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EC GASTROENTEROLOGY AND DIGESTIVE SYSTEM

Research Article

Vagus Nerve: The Possibility of Regulating the Contractile Function of the Uterine Floor

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Received: January 23, 2020; **Published:** February 11, 2020

Abstract

Electromotor activity of the smooth muscles of the rabbit uterus bottom by the peripheral segment of the vagus nerve at the level of C5-C6 electro irritation was stimulated. The peripheral parts of the trunk of both vagus nerves were stained with the toluidine blue administration, and a morphological study of biopsy specimens was undertaken. Staining of intramural ganglia, i.e. the presence of synaptic contacts with preganglionic cholinergic fibers, was revealed.

Keywords: *Uterus; Innervation; Vagus Nerve*

Introduction

It is believed that the bulbar section of the parasympathetic nervous system does not Innervate the pelvic organs [1]. However, according to other researchers, it is through the vagus nerve that cholinergic innervation of the uterine floor is performed [2]. Cholinergic neurons form moderately dense plexuses in the myometrium, the microarterial system of the fallopian tubes. Acetylcholine is known to stimulate uterine contractions [3].

Studies of uterine innervation in mice have shown that acetylcholine, norepinephrine, and serotonin dose-dependently regulate uterine motility and hormonal status. Blockade of прод-adrenoreceptors of longitudinal muscles prevents a decrease in contractile activity of the myometrium, while blockade of circus-adrenoreceptors of circular muscle fibers prevents a decrease in muscle tone caused by the action of norepinephrine [4]. Other researchers have shown in experiments on rat uterus that acetylcholine, histamine, serotonin, phenylepinephrine and oxytocin cause uterine contractions that are inhibited by an ATP-Aza blocker [5].

Immunohistochemically, it has been shown that the myometrium of young mice contains P2x1 purinoreceptors [6], which play a role in the mechanisms of contraction of the smooth muscles of the uterus and its tubes. In particular, activation of P2 receptors leads to a reduction in the non-pregnant uterus of a Guinea pig [7].

Smooth muscle contractions are also caused by the introduction of serotonin. R Bello., *et al.* (2002) showed that preincubation of the rat uterus with dichloromethane extract causes dose-dependent inhibition of the contractile effect of serotonin. At the same time, neither dichloromethane nor methanol inhibited norepinephrine-induced contractions of the uterus and tubes [8].

In the smooth muscles of the uterus, it is assumed that there is a noncholinergic excitatory motor innervation, which is mediated by serotonin. Moreover, oxytocin slows down the absorption of serotonin by mast cells and has a potentiating effect on uterine contractions [9]. However, T Kitazawa., *et al*. (1999) reports on the possible inhibitory effect of serotonin on the motor activity of the circular muscle of the swine uterus. Histochemical research using antibodies specific to 5-HT1B/1D receptors that cause contraction of isolated blood vessels in the human uterus revealed the presence of 5-HT1B-in the smooth muscle layer of the uterine vessels, and the absence of 5-HT1D-receptors [10]. According to our data, the rabbit's uterus contains 5-2,3,4 receptors, activating which serotonin causes uterine contraction [11]. Sumatriptan can cause uterine vascular contractions by acting on 5-HT1B receptors [12].

At the same time, other researchers Express a different opinion. In particular, a pharmacological study of the contractility of the cervical strips of the Guinea pig's uterus revealed no effect of the serotonin antagonist on the contraction of the uterine tissue strips caused by the compound "48/80" [13]. Perhaps the difference in research results obtained by these authors is due to the fact that the sensitivity of different parts of the uterus to serotonin, as well as to other contractile agents, is not the same. Thus, the ovarian region of the uterus of an adult rat was less sensitive to serotonin than the cervical region. The authors concluded that not only the number of receptors, but also anatomical differences determine the hormonal regulation of the uterus's sensitivity to serotonin [14].

The nature of the response of the uterus and tubes also depends on the hormonal background, on the estrus phase in which the animal is located. Cells of Cajal of the human myometrium Express receptors of estrogen and progesterone. Rabbit myometrial strips treated with estrogen or progesterone, in response to a series of electrical stimuli, show multidirectional contractile reactions: strips treated with estrogen give the phenomenon of a positive ladder, and strips treated with progesterone, in response to each successive electrical impulse, detected the phenomenon of a negative ladder [15].

In view of the need to conduct studies of cholinergic mechanisms of regulation of contractile activity of the uterine floor on a tested hormonal background, the task of selecting an experimental animal was very relevant. The rabbit, as we know, is unique not only in that the vagus nerve and the sympathetic trunk pass separately on its neck and do not form anastomoses, but also in that when animals are kept separately, females do not ovulate, and they have a natural stable background of the first phase of estrus.

Materials and Methods

Experiments were performed on 5 chinchilla rabbits, females weighing 3.5-4 kg. in the sparing conditions of the surgical stage of Nembutal anesthesia (40 mg/kg), the peripheral segment of the vagus nerve was stimulated at the level of C5-C6 at the first stage of the experiment. electro-motor activity (EMA) of the smooth muscles of the uterine floor was recorded using bipolar silver electrodes with a contact surface area of 1.5 - 2 mm^2 placed on the surface of the organ. EM registration was performed on a nichon-Cohden polygraph under pre-amplification conditions. At the second stage of the experiment, toluidine blue was injected into the peripheral part of the trunk of both vagus nerves at the level of the neck. Axoplasmic current transfers the dye to organs and tissues innervated by the vagus nerve for 10 hours. then, the tissues of the uterine floor were taken. The biopsy was fixed in 10% neutral formalin, dehydrated in alcohols of increasing concentration and enclosed in paraffin. The obtained sections were stained with hematoxylin and eosin and visualized at the light-optical level at an increase of 240-600. The control was the uterus of intact rabbits.

Statistical analysis was performed using the student's t-test at $p < 0.05$.

Results and Discussion

The results of the study and their discussion. Irritation of the right vagus nerve increases the amplitude and frequency of slow waves of electromotor activity of the uterine floor (Table 1).

The value of the studied stimulatory effect is 30.2% in frequency and 62.5% in amplitude.

Background EMA		Stimulation vagus nerve	
Frequency/min	**Amplitude, mV**	**Frequency/min**	**Amplitude, mV**
8,6 ± 1,1	0,16 ± 0,04	11,2 ± 1,5	0,26 ± 0,09
P < 0,05		P < 0,05	

Table 1: *Electromotor activity of the uterine floor when the vagus nerve is irritated.*

It should be noted that the vagal stimulatory effect on the EMA of the uterine floor is detected with intact α -and β-adrenoreceptors. Isolated stimulation of the sympathetic stem in any of the experiments on rabbits weighing 3.5-4 kg did not lead to an increase in motility of smooth muscle cells of the uterine floor. Thus, using the physiological method, the presence of a vagal stimulatory effect on the EMMA of the smooth muscles of the uterine floor was established.

Anatomical evidence for the presence of vagal innervation of the uterine floor was provided by experiments with *in vivo* endoneural injection of toluidine blue under the myelin sheath of the right and left vagus nerves, followed by staining of the neural structures of the uterine floor.

Vessels of fundus enlarged, full-blooded, muscular tissue in the subserous layer are defined nerve trunks. There is a transition of smooth muscle bundles from the tube to the uterine tissue with a slight dilution of muscle fibers. Bundles of smooth muscle cells go in different directions. In the thickness of the muscle tissue, the nerve ganglia, colored toluidine blue, surrounded by the perineum and containing a different number of neurons - from 3-4 to 15-20 cells (Figure 1).

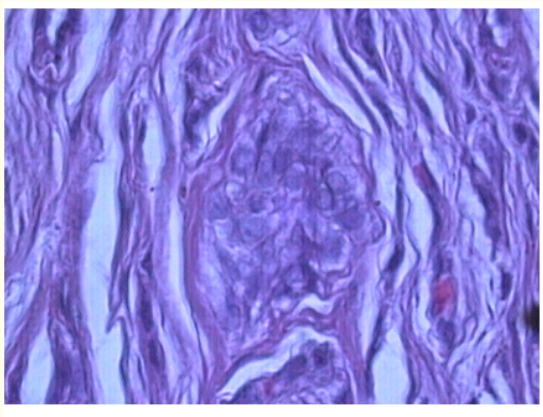

Figure 1: *Rabbit uterus of the experimental group. The nerve ganglion. Staining with hematoxylin and eosin. Coloring of nerve structures with toluidine blue. HC. x 600.*

The muscle layer of the uterine floor of the control group of animals contains only smooth muscle cells that go in different directions. Intramural ganglia were not detected. Connective tissue layers are located between the bundles of smooth muscle cells (Figure 2).

Thus, intramural ganglia that have synaptic contacts with preganglionic cholinergic fibers are visualized when staining the vagus trunks. Staining of intramural ganglia confirms their presynaptic regulation by cholinergic fibers of the vagus nerve. Studies have confirmed the functional role of the vagus nerve in regulating the electromotor activity of the uterine floor.

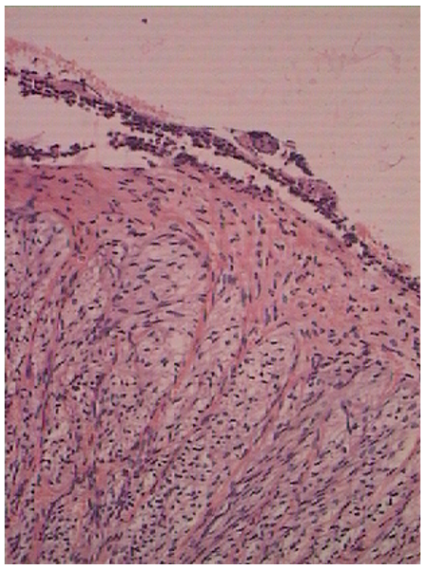

Figure 2: *The uterus of the rabbit in the control group. Vessels of the venous type, full-blooded Connective tissue layer between the bundles of smooth muscle cells. Staining with hematoxylin and eosin. HC. x 120.*

Conclusion

The existence of bulbar cholinergic innervation of uterus was demonstrated for the first time. Cholinergic enhancement of contractile activity of the uterus was confirmed.

Bibliography

1. Dindyaev S., *et al*. "Intra- and extraorgan bioamine supply in rat uterus". *Nauka i Studia* 3 (2016): 338-344.
2. Collins JJ., *et al*. "Vagal afferent flow the uterus and cervix provide direct connections to the brainstem". *Cell and Tissue Research* 295.1 (1999): 43-54.
3. Ushakova GA and Petrich LN. "Modern ideas about the mechanisms of development of labor activity: Overview". Mother and Child in Kuzbass 2 (2016): 4-10.
4. Konstantinova MM., *et al*. "The effect of transmitters on the spontaneous activity of the uterus of the mouse". Ross Fiziol. I.M. Sechenova. 86.9 (2000): 1081-1092.
5. Lee B., *et al*. "General pharmacological properties of YJA20379-8., a new H+/K(+)-ATPase inhibitor with anti-ulcer activities". *Arzneimittelforschung* 51.8 (2001): 659-666.
6. Vial C and Evans RJ. "Smooth muscles does not have a common P2X receptor phenotype: expression, ontogeny and function of P2x1 receptors in mouse ileum, bladder and reproductive systems". *Autonomic Neuroscience* 92.1-2 (2001): 56-64.
7. Ziganshin AU. "P2 receptors as promising targets for the action of future drugs". *Kazan Medical Journal* 97.1 (2016): 135-141.

8. Bello R., *et al*. "Globularia alypum L. extracts reduced histamine and serotonin contraction in vitro". *Phytotherapy Research* 16.4 (2002): 389-392.

9. Theoharides TC and Stewart JM. "Genitourinary mast cells and survival". *Translational Andrology and Urology* 4.5 (2015): 579-586.

10. Ontsouka EC., *et al*. "Expression of Messenger RNA Coding for 5-HT Receptor, Alpha and Beta Adrenoreceptor (Subtypes) during Oestrus and Dioestrus in the Bovine Uterus". *Transboundary and Emerging Diseases* 51.9-10 (2004): 385-393.

11. Lychkova AE., *et al*. "Serotonin regulates contractile activity of the uterus in non-pregnant rabbits". *Comparative Biochemistry and Physiology Part C: Toxicology and Pharmacology* 165 (2014): 53-59.

12. Razzaque Z., *et al*. "5-HT1B-receptors and vascular reactivity in human isolated blood vessels: assessment of the potential craniovascular selectivity of sumatriptan". *British Journal of Clinical Pharmacology* 53.3 (2002): 266-274.

13. Bytautiene E., *et al*. "Endogenous mast cell degranulation modulates cervical contractility in the guinea pig". *American Journal of Obstetrics and Gynecology* 186.3 (2002): 438-445.

14. Oropeza MV., *et al*. "Anatomical differences in uterine sensitivity to prostaglandin F(2alpha) and serotonin in non-pregnant rats". *European Journal of Pharmacology* 446.1-3 (2002): 161-166.

15. Cretoiu SM., *et al*. "Interstitial Cajal-like cells of human Fallopian tube express estrogen and progesterone receptors". *Journal of Molecular Histology* 40.5-6 (2009): 387-394.

Volume 7 Issue 3 March 2020