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Bioelectrical activity of porcine oviduct and uterus during spontaneous and induced estrus associated with cyclic hormone changes

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ABSTRACT

It is widely accepted that uterine contraction is initiated by spontaneous generation of electrical activity at a cellular level in the form of action potentials. Such action potential events, when they involve many myometrial cells and occur in immediate succession, are described by their amplitude and duration. In an effort to improve clinical management of uterine contractions, research has focused on determination of the properties of the reproductive tract's electrical activity under hormonal stimulation. The aim of this study was to evaluate the myoelectric activity (amplitude and duration) of the oviduct and the uterus in relation to plasma concentration of LH, estradiol (E2), and progesterone (P4) during spontaneous and induced estrus in gilts. The course of the experiment was divided into eight periods defined by hormone concentrations (LH, P4, and E2) and time intervals before and after the start of the LH surge. Myoelectric signals were recorded, and the hormone levels were measured during proestrus and estrus in natural and hormone-induced estrus cycle. During the natural estrus, the LH surge was longer than after hormonal stimulation (28 vs. 20 hours) and suggested an inverse relationship between the LH concentration and the duration of myoelectric activity ($S_R = -0.68$). Analyses of the records of the amplitudes and durations of the electromyography activity in uterine horns and oviducts showed significant differences between spontaneous and induced estrus ($P < 0.05$). During induced estrus, the LH surge began earlier (T1 vs. T2) and increased more (7.46 vs. 6.50 ng/mL) than during spontaneous estrus. This observation suggests a direct relationship between the LH concentration and the amplitude of the myoelectric activity (Spearman rank correlation = 0.71). The significantly higher duration and amplitude of the activity in the isthmus of the oviduct and the uterus during induced estrus shortly after the onset of standing heat (4–8 hours after the LH surge) suggested more favorable conditions for effective artificial insemination.

1. Introduction

The need for a better understanding of how the mechanical myometrial contractility output can be controlled requires a detailed *in vivo* examination of the reproductive tract. The commonly encountered clinical problems caused by failure in contractile activity, such as preterm labor, dystocia, and infertility, are often described as disorders in embryo transport and implantation [1]. It is widely accepted that uterine contraction is initiated by a spontaneous generation, at a cellular level, of electrical activity in

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the form of action potentials. Such action potential events, when they involve many myometrial cells and occur in immediate succession, are described by amplitude and duration. In the human, this electrical activity is low and unco-ordinated early in gestation but becomes intense and synchronized later in pregnancy and peaks at term [2]. In animals, only a few articles report electrical activity in the reproductive tract of cattle [3,4], mares [5,6], pigs [7–9], and sheep [10] in different phases of the estrus cycle and gestation. Most studies were performed *in vivo* in rats and mice, where the length of pregnancy and the labor could be controlled and perhaps compared with the myometrium of nonpregnant females with a good degree of precision [1,11,12]. A study of the exact relation between the changes in the action potential and the hormonal status and the impact of the administrated medications is possible only in a long-term *in vivo* experiment. In a vast majority of the reviewed studies, it is indicated that prostaglandins [13], nitrogen oxide [14], the autonomic nervous system [15,16], and steroid hormones [17,18] affect the reproductive tract contractions. In those reviews, the electromyography (EMG) activity has been analyzed mainly during pregnancy, labor, postpartum, or spontaneous estrus cycle but not during an induced estrus cycle. In attempts to improve the clinical management of uterine contractions during estrus cycle, significant attention has been dedicated to measurements of the electrical activity in the uterus and oviduct after stimulation with eCG, hCG, and GnRH agonists. The results of the associated bioelectrical activity, recorded in hormonally stimulated gilts, were compared with the results obtained in gilts expressing a spontaneous estrus.

The earliest uterine EMG studies had established that the electrical activity of the myometrium is responsible for myometrial contractions [2–4], but there is still lack of evidence of oviductal contraction control [19]. In the human, two common methods of acquiring the uterine (EMG) signals abdominally are used: a direct method involving entering the uterus via needle electrodes through the abdomen and a noninvasive method using abdominal surface electrodes [2]. In animal model, the telemetry method allows to reduce disadvantages and to conduct the long-term recordings with animals in a state of well-being, eliminating the stress associated with immobilization. When large animal studies are essential before moving to clinical trials, it is important to find ways to reduce the number of experimental animals used [20]. The telemetry method facilitates the reduction of the number of animals used in the experiment [21]. Here, we describe the design features of a uterine and oviductal EMG telemetry system and the surgical techniques that may be used in porcine reproductive tract during a long-term study. Recently, an implantable telemetry method using commercially available equipment was implemented in the electromyography studies of the gastrointestinal tract in weaned piglets [22] and in the reproductive tract in cows [3,4] and pigs [23–25]. Pigs are widely used as experimental models in research involving the reproductive tracts. At the Center for the Development of Advanced Medical Technology, “medical” pigs were considered ideal preclinical model systems and in the investigations that were carried out pigs were treated as a referential species [7–9,20,21]. Obtaining a better basic understanding of the bioelectrical activity in the smooth muscle layer of the oviduct and the uterus will improve the power and usefulness of these models.

In an effort to improve clinical management of uterine contractions, research was focused on understanding of the properties of the electrical activity of the reproductive tract under hormonal stimulation. The aim of this study was to evaluate the myoelectric activity (amplitude and duration) in the oviduct and uterus in relation to the plasma concentration of luteinizing hormone (LH), estradiol (E2), and progesterone (P4) in gilts during spontaneous and induced estrus.

2. Materials and methods

2.1. Animals and surgery

The study was conducted using eight sexually mature Polish landrace breed gilts, 95 to 115 kg bodyweight (bw). The recordings were repeated on two occasions. The sows were adapted to the animal facilities for 7 days before the studies. During the entire experiment, the animals were housed in metabolic cages equipped with automatic drinkers. The gilts were fed and watered *ad libitum*. During the adaptation period and throughout the experiment, the animals did not manifest any signs of disease. General inclusion criteria into this study were age older than 4 months and single estrus cycle. Boar exposure was used to perform the first estrus detection. Gilts with no specific signs of heat (“silent heat”) were excluded from the experiment ($n = 5$). Animals with spontaneous (natural) estrus constituted a control group for animals with induced estrus. The experiment protocols and procedures were approved by the local ethical committee.

The surgery was carried out under general anesthesia. The animals were premedicated with an intramuscular injection of azaperone (3.0 mg/kg bw, im; Stresnil; Janssen Pharmaceutica, Belgium) after which a catheter was inserted into the auricular vein. The surgery was performed under general anesthesia consisting of a combined administration of medetomidine (1.0 mg/kg bw, iv; Cepetor; CP-Pharma Handelsges), butorphanol (0.2 mg/kg bw, iv; Butomidor; Richter Pharma AG), ketamine (3.0 mg/kg bw, iv; Bioketan; Vetoquinol Biowet), and propofol (2.0–4.0 mg/kg bw, iv; Propofol; Pfizer) and in strictly aseptic conditions. In brief, an incision, 15 cm long, was made on the right side, just behind the rib arch. The skin, the external and internal oblique muscles, the straight muscle, and the peritoneum were cut. Then the uterus, oviducts, and ovaries were extracted from the abdominal cavity. The electrodes were sutured on the isthmus and ampulla of the right oviduct and on the middle part of the horn of uterus with nonabsorbable sutures (Amifil 5–0; SINPO, Poland). In the next step, the oviducts and uterus were positioned back in the abdominal cavity and a transmitter implant was fixed in a pocket made in the external oblique muscle. The ground electrode was fixed to the abdominal muscles near the transmitter and the laparotomy was closed in a standard