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INDICATORS OF THE ACTIVITY OF DIGESTIVE ENZYMES AND TRANSAMINASES IN SALIVA AND COPROFILTRATE IN WOMEN DURING PREGNANCY

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Abstract.*Introduction.* The characteristics of enzymes and transaminases in saliva and coprofiltrate in the "Mother–placenta–fetus" system in women were studied by trimester of pregnancy and in the postpartum period. ***The purpose of the work*** — to study the enzyme profile of biological fluids during pregnancy, to establish a relationship between the content of enzymes in the blood, their excretion in the composition of excretes and recretes with the activity of transaminases in the corresponding substrates. ***Materials and methods.*** The material for the study was taken from non-pregnant and pregnant women. The dynamics of changes in the activity of hydrolases in biological fluids was studied. ***Results.*** The participation of secretory and excretory pathways of enzyme excretion from the blood and body during pregnancy has been shown, the participation of salivary glands in the recreation of hydrolases in enzyme homeostasis has been isolated. ***Conclusions.*** The participation of transaminases and alkaline phosphatase in the homeostasis of hydrolases is not excluded, which is proved by the enzyme profile of biofluids during pregnancy.

Keywords: enzymes, incretion; recreation, excretion, pregnancy, salivadiagnostics

ПОКАЗАТЕЛИ АКТИВНОСТИ ПИЩЕВАРИТЕЛЬНЫХ ФЕРМЕНТОВ И ТРАНСАМИНАЗ В СЛЮНЕ И КОПРОФИЛЬТРАТЕ У ЖЕНЩИН В ПРОЦЕССЕ БЕРЕМЕННОСТИ

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Резюме. ***Введение.*** Изучались особенности ферментов и трансаминаз в слюне и копрофильтрате в системе «Мать–плацента–плод» у женщин по триместрам беременности и в послеродовый период. ***Цель исследования***—изучить ферментный профиль биологических жидкостей при беременности, установить связь между содержанием ферментов в крови, выделением их в составе экскретов и рекретов с активностью трансаминаз в соответствующих субстратах. ***Материалы и методы.*** Материал для исследования брался у небеременных и беременных женщин. Изучалась динамика изменения активности гидролаз в биологических жидкостях. ***Результаты.*** Показано участие рекреторного и экскреторного путей выделения ферментов из крови и организма при беременности, обособлено участие слюнных желез в рекреции гидролаз в ферментном гомеостазе. ***Выводы.*** В гомеостазировании гидролаз не исключено участие трансаминаз и щелочной фосфатазы, что доказывается ферментным профилем биожидкостей при беременности.

Ключевые слова: ферменты, инкреция, рекреция, экскреция, беременность, саливадиагностика

INTRODUCTION

Enzymes increted by digestive glands are irretrievably excreted from the body as part of urine, sweat, and feces, as well as excreted from the blood by recreation with their subsequent participation in the polyenzyme supply of secretions entering the gastrointestinal (GI) tract [2–4, 8, 9, 11]. A special role is assigned to the incretin enzymes, whose homeostasis is dynamically maintained under various functional states of the body, one of which is pregnancy [19]. Metabolic relations between the maternal organism and the growing fetus are established during pregnancy, which actively absorbs amino acids for protein synthesis. The fetus absorbs nutrients with amniotic fluid, which are hydrolyzed to monomers in the GI tract of the developing organism by enzymes that are recreted into the aquafetal environment (an autolytic digestion) [1, 15, 16].

The processes of excretion and recreation of such enzymes as pepsinogen, amylase, lipase, and alkaline phosphatase were previously studied by measuring their concentration/activity in urine and feces (coprofiltrate), as well as their excretion by salivary glands [5, 6, 10].

In parallel with hydrolases, transaminases were studied in the same biological fluids.

The excretion of hydrolases (pepsinogen, amylase, lipase) with excreta or as part of recretes is associated with transaminase and alkaline phosphatase activities that supply energy for translocation processes and pinocytosis (transcytosis) [14].

Cholestasis, destructive processes in hepatocytes or tension of biliary function specifically change the activity of transaminases and alkaline phosphatase [14].

De Ritis ratio (aspartate aminotransferase/alanine aminotransferase (AST/ALT)) reflects central or peripheral types of metabolic shifts, and alkaline phosphatase serves as an indicator of metabolic processes, in particular, changes in glucose levels [12].

Enzymological changes in blood reflect both diagnostic and especially metabolic sense, and in general characterize the biochemical status of the organism. Alkaline phosphatase is responsible for glucose output from cells and for the formation of phosphate pool. It is a marker of ontogenetic maturity and a regulator of transmembrane fluxes [14, 20].

AST and ALT are stable indicators. They are in a tight metabolic relationship, forming the de Ritis ratio, which integratively relates protein metabolism and characterizes total blood protein [12–14].

AIM

The aim of the study is to investigate the enzyme profile of biological fluids in pregnancy, to establish the relationship between the content of enzymes in the blood, their excreta and recreta with the activity of transaminases in the corresponding substrates.

MATERIALS AND METHODS

The material for the study was taken from non-pregnant (n=45) — control and pregnant (n=86) women — women in labor at full term.

The content and activity of pepsinogen, amylase, lipase, alkaline phosphatase and transaminases (AST, ALT) in fluids (blood, saliva, urine and coprofiltrate) in non-pregnant and pregnant women in trimesters of pregnancy and in the postpartum period were studied. The de Ritis ratio (AST/ALT) was calculated.

Total proteolytic activity was determined at low pH values of 1.5–2.0 by spectrophotometric (tyrosine) Kunitz–Northrop method in modification. Amylolytic activity was determined by amyloclastic method according to Karavey. Alkaline phosphatase activity was determined by standard constant time method using biotests by Lahema diagnosticum (Czech Republic). Lipolytic activity was

determined by unified method using olive oil as a substrate [13]. Transaminase activity (AST, ALT) was determined by colorimetric dinitrophenylhydrazine method according to Reitman and Frenkel [21].

Statistical processing of the results was performed using Microsoft Excel 2003 spreadsheets, SPSS 11.0 and Primer of biostatistics 4.03 programs.

RESULTS

Serum amylolytic activity was 13.5±0.8 units/mL in non-pregnant women. It remained almost the same in pregnant women in the I trimester, whereas in the II and especially in the III trimester it significantly increased — 2-fold (p <0.001) compared with the control group and the I trimester of pregnancy. In the postpartum period, the enzyme activity decreased, not reaching the indicators of non-pregnant women (Table 1).

Urinary amylase excretion in the control group was higher (64.1±1.6 units/mL) than in pregnant women during the I trimester of pregnancy. After the labor, there was a decrease in urinary amylase activity (1.5-fold; p <0.001).

Amylase synthesis by salivary glands tended to increase from control values and from the beginning to the end of pregnancy (Table 2).

Amylase activity decreased in the postpartum period, not reaching the values in non-pregnant women.

Table 1

Indicators of the activity of digestive enzymes and transaminases in blood and urine in the control group and pregnant women who gave birth on time, during trimesters of pregnancy and after childbirth)

Таблица 1

Показатели активности пищеварительных ферментов и трансаминаз в крови и моче у лиц контрольной группы и беременных женщин, родивших в срок, по триместрам беременности и после родов

Показатели / Indicators	Контрольная группа / Control group (n=45)	Беременные со срочными родами / Pregnant women with an urgent delivery (n=86)			
		I триместр / I trimester	II триместр / II trimester	III триместр III trimester	После родов / After giving birth
Кровь / Blood					
Амилаза (ед/мл) / Amylase) (units/ml)	13,5±0,8	11,3± 1,1	18,2±1,7**	25,0±1,3*	17,8±0,8**
Пепсиноген (тир. ед/мл) / Pepsinogen (tyr. units/ml)	58,1±1,1	44,2±3,3**	53,8±4,1**	48,2±2,6**	44,4±1,8**
Липаза (ед/мл) / Lipase (units/ml)	18,1±0,7	15,8±1,5**	21,4±1,6**	32,1±1,8*	21,3±1,7**
Щелочная фосфатаза (ед/мл) / Alkaline phosphatase (units/ml)	722,1±50,6	1015,6±102,2**	1200,1±114,2*	1287,8±102,3**	855,6±67,4
АСТ (ед/мл) / AST (units/ml)	11,1±1,2	12,1±1,2	14,3±1,2**	18,5±1,3*	14,0±1,2
АЛТ (ед/мл) / ALT) (units/ml)	8,8±0,7	13,7±1,1**	15,9±1,3**	20,5±1,7*	14,5±1,2**
АСТ/АЛТ / AST/ALT	1,26±0,04	0,88±0,01**	0,89±0,01**	0,90±0,01**	0,96±0,02**
Моча / Urine					
Амилаза (ед/мл) / Amylase (units/ml)	64,1±1,6	42,2±0,8*	50,6±1,4*	67,2±2,1	41,2±0,9*
Пепсиноген (тир. ед/мл) / Pepsinogen (tyr. units/ml)	4520,3±212,0	5200,8±186,1**	7800,1±204,1*	9650,1±211,5*	3698,5±146,7**
Липаза (ед/мл) / Lipase (units/ml)	20,6±0,8	24,4±0,4**	35,2±1,6*	41,2±1,9*	27,5±0,5
Щелочная фосфатаза (ед/мл) / Alkaline phosphatase (units/ml)	428,6±18,1	320,1±16,7**	480,7±20,6	410,9±19,1	240,4±16,2**
АСТ (ед/мл) / AST (units/ml)	5,7±0,7	4,3±0,3*	4,5±0,3*	5,1±0,4	4,7±0,3**
АЛТ (ед/мл) / (ALT) (units/ml)	5,1±0,6	4,8±0,3**	5,2±0,4	5,3±0,4	4,8±0,3**
АСТ/АЛТ / AST/ALT	1,1±0,03	0,89±0,01**	0,86±0,01**	0,96±0,02	0,98±0,02

Примечание: достоверность различий с показателями контрольной группы: * — p <0,001; ** — p <0,05.

Note: significance of differences with the indicators of the control group: * — p <0.001; ** — p <0.05.

Table 2

Indicators of the activity of digestive enzymes and transaminases in saliva and coprofiltrate in the control group and pregnant women who gave birth on time, during trimesters of pregnancy and after childbirth

Таблица 2

Показатели активности пищеварительных ферментов и трансаминаз в слюне и копрофильтрате у лиц контрольной группы и беременных женщин, родивших в срок, по триместрам беременности и после родов

Показатели / Indicators	Контрольная группа / Control group (n=45)	Беременные со срочными родами / Pregnant women with an urgent delivery (n=86)			
		I триместр / I trimester	II триместр / II trimester	III триместр / III trimester	После родов / After giving birth
Слюна / Saliva					
Амилаза (ед/мл) / Amylase (units/ml)	2385,3±264,7	2506,2±285,1	3515,1±440,8**	4781,6±423,8*	3109,0±294,2**
Пепсиноген (тир. ед/мл) / Pepsinogen (tyr. units/ml)	1520,9±247,6	1208,6±296,2**	1807,0±215,6	2612,9±218,1*	1463,3±221,6
Липаза (ед/мл) / Lipase (units/ml)	64,8±7,0	78,1±15,2**	90,3±8,4*	121,1±11,6*	70,9±5,4
Щелочная фосфатаза (ед/мл) / Alkaline phosphatase (units/ml)	215,6±22,3	722,0±38,3*	518,2±45,4*	361,8±30,2	475,3±31,6**
АСТ (ед/мл) / AST (units/ml)	8,1±1,1	7,2±0,6**	8,6±0,6	14,0±1,2*	12,5±1,0*
АЛТ (ед/мл) / (ALT) (units/ml)	6,4±0,8	6,6±0,5	10,4±0,8*	13,1±1,1*	11,2 ± 0,9*
АСТ/АЛТ / AST/ALT	1,26±0,04	1,09± 0,03	0,83±0,01**	1,07±0,03**	1,12±0,03
Копрофильтрат / Coprofiltrate					
Амилаза (ед/мл) / Amylase (units/ml)	19,5±0,8	21,6±1,5	30,2±2,2**	44,4±3,9*	18,3±0,9
Пепсиноген (тир. ед/мл) / Pepsinogen (tyr. units/ml)	442,2±20,5	410,2±16,1	270,8±20,4**	153,8±10,9*	315,3±16,8**
Липаза (ед/мл) / Lipase (units/ml)	320,8±12,6	420,3±16,0**	390,4±15,5	344,4±17,2	324,3±13,6
Щелочная фосфатаза (ед/мл) / Alkaline phosphatase (units/ml)	6220,4±248,0	5740,2±218,7	3483,1±113,2**	2236,6±158,6*	3229,2±122,1**
АСТ (ед/мл) / AST (units/ml)	4,2±0,3	9,6±0,8*	9,8±0,8*	10,7±0,8*	8,6±0,6**
АЛТ (ед/мл) / (ALT) (units/ml)	4,2±0,3	9,4±0,7*	9,4±0,6*	10,7±0,8*	8,5±0,6**
АСТ/АЛТ / AST/ALT	1,0±0,02	1,02±0,02	1,04±0,02	1,0±0,02	1,01±0,02

Примечание: достоверность различий с показателями контрольной группы: * — p <0,001; ** — p <0,05.

Note: significance of differences with the indicators of the control group: * — p <0.001; ** — p <0.05.

Coprofiltrate (fecal dilution 1:4) had a slightly higher activity than serum amylase, which acquired greater amylolytic activity during pregnancy, amounting at the end of pregnancy to values 2 times higher than the control. After delivery the values were comparable to those of non-pregnant women (Table 2).

As for the lipolytic activity of serum, except for the I trimester of pregnancy, there is an increase in its growth in the II and III trimesters, and after labor it decreases almost to the values of the control group. From trimester to trimester the excretion of lipase with urine and saliva increases, remaining above the control and after delivery. Lipolytic activity in coprofiltrate increases in the I trimester and remains elevated in the subsequent periods of pregnancy.

With regard to alkaline phosphatase, there is a high level of the enzyme in the blood in the II, III trimester of pregnancy and in the postpartum period. There is an increase in the excretion of the enzyme in the urine in the I and II trimesters, and subsequently its concentration decreases, remaining after delivery below the control values. Having increased in the I trimester, the alkaline phosphatase activity of saliva remains high compared to the data in non-pregnant women. Being high in the control group, the enzyme activity in coprofiltrate decreases during pregnancy almost 3 times (p <0.001), holding the energy reserve for the development of pregnancy.

There is an increase in both AST and ALT in serum during pregnancy compared to the control group. However, the de Ritis ratio (an indicator of adaptation of metabolic fluxes), equal to 1.26±0.04 in the control, becomes less

than 1 due to a greater increase in ALT, which is included in glucose-alanine shunt and catabolism. AST acts as an integrator of metabolism, an indicator of lipid peroxidation in the mechanism of cytolysis.

In urine, transaminase activity is not so great and decreases in pregnancy by AST in all trimesters and ALT in the I trimester. The de Ritis ratio changes accordingly to the indicator in the blood.

In the saliva of the control group, the content of AST and ALT is almost equal to that in blood, i.e. transaminase activity in these fluids is the highest. In pregnancy in the I trimester in saliva it decreases, in the II and III trimesters AST activity increases, and ALT remains decreased in the II and increases in the III trimester. Accordingly, the AST/ALT ratio, which is greater than one, changes.

While in coprofiltrate in non-pregnant women the activity of transaminases is minimal (4.2±0.3 units/mL), in pregnancy it increases more than 2-fold for AST ($p < 0.001$) and 1.8–1.9-fold for ALT ($p < 0.05$). The de Ritis ratio of coprofiltrate in pregnancy is higher than one.

DISCUSSION

The obtained results indicate an increase in amylolytic activity of blood serum, saliva and coprofiltrate during pregnancy. Moreover, the amylolytic activity of the biological fluids studied remained higher than that of the control group in the postpartum period. According to the secretion of amylase with saliva, it is possible to refer to the dynamics of pregnancy, which is currently used in salivadiagnostics [7, 9, 10, 13, 17–19, 21].

A different dynamics was observed in relation to amylase in urine: the control group had a higher index than pregnant women in the I trimester. The activity of amylase in urine decreased after the labor.

The proteolytic activity of serum and coprofiltrate decreased during pregnancy and remained at a low level in the postpartum period. Blood plasma pepsinogen reflects the metabolism of amino acids and their anabolism [5]. Its value in the control group corresponded to the average values of literature data in the control group [8].

The fate of plasma pepsinogen depends on urinary excretion of pepsinogen, which increases from trimester to trimester and sharply decreases after delivery. In addition, saliva in the II and II trimesters of pregnancy had greater proteolytic activity than the control group. Its indices decrease in the postpartum period, which corresponds to the dynamics of protein-producing function in the “mother–fetus” system [8, 10].

The data on alkaline phosphatase parameters had differently directed changes throughout pregnancy in the women studied. In serum and urine there was an increase in the level of alkaline phosphatase by the end of pregnancy compared to the values in non-pregnant women. At the same time, in saliva, the highest values of the enzyme were detected in the I trimester of pregnancy with a subsequent decrease in the postpartum period. The alkaline phosphatase activity of coprofiltrate throughout pregnancy remained lower than that of non-pregnant women.

Alkaline phosphatase occupies an intermediate position in the classification of enzymes between hydrolases and transaminases [13]. Its hydrolytic activity in blood has multiple sources (gut, pancreas, liver, bone tissue, fallopian tubes). This also dictates its polyfunctionality, namely its participation in transport, regulatory, and integrative systems [5]. Alkaline phosphatase reflects its inclusion in the process of pregnancy, especially in the I trimester, in connection with the transport of substances-metabolites during the formation of the “mother–fetus” system.

In all the biological fluids studied, we found the presence of transaminases in women in all trimesters of pregnancy with the greatest changes in serum and coprofiltrate. The data on the ratios of enzyme content in blood, saliva, urine and coprofiltrate in pregnancy are presented to illustrate this phenomenon.

CONCLUSION

1. In pregnancy, there is an increase in the activity of serum amylase, saliva and coprofiltrate with preservation of the level of indicators above the control group in the postpartum period.

2. A different dynamics is observed with respect to proteolytic activity of serum and coprofiltrate with the lowest values at the end of pregnancy.

3. Alkaline phosphatase activity has multidirectional changes from I to III trimester of pregnancy with the greatest changes in enzyme values in saliva.

4. Transaminase activity of blood serum, saliva, urine and coprofiltrate with predominant enzyme levels in serum and coprofiltrate was detected in pregnant women.

5. The obtained results indicate the presence of homeostasis pathways of hydrolases due to recretory and excretory excretion of them from blood by salivary glands, intestine and kidneys.

6. The data on the secretion of enzymes in saliva may be the basis for the use of salivadiagnostics as a noninvasive method of diagnosis.

ADDITIONAL INFORMATION

Author contribution. Thereby, all authors made a substantial contribution to the conception of the study,

acquisition, analysis, interpretation of data for the work, drafting and revising the article, final approval of the version to be published and agree to be accountable for all aspects of the study.

Competing interests. The authors declare that they have no competing interests.

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