EFFICACY AND SAFETY PROFILE OF CHOPHYTOL AT COURSE TREATMENT THE SYNDROME OF INTESTINAL DYSPEPSIA IN PREGNANT WOMEN

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The phenomena of intestinal dyspepsia, constipation in particular - it is quite frequent during pregnancy. According to statistics, about 58% of pregnant women and 35% women after childbirth suffering from this pathology. This is facilitated during pregnancy increased the concentration of progesterone. This hormone not only protects the pregnancy, but also significantly reduces the tone of smooth muscles of the intestine. In addition during pregnancy especially during the second and third trimester uterine size significantly increased. This leads to compression of the bowel and violation of his motor and evacuation activities. Additional factors contributing to the occurrence of constipation include nausea, vomiting and lack of appetite in early gestosis, physical inactivity, bed rest under the threat of miscarriage, the use of iron preparations with prophylactic and therapeutic purposes, and some others [7, 9].

Constipation is one of the manifestations of intestinal dyspepsia syndrome and is characterized by the frequency of stool less than 3 times a week, a delay bowel movement for more than 48 hours, stool weight of less than 35 grams per day, feeling of incomplete bowel evacuation, dense feces and straining during defecation. In general, said syndrome includes dysbiosis, constipation, flatulence, which adversely affect the overall health of the pregnant, the course of pregnancy and fetal status [4, 8, 10].

The main method of prevention and correction of intestinal dyspepsia in pregnancy is a diet because taking laxatives undesirable due to possible miscarriage. In intestines should come as many as possible fiber. Some laxative effect is given milk products: kefir, yogurt and kvass. Also useful are vegetable fats: they form the splitting of fatty acids, stimulating peristalsis. At the same time, with the expressed symptoms of intestinal dyspepsia efficacy of this approach is quite low [4, 7].

Recently as a drug for combination therapy of intestinal dyspepsia proposed hepatoprotective drug Chophytol. Its reception should be possible from the 10-12 weeks of pregnancy. Chophytol has a positive effect on the fat metabolism and on blood chemistry, protein and nitrogen metabolism, provides antioxidant protection of cell membranes from the damaging of exogenous and endogenous factors, normalizing antioxidant defense cells, activated respiratory enzymes and normalizing the intracellular synthesis of lipids, which is very promising for use in obstetric practice [1, 10]. It confirmed its high efficacy for the prevention of fetoplacental insufficiency in groups of women with a high risk of its development [5, 6].

The aim of our study was to investigate the efficacy and safety of Chophytol in the treatment of intestinal dyspepsia during pregnancy. Particular attention was paid to the nature and severity of adverse reactions to preparation reception.

Materials and methods. A clinical investigation was carried out as an open clinical trial in accordance with approved protocol on the base of University Hospital of Kharkiv National Medical University. The subject of the study were clinical and

pharmaceutical criteria of safety and efficacy of Chophytol. Apply a preparation "Chophytol", produced by the pharmaceutical company «Lab. Rosa-Phytopharma» in the form of 200 mg tablets containing the dry aqueous extract of artichoke leaves (Cynara scolymus) [2, 5].

During the period from January 2014 by October 2016 under the supervision and treatment were 54 pregnant women aged between 18 and 42 years, in various stages of pregnancy (from 14 to 35 weeks) suffering from a syndrome of intestinal dyspepsia. Inclusion criteria were the presence of concomitant extragenital pathology in the form of chronic constipation. The study included screening period (survey) and the period of receiving Chophytol. Evaluation of the clinical picture of the patient was carried out on the basis of complaints, data of clinical examination and laboratory investigations. All patients received oral Chophytol 1 tablet of 200 mg 3 times per day before meals. The total duration of treatment was 25-30 days. After completing the course of treatment carried out re-examination and questioning of the patient. All findings were introduced in individual card of pregnant and individual registration form. The study was conducted taking into account of patient's compliance. In the course of treatment carried out the control of appointments performance of patients. Indices and criteria of effectiveness of the treatment was to evaluate the doctor-researcher based on subjective feelings of patients taking into account the objective of the survey data.

During the survey the patient were taken into account the severity of the following symptoms:

- abdominal pain during straining and defecation (in scores);
- delayed stool for 2-3 days or more (in scores);
- active delay of stool associated with the fear of defecation (in scores);
- abdominal overflow, flatulence and bloating (in scores);

Severity of studied symptoms of intestinal dyspepsia took into account in accordance with the following scale:

0 - absent;
1 - slight;
2 - moderate;
3 - expressed

At the end of taking Chophytol, patients rated their condition according to the following subjective scale:

- significant reduction in the severity of subjective complaints;
- reduction of subjective complaints;
- no change;
- an increase in the severity of subjective complaints.

The data of clinical examination is mandatory supplemented by laboratory studies conducted at all stages of the study. Chophytol tolerability was assessed on the basis of subjective symptoms and sensations reported by patients and objective data obtained by researchers in the process of treatment. Take into account dynamics of laboratory parameters, as well as the incidence and nature of adverse reactions [3, 4].

Results and discussion. Clinical and pharmaceutical performance criteria and the results of treatment of intestinal dyspepsia syndrome during pregnancy assessed by the dynamics of constipation symptoms observed with different terms of pregnancy under the influence of the reception "Chophytol" are in the table. The results were compared with the international standards of functional defecation disorders (Rome II). At the same time we take into account and related intestinal dyspepsia symptoms associated with constipation, and patient compliance in relation to the successful treatment of symptoms, as well as readiness for change their traditional way of life [7, 11].

Table

Dynamics of constipation symptoms in pregnant women under the influence of Chophytol reception

Symptoms of disease and degree of its severity		Visits (observation point)			
		Start reception visit 1	10th day visit 2	27-30th days visit 3	
		n=54	*n=54*	*n=54*	*%*
Abdominal pain during straining and defecation	Absent	1	19	42	68,2
	Slight	14	16	6	17,2
	Moderate	19	12	4	10,9
	Expressed	20	7	2	3,7
Delayed stool for 2-3 days or more	Absent	1	34	47	85,3
	Slight	11	8	4	8,5
	Moderate	20	7	2	4,1
	Expressed	22	5	1	2,1
Active delay of stool associated with the fear of defecation	Absent	2	31	44	80,7
	Slight	14	12	6	13,1
	Moderate	18	7	2	3,1
	Expressed	20	4	2	3,1
Abdominal overflow, flatulence and bloating	Absent	2	30	46	82,7
	Slight	11	12	5	12,3
	Moderate	16	8	2	3,1
	Expressed	25	4	1	1,9

Note: n - number of patients in the observation group

As follows from the table, all pregnant before you start taking the drug Chophytol bothered delayed stool for 2-3 days or more as a manifestation of the syndrome of intestinal dyspepsia. Almost all patients (51 women, or 95.3%) is also bothered by other manifestations of dyspepsia - abdominal overflow, flatulence and bloating. Active stool retention associated with the fear of an act of defecation marked at 52 pregnant women (96.8%).

It should be noted that the manifestations of constipation symptoms in many of studied were expressed significantly. So, pain in the abdomen during straining and at defecation was observed in 21 cases (39.1%); chronic chair delay of 2-3 days or more

were 19 (32.8%); active chair delay associated with the fear of an act of defecation were observed 20 patients (34.3%) and abdominal overflow, flatulence and bloating noted in 22 cases (41.2%).

The study demonstrated that the use of Chophytol as a single therapeutic agent resulting in reduction of clinical manifestations of chronic constipation in the vast number of subjects. So, on the tenth day of receiving more than half of the decrease in the number of patients with severe symptoms and has dramatically increased the number of cases the lack of basic signs of the disease. Many patients have also noted an overall improvement in bowel function, improvement of appetite and mood. By the end of treatment (27-30th day) clinical signs of chronic constipation were absent or only slightly manifested in the vast majority of patients - from 84.4 to 93.8%, and significant symptoms remained no more than at 3.7% of cases. Moreover, among the observed patients there were no notable adverse effects of the preparation used. Consequently, the rate of effectiveness of herbal preparation Chophytol applied in the form of tablets for oral use in pregnant women with chronic constipation symptoms ranged from 84.4 to 93.8%.

Based on the analysis of the dynamics of clinical manifestations of chronic constipation under the influence of Chophytol it was concluded that in almost all cases the safety and tolerability of the observations should be evaluated in accordance with the scale, as "good". Tolerability of Chophytol with the level of "good" is installed in 52 of the 54 patients included in the clinical trial, which is 95.7%.

According to the literature, the efficiency of the group of hepatoprotective drugs in general is not in doubt. Previously, high efficiency Chophytol for the prevention of fetoplacental insufficiency in pregnant group of high perinatal risk was confirmed. Compared with the traditional multi-component schemes of preventive measures the treatment of Chophytol appear more favorable outlook for the carrying of a pregnancy and its outcome. Chophytol provides etiopathogenic mechanism of clinical exposure, allowing the treatment of chronic constipation manifestations of the syndrome of intestinal dyspepsia. Thus, Chophytol occupies a worthy place in the arsenal of agents for the treatment of obstetric pathologies. It has a solid reputation and many years of application history, so stable is available for patients in the pharmaceutical market in Ukraine [1, 5, 6, 10].

The clinical study allowed us to confirm the previously established safety and good tolerability of the preparation Chophytol and draw some conclusions.

Conclusions

Based on results of this clinical study found high positive criteria of efficiency (up to 93.8%) Chophytol action in the treatment of chronic constipation symptoms in pregnant women. Based on previous experience of application Chophytol in obstetric practice, it proved a good its efficacy and safety when used in pregnant women with chronic constipation. According to the criteria presented in this study, Chophytol can be recommended for wide use in the treatment of pregnant women with the given pathology.

The clinical effect fully manifested after 2-3 weeks from initiation of Chophytol therapy. Maximum medication bioavailability observed at the reception before the

meal. After a single dose, maximum concentration of Chophytol in plasma is achieved in 3-4 hours. With prolonged use, stable concentration of medication in the blood plasma is reached after 1-1.5 weeks. With the plasma proteins bound 91.2% of active substance [5].

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