THE RESULTS OF MEDICAL TRIALS OF ELI-P-COMPLEX METHOD

During 1995-2008, ELI-P-Complex method underwent medical trials by population screenings in the following institutions:

1. Russian State Medical University, Moscow, Russia.
2. University of Peoples' Friendship, Moscow, Russia.
3. Kazan State Medical University, Kazan, Russia.
4. Kazan State Medical Academy, Kazan, Russia.
5. Medical Research Center "Immunity and Health", Moscow.
6. Moscow Regional Research Institute for Obstetrics and Gynecology, Moscow, Russia.
7. Center for Medical and Social Rehabilitation, Kaliningrad, Russia.
8. Medical Center, Magnitogorsk, Russia.

7296 women aged from 17 to 45 years (2352 before pregnancy and 4944 during 4-16 weeks of pregnancy), of whom 6568 results of pregnancy were observed. A correlation between the results of ELI-P-Complex method and pregnancy development and results were analyzed.

Non-parametric methods Chi-square test and Mann-Whitney test, were used for statistical calculations conducted with "SPSS for Windows" and "STATISTICA" software.

Results obtained are presented in the tables below.

Conclusions:

1. Women with general immune suppression, that is with abnormally low serum content of auto-Abs evaluated by ELI-P-Complex method (n = 948), were characterized by non-physiological development of pregnancy nearly 5 times more often compare to women with normal serum content of auto-Abs evaluated by ELI-P-Complex method (table 1) ($p < 0.01$). Situation of pre-eclampsy was especially typical and revealed at 20.8% of pregnancies in women with general immune suppression ($p < 0.0001$).
2. Women with general immune activation, that is with abnormally high serum content of auto-Abs evaluated by ELI-P-Complex method (n = 182), were characterized by non-physiological development of pregnancy nearly 9 times more often compare to women with normal serum content of auto-Abs evaluated by ELI-P-Complex method (table 1) ($p < 0.01$). Rise of frequency of severe deviations (9.3% of cases) were typical for newborns from women with general immune activation ($p < 0.01$).
3. Pregnancies in both women with general immune suppression (23.8%), and women with general immune activation (36%) were much more frequently ended by miscarriages or stillbirths compare to 1.3% in women with normal serum content of auto-Abs evaluated by ELI-P-Complex method (table 1) ($p < 0.01$ for both).
4. Elevated frequency of miscarriages or stillbirths (more then 25% from all pregnancies) were typical for women with selective elevation of the next auto-Abs: against S100 (34.9%), against ß2-Glycoprotein I (29.9%), against Choriogonadotropin (28.1%), against collagen 26.2%), against Spr-06 (25.3%). ($p < 0.05$ - 0.01) (table 2).
5. Elevated frequency of severe deviations in newborn health state and malformations (more then 2.5% from all newborns) were typical for women with selective elevation of the next auto-Abs: against S100 (8.3%), against Thyroglobulin (5%), against Insulin (2.9%), against Choriogonadotropin (2.7%). ($p < 0.05$ - 0.01) (table 2).
6. Cases of non satisfactory results of pregnancies in women with normal (physiologic) results of ELI-P-Complex – 1.3% of miscarriages and stillbirths and 0.2% of newborns with severe deviations or malformations – may be supposedly related to genetic deviations affects upon pregnancy development.

Table 1.

Result of pregnancy in investigated women of fertile ages (n = 6568; Women with reproducible results of investigations by ELI-P-Complex were taken into account (at least two investigations with intervals of 3-4 weeks were executed)

Pregnancy development				Newborn Health State		
Physiological development of Pregnancy	Deviations in pregnancy development		Miscarriages and stillbirths	Alive and Healthy Newborns	Moderate deviations in health state	Severe deviations and malformations
	Threat of Miscarriage	Pre-eclampsy				
Group 1. Women which were characterized by normal results of ELI-P-Complex (level of immune reactivity for any antigen is in range between -20% ... +10%) (n = 1642)						
1563	58	-	21	1563	53	3
Group 2. Women which were characterized by moderate deviations of immune reactivity level for one or more antigens i.e. IR fall in ranges -21...-60% or +11...+40%) (n = 948)						
182	349	197	220	408	240	80
Group 3. Women which were characterized by severe deviations of immune reactivity lever with one or more antigens is lower than -60% or higher than +40%) (n = 86)						
9	42	4	31	13	19	22

Positive predictive value (PPV) of ELI-P-Complex Test

$$PPV = \frac{True\ Positive}{True\ Positive + False\ Positive}$$

For prediction of pregnancy development and outcome

True Positive - *Women from 2 and 3 group with complicated pregnancy development and outcomes (Miscarriages, stillbirths, pre-eclampsy, etc)*
False Positive - *Women from 2 and 3 group with physiological development of pregnancy.*

$$PPV = \frac{(349+197+220)+(42+4+31)}{843+182+9} * 100 = 81{,}5\%$$

For prediction of newborn health state

True Positive - *Women from 2 and 3 group with moderate and severe deviations in health state and malformations*
False Positive - *Women from 2 and 3 group with alive and healthy newborns.*

$$PPV = \frac{(240+80)+(19+22)}{361+408+13} * 100 = 46{,}1\%$$

NB: *Relative low PPV (prediction of newborn health state) supposedly is related to high adaptive potential of fetus/newborns organism, which provides satisfactory resistance to unfavorable maternal influences.*

Sensitivity and Specificity of ELI-P-Complex Test

$$Sensitivity = \frac{True\ Positive}{True\ Positive + False\ Negative}$$

$$Specificity = \frac{True\ Negative}{True\ Negative + False\ Positive}$$

For prediction of pregnancy development and outcome

True Positive - *Women from 2 and 3 group with complicated pregnancy development and outcomes (Miscarriages, stillbirths, pre-eclampsy, etc)*
False Negative - *Women from 1 group with moderate, severe deviations in health state and malformations*

$$Sensitivity = \frac{(349+197+220)+(42+4+31)}{843+58+21} *100 = 91\%$$

True Negative - *Women from 1 group with physiological development of pregnancy*
False Positive - *Women from 2 and 3 group with physiological development of pregnancy.*

$$Specificity = \frac{1563}{1563+182+9} *100 = 89,1\%$$

For prediction of newborn health state

True Positive - *Women from 2 and 3 group with moderate, severe deviations in health state and malformations*
False Negative - *Women from 1 group with moderate, severe deviations in health state and malformations*

$$Sensitivity = \frac{(240+80)+(19+22)}{361+53+3} *100 = 86,5\%$$

True Negative - Women from 1 group with physiological development of pregnancy
False Positive - *Women from 2 and 3 group with alive and healthy newborns.*

$$Specificity = \frac{1563}{1563+408+13} *100 = 78,7\%$$

Table 2.

Result of pregnancy of women which were characterized by selective elevation of any one or few of investigated auto-Abs (more then 20% above an average level of individual immune reactivity) (Group-4; n = 3892; Women with reproducible results of investigations by ELI-P-Complex were takes into account (at least two investigations with intervals of 3-4 weeks were executed)

Pregnancy development				**Newborn Health State**		
Physiological development of Pregnancy	Deviations in pregnancy development		Miscarriages and stillbirths	Alive and Healthy Newborns	Minimal deviations in health state	Severe deviations and malformations
	Threat of Miscarriage	Pre-eclampsy				
Elevated auto-Abs against Choriogonadotropin (n = 146)						
31 (21.2%)	115 (78.8%)	2 (1.4%)	41 (28.1%)	14 (9.6%)	87 (59.6%)	4 (2.7%)
Elevated auto-Abs against dsDNA (n = 968)						
566 (58.5%)	402 (41.5%)	7 (0.7%)	219 (22.6%)	228 (23.6%)	512 (52.9%)	9 (0.9%)
Elevated auto-Abs against ß2-Glycoprotein I (n = 1146)						
361 (31.5%)	785 (68.5%)	22 (1.9%)	339 (29.9%)	276 (24.1%)	516 (45%)	15 (1.3%)
Elevated auto-Abs against Fc-Ig (n = 1514)						
963 (63.6%)	551 (36.4%)	21 (1.4%)	214 (14.1%)	414 (27.3%)	873 (57.7%)	13 (0.9%)
Elevated auto-Abs against Collagen (n = 461)						
268 (58.1%)	193 (41.9%)	8 (1.7%)	121 (26.2%)	96 (20.8%)	238 (51.6%)	6 (1.3%)
Elevated auto-Abs against Insulin (n = 68)						
13 (19.1%)	55 (81.9%)	- (0%)	17 (25%)	11 (16.2%)	38 (55.9%)	2 (2.9%)
Elevated auto-Abs against S100 (n = 459)						
81 (17.6%)	378 (82.4%)	2 (0.4%)	160 (34.9%)	122 (26.5%)	139 (30.3%)	38 (8.3%)
Elevated auto-Abs against Thyroglobulin (n = 160)						
51 (31.9%)	109 (68.1%)	2 (1.3%)	31 (19.4%)	41 (25.6%)	80 (50%)	8 (5%)
Elevated auto-Abs against Spr-06 (n = 79)						
21 (26.6%)	58 (73.4%)	0 (0%)	20 (25.3%)	26 (32.9%)	32 (40.5%)	1 (1.3%)
Elevated auto-Abs against KiM-05 (n = 467)						
161 (34%)	306 (65.5%)	9 (1.9%)	92 (19.7%)	113 (24.2%)	259 (55.5%)	3 (0.6%)
Elevated auto-Abs against ANCA and/or TrM-03 (n = 974)						
261 (26.8%)	713 (73.2%)	17 (1.7%)	221 (22.7%)	214 (22%)	537 (55.1%)	2 (0.2%)

Notes:

1) The same individual data may be presented in a different columns simultaneously, because in woman with treat of miscarriage, pre-eclampsy or miscarriage may happen later;

2) The same individual data may simultaneously be presented in a different rows, because in woman with abnormal elevation of auto-Abs against, for example, S100, may simultaneously have an elevated auto-Abs against, for example, insulin.

Data presented in the next Dissertation works (mentioned below) were used for compiling of Table 1 and 2.

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