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The Gastrointestinal Motility in Rats at First Trimester of Pregnancy.

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ABSTRACT

The aim of the study was to investigate the spontaneous and stimulated motility of stomach and colon in rats on different days of pregnancy. Gastrointestinal motility was recorded by the balloon graphic method on the anesthetized rats. It was established that in pregnant rats amplitude of spontaneous and stimulated by carbachol contractions in stomach and colon was decreased on the 3rd, 4th, 5th and 7th day of pregnancy. In pregnant rats index of spontaneous and stimulated by carbachol gastric motility was diminished on the all days of investigations. Index of spontaneous motor activity of colon on the 3rd day of pregnancy was not statistically significantly different from control but on the 4th, 5th and 7th day of pregnancy index of spontaneous motor activity of colon was reduced. . In pregnant rats index stimulated by carbachol colon motility was diminished on the all days of investigations.

Keywords: pregnancy, toxicosis, stomach, colon, motility, rats.

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INTRODUCTION

Nausea is the most common complaint of pregnant women in early pregnancy, during the first 12 weeks of pregnancy [1]. Sometimes nausea is the first sign that the women is pregnant. Also, first trimester of pregnancy is characterized by nausea, vomiting, hyperemesis gravidarum, gastroesophageal reflux disease, constipation, and diarrhea [2]. All these clinical signs are combined with the term "early toxicosis."

Approximately 85% of pregnant women encounter nausea and vomiting. Hyperemesis gravidarum, the most severe form of early toxicosis, is reported in 3% of pregnant women and can significantly affect the physical and psychological state of women [3]. Complications hyperemesis gravidarum is dehydration, violation nutrition and digestion and so on. They are found in 1.5-2% of pregnant women, in connection with what only in the US for this reason more than 50,000 pregnant women are sent annually to hospitalization [4,5].

Scientists have not yet come to a common opinion about the causes of early toxicosis. For today there are several theories that explain the development of early toxicosis.

Immunological theory. This theory is based on the fact that the parent organism perceives the fetus as an alien object (the cells of the parent), which causes its rejection in the form of signs of toxicosis in the early terms [6]. An interesting theory is Sherman P. and Flaxman S., who suggested that early pregnancy toxicosis protects the pregnant woman and the fetus from the effects of infections and toxins contained in food [7]. Thus, in their opinion, the body of the pregnant woman, which has intrusion of cellular immunity, and the fetus, which at the time of early onset of toxicosis in the mother does not yet have its own detoxification mechanisms, protected from the possible influence of factors that can lead to miscarriage, birth defects , a serious mother's disease [7,8].

Psychological theory. The psychological theory explains the signs of early toxicosis of a woman's moral unpreparedness before pregnancy and all changes in the body, figure and livelihood associated with it.

Vegetative theory. This theory is based on the fact that pregnancy requires intensified work of all organs and systems, and the body of a woman is not yet ready for changes. Failures in the functioning of the nervous system are manifested as signs of early toxicosis

Some considers that the main mechanism of toxicosis is connected with the central nervous system (CNS) of women. According to these theories at the moment of fertilization the functioning of CNS changes, as the result CNS causes nausea, vomiting, increased salivation, changes in sapor (taste) and olfaction.

Hormonal theory. Hormonal theory justifies the manifestation of toxicosis in the early stages of the development of hormones of pregnancy.

All these theories are well described in Ogorodnik's and Davydova's work [9]. Taking into account the known data on the role of gastrointestinal motility disorders in the genesis of nausea and vomiting, we hypothesized that the inhibition of the motor-evacuation function of the stomach and colon that may be one of the important causes of early toxicosis. The aim of the work was to investigate the spontaneous and stimulated motility of stomach and colon in first week of pregnancy in rats that which corresponds to the first trimester of pregnancy in women.

MATHERIALS AND METHODS

Animals

The study was done on white nonlinear rats 4-5 month old in accordance with the recommendations of the Guide for the Care and Use of Laboratory Animals of the National Institutes of Health and the general ethical principles of animal experiments, approved by the First National Congress on Bioethics Ukraine (September 2001). The protocol was approved by the Committee on the Ethics of Animal Experiments of the Taras Shevchenko National University of Kyiv. Females were kept separately from males since 1.5 months age.

The rats were kept in collective cages in controlled conditions of temperature (22±3°C), light (12h light/dark cycle) and relative humidity (60±5 %). The animals were fed laboratory chow and tap water ad libitum.

Determination of estrous cycle phase and dated of pregnancy

For mating healthy females and males were selected. Only young females were observed, because with age estrous cycle phase become uneven and irregular. To make mating successful only females in proestrous phase were used [10]. Breeding rats were housed together (in ratios of 1:1) overnight until the start of light cycle the next day. In the morning after mating female was removed from cage and observation of spermatozoids in vaginal smears were conducted to prove mating. Female has been engaged in the subsequent experiment in case of spermatozoids presence. The day on which spermatozoids were found in a vaginal smear was called the first day of gestation [10-12].

Method of gastrointestinal motility study in rats

On 3rd, 4th, 5th and 7th day of gestation the motor activity of the stomach and colon were recorded by the balloon graphic method [13]. The animals were taken in the test immediately after 12 hours after the last meal. Rats were narcotized with urethane (1.1 g / kg, i.p.). Into the stomach and colon of rats a latex balloon was injected which were filled with water. The volume of gastric balloon was 1.2 ml and the volume of colon balloon was 0.8 ml. Then the balloons were attached to the automated complex "Jaguar" manufactured by PAO NPP “Saturn” (Kyiv, Ukraine). After 20 minutes of the equilibrium period, spontaneous motor activity of the stomach and colon were recorded within two hours, after which a standard motility stimulator of the non-selective agonist of the acetylcholine receptors carbachol (manufactured by Sigma-Aldrich Co. (St. Louis, MO, USA)) in a dose of 10 μg/kg was injected i.p. Further, the recording was continued for another 2 hours, based on the duration of action of carbachol, which is 1.5-2 hours. After the experiments conducted, the calculation and analysis of data was performed.

The motor activity of the stomach and colon was characterized by a total motor index (MI) for 1 minute. The latter is calculated by the formula:

$$MI=\sum(hd)/T,$$

where h is the amplitude of the reductions in mmHg, d - the length of each wave in mm., T is the time of the plot of the calculated curve.

Also expected average amplitude of spontaneous and stimulated abdominal cramps in centimeters of water column (cm wc).

After the experiment, the rats were killed by the introduction of a triple dose of anesthesia.

Statistical analysis

Statistical data was processed in the "Statistica 8.0" program package. To test the samples, the W Shapiro–Wilk test was used for the distribution of the investigated indicator. Since the sample checks showed a normal distribution of the studied parameters, the reliability of the data difference in the samples was estimated using Student's t-tests for independent samples. At the same time, the average value (M) and the standard error of the average (m) were calculated.

RESULTS AND DISCUSSION

Figure 1 shows typical original records of gastric motor activity in rats of control group and in rats on different days of pregnancy. We can see that motor activity of stomach in rats on different days of pregnancy was lower in comparison with motor activity of stomach in rats of control group. Amplitude of spontaneous contractions in stomach on the 3rd, 4th, 5th and 7th day of pregnancy decreased by 32,1% ($p<0,01$), 37,8% ($p<0,01$), 60,8% ($p<0,01$) and 71,7% ($p<0,001$) consequently in comparison with the control (table 1).

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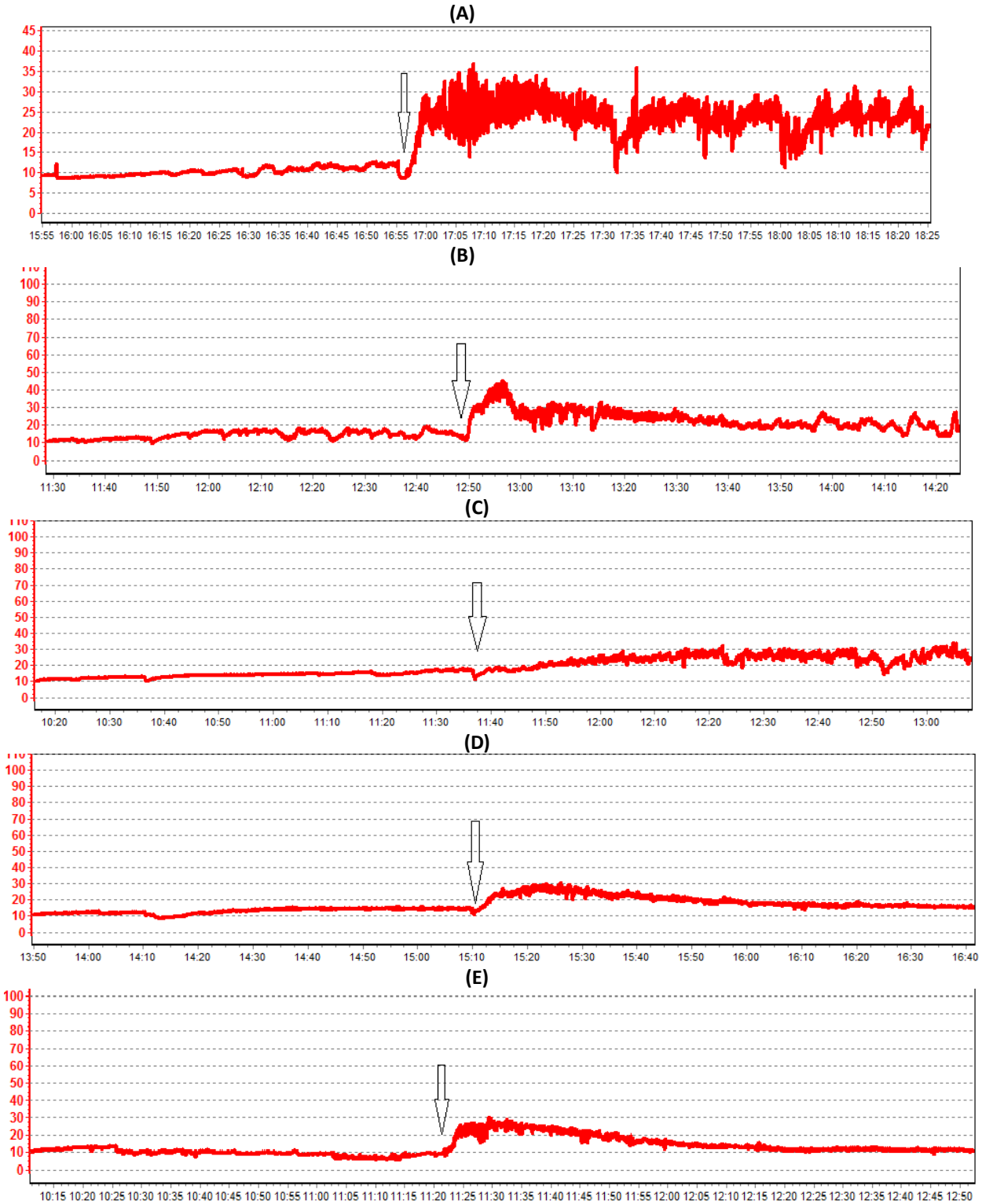

Figure 1. Typical original records of gastric motor activity in control and pregnancy rats: A – control rats; B - rats on the 3rd day of pregnancy, C - rats on the 4rd day of pregnancy ,D - rats on the 5rd day of pregnancy and E - rats on the 7rd day of pregnancy; ↓ - moment of carbachol injection.

Amplitude of gastric contractions stimulated by carbachol on the 3rd, 4th, 5th and 7th day of pregnancy was decreased by 25,4% ($p<0,01$), 28,8% ($p<0,01$), 44,1% ($p<0,001$) and 45,8% ($p<0,001$) consequently in relation to control (table 1).

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Table 1. Amplitude of gastric contractions in non pregnant and pregnant rats (M±m, n=10)

	Amplitude of gastric contractions (centimeters of water column)				
	Control (non pregnant rats)	Pregnant rats			
		3rd day of pregnancy	4th day of pregnancy	5th day of pregnancy	7th day of pregnancy
Spontaneous contractions of stomach	2,09±0,4	1,42±0,3**	1,3±0,2**	0,82±0,1**	0,80±0,1***
Contractions of stomach stimulated by carbachol	5,9±0,6	4,4±0,5**	4,2±0,5**	3,3±0,4***	3,2±0,4***

** - p<0,01, *** - p<0,001 compared with control.

On the rd, 4th, 5th and 7th day of pregnancy index of spontaneous motor activity of stomach diminished by 24,7% (p<0,01), 26,4% (p<0,01), 30,4% (p<0,01) and 29,3% (p<0,01) consequently (table 2).

Table 2. Index of gastric motility in in non pregnant and pregnant rats (M±m, n=10)

	Index of gastric motility				
	Control (non pregnant rats)	Pregnant rats			
		3rd day of pregnancy	4th day of pregnancy	5th day of pregnancy	7th day of pregnancy
Spontaneous gastric motility	146,9±8,2	110,4±3,7**	108,1±4,7**	102,2±3,3**	103,8±3,4**
Gastric motility stimulated by carbachol	214,1±7,1	150,4±6,4**	130,2±3,4**	128,5±2,1***	131,3±3,3***

** - p<0,01, *** - p<0,001 compared with control.

In pregnant rats carbachol stimulated gastric motility but reaction on carbachol was much weaker than in control (non-pregnant) rats. On the 3rd, 4th, 5th and 7th day of pregnancy index of stimulated by carbachol motor activity of stomach diminished by 29,8% (p<0,01), 39,4% (p<0,01), 40,0% (p<0,001) and 38,7% (p<0,001) consequently (table 2).

Figure 2 shows typical original records of colon motor activity in rats of control group and in rats on different days of pregnancy. Amplitude of colon spontaneous contractions on the 3rd, 4th, 5th and 7th day of pregnancy was lowered by 27,9% (p<0,05), 39,5% (p<0,01), 53,5% (p<0,01) and 51,2% (p<0,001) consequently in comparison with the control (table 3).

Table 3. Amplitude of colon contractions in non pregnant and pregnant rats (M±m, n=10)

	Amplitude of colon contractions (centimeters of water column)				
	Control (non pregnant rats)	Pregnant rats			
		3rd day of pregnancy	4th day of pregnancy	5th day of pregnancy	7th day of pregnancy
Spontaneous contractions of stomach	4,3±0,14	3,1±0,1*	2,6±0,13**	2,0±0,13**	2,1±0,12***
Contractions of stomach stimulated by carbachol	8,4±0,4	6,2±0,16**	6,6±0,2**	5,5±0,17***	5,1±0,2***

* - p<0,05, ** - p<0,01, *** - p<0,001 compared with control.

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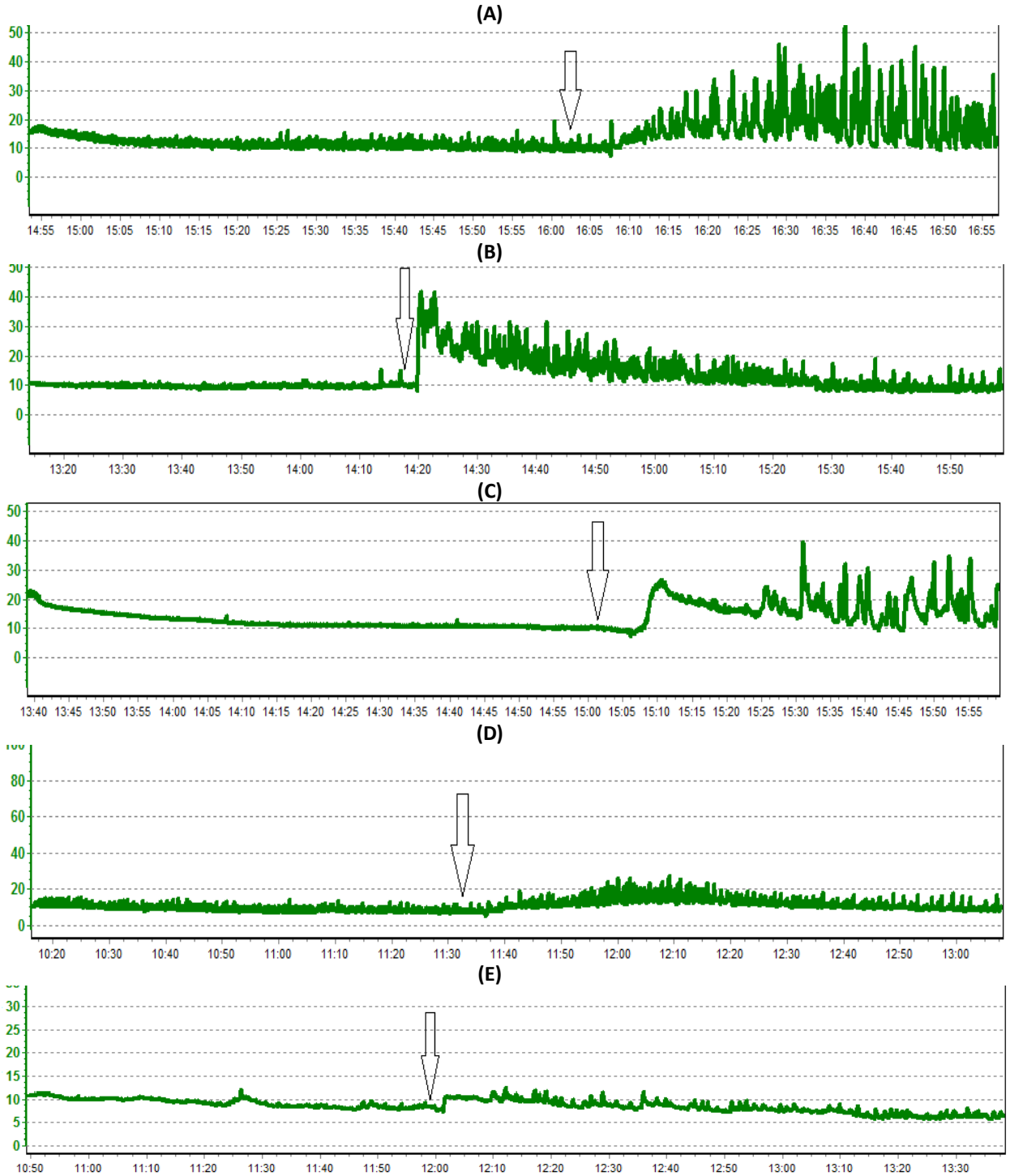

Figure 2. Typical original records of colon motor activity in control and pregnancy rats: A – control rats; B - rats on the 3rd day of pregnancy, C - rats on the 4rd day of pregnancy ,D - rats on the 5rd day of pregnancy and E - rats on the 7rd day of pregnancy; - moment of carbachol injection.

Amplitude of colon contractions stimulated by carbachol diminished on the 3rd, 4th, 5th and 7th day of pregnancy was lowered by 27,9% ($p<0,05$), 39,5% ($p<0,01$), 53,5% ($p<0,01$) and 51,2% ($p<0,001$) consequently in comparison with the control (table 3).

Index of spontaneous motor activity of colon on the 3rd day of pregnancy was not statistically significantly different from control (table 4). But on the 4th, 5th and 7th day of pregnancy index of spontaneous

motor activity of colon reduced by 13,1% (p<0,05), 20,3% (p<0,05) and 22,1% (p<0,05) consequently in comparison with the control (table 4).

In rats on the 3rd, 4th, 5th and 7th day of pregnancy index of colon motility stimulated by carbachol was decreased by 26,9% (p<0,01), 28,2% (p<0,01), 25,1% (p<0,01) and 28,2% (p<0,01) consequently in comparison with the non pregnant rats (table 4).

Table 4. Index of colon motility in non pregnant and pregnant rats (M±m, n=10)

	Index of colon motility				
	Control (non pregnant rats)	Pregnant rats			
		3rd day of pregnancy	4th day of pregnancy	5th day of pregnancy	7th day of pregnancy
Spontaneous colon motility	113,3±2,1	108,0±3,3	98,5±2,6*	90,3±1,5*	88,3±1,9*
Colon motility stimulated by carbachol	150,8±4,4	110,2±4,1**	108,3±3,1**	113,0±3,3**	108,2±2,1**

* - p<0,05, ** - p<0,01 compared with control.

CONCLUSIONS

In the results of our investigations it was established that spontaneous and stimulated by carbachol motility of stomach and colon decreased that leads to violation of the evacuation of the stomach and constipation. As a result, endogenous intoxication occurs, which causes nausea and vomiting.

In the first months after conception, an active hormonal change takes place in the body after the conception in order to prepare for the child's nursing, in particular, the development of progesterone is substantially increased. It reduces the smooth muscle tone of the pelvic organs so that the fertilized egg is safely secured in the uterus. Unfortunately, it also has a peculiar side effect - the contractile activity of the digestive tract slows down, intestinal peristalsis worsens, constipation can occur [14].

During pregnancy also concentration of oestrogen is rising. Oestrogen inhibited colonic contractility that leads to development of constipation [15,16]. Indeed, literature data indicate the development of constipation in pregnant women [17,18].

Therefore, we assume that one of the causes of early toxicosis may be the suppression of gastrointestinal motility because of influence of high concentration of hormones such as the estrogen, progesterone, human chorionic gonadotropin on the smooth muscles.

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