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The Impact Of Medicinal-Prophylactic Trousers' Daily Wearing On Pregnancy Course In The Third Term Of Women With Habitual Miscarriage Of Fetus.

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ABSTRACT

Notwithstanding the intensive development of medical science, the prevalence of habitual miscarriage of pregnancy has no downtrend in the whole world. The etiology of the given state is rather wide. It underlines the great perspective of further perfection of its pathogenetic treatment. Taking into account the high degree of readiness of pharmacological impacts at the given state, it seems perspective to conduct the search of non-pharmacological impacts able to potentiate pharmacological therapy. In the conducted study of women with habitual miscarriage of pregnancy in its third term we estimated the capacities of the author's variant of medicinal-prophylactic trousers in respect of maintenance of pregnancy. It was established that wearing of the author's trousers provided great efficiency of treatment and delivery in time in all the cases against the background of identical pharmacological therapy aimed at maintenance of pregnancy of patients with its habitual miscarriage. In the group of women with habitual miscarriage of pregnancy who received only pharmacological therapy in the course of the third pregnancy term they managed to bear pregnancy in 71.4% of cases. Perhaps, high efficiency of application of the author's variant of medicinal-prophylactic trousers is connected with their positive impact on microcirculation processes in the region of pelvis of pregnant women on behalf of detected normalization of platelets' aggregative properties. Received results allow considering medicinal-prophylactic trousers' wearing an important component of medical events aimed at maintenance of pregnancy in its third term in women with habitual miscarriage of pregnancy.

Keywords: habitual miscarriage of pregnancy, women, pregnancy, platelets, aggregation, medicinal-prophylactic clothes.

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INTRODUCTION

One of the most important modern social and medical problems is preserving high level of habitual miscarriage of pregnancy [1, 2]. This diagnosis is met in developed countries in 10-25 % of women. Habitual miscarriage of pregnancy is determined by WHO (World Health Organization) as three and more earlier losses of pregnancy at the term before 20 weeks with the mass of fetus less than 500gr. In women suffering from habitual miscarriage of pregnancy the probability of abortion is much higher than in the population and is equal to 40-45% [3].

We found a large quantity of factors promoting the formation of habitual miscarriage of pregnancy. They include genetic factors [4], persistent infections of genitals [5], pathology of womb [6], hyperandrogenia of various geneses, inferiority of lute in phase, diseases of thyroid gland, syndrome of polycystic ovary [7] and immune disturbances [8]. At the same time, these disturbances were not found in approximately 50% of cases of habitual miscarriage of pregnancy. Some researchers incline to the opinion that surplus activation of hemostasis system plays special role in these cases. It surpasses the degree of its strengthening at physiological pregnancy [9]. It is known that in the norm pregnant women have some hyper coagulation and hyper aggregation of platelets which don't lead to the development of vessels' thromboses as they are effectively blocked by natural anticoagulants, fibrinolytics and disaggregants [10]. Physiological surplus activity of hemostasis components provides optimal conditions for placentation and at childbirth - complete and timely hemostasis [11]. Pregnant women with habitual miscarriage of pregnancy are found to have surplus strengthening of hemostasis, especially in the form of platelets' hyper aggregation. It takes place faster than changes of hemostasis at pregnancy in the norm. In women with habitual miscarriage of pregnancy hemostasis is activated already in the first term till the level of the second-third term of pregnancy. In such cases hemostasis activity in the second and third terms of these women's pregnancy can rise till the level which makes normal hem circulation in the placenta impossible and leads to premature abortion [12].

Conducted at present therapy aimed at maintenance of pregnancy in the third term in women with habitual miscarriage of pregnancy not always can have satisfactory effect and allow bearing pregnancy [9, 12]. Evidently, additional rehabilitating impact on these women's bodies positively influencing platelets' activity can become one of the variants of efficiency rise of medical impacts on the given category of women. Non-pharmacological impacts having no side effects [13] can have special perspectivity in this respect.

In previous clinical [14] and experimental [15,16] researches there was shown the capacity of some medicinal impacts to lower platelets' aggregation [17] till the level near to the norm. High activity in this respect was shown by non-pharmacological impacts which can potentiate traditionally applied at many states pharmacological drugs [18]. At the same time, basic mass of population and especially pregnant women are characterized by low attachment to regular physical exercises [19]. That's why the search of variants of non-pharmacological correction is being continued. It will be more popular in basic mass of pregnant women with habitual miscarriage of pregnancy [20,21] and will be able to influence positively platelets' aggregation which is very significant for placental metabolism at late periods. The author considers daily wearing of medicinal-prophylactic trousers (MPT) as an alternative to medicinal physical training at habitual miscarriage of pregnancy. From one side, the attachment to MPT among pregnant women is much higher than to medicinal physical training [22]. From the other side, MPT application can provide more functionally favorable womb state of a pregnant woman and lower the level of existing in her body disturbances [23,24]. Taking all this into account, we put the following aim in our research: to estimate the dynamics of pregnancy course and platelets' aggregation activity in women with habitual miscarriage of pregnancy who daily wore the author's MPT in the third term of pregnancy.

MATERIALS AND METHODS

The conducted research was approved by the Local Ethic Committee of the Russian State Social University in May,17th, 2016 (Record №5). All the examined women gave written informed agreement on participation in the conducted research. The research involved pregnant women in the third term living in Central Russia (Moscow city and Moscow region). The age of all the observed women was 22-30 years. Under observation we took women either without deviations in the reproductive field (the control group) or having habitual miscarriage of pregnancy (two groups of observation).



The control group was composed [35] of clinically healthy pregnant women being at the term of 28 weeks with two and more physiological childbirths in the anamnesis. The women from this group were known to have favorable obstetrical anamnesis, absence of spontaneous abortions and other obstetrical disturbances.

The criterion of involvement into the groups of observation was the following one — habitual miscarriage of pregnancy, i.e. the presence of three and more spontaneous abortions iteratively at the terms before 22 weeks in the anamnesis of a woman. There were formed two groups of observation out of the examined pregnant women with habitual miscarriage of pregnancy. The first group of observation was composed of 42 women being at the term of 28 weeks' pregnancy and receiving standard maintaining pregnancy therapy. The second group of observation involved 44 women with habitual miscarriage of pregnancy also at the term of 28 weeks. The women from the second group of observation, except traditional therapy maintaining pregnancy, daily wore the author's variant of MPT.

Applied MPT had front and back halves. The upper part of the front half was made as a cut out detail of elastic material with raised belt-line and enlarged free fitting allowance. The upper part of trousers' back half was cut out of elastic material. Vertical leather stripes were stitched on it. They formed pockets where rigid plates were put. Similar leather stripes were also stitched on the upper part of trousers' front part. The lower line of vertical leather stripes' stitching had semicircular form on the front half of trousers and smoothly descended from the point 8-12cm lower than the top of the side seam till the point 10-15cm higher than the connection point of pace and middle seams of trousers. Besides, on the front half of trousers in the fields of side seams at the level of vertical leather stripes' disposition in MPT there were stitched some rebounded regulating details which were provided by the band VELKRO. Its reciprocal fragments were situated on the back half of trousers. Vertical leather stripes were 2.5-3 cm wide and were evenly stitched on the front and back halves of trousers. Used for MPT production rigid plates were made from fluoroplastic and were 1-3 mm thick [25].

Pregnant women from both groups of observation were under dynamic control with examination according to mentioned below methods at 28 weeks' and 38 weeks' pregnancy terms. The control group was observed and examined in the same terms. In the result of absence of reliable differences between both results of researches the control values are presented by one value – arithmetic average between both examinations.

All the pregnant women were examined in the following fields – common state, womb tone, fetal heartbeats, presence or absence of genital tracts' discharges. In laboratories we determined the activity of lipids' peroxidation (LPO) in blood plasma of the pregnant women. It was registered according to the content of thiobarbituric acid (TBA)-active products in it with the help of a kit produced by the firm "Agat-Med" (Russia) and according to the level of acylhydroperoxides (AHP) [26]. We also registered antioxidant blood activity [27]. We determined the concentration of P-selectin molecules and PECAM-1 (Bender MedSystems GmbH, Austria) by the method of enzymoimmunoassay in plasma.

After washing and resuspending we estimated quantitatively in platelets the levels of cholesterol (CS) by enzymatic colorimetric method with the help of a kit of the firm "Vital Diagnostikum" (Russia) and common phospholipids (CPL) according to the quantity of phosphorus content in them [28]. The evidence of intraplatelet LPO processes was found in washed and resuspended platelets according to concentration of malondialdehyde (MDA) in reduction reaction of thiobarbituric acid and AHP quantity [26].

In capillary blood of the pregnant women with the help of Gorjaev's box we conducted the calculation of platelets' quantity. Platelets' aggregation (PA) was estimated by visual micro method with the usage of the following inductors – ADP (0.5×10^{-4} M.), collagen (dilution 1:2 of the basic suspension), thrombin (0.125 un/ml.), adrenaline (5.0×10^{-6} M) and hydrogen peroxide (7.3×10^{-3} M) [28]. Received in the research results were processed by Student's t-criterion.

RESULTS AND DISCUSSION

Dynamic observation of the pregnant women from both groups of observation showed that only women wearing MPT managed in 100% of cases to maintain pregnancy till the term of 38 weeks and fulfill delivery as it was planned with receiving of alive full-term newborns. This group of pregnant women in the



course of the third term of pregnancy was noted to have satisfactory general state and normal womb tone; fetal heartbeats were clearly heard and genital tracts' discharges were absent. In the first group of observation only 30 women (71.4%) reached 38 weeks' term of pregnancy with consequent planned delivery. Pregnancy came to a standstill in two women from this group (4.8%) at the terms of 30 and 32 weeks. The rest women (23.8%) were registered to have preterm delivery with receiving of alive premature newborns in all the cases.

Existing at the beginning LPO activation gradually lowered in women from the groups of observation by the 38^{th} week of pregnancy. In the group with daily MPT wearing it turned out to be possible to lower its intensity till the control level. So, in this group the quantity of AHP and TBA-products in plasma lowered by the end of observation from 2.52 ± 0.39 D₂₃₃/1ml and 4.72 ± 0.54 mkmol/l (control values -1.82 ± 0.27 D₂₃₃/1ml and 3.37 ± 0.32 mkmol/l respectively) till 1.96 ± 0.34 D₂₃₃/1ml and 3.45 ± 0.41 mkmol/l respectively. It turned out to be possible in the result of evident strengthening of plasma AOA in them till $34.0\pm0.38\%$ by the end of observation (control value $-34.7\pm0.45\%$). Positive results of women who didn't wear MPT were less significant. In the result of MPT wearing by women with habitual miscarriage of pregnancy there was noted more evident lowering of initially high concentrations of adhesion molecules in their plasma (Table 1). So, by the 38^{th} week of pregnancy in the second group of observation the levels of P-selectin and PECAM-1 lowered more evidently (by 15.6% and 16.3% respectively) and reached the control values.

In the result of daily MPT wearing platelets' membranes of women with habitual miscarriage of pregnancy in its third term were noted to have more evident lowering of CS level (till 0.88 ± 0.012 mkmol/ 10^9 platelets) and CPL rise (till 0.76 ± 0.006 mkmol/ 10^9 platelets). In the first group of women these indices reached 0.96 ± 0.011 mkmol/ 10^9 platelets and 0.69 ± 0.008 mkmol/ 10^9 platelets respectively.

Initially activated LPO in platelets of pregnant women with habitual miscarriage of pregnancy (AHP – by 29.2%, MDA – by 32.6%) weakened till the control level only against the background of MPT wearing. By the end of observation the content of LPO products in platelets of women who continuously wore MPT, lowered (AHP – till $3.27\pm0.017~D_{233}/10^9~p$ platelets and MDA – till $1.46\pm0.013~n$ mol/ $10^9~p$ platelets respectively) and became equal with the control level.

Application of MPT to pregnant women with habitual miscarriage of pregnancy against the background of maintaining pregnancy treatment was accompanied by more evident positive dynamics of platelet hemostasis. The quantity of platelets in their blood didn't change and remained at the level of the norm. But initially accelerated platelets' aggregation in pregnant women with habitual miscarriage of pregnancy was evidently decelerated in the third term against the background of MPT. In the result of daily MPT wearing the observed pregnant women were registered to have increase of PA time in response to all the used inductors till the level near to the corresponding control. Their most evident reaction of platelets was on collagen, ADP and H_2O_2 , less active PA was with ristomicin and thrombin. Maximal duration of PA development was observed in pregnant women who wore MPT in the third term, in response to adrenaline -86.7 ± 0.27 s. (Table 1).

Table 1: The dynamics of hematological indices of the examined pregnant women with habitual miscarriage of pregnancy in the third term who wore medicinal-prophylactic trousers

Parameters	Pregnant women with habitual miscarriage				
	traditional treatment		additional wearing of medical and preventive pants		n=34 <i>,</i> M±m
	28weeksofpregnancy,	38weeks	28weeksofpregnancy,	38weeksofpregnancy,	
	n=42	of	n=44	n=44	
		pregnancy,			
		n=30			
Acylhydroperoxides	2.56±0.57	2.21±0.49	2.52±0.39	1.96±0.34	1.82±0.27
of plasma, D ₂₃₃ /I ml	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Thiobarbituric	4.67±0.50	3.92±0.45	4.72±0.54	3.45±0.41	3.37±0.32
acid-products of	p<0.01	p ₁ <0.01	p<0.01	p ₁ <0.01	
plasma, umol/l		p ₂ <0.05			
Antioxidant activity	24.0±0.48	29.2±0.36	23.7±0.42	34.0±0.38	34.7±0.45



of plasma, %	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
P-selectin, ng/ml	123.6±0.45	112.5±0.52	124.6±0.59	105.1±0.41	103.2±0.48
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
PECAM-1, ng/ml	60.2±0.32	56.0±0.29	61.3±0.28	51.3±0.24	49.8±0.34
	p<0.01	p ₂ <0.05	p<0.01	p ₁ <0.01	
Cholesterol in thrombocytes, umol/10 ⁹ platelets	1.02±0.014	0.96±0.011	1.03±0.009	0.88±0.012	0.85±0.012
	p<0.01	p ₂ <0.05	p<0.01	p ₁ <0.01	
Total phospholipids in thrombocytes,	0.63±0.007	0.69±0.008	0.62±0.009	0.76±0.006	0.75±0.011
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
umol/10 ⁹ platelets		p ₂ <0.05			
Acylhydroperoxidesplatelets,	4.16±0.019	3.71±0.016	4.19±0.018	3.27±0.017	3.22±0.017
D ₂₃₃ /10 ⁹ platelets	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
, ,	·	p ₂ <0.05	·		
Malondialdehydein	1.91±0.014	1.65±0.015	1.88±0.012	1.46±0.013	1.44±0.011
thrombocytes,	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
nmol/10 ⁹ platelets		p ₂ <0.05			
Aggregation of platelets with ADP, s	31.2±0.19	35.7±0.21	30.9±0.17	39.9±0.15	40.1±0.14
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Aggregation of platelets	23.7±0.24	27.1±0.20	24.0±0.19	29.7±0.17	30.2±0.10
Aggregation of platelets with collagen, s	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Aggregation of platelets	40.7±0.12	47.2±0.15	41.1±0.19	50.6±0.27	51.2±0.12
with thrombin, s	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Aggregation of platelets with ristomycin, s	34.1±0.22	38.7±0.16	33.9±0.14	41.6±0.10	42.4±0.16
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Aggregation of platelets with H ₂ O ₂ , s	35.8±0.27	38.4±0.24	36.2±0.32	41.0±0.13	41.8±0.22
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			
Aggregation of platelets with epinephrine, s	74.5±0.36	81.0±0.29	73.1±0.039	86.7±0.27	88.5±0.034
	p<0.01	p ₁ <0.05	p<0.01	p ₁ <0.01	
		p ₂ <0.05			

Conventional signs: p – signification of initial parameters' differences in groups of observation and control group; p_1 – signification of accountable indices' dynamics in groups of observation; p_2 – signification of results' differences of correction impact in groups of observation and values of control group.

Habitual miscarriage of pregnancy is at present a widespread state. It attracts much attention from the side of specialists of various profiles. Modern medicine acknowledges polyetiology of habitual miscarriage of pregnancy what points at the necessity of the search and detailed analysis of pathogenetic mechanisms of various etiological factors' realization. Last time many researchers incline to the opinion that an important role in the development of habitual miscarriage of pregnancy is played by surplus activity of hemostasis system, especially in respect of platelet aggregation [30].

It is clear that presence of these changes at habitual miscarriage of pregnancy worsens metabolism and circulation processes in the womb thus weakening trophism of placenta and fetus [31,32]. Surplus platelets' aggregation lies in the basis of these disturbances [33]. Weakening of a body's antioxidant protection with the increase of LPO intensity in its plasma and cells is very significant here. Free radicals mostly disturb functioning of platelet membranes. It is aggravated by CS growth in them in pregnant women with habitual miscarriage of pregnancy and decrease of CPL promoting the development of membrane-pathy [34]. It declares itself in



pregnant women with habitual miscarriage of pregnancy by the increase of their platelets' capacity to hyper aggregation and formation of preconditions for metabolism inhibition [35,36].

Concentrations of the molecule of cellular adhesion P-selectin and PECAM-1 are important markers of high platelet activity. They have platelet and endothelial origin. It is acknowledged that fluctuations of concentrations' levels of P-selectin and PECAM-1 are connected with modifications of platelets' capacity to aggregation and disaggregation. Their increased concentrations in the examined women point at surplus level of their expression and, thus, at high interaction potential of platelets and endothelium at habitual miscarriage of pregnancy [37,38].

Last time modern society starts to look for new forms of rehabilitation (including pregnant women) [39] more and more actively. Application of medicinal-prophylactic clothes [40,41] is one of new rehabilitation variants. The design of these clothes is conducted with the account of last achievements of physiological science [42]. Because of wide prevalence of habitual miscarriage of pregnancy, designing of MPT for pregnant women with this pathology acquires great signification. But additional researches are needed for final clarification of all the aspects of MPT positive impact on a body against the background of maintaining pregnancy therapy. It was begun in the present research.

Daily MPT wearing in the third term of pregnancy by women with the diagnosis of its habitual miscarriage showed their potentiating impact on maintaining pregnancy treatment. So, at the absence of MPT wearing planned delivery was possible in this category of women only in 71.4% of cases. But in case of their wearing the efficiency of such treatment reached 100% what underlined high rehabilitating potential of MPT. It is evident that reached results are conditioned by specific impact of MPT which is mostly based on weakening of trophic disturbances on behalf of hematological indices' improvement.

It was found out in our research that LPO intensity in blood plasma in the third term of pregnant women with habitual miscarriage of pregnancy was lowered more evidently at daily MPT wearing. Thus, it improved functioning of their internals. At the same time, weakening of LPO activity in platelets' membranes provided activity optimization of enzymatic systems of blood platelets and receptors on their surface. Detected in pregnant women from the second group of observation who daily wore MPT, lowering of plasma level of P-selectin and PECAM-1 contributed greatly to the decrease of platelet activity and pointed at risk minimization of episodes of capillary course's blocking by platelet micro thrombi and formation of optimal conditions for metabolism in tissues [43,44].

Detected more evident PA lowering in the second group of observation against the background of daily MPT wearing could be estimated as consequence of significant decrease of LPO intensity in plasma and platelets and minimization of platelet membrane-pathy's manifestations. It led to alleviation of functioning of platelets' receptor and post-receptor mechanisms [45]. Inhibition of PA development in response to ristomicin in pregnant women with habitual miscarriage of pregnancy against the background of MPT could be connected with the decrease of von Willebrand's Factor inflow into their blood [38]. The growth of platelets' resistance to hydrogen peroxide (what was judged by the increase of PA time with H_2O_2) pointed at strengthening of the system of platelets' ant oxidation. Found PA weakening against the background of daily MPT wearing provided greater efficiency of maintaining pregnancy therapy not only on behalf of more evident LPO weakening in platelets' membranes but also in the result of larger lowering of the activity of thromboxane-formation system. It was told by evident PA inhibition with weak inductors which was realized through thromboxane-formation [38].

It can be claimed that application of MPT to women with habitual miscarriage of pregnancy in the third term strengthens the efficiency of maintaining pregnancy treatment on behalf of significant weakening of LPO processes in plasma and platelets, improvement of their aggregation indices till the control level. Reached weakening of platelet aggregation indices (mostly determining blood rheological properties in capillaries) is the basis of a woman's rehabilitation and provision of functionally favorable situation in her body [46,47].

CONCLUSION

Preservation of high frequency of habitual miscarriage of pregnancy is a serious problem of modern society and medicine. Hemostasio logical disturbances have rather great signification in formation of the given



state. They cause worsening of metabolic processes in the womb of the pregnant woman. Taking into account the high degree of readiness of pharmacological treatment of habitual miscarriage of pregnancy, it seemed to be very significant to conduct the search of non-pharmacological impact on a woman's body able to potentiate pharmacological therapy in the third term of pregnancy. Daily wearing of medicinal-prophylactic trousers from the 28th week till the 38th week of pregnancy was accompanied in all the cases by maintenance of pregnancy till planned delivery at normalization of platelets' aggregative activity. Received results allowed considering wearing of medicinal-prophylactic trousers to be an important and effective component of treatment maintaining pregnancy in its third term in women with habitual miscarriage of pregnancy, and give possibility to recommend their application as widely as possible.

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