarify these conflicting data.

The effects of acepromazine, detomidine, and xylazine on myometrial activity could be significant in various clinical situations, including routine exams of the mare’s reproductive tract, hysteroscopic exams, uterine lavages, and dystocias. When a reproductive examination is performed on a mare, transrectal palpation of uterine tone is an important diagnostic finding. Results from the present study suggest that the use of acepromazine, detomidine, or xylazine to facilitate such an exam may change uterine tone significantly. Endoscopic examination of the uterus requires distention of the uterine lumen with gas or fluid. Suppressive action on myoelectrical activity after pretreatment with acepromazine, rather than detomidine or xylazine, to allow adequate distention of the uterine body and both horns may be beneficial.

Lavage of the uterus is performed to recover embryos and to treat and prevent endometritis [Squires et al., 1985; Troedsson et al., 1992]. In both situations, recovery of all of the fluid from the uterus is important. Results from this study suggest that the α-agonist sedatives may aid in this regard whereas acepromazine could negatively affect fluid recovery. For the veterinarian working on a dystocia without the aid of general anesthesia, adequate restraint of the mare is a major factor in success. It is also important to have enough space within the uterus between myometrial contractions to make the manipulations necessary to correct the position of the foal. For this reason, the effect of detomidine and xylazine on the myometrium during dystocias should be considered.

Finally, when natural cover is required, acepromazine is occasionally used to aid in the restraint of uncooperative mares. There is a need
to investigate the consequences of this drug's suppressive effects on myoelectrical activity of the uterus on uterine sperm transport and physical clearance from the uterus.

REFERENCES


