Study Comparing The Incidence of DLIS in Pregnant Women with EPH-gestosis vs Normal Pregnancy

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Porovnanie incidencie DLIS u tehotných žien s EPH gestózou a u žien s normálnou tehotnosťou

Summary

Our studies demonstrate that of the highest value in the diagnosis of risk for EPH-gestosis can be the determinations of digoxin-like immunoreactive substances (DLIS) and uric acid in the serum of pregnant women. In the serum of pregnant women who were never given digitalis preparations, in 83 % of studied cases the presence of digoxin-like immunoreactive substances (DLIS) was found. Significantly higher DLIS concentrations occur in pregnant women with EPH-gestosis and correlate with uric acid concentrations while they are independent of the concentrations of total protein, albumins, urea, creatinine and bilirubin. DLIS exerts no effect on the shape and temporal conditions of ECG record. Determination of DLIS can be helpful in early diagnosis of oligosymptomatic gestosis *(Tab. 3, Fig. 2, Ref. 23)*.

Key words: risk for EPH-gestosis, digoxin-like immunoreactive substances (DLIS), uric acid, oligosymptomatic gestosis.

Súhrn

Štúdia ukázala, že pri diagnostike rizika EPH gestózy má najvyšší prínos určenie digoxínu-podobných imunoreaktívnych látok (DLIS) a kyseliny močovej v sére tehotných žien. V sére tehotných žien, ktoré nikdy neužívali digitálisové preparáty, sa až v 83 % zistila prítomnosť digoxínu-podobných imunoreaktívnych látok (DLIS). Signifikantne vyššia bola koncentrácia DLIS u tehotných žien s EPH-gestózou a korelovala s koncentráciou kyseliny močovej, ale bola nezávislá od koncentrácie celkových bielkovín, albumínov, urey, kreatinínu a bilirubínu. DLIS neovplyvňovali tvar EKG. Určenie DLIS môže byť nápomocné pri skorej diagnostike oligosymptomatickej gestózy *(tab. 3, obr. 2, lit. 23)*.

Kľúčové slová: riziko EPH gestózy, digoxínu-podobné imunoreaktívne látky (DLIS), kyselina močová, oligosymptomatické gestózy.

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One of the more frequent and dangerous pathological conditions occurring in pregnancy, usually in its last trimester or in early puerperium, requiring hospital treatment, is EPH-gestosis – a complex of signs characterized by arterial hypertension (H), oedema (E), and proteinuria (P).

In spite of continuous progress in the diagnosis and treatment, gestosis still opens the list of causes of intrauterine fetal wasting and neonatal death in the perinatal period (3, 14).

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The etiology of gestosis is still unknown. It is called "the disease of theory". In blood of pregnant woman biochemical markers appear, indicating the risk for gestosis (12, 17). Due to glomerular filtration disturbances, serum concentrations of uric acid, urea and creatinine increase (12, 13, 20).

Determination of uric acid in the serum of pregnant women with perinatal EPH-gestosis is great diagnostic value (20).

In the second half of 1980s reports appeared on the occurrence of digoxin-like immunoreactive substances (DLIS) in the serum and urine of women in the third trimester of pregnancy (6, 9, 15), in amniotic fluid (5, 10) and in the serum of newborns.

The reports on the occurrence of digoxin-like substances in pregnant women were not touching as yet the presence of DLIS in EPH-gestosis and the possible correlation between

gestosis intensity and DLIS concentration. Therefore, own studies have been undertaken on the assessment of determination of digoxin-like substance concentrations in the serum of pregnant women with EPH-gestosis.

Own studies

The aim of the study was the assessment of the incidence and comparison of the dynamics of concentration changes of digoxin-like immunoreactive substances (DLIS) in the serum of pregnant women in the third semester of normal pregnancy and pregnancy complicated with EPH-gestosis.

Material and Method

The studies included 114 pregnant women, aged 19-40 years (mean age 27.7 yrs), in 37th-42nd week pregnancy, treated as inpatients in the Institute of Gynaecology and Obstetrics, Central Clinical Hospital, Military Medical Academy in Warsaw in the years 1993-1994. The studied women were never given digitalis preparations.

The studied subjects were divided into two groups:

Table 1. Incidence of mild, moderately severe and severe gestosis in multiparas and primiparas.

Gestosis / Group	Mild		Moderately		Severe		Total	
	number	%	number	%	number	%	number	%
Multigravida	27	45.3	2	3.1	1	1.6	32	50
Primigravida	23	42.2	4	6.3	1	1.6	32	50
Total	50	87.5	6	9.4	2	3.1	64	100

1. 64 women (32 multiparas and 32 primiparas) with EPH-gestosis.

2. 50 women (27 multiparas and 23 primiparas) with uncomplicated pregnancy, without signs of gestosis (Tab. 1).

DLIS concentration was determined by fluorescent-polarization immunohistochemical method in the Medical Analysis Laboratory, CCH, MMA, using a Tdx analyzer with Abbott kits. The determination were performed three times: in the third trimester of pregnancy, on the first and fifth day of the puerperium. As the borderline value DLIS concentration of 0.1 ng/ml was accepted. Lower values were regarded as absence of digoxine-like substances in the serum.

On the days of DLIS determination, serum concentrations were studied of: total protein, albumins, bilirubin, glucose, urea, creatinine and uric acid.

Simultaneously, routine, 12-lead ECG was recorded by means of a unit produced by Chiller, with evaluation of duration of R-R intervals, PQ/R/, QT, Qtc, QRS complexes, and the shape of the waves, espetially of ST-T complex.

Arterial blood pressure was also checked, and during qualification of the pregnant women into the gestosis group, the presence of oedema was assessed in 1-3 point scale according to gestosis index, and urine was analyzed for protein presence.

Birth control of newborns was assessed in the 1st and 5th minutes after birth according to Apgar score. In the cases of score below 7 points, umbilical arterial gasometry in newborn was performed.

The results were analyzed statistically using Student t-test for independent variables. It was accepted that distributions of variables differed significantly when the established value of the significance level was lower than p_0=0.05.

Results

Among 64 pregnant women in group I (32 multiparas and 32 primiparas) in 58 cases (98.6 %) increased DLIS concentration was found in the serum. Only in six pregnant women (five multiparas and one primipara) which accounted for 9.4 % of the studied group, digoxin-like substances were not found in clinically significant concentration, that is 0.1 ng/ml (Fig. 1).

Among 50 pregnant women in group II (27 multiparas and 23 primiparas) in 37 cases (74 %) increased DLIS concentration was found; in 13 women (eight multiparas and five primiparas) which accounted for 26 % of the studied group, digoxin-like substances were not found (Fig. 2).

The mean DLIS concentrations were significantly higher (p=0.00002) in the group with EPH-gestosis (0.32 ng/ml) than in the group with normal pregnancy (0.14 ng/ml) and correlated with uric acid concentrations (p=0.00001) (Tab. 2).

No significance was found of the correlation between DLIS concentration and the concentrations of urea, creatinine, bilirubin, glucose, albumins and total protein (p=0.005) nor any influence was observed of DLIS concentration on the ECG (p=0.05) (Tab. 3).

Digoxin-like immunoreactive substances (DLIS), even in significant concentrations exerted no effect on birth weight of newborns (p=0.72) while they had unfavorable influence on their birth condition (p=0.03).

Discussion

The diagnosis of EPH-gestosis is based mainly on the presence of hypertension, proteinuria and oedema or one of them (1, 19) which enables to determine the degree of gestosis intensity. Gestosis or risk for gestosis are also suggested by concentration increase of uric acid, urea and creatinine in the serum of pregnant women (1, 2, 13, 20).

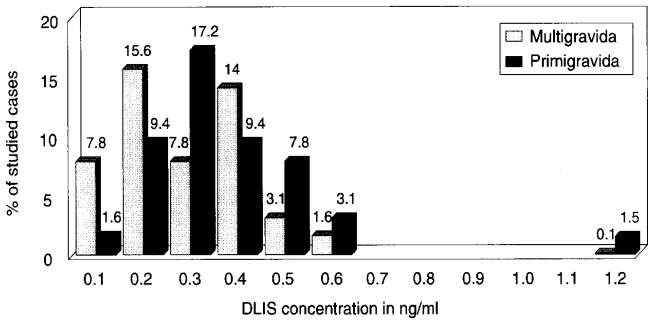

Figure 1. Serum DLIS concentration in group I of pregnant women (n=64).

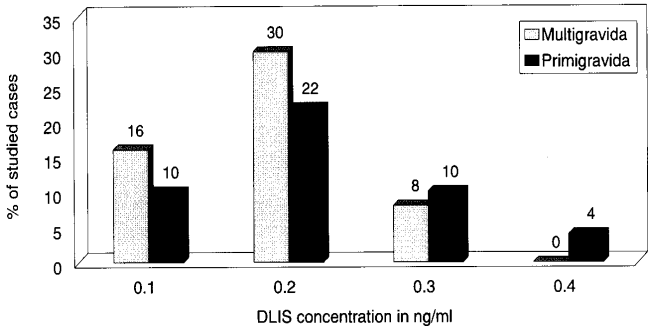

Figure 2. Serum DLIS concentration in group II (n=50).

Table 2. Mean concentration of uric acid in relation to serum DLIS concentration.

DLIS ng/ml	Number of pregnants	Mean concentration of U. A. mg %
<0.1	6	4.8
≥0.1÷1.0	58	5.97

Table 3. Comparison of the concentrations of the studied substances in the serum of pregnant women with DLIS concentrations in group I.

DLIS ng/ml	Number of pregnants	Mean concentrations of the studied substances					
		Bilirub.	Glicosae	Urea	Creatine	Protein	Albumin
<0,1	6	0.3	72.5	10.0	0.78	6.02	3.2
≥0.1÷1.0	58	0.46	75.2	9.57	0.74	6.04	3.39

In western literature reports appeared on the occurrence of digoxin-like immunoreactive substances (DLIS) in the serum of pregnant women (5, 6, 7, 9).

The incidence of DLIS occurrence in pregnant women with gestosis was not studied and DLIS concentrations in EPH-gestosis were not assessed.

Ebara et al. (5) found only DLIS presence in amniotic fluid, umbilical blood and serum of newborns (by RIA).

Graves et al. (9) demonstrated the presence of DLIS in the serum of women in the third trimester of pregnancy, during labour and 24 hours after delivery.

In own study, increased concentrations of digoxin-like substances were found in 90.6 % of pregnant women with EPH-gestosis (group I) and in 74 % of pregnant women with uncomplicated pregnancy (group II). Mean DLIS concentrations were significantly lower in group II (0.14 ng/ml) which confirmed the earlier accepted hypothesis that determination of digoxin-like substances can be of practical value in monitoring of pregnancy at risk for gestosis.

Dasgupta et al. (4) also found presence of DLIS in pregnant women with imminent eclampsia in preterm labour.

In the available literature no reports were found in which a comparative analysis was carried out of digoxin-like substance concentration in relation to other biochemical factors in the serum.

According to Szpakowski et al. (20), uric acid is one of biochemical indices of great diagnostic value of perinatal EPH-gestosis and its intensity. Own studies confirm the existence of a relationship between increased DLIS concentrations and increased uric acid concentrations.

Valdes and Graves, (21) and Kelly (11) suggested a relationship between the occurrence of digoxin-like substances and total protein concentration in the serum and type of diet.

In all studied subjects the concentrations of total protein and albumins were normal and type of diet was uniform.

Taking into account the suggestions of Bertrand et al. (2) and Yiannakou et al. (23) on the occurrence of false positive DLIS concentrations depending on the presence of steroids, androgens, estrogens and bilirubin in the serum, digoxin-like substances were determined by Tdx test practically excluding any cross-reactions (8, 16, 18, 22). It was proved that DLIS presence in the serum was a real and not a false positive result, depending on cross-reactions.

Our studies demonstrate that of the highest value in the diagnosis of risk for EPH-gestosis can be the determinations of digoxin-like immunoreactive substances (DLIS) and uric acid in the serum of pregnant women.

Conclusions

1. In the serum of pregnant women who were never given digitalis preparations, in 83 % of studied cases the presence of digoxin-like immunoreactive substances (DLIS) was found.

2. Significantly higher DLIS concentrations occur in pregnant women with EPH-gestosis and correlate with uric acid concentrations while they are independent of the concentrations of total protein, albumins, urea, creatinine and bilirubin. DLIS exerts no effect on the shape and temporal conditions of ECG record.

3. Determination of DLIS can be helpful in early diagnosis of oligosymptomatic gestosis.

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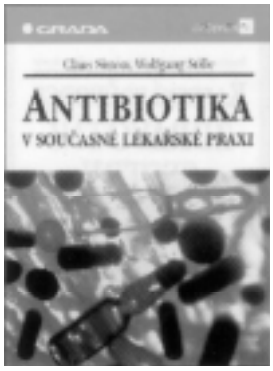

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M. Bernadič