INTRODUCTION

Nausea and vomiting are most frequent complaints of first pregnancy weeks. Emotional component, significant impact on wellbeing and quality of life has put these symptoms in the center of plenty of investigations. The majority of them deal with treatment methods and comparison of their effectiveness.

From 50 to 80% of all pregnant women have complaints on vomiting or nausea or both, but only in 2–3% cases the severity of vomiting is a reason of hospitalization and an indication to parenteral nutrition [12]. This is very important to notice, that this diagnosis should be a one of exclusion – absence of other diseases; vomiting is a proper clinical symptom, as gastrointestinal inflammation or enteral infection.

Race, age, number of pregnancy and labor role in nausea and vomiting genesis was discussed [4], some authors proposed an influence of maternal, social and psychological status [5] and even educational status [14]. One investigation has proposed the less frequency of nausea and vomiting in multiparous women as a result of smaller placental volume [6]. Human chorionic gonadotropin is considered to be a main pathogenic factor of nausea, as it stimulates estrogen production in ovarian and thus provokes symptoms. That’s why twin or molar pregnancy is in more risk of nausea and vomiting [6].

Thus, the real etiological factor of both nausea and vomiting are unknown, investigators have been concentrated for the search of association between this early pregnancy symptoms and more late pregnancy complications. Q. Zhou et al. (2019) reported about increased risk of low weight newborn by severe form of first-trimester vomiting. On the contrary, S. Hinkle et al. (2016) proved a strong association of vomiting and nausea with a reduced risk of clinical pregnancy loss. Discussing the absence of this association with losses on preclinical or preimplantation pregnancy, authors propose protective role of vomiting and nausea, but realized only after complete implantation. In 1986 F. Tierson et al. proposed an explanation, what is the reason of small newborn weight by first trimester nausea and vomiting. It may be caused by a more quick fetus maturation because of an increased protein intake. S. Poeran-Bahadoer et al. (2019) studied more longer the catamnesis of patients with vomiting of first trimester and their children till adulthood in population of Rotterdam. According to their results, vomiting, not depending on its severity, increases the risk of obesity and excess body mass of an offspring in adulthood. Any other cardiovascular risk factor increasing was not revealed, in the same time authors cannot propose any explanation of this trend, in spite of possible risk of fetal growth restriction at these patients [10]. A. Ayvcrevoe et al. (2013) have reported about decreased insulin sensitivity, revealed at offsprings’ of women with vomiting of first trimester. The number of cases in this report was less than 100, totally with control group, and authors dialed only with severe forms of disease, so the possibility of their application to all vomiting women is discussable.

The same difficult as an etiology question, the first trimester vomiting management problem is. I. Tsikiridis et al. (2019), reporting about evidence based recommendations for nausea and vomiting treatment, marked only two ones – frequent small meal and avoidance of iron supplementation [12]. Speaking about other popular remedies, they mentioned ginger, antihistamines, acustimulations, phenothiazines, dopamine, and serotonin 5-hydroxytryptamine type 3 receptor antagonists, those are often used, but do not have enough evidences of effectiveness. As an example of those methods, N. Michihata et al (2019) have demonstrated that use of one of Japanese herbal drug, leading not to decreasing frequency of vomiting, let to avoid staying in hospital for these patients.

Speaking about possible consequences of first trimester vomiting we performed a prospective investigation, devoted to electrolytic balance in first and second trimester. The goal was to reveal if vomiting in first 12 weeks of pregnancy leads to significant or non-significant changes in electrolytic balance and are there any changes in more late terms.

Objective of the study – to study changes in electrolyte balance and hematocrit concentration by vomiting of first trimester and by uncomplicated pregnancy.

MATERIALS AND METHODS

109 women in first pregnancy trimester were investigated. All of them were nulliparous and had single-fetus pregnancy. They were divided in 2 groups, depending on having vomiting. 58 patients of group I had vomiting from 1 till 10 times a day; we excluded women with emesis gravidarum, as well as patients with other objective reasons of vomiting – severe gastrointestinal diseases, intesti-
RESULTS AND DISCUSSION

By pregnancy progress the female body undergoes significant overload due to the growing need of fetus-placental complex. One of the ways to achieve it is to make circulating blood volume according to persistently increasing volume of vascular bed. The mechanisms of this are still discovering, but scientists have no doubt, that the main one is an asymmetric change of circulation volume – while totally it is increased on 30%, the volume of plasma becomes bigger on 40% and volume of blood cells – only on 20%. The first result is physiological for pregnancy anemia. But the plasma itself also is not a homogenic medium; it contains a lot of non-polar molecules, proteins first of all. So, the next result of hemodilution is a relative hypoproteinemia that is not corrected by significant increasing of fibrinogen concentration. So, changes in electrolyte balance are avoidless. But possible borders of these changes are very narrow, because electrolytic gradient on both sides of membrane is a base of cell wellbeing and function. An additional factor, that can influence this balance, is vomiting, being a reason of sodium-ion and chloride-ion loss.

Our previous researches have demonstrated, that women with severe forms of preeclampsia by detailed questioning in majority of cases didn’t remind nausea and vomiting in first trimester of current pregnancy [15]. On contrast, women with uncomplicated pregnancy beginning of study showed lower concentrations of sodium-ion concentration in first pregnancy trimester, in the beginning of study showed lower concentrations of sodium-ion – 145 mmol/l, in group of non-vomiting women – 145 mmol/l. That’s why the group of patients with vomiting in first trimester was collected with the aim to find correlation between possible electrolyte changes and pregnancy progress.

As our results demonstrate, that medium concentrations of studied ions didn’t differ between groups on the start of investigation (Table).

So, vomiting of first pregnancy trimester does not lead to dramatically changes of electrolyte balance, and according to good pregnancy results in most cases of vomiting women, cannot be considered as a serious complication. In any case, vomiting should lead to electrolytes losses, and sodium-ion is one of the first to lose. But the stability of electrolytes balance is so important for organism wellbeing, and regulating mechanisms, including aldosterone with its angioten

<table>
<thead>
<tr>
<th>Electrolyte Concentration (mmol/l)</th>
<th>Group I (n = 58)</th>
<th>Group II (n = 51)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na⁺)</td>
<td>138.5 ± 2.80</td>
<td>141.1 ± 4.57</td>
</tr>
<tr>
<td>Potassium (K⁺)</td>
<td>4.0 ± 0.22</td>
<td>4.1 ± 0.19</td>
</tr>
<tr>
<td>Calcium (Ca²⁺)</td>
<td>2.3 ± 0.12</td>
<td>2.1 ± 0.29</td>
</tr>
<tr>
<td>Bicarbonate (HCO₃⁻)</td>
<td>24.5 ± 2.25</td>
<td>25.9 ± 2.71</td>
</tr>
</tbody>
</table>

Table: Ion concentrations in plasma of surveyed women.

Figure 1. Distribution of patients by sodium-ion concentration.
of physiological for pregnancy hemodilution, and this tendency is proper majority of women with vomiting of first trimester, albeit they are losing fluid. In the same time, part of women, despite absence of any complains during first trimester, are in a dangerous tendency of insufficient hemodilution.

Researchers are minded to consider hemodilution by pregnancy first of all from the point of view hemoglobin decreasing. Nevertheless, hemodilution is rather a reflection of normal regulation of electrolyte–protein balance by pregnancy. Initial hypoproteinemia, that is considered to be one of possible pathogenic mechanisms of pre-eclampsia, and perhaps – other obstetrics complications, results an oncotic pressure decreasing. In this condition the increasing of sodium-ion concentration that does not exceed physiological borders, is well explained. It can be proposed, that vomiting in first pregnancy trimester is a possible way to confirm normal sodium-ion concentration in the beginning of gestation. From this point of view a question of any kinds of infusion, used for nausea and vomiting treatment, becomes very discussable. The regulation of osmotic homeostasis may be very fragile, so excess volume of different electrolytes formula may by not only useless, but sometimes harmful for future pregnancy currency.

Hyponatremia is divided into absolute and relative. Absolute one is a result of profuse diarrhea or vomiting, excessive sweating, renal and adrenal insufficiency, hemorrhage and diabetic acidosis. Relative hyponatremia is a consequence of water delay in circulation, as it is necessary by physiological pregnancy [24].

Difference in concentration of other electrolytes between groups is not significant, as well as distribution patients by this concentration.

In the beginning of second pregnancy trimester the moderate concentrations of all studied ions also didn’t have differences between groups. But discussing the direction of changes with pregnancy progress, they are opposite in two studied groups. Patients, that had vomiting of first trimester, till 20 weeks had registered decreasing of sodium-ion concentration. On the contrary, women, having any complain in first trimester, till second trimester demonstrates increasing of sodium-ion concentration. It means, first group of patients have more favorable changes in blood circulation, meaning more expressed hemodilution. The increasing concentration of sodium-ion in second group testifies the inadequate hemodilution in these patients.

To prove the idea of incomplete hemodilution at some patients without vomiting and nausea, we studied the moderate hematocrit value and distribution of patients for this criteria in the end of first trimester. For evaluation of hemodilution hematocrit is more favorable, than hemoglobin, because of possible influence of iron deficiency. The moderate hematocrit volume in first trimester was similar in both groups, hesitating in physiological measures – 38.9 ± 3.52% for group I and 36.7 ± 4.53% – for group II. The distribution of patients by this sign demonstrates difference, similar to the sodium-ion concentration (Fig. 2).

In spite of similar moderate value in groups, 35.3% patients of group II demonstrate hematocrit level 40% and more, in group I – only 18.9%. This deviation also can be considered as an argument of insufficient hemodilution at part of women without nausea and vomiting in first trimester. The hematocrit volume in first trimester correlates negatively with sodium-ion concentration (correlation index – 0.7), that can prove the role of additional osmotic regulation by the vomiting.

In the middle of second trimester the trend of hematocrit level is also similar to sodium concentration – at patients, having vomiting in first trimester it has decreased from 38.9 ± 3.52% to 34.4 ± 1.98%, that argues hemodilution progressing. The group II (patients, having any nausea and vomiting in first 12 weeks), contrary demonstrate increasing of this parameter – from 36.7 ± 4.53% to 37.9 ± 2.79%. Some of these patients, having comfortable and uncomplicated passing of first trimester, really have inadequate adaptation of blood circulation, including lack of circulating volume. The decreasing of this parameter in 14–17 gestational weeks is proved as prognostic factor of early pre-eclampsia onset [13]. A. Stangret et al. (2017) tried to explain it by a significant dysfunction of renin-angiotensin-aldosterone system, occurring as a predictor of fetal growth restriction.

According to modern point of view, reduced blood flow in placenta leads to a specific kind of injury – hypoxia reoxygenation process caused by free radicals. They damage placental tissue, provoking excess releasing of placental vasoconstrictor factors to systemic maternal circulation. The activation of proinflammatory cytokines synthesis makes the pathological changes in endothelium deeper [7].

**CONCLUSION**

Vomiting of first pregnancy trimester does not lead to significant changes electrolyte balance. These patients in progress of pregnancy demonstrate adequate hemodilution, that mean decreasing of hematocrit value and sodium-ion concentration. At the same time, at some patients without vomiting and nausea the trend to incomplete hemodilution is revealed. This trend may result progressing of endothelial dysfunction, what will lead to different pregnancy complications.
ВОТЙНИНУ ПЕРШОГО ТРИМЕСТРА БЕРЕМЕННОСТІ: ЯК ОЦЕНИВАТЬ?

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Історичний розвиток

Цель исследования: изучить изменения электролитного баланса и гематокрита при рвоте первого триместра и при неосложненном течении беременности.

Материалы и методы: Обследовано 109 женщин в первом триместре беременности, разделенные на 2 группы. Группу I составили 58 пациенток с жалобами на рвоту от 1 до 10 раз в день, группа II — 51 женщина без жалоб на рвоту и блювоту. В обеих группах проводили исследование на наличие гиперемии ротовой полости, гемодилюцию, что предполагает снижение концентрации натрия и показателя гематокрита. В то же время у части пациенток с благополучным и неосложненным течением первого триместра беременности выявлена динамика прогрессирования беременности у женщин I группы отмечено снижение концентрации натрия, а у беременных II группы — наоборот, тенденция к повышению этого показателя. Однако при распределении участниц исследования по показателям установлено, что большая часть женщин II группы имела высокое содержание натрия в сыворотке крови и высокий уровень гематокрита. Кроме того, в динамике прогрессирования ретроспективный анализ

Выводы: Результаты исследования указывают на то, что при рвоте первого триместра беременности у женщин нарушается гемодилюция, что приводит к снижению концентрации натрия и повышению гематокрита. В то же время у части пациенток с благополучным и неосложненным течением первого триместра беременности выявлены тенденции к увеличению этих показателей. Эти данные могут быть использованы при планировании перинатальной мониторинга.

Ключевые слова: рвота, беременность, гемодилюция, гематокрит.