

EX VIVO PHARMACOLOGY OF SMOOTH MUSCLE IN THE UTEROSACRAL LIGAMENT: ADRENERGIC AND CHOLINERGIC EFFECTS AND THEIR MODULATION BY OXYTOCIN AND RELAXIN

Hypothesis / aims of study

The uterosacral ligament is a constitutive component of the pelvic floor involved in pelvic organ prolapse. A previous study observed that in premenopausal women with pelvic organ prolapse the smooth muscle structure of the ligament was impaired. The functional role of the smooth muscle component is not clear. The goal of the present study was to characterize the normal function and pharmacology of the smooth muscle via an *ex vivo* micro perfusion system for native live tissues obtained during surgery.

Study design, materials and methods

Samples from the cervical third of the uterosacral ligaments (Figure 1) were preserved during hysterectomy of 39 premenopausal women with benign indications, excepting prolapse and endometriosis. Microscopically small cross sections of arterioles and translucent chips of connective tissue with collagen fibrils and smooth muscle (ground reticulum) were prepared with micro instruments, mounted in a perfusion chamber (400 μ l). The structure of the tissue was visualized by birefringence of collagen between crossed polar filters. Contraction of smooth muscle on perfusion with drugs was monitored by digital time-lapse video. Contraction movements were analysed with the Image J software and quantified by image subtraction.

Results

First, we tested the feasibility of the perfusion assay by measuring the contraction of arterioles on perfusion with Arterenol in a dose response experiment. In a second step we identified smooth muscle between collagen fibrils of the ground reticulum via stimulation of contractions with KCl. Then the sample was perfused with increasing concentrations of Carbachol. The smooth muscle contracted in the physiological range of 10^{-4} M. Oxytocin elicited rhythmic contractions of the smooth muscle in the ground reticulum. Relaxin-2 widened the lumen of the arterioles, often accompanied by rhythmic contractions, shifted the dose response to the right, and enhanced the rhythmic contractions of the reticular muscle on Oxytocin. Helical arterioles, sinusoids and special veins together with the surrounding smooth muscle bundles of the connective tissue formed a functional cavernous unit, the pharmacology of which was analysed under the microscope. Data is presented as video clips and time scans of contraction.

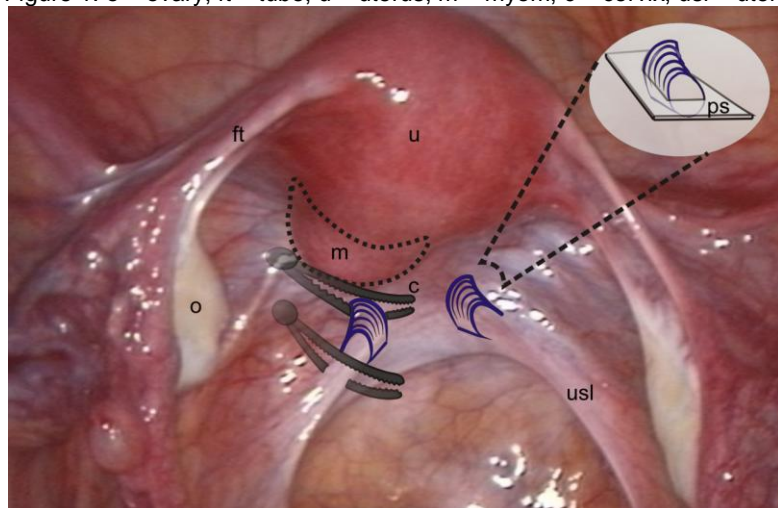
Interpretation of results

(1) *Ex vivo* pharmacology of surgical samples in the microscopic scale is a novel approach and a new option for functional investigations of the pelvic floor. (2) Smooth muscles and vessels in the sacrouterin ligament are differentially regulated by sympathetic and parasympathetic neurotransmitters and modulated via Relaxin and Oxytocin. (3) Further studies along these lines may be a point of departure for the pharmacological treatment of pelvic organ prolapse.

Concluding message

Smooth muscles components in the sacrouterin ligament are differentially regulated by sympathetic and parasympathetic neurotransmitters and modulated via Relaxin and Oxytocin.

Figure 1: o – ovary, ft – tube, u – uterus, m – myom, c – cervix, usl – uterosacral ligament



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Is this a clinical trial?	No
What were the subjects in the study?	HUMAN
Was this study approved by an ethics committee?	Yes

<i>Specify Name of Ethics Committee</i>	Ethics Committee University Tuebingen, Germany
<i>Was the Declaration of Helsinki followed?</i>	Yes
<i>Was informed consent obtained from the patients?</i>	Yes