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# USE OF ENZYMES IN COMPLEX TREATMENT OF ANTIPHOSPHOLIPID SYNDROME IN WOMEN WITH REPRODUCTIVE LOSSES OF ANDIJAN STATE

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## ABSTRACT

Background: Obstetric complications developing at antiphospholipid syndrome are serious medical-social problem. Seeking of the treatment methods sets conditions for urgency of the article reviewed. Enzyme preparations are widely applied for treatment of women with fecundity disorder and hemorheology changes. Research objective was in clinico-laboratorial evaluation of Serrata drug impact in antiphospholipid syndrome in women with reproductive losses of Andijan state. Methods: Data of 43 women in the non-pregnancy state with reproductive losses (RL) in past history with revealed APS had been studied by us. Results: Thus, conducted therapy with Serrata was conductive to haemostasis. Conducted researches confirm the safety of application.

## UDC CODE & KEYWORDS

■ UDC: 618 ■ Antiphospholipid syndrome ■ Reproductive losses ■ Autoimmune response

## INTRODUCTION

Research of autoimmune response impacts (formation of antibodies to certain proper phospholipids) on implantation, growth, fetal and fetus development processes, gestation course and outcome of labor is taking on special significance in studying function of immune-associated processes and in pathogenesis habitual noncarrying of pregnancy.

Antiphospholipid antibodies have multifarious influence on haemostasis system by damaging all its protective links: endothelial barrier, function of natural anticoagulants, endogenous fibrinolysis by activating platelet link of haemostasis and procoagulant factors.

At present specialists of all medical sectors are involved in studying of APS. It's time to apply this knowledge in interpretation of diversified clinical picture of APS, studying critical conditions, recurrent thromboses which contribute to progress of obstetric and perinatal complications (Linnikov at all. 2005; Makatsaria at al. 2007; Linnikov, 2013).

It is known that rise in coagulation potential primarily by increasing in concentration of blood coagulation factors and functional activity of platelets is an adaptive response for haemostasis system during physiologically proceeding pregnancy (Linnikov, 2013). As far as pregnancy progression with diseases proceeding with haemostasis system disturbance the risk of blood clot development in vessels of placenta, fetus, maternal body increases.

Thrombophilic type disturbance of gestational adaptation is observed in antiphospholipid syndrome (APS), hereditary and acquired defects of haemostasis system (Brenner, 1999; Dahlback, 1999; D'Angelo at al. 2000; Frenkel at al. 1999).

### The aim of the research

Research objective was in clinico-laboratorial evaluation of Serrata drug impact in APS in women with reproductive losses of Andijan state.

### Materials and methods

Data of 43 women in the non-pregnancy state with reproductive losses (RL) in past history with revealed APS (main group) had been studied by us. Main group was divided into two groups depending on treatment. In group I (n = 20) the patients had received conventional anticoagulant, antiaggregant and antioxidant therapy. The patients of group II (n = 23) in addition to conventional therapy had received preconceptively enzymatic drug Serrata (manufactured by Kusum, India) at course dose in 10 mg (1 tablet) t.i.d. within 1 month prior to estimated pregnancy with further maintaining dose depending on haemostasis indices over a period of pregnancy. Serrata does not have teratogenic effect; it has fibrinolytic, anti-inflammatory and anti-edematous activity as well as regenerates microcirculation and oxygenation of tissues.

Control group (III) was comprised of 10 women (n = 10) with physiologically proceeding pregnancy and without APS at the same terms of gestation. Groups were comparable by age, number of gestation and childbirth in past history. Determination of lupus anticoagulant (LA) in plasma had been carried out with 6 – 8 weeks interval according to Scientific and Standardization Committee of International Society on Thrombosis and Haemostasis since LA determination according to literary data in 75 per cent of cases is reliable while the concentration of anticardiolipin antibodies is reliable only in 65 per cent of cases. Basis of test on LA (lupus-test) was taken its property to inhibit phospholipids by extending the coagulation time in APTT tests, the dilute Russell's viper venom time, PT and the activated recalcification time.

Diagnosis of thrombophilic state of the blood was included determination of platelet aggregation: detection of fibrin monomers soluble complex concentration (FMSC), D-Dimmer (fibrin polymerization). Determination of the main links of haemostasis system before and after treatment that included the following parameters: prothrombin time (PT, s), International Normalized Ratio (INR, units), Prothrombin Index (PI, %), Activated Partial Thromboplastin Time (APTT, s), Fibrin Monomers Soluble Complex (FMSC, mg/100 ml), Fibrinogen (g/l).

All observations had been carried out on the basis of central research laboratory (CRL) of the Andijan State Medical Institute.

Findings had been exposed to statistical data processing on personal computer Pentium-IV by means of Microsoft Office Excel-2003 software package including use of embedded functions for statistical manipulation.

## Results

Activation of plasmatic links of haemostasis system had been observed when compared indices of haemostasiogram before treatment of women with RL caused by APS as compared with control group.

The results of the study provided in the Table 1 show that study of haemostasis system shows general trend to hypercoagulation of procoagulant link. Trend to extension of APTT is observed in patients from group I for 1.4 times as compared with control group while in group II for 1.2 times when plasma procoagulant activity was evaluated. Parameters of D-Dimmer indices in both groups were higher for 5 times. However, other indices were also higher in patients of the main group as compared with control group.

Table 1: Parameters of haemostasis system indices in women with APS before treatment

| Index | n=23 | n=20 | n=10 |
|---|---|---|---|
| **PT. s** | 19.96 ± 1.09***** | 19.9 ± 0.25*** | 17.5 ± 0.42 |
| **INR. unit** | 1.15 ± 0.09* | 1.23 ± 0.01**** | 1 ± 0.02 |
| **PI. %** | 102.65 ± 3.38***** | 107.25 ± 0.63** | 94.1 ± 1.30 |
| **APTT, s** | 37.52 ± 1.42*** | 44.6 ± 0.50*** | 31.9 ± 0.56 |
| **FMSC. mg/100 ml** | 4.93 ± 0.30*** | 5.85 ± 0.14***** | 3.93 ± 0.08 |
| **Fibrinogen. g/l** | 3.07 ± 0.19 | 3.43 ± 0.13* | 3.0 ± 0.13 |
| **D-Dimmer. mg/ml** | 1164.35 ± 104.52*** | 1342.5 ± 35.98**** | 233.3 ± 22.57 |
| * - reliable P<0,1 ; **-P<0,01; ***-P<0,001; ***-P<0,02; ****-P<0,002; *****-P<0,05 as compared with control group. | | | |

Source: Authors

Laboratory test values of groups I and II had been compared with control group after completion of enzymotherapy course.

The results of the study provided in the Table 2 show that number of distinction had been detected in surveyed patients during evaluation of haemostasiogram indices first of all in platelet link.

Table 2: Parameters of haemostasis system indices in women with APS after treatment

| Index | n=23 | N=20 | n=10 |
|---|---|---|---|
| **PT. s** | 17.04 ± 0,53 | 18.65 ± 0.43**** | 17.5 ± 0.42 |
| **INR. unit** | 1.02 ± 0.03 | 1.18 ± 0.01*** | 1 ± 0.02 |
| **PI. %** | 77.26 ± 1.63** | 105 ± 0.81*** | 94.1 ± 1.30 |
| **APTT,.s** | 32.48 ± 1.37 | 43 ± 0.63** | 31.9 ± 0.56 |
| **FMSC. mg/100 ml** | 3.47 ± 0.13* | 5.5 ± 0.16** | 3.93 ± 0.08 |
| **Fibrinogen. g/l** | 2.98 ± 0.2 | 3.13 ± 0.14 | 3.0 ± 0.13 |
| **D-Dimmer.mg/ml** | 240.13 ± 21.63 | 1305 ± 38.79** | 233.3 ± 2257 |
| *- reliable P<0,01; **-P<0,001; ***-P<0,002; ****-P<0,05 as compared with control group. | | | |

Source: Authors

Indices were acquired values to be typical for physiological gestation. It should be noted that normalization of these values occurred faster in surveyed group II as compared with surveyed group I. Markers of thrombophilia became normal values faster in women from group II in relation to control group than in women from group I respectively.

Thus, conducted therapy with Serrata was conductive to haemostasis. Conducted researches confirm the safety of application. Elevation of D-dimer and FMSC levels is the reflection of haemostasis system since such factors in APS and thrombophilia are elevating long before estimated pregnancy and markers of such processes.

## Conclusion

If to take into account that increase in coagulation potential is an adaptive response for haemostasis system during physiologically proceeding pregnancy then thrombophilic type disturbance of gestational adaptation to be observed in APS often points to advisability to study of coagulation system and devise of preconceptive therapy long before the estimated pregnancy.

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