Exercise and Human Health: The Example of the Effect of Moderate Physical Exercise on Von Willebrand's Factor's Activity and Concentration in Blood

Ryszard Paczuski, Mirosława Cieslicka, Paweł Wojtacha and Błażej Stankiewicz

I. Introduction

THE opinion about benefits of training for human health is very common. Physical activity is recommended as prophylactics of various diseases especially forms of arteriosclerosis including myocardial infarction. Exercise induces a sequence o physiological changes among which is the activation of fibrinolytic system. The release of tissue type of plasminogen activator (t-PA) from activated endothelial cells is one of the most important component of this phenomena [11,13,14,18,24,25,27]. Statistical analyses of the exercise therapy clearly show positive results, but they do not reflect the existence of a group of people who did not respond to such treatment or respond negatively. On the other hand the circulation problems are commonly reported after exercise and known since the times of first Marathon runner. Myocardial infarction each year causes death of very young sportsmen, including those of master class.

The mechanism of the negative effect of exercise on human health is multifactorial an as a result complicated and uncertain. From many coagulation factors realised after exercise probably the most important is von Willebrand factor. It is multimeric glycoprotein with molecular mass up to 20 x 10^6 D and complex adhesive activity which includes at least two basic functions (I) adhesion of platelets on site of vessels wall damage and (II) protection it against proteolysis of coagulation factor IIIV (FIIIV) and it's transport to place of vessel injury [1,2,3]. The conformation properties of vWf cause especially high vWf adhesion to injured vessel wall under conditions of high shear stress which appear in arteries and arterioles, and for this reason vWf has essential significance for thrombus formation there. Von Willebrand's factor is synthesized in megacarocytes and endothelium of blood vessels and released in a continuous (I) and controlled (II) manner. It is stored in structures termed Weibel-Palade bodies which also contain other coagulation proteins including t-PA, . After stimulation all these proteins are released to blood [1,2].

The significance of the increased concentration and activity of vWf for the risk of myocardial infarction explains the phenomena of double higher incidence of MI among people with A, B or AB blood group than those with O group. The molecules of vWf after glycosylation poses blood group substances according to individual phenotype. The speed of enzymatic degradation and elimination of vWf from blood is faster among individuals with H antigen (O group) than others, which causes about 20% lower plasma activity and concentration of vWf. This mechanism causes also similar decrease of concentration and activity of FVIII [3,4,6,7, 29,30,31,32].

Along with pathological processes, physiological factors such as physical effort, stress or pregnancy have an impact on concentration and activity of plasma vWf. The effect of physical exercise being probably the most often interfering factor, in spite of being listed in publications, is not researched thoroughly. Publications concerning this issue are based on, for the most part, small group of subjects, and, moreover, it is difficult to determine the reason for changes – whether they were caused by physical effort itself or perhaps tissue constriction or local circulation stasis [8-14].

To study the procoagulation effect of physical effort we measured changes of on Willebrand's factor's concentration (vWf:Ag) and activity (vWf:CBA) in blood. To eliminate other than effort factors we decided to study it's blood level changes after swimming.

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II. MATERIAL AND METHODS

The study was preceded in the group of 61 young volunteers (32 men and 29 women) aged 19-22 (mean 20, SD 7 months). This effort consisted in 35 mutes of swimming in indoor swimming pool. The levels of swimming abilities across the group were similar and determined intermediate. Blood used to determinate the vWf:Ag concentration and vWf:CBA activity was drawn approximately 10 minutes before a 35-minute period of freestyle swimming and immediately afterwards. Blood was drawn in accordance to standard procedure from cubital vein, using sodium citrate in 1:9 ratio as anticoagulant, centrifuged for obtaining platelet pour plasma, which was then frozen and stored until the examination date in refrigerator at the temperature -20º C. The von Willebrand concentration (vWf:Ag) was measured with ELISA test using DAKO (Danmark) reagents according to manufactural procedure. The activity of was measured with collagen binding assay (vWf:CBA) using Favaloro method with small modifications [5,15]. The coating collagen was human type III (SIGMA, USA), the conjugate of peroxidase was obtained from DAKO. The research was carried out upon the approval of the committee of bioethics, as well as written approval of a subject. The project was approved by regional Bioetics Commiettee and followed by confirmed agreement of all participants according to required procedure.

Results

An increase of blood concentration and activity of von Willebrand factor after exercise was observed in the whole group. Both parameters evaluated in the group increased considerably – vWf:Ag by 59%, SD 60, p<0,001 and vWf:CBA by 70%, SD 62%, p<0,001. A big difference in reaction after effort was observed between male and female group (tables 1 and 2, figures 1,2,3,4).

Table 1: The plasma concentration of von Willebrand factor (vWf:Ag) in male group (n=32) and female group (n=29) before and after 35 minutes of swimming.

Study group	Before effort		After effort		Statistical signifficence	Difference of vWf :Ag	
	mean	SD	mean	SD		mean	SD
Male	105%	26%	189%	81%	p<0,001	84%	71%
Female	92%	18%	120%	23%	p<0,001	28%	20%
Whole group	99%	23%	156%	70%	P<0,005	59%	60%

Table 2 The plasma activity of von Willebrand factor (vWf:CBA) in male group (n=32) and female group (n=29) before and after 35 minutes of swimming.

Study group	Before effort		After effort		Statistical signifficence	Difference of CBA activity	
	mean	SD	mean	SD		mean	SD
Male	96%	34%	195%	85	p<0,001	99%	67%
Female	98%	24%	134%	46%	p<0,001	36%	37%
Whole group	97%	29%	165%	74%	p<0,001	69%	63%

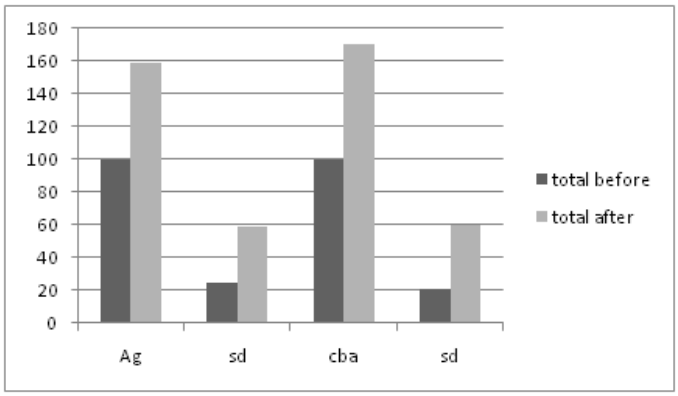

Figure 1: Individual changes of plasma concentration of von Willebrand factor (vWf:Ag) in male group (n=32) after 35 minutes of swimming.

In male group von Willebrand's factor's activity (AWF:Ag) was increasing by 81% on average, and its vWf:CBA activity by 99% (p<0.001, tables 1 and 2, figure 2).

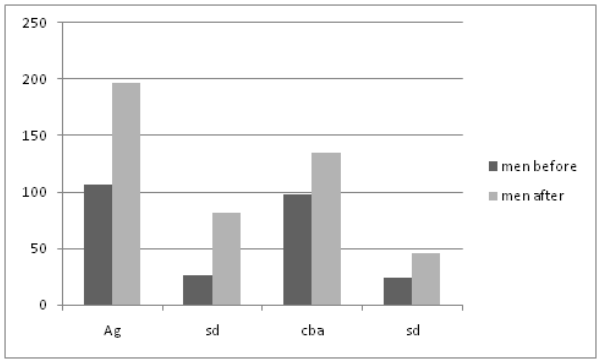

Figure 2: Individual changes of plasma concentration of von Willebrand factor (vWf:Ag) in female group (n=29) after 35 minutes of swimming.

In female group the scale of increase was lower and was 28% for vWf:Ag and 36% for vWf:CBA activity (p<0.001, tables 1 and 2, figure 3).

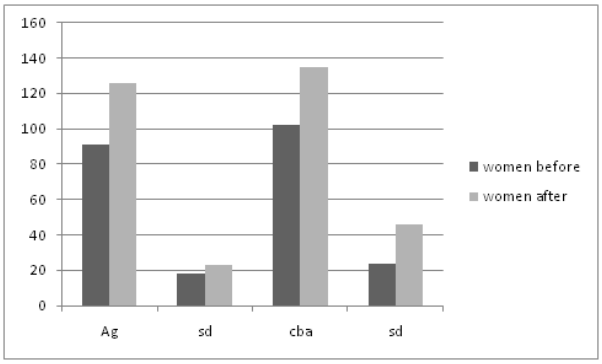

Figure 3: Individual changes of plasma activity of von Willebrand factor (vWf:CBA) in male group (n=32) after 35 minutes of swimming.

The difference between increase of vWf:Ag and vWf:CBA between male and female group was significant at p<0,001. The subjects differed considerably in the scale of reaction to effort, differing both in the scale of increase of vWf:Ag plasma concentration and vWf:CBA plasma activity. Some individuals shown no reaction after effort while some others reacted with extremely high release of vWf to blood reaching almost 300% (figure 4).

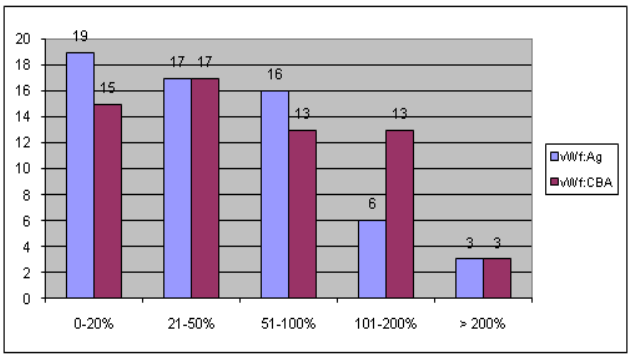

Figure 4: Individual changes of plasma activity of von Willebrand factor (vWf:CBA) in female group (n=29) after 35 minutes of swimming.

About ¼ of population shown a week release of vWf. But also a large part of population – 27% reacted after exercise with intense increase of vWf:CBA in range exceeding 100%.

III. Discussion and Conclusions

The experimental model of the moderate physical exercise based on 30 minutes of swimming induced significantly increases the levels von Willebrand's factor's activity and concentration in blood. Observed interontogenetic differences are considerable (fig. 1-4), yet they do not affect statistic inferencing. Significant statistic differences were observed in the scale of vWf concentration and activity increase between male and female groups. Physical effort has been deemed the

reason for von Willebrand's factor increase in blood, yet, as we have determined in the introduction, literature data confirming this fact are not numerous, while for vWf:CBA activity there are none at all. The results of early experiments were not clear, and in some subjects the exercise caused the release of vWf [8], and in others did not [16]. At present, this fact leaves no doubt. The highest two-, threefold increase of plasma concentration was observed as a result of a long-distance run [9, 10]. Admittedly there is a report on vWf increase up to 800%; nonetheless, in the evaluation of probability for such a significant increase it should be treated with caution [11]. In other experiments the increase in vWf level was obseved as well, but not that significant, since in the range of 10%-80% [12-14, 17-23]. The differences in the method of evaluation (gait, run, bike, cycloergometer) influenced the discrepancies in the scale of increase. The duration of exercise proved to be significant as well, along with the increase in the duration, vWf [24,25] activity and concentration increased as well. The increase in vWf concentration occurred for 15 minutes following the exercise, and then normalization was commencing [25, 26]. Subjects age turned out to be significant as well, as the phenomenon apparently manifested itself in persons aged 20 to 30 [19, 25].

In spite of the facts above, there can be some reservations about the methodology of research conducted and interpretations of their results, indicating other possible reasons for vWf release, e.g. recurring local tissue constriction or circulation stasis. The report that even the kind of shoes worn or their lack can influence test results indicate that caution in the evaluation of examinations on exercises should be preserved. The rate of feet tissue endothelium excitation was responsible for these differences [27]. The sort of exercise applied in our research, consisting in swimming in swimming pool is an optimal model of an experiment, as is excludes the factors similar to those cited above and eliminating other reasons for releasing vWf into blood. However, it should be assumed that in most situations the mechanism of releasing vWf as a result of exercise is complex, entailing both local and bodily factors.

Another interesting observation that we have not come across analyzing literature data is the assertion of a significant difference in men's and women's reaction to exercise. In men both vWf:Ag concentration and its vWf:CBA activity increased threefold in comparison with women (tables 1 and 2, figures 1, 2, 3, 4). This difference might have been overlooked by other researchers since only the representatives of one sex underwent scrutiny or there have been disproportions within the group [14,18,20,23,25,26]. Usually only men were examined [9,13,22,28] or they dominated the group. The fact that even small, 5- or 7- person groups underwent examination is probably of significance as well [9,24]. Both physical conditions (pool's size, temperature of water and air), exercise duration, swimming skills level in both groups did not differ, thus they should not be considered the reason. Admittedly, subjective factors cannot be excluded, e.g. more ambitional attitude towards set task, so putting more effort into it in male groups, it is not very likely that it might be the reason for threefold increase scale. This effect probably partially explains the differences of the incidence of atheriosclerosis and myocardial infarction between male and female populations. It also consists a strong argument suggesting significance of vWf in patomechanis of atheriosclerosis.

The individual differences in reaction to physical effort (fig 1-4) are especially significant. A large part of human population do not release a vWf after exercise or release a week amount of these protein, while others release over 200%. Such big individual changes of vWf concentration and activity are not only responsible for the confusing differences in conclusions after early studies on the effect of exercise on vWf concentration [8,16] but also essential for existence of differences of the individual of reaction for exercise therapy. The difference will interfere with the changes of other coagulation proteins creating individual gene dependent profile. If these phenomena are unbalanced with the increase of fibrinolytic activity it may cause various thrombotic episodes including myocardial infarction. In conclusion for a part of human population even moderate exercise may cause negative health results. But on the other hand it's measurements may be essential for predicting physiological results of training and application of exercise therapy.

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