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Isthmus of the Uterus: Whether Vagal Innervation is Possible

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Abstract

The goal is to identify possible vagal innervation of the uterine isthmus and the role of exogenous and endogenous serotonin in the regulation of contractile activity of smooth muscles in this organ.

Material and methods: The electric motor activity of the smooth muscle of the isthmus of the rabbit, s uterus was stimulated by the electrical stimulation of peripheral segment of the vagus at the level of C5-C6. Serotonin was administered against the background of vagus nerve irritation and 5HT2 receptors were turned off. Isolated vagus nerve stimulation was performed against the background of switching off 5 HT2 receptors.

Results: Electrophysiological studing showed that irritation of the peripheral segment of the vagus nerve causes an increase in the electromotor activity of the isthmus of the rabbit's uterus. Endogenous serotonin increases the parasympathetic effect by activating mainly 5HT1-receptors, exogenous-by activating 5HT2-receptors.

Keywords: Isthmus of the uterus; Vagus nerve innervation

Introduction

The works of leading anatomists show parasympathetic innervation of the pelvic organs including the uterus with the pelvic plexus [1]. Some reports provide data on possible vagal innervation of the uterine floor [2]. Regarding the double innervation (bulbar and sacral), it is known that the colon in the transversely-rimmed department has a bulbar innervation, successively replaced by a sacral parasympathetic innervation. A number of studies have shown that parasympathetic nerves have a stimulating effect on the motility of the colon [3]. Studies have shown the predominant vagal innervation of the caecum with minor sacral, in the rectosigmoid department, sacral innervation prevails, however, bulbar has a certain corrective value. It is known that in the composition of the parasympathetic nerve regulation, in addition to acetylcholine, VIP, purines, there is serotonin [4-7]. The role of serotonin in the vagus nerve in possible innervation of the uterine isthmus remains insufficiently elucidated.

The goal is to identify possible vagal innervation of the uterine isthmus and the role of exogenous and endogenous serotonin in the regulation of contractile activity of smooth muscles in this part of the organ. Materials and methods. The research was carried out on 18 chinchilla rabbits (females) with a body weight of 3.4 – 3.8 kg, under sparing conditions in accordance with the Helsinki Convention, approved in 2000. Rabbits underwent a lower-midline laparotomy, isolated the isthmic part of the uterus, and applied bipolar platinum electrodes to register an electromyogram (EMG). The EMG curve was used to determine the amplitude-frequency characteristics of slow waves and spikes, the power of tonic and phase contractions, and propulsive activity using the CONAN-M hardware and software complex (sensitivity 95%, specificity 93%).

A median incision was made on the neck, the right and left vagus nerves were dissected, and their decentralization was performed. The peripheral end of the right vagus nerve was placed on bipolar platinum electrodes, through which nerve stimulation was performed with an amplitude of 1.5-7 V, 10 Hz, 2 MS. Pharmacological analysis of the resulting phenomenon was performed using 5nt2 blockers of the spiperone receptors at a dose of 1 mg \ kg. The experiments were carried out according to the following scheme: 1 group of rabbits (n=9) underwent control vagus nerve stimulation in order to test its functional state; then 5nt2 receptors were blocked with spiperone and again the vagus nerve was irritated

and the value of the vagus stimulatory phenomenon was studied The second group of rabbits /n=9/ had no control irritation of the vagus nerve. Picked up next, the dose of serotonin, which does not have an independent stimulant effect, is 50 mg/kg. Then injected serotonin on a background of irritation of the vagus nerve before and after blockade of 5HT2 receptors.

The control group consisted of 5 female rabbits, which were registered with the EMG of the isthmic department of the uterus for 3-4. 5 hours, as in the experimental groups. Statistical analysis was performed using the Mann-Whitney software package.

Results

The frequency of slow waves EMG istmus was 7.5 ± 0.5 V min, the amplitude 0.09 ± 0.02 mV, the power of tonic contractions - 0.675 ± 0.031. The frequency of spikes was 0.8 ± 0.02, the amplitude was 0.02 ± 0.003 mV, the power of phase contractions was 0.016 ± 0.0012, and the propulsive activity was 42.2 ± 1.5. Vagus nerve irritation leads to an increase in the frequency of slow EMG waves to 12.0 ± 0.9 (by 60%, $p<0.05$), the amplitude to 0.11 ± 0.003 mV (an increase of 22.2%, $p< 0.05$), the power of tonic contractions was 1.32 ± 0.015 (an increase of 98%, $p<0.01$) the Frequency of spikes increased to 1.0 ± 0.08 (increase by 20%, $p<0.05$), the amplitude - up to 0.03 ± 0.002 mV (increase by 50.1% $p<0.05$). The power of phase contractions was 0.03 ± 0.0032 (an increase of 82.9%, $p< 0.05$), propulsive activity – 44.0 ± 1.8 (an increase of 4.3%, $p>0.05$). That is, irritation of the vagus nerve leads to an increase in tonic and phase contractions with a slight increase in the propulsive activity of the isthmus smooth muscles.

Subsequent blockade of 5NT2 receptors with spiperon leads to an increase in the frequency of slow EMG waves from 8.0 ± 0.6 to 16.0 ± 1.5 when the vagus nerve is irritated in min (increase by 100.1%, $p<0.01$) with a stable amplitude-0.07 ± 0.03 mV. The power of tonic contractions changes from 0.56 ± 0.034 to 1.12 ± 0.012 (increase by 100.1%, $p<0.01$). The frequency of spikes increases from 0.3 ± 0.04 to 0.5 ± 0.06 (an increase of 66.7%, $p<0.05$), the amplitude – from 0.01 ± 0.018 to 0.02 ± 0.03 mV (an increase of 100.3%, $p<0.01$), the power of phase contractions - from 0.003 ± 0.0012 to 0.010 ± 0.0014 (an increase of 66.7%, $p<0.05$), the propulsive activity - from 18.7 ± 0.24 to 112 ± 0.27 (an increase of 598%, $p<0.05$). That is, the blockade of 5NT2-receptors increases the power of tonic and phase contractions of smooth muscles and propulsive activity when the vagus nerve is irritated, therefore, through the 5NT1 - receptor, the influence of endogenous serotonin, which is part of the vagus nerve, is carried out when the vagus is irritated.

In rabbits of the second group isolated administration of small doses of serotonin does not cause independent chronotropic and inotropic effect on motor function the smooth muscles of the isthmus. However, the introduction of serotonin against the background of vagus nerve irritation increases the motor function of smooth muscles (Table 1).

Indicators	Background	Irritation of the vagus nerve	Irritation of the vagus nerve + serotonin
Slow waves, frequency	7,0±0,08	12±0,7	18,0±1,2
Slow waves, amplitude	0,08±0,009	0,1±0,03	0,14±0,005
Spikes, frequency	0,7±0,03	1,0±0,11	1,5±0,08
Spikes, amplitude	0,12±0,004	0,05±0,004	0,08±0,0003

Table 1: Electromyogram indicators when serotonin administration is connected to vagus nerve irritation.

The power of tonic contractions when the vagus nerve is irritated changes from 0.56 ± 0.04 to 1.2 ± 0.02 (an increase of 112%, $p<0.01$), when serotonin is administered against this background – from 1.2 ± 0.02 to 2.52 ± 0.31 (an increase of 110%, $p<0.01$). The power of phase contractions when serotonin is administered against the background of vagus nerve irritation increases from 0.014 ± 0.0025 to 0.05 ± 0.003 (an increase of 257%, $p<0.01$). Propulsive activity was 24.0 ± 1.5 (an increase of 22.1% $p<0.05$). Thus, serotonin, introduced against the background of vagus nerve irritation, has an additional stimulating effect on the motor function of the isthmus of the uterus.

Blockade of 5nt2-receptors with spiperon led to a change in the power of tonic contractions when the vagus nerve was irritated from 0.5 = 0.02 to 1.2 = 0.15 (an increase of 140%, $p<0.01$). The power of phase contractions in these conditions changed from 0.05 ± 0.0013 to 0.15 ± 0.05 (an increase of 199.8%, $p<0.01$). That is, vagal irritation against the background of 5nt2-receptor blockade has a greater effect on phase contractions, less on tonic contractions, and the propulsive activity changes from 10.0 ± 1.3 to 8.0 ± 0.4 (a decrease of 20%, $p<0.05$). This suggests a significant contribution of serotonin of vagal origin to the activation of the motor function of the uterine isthmus when exposed TO 5nt1 receptors of effector cells. The introduction of serotonin on the background of vagal turning off 5HT2-receptors leads to a change in power

tonic contractions with 1.2 of ± 0.15 to 1.1 ± 0.14 (20% reduction, $p<0.05$), power of phase reductions from 0.15 ± 0.008 to 0.12 ± 0,003 (a decrease of 20.1%, $p<0.05$). Propulsive activity increases from 8.0 ± 0.4 to 9.2 ± 0.3 (an increase of 15%, $p<0.05$). That is, the introduction of exogenous serotonin against the background of vagus irritation has a negative effect on the motor function of the isthmus through the activation of 5HT2 receptors.

Thus, endogenous vagus serotonin, released when the vagus nerve is irritated, has a stimulating effect by activating 5HT1-receptors, while exogenous serotonin-mainly due to 5HT2 - receptors of effector tissues.

A similar effect of endogenous serotonin on 5HT1 receptors was shown in the example of postprandial motility [8].

Conclusions

The vagus nerve innervates the isthmic part of the uterus. Endogenous serotonin has a predominant effect by activating 5HT1-receptors of smooth muscle cells. Exogenous serotonin has a predominant effect on 5HT2 receptors of effector cells.

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