STATE OF THE PLATELET HEMOSTASIS IN THE MIDDLE-AGED AND THE ELDERLY HYPERTENSIVE PATIENTS

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It has long been known that complications of essential hypertension (EH) are associated mostly with disorders of blood coagulation system [4, 14] and degree of absolute risk of cardiovascular events is growing with increasing of age [10, 12, 13]. That is why much attention is paid to more detailed study of mechanisms of thrombosis as the component of complications of EH through lens of hemostatic changes at present [6]. Therefore, regulatory
mechanisms of initiation of thrombus formation and participation of platelet hemostasis are studied in hypertensive patients insufficiently today.

Situation has changed in recent years: epidemiological and experimental data have emerged to ascertain presence of prothrombotic changes in system of hemostasis in EH. Typical disorders in hemostasis system in EH are considered as a significant risk factor for thrombophilic complications [1, 2, 5, 15]. Thromboembolic conditions are observed in 56% of patients and are a direct cause of death in 49% of cases, hemorrhage – in 35% [11].

Data on importance in predicting development of cerebral stroke and myocardial infarction of such factor of hemocoagulation as platelet dysfunction have been obtained in recent years [2, 9]. The key element in processes of atherothrombosis is platelet activation [11]. The blood platelets are the matrix for the coagulation cascade [3, 5]. Changes in a functional state of platelets, bioenergetic and plastic processes occurring in these cells are related directly to hemostasis as a whole and may indicate severity of cardiovascular damage [8]. However a functional activity of platelets is understood poorly still.

One of the components of VirkhoV triad is an impaired blood composition namely the factors of platelet coagulation and activation. Imbalance of platelet-plasma hemostasis leads to development of complications in arterial hypertension (AH) [16].

Changes in functional properties of platelets in patients with EH are accompanied by release of vasoactive mediators that provoke local vasospasm and increase platelet aggregation which magnifies risk of thrombotic complications. The leading link of enhanced thrombus formation is increased platelet aggregation in AH [9]. The platelets of the patients with EH have the increased sensitivity to ADP. Dockrell M. et al. showed the positive correlation of blood pressure with potentiation by endothelin-1 of the adrenaline-induced platelet aggregation which can be considered as the manifestation of familial susceptibility to EH in their studies [13].

There are few work concerns study of platelet hemostasis in patients with AH especially in older age groups.

This article is an attempt to systematize and analyze few literary data on role of hemostasis system in pathogenesis of EH in the elderly.

The objective of the study. To identify the baseline levels of the platelet hemostasis indices in the middle-aged and the elderly hypertensive patients.

MATHERIAL AND METHODS

We performed the comparative assessment of status of the platelet hemostasis in 63 middle-aged (group I) and 53 elderly patients (group II) respectively to clarify this issue in our work. Patients of the surveyed groups were comparable in age, sex and related pathology. The control group consisted of 15 patients for every of the surveyed groups (group III the middle-aged and group IV the elderly respectively) matched with basic by age and gender. The control was presented with patients without AH who were hospitalized with diagnoses of chronic gastritis, duodenitis, cholecystitis, atherosclerotic cardioisclerosis, with angina functional class that is not above I, without cardiac arrhythmias and heart failure that is not above II A stage for Strazhesko M. D. – Vasylenko V. Kh.

The diagnosis and stage of EH was set according to the criteria of WHO and the International Society of Hypertension (2013). Patients with significant heart rhythm disorders, angina functional class that is above I, heart failure that is above II A stage for Strazhesko M. D. – Vasylenko V. Kh. were not involved in the study. Cases with symptomatic hypertension and obesity more than the second degree were also excluded.

Spontaneous and induced platelet aggregations were determined. Platelets were activated with adenosine diphosphate (ADP) (1×10⁻⁵ mM/L), adrenaline (1 μg/mL) and analysed by optical aggregometry (SOLAR AP-2110). We determined and analyzed the following indices: amplitude of aggregation (AA) (%), time of maximal aggregation (TMA) (min.), slope of aggregation (SA) (%/min.).

RESULTS AND DISCUSSION

The parameters of the platelet hemostasis in the middle-aged hypertensive patients were compared with the corresponding indicators of the elderly hypertensive patients according to the stated purpose and tasks. Analyzing the obtained data of the platelet hemostasis indices in particular the spontaneous aggregation it is noteworthy that AA and SA were different significantly among the compared indicators.

So, AA was higher by 23,1% (p<0,05) in the elderly and was 3,2±1,7% respectively and 2,6±1,7% in the middle-aged; SA – by 46,7% (2,2±1,7%/min. and 1,5±1,2%/ min. respectively). The acceleration of the aggregation process was detected by 46,7% (p<0,05) in the elderly compared with the patients of the middle age (tab. 1).

TMA index in the middle-aged patients was 27,3% (p<0,05) higher than in the control group.

We found the significant slowdown of the aggregation process in the elderly patients by 33,3% (p<0,05) compared to the control values analyzing the velocity of it.

Thus, the comparison of the obtained indices of the spontaneous platelet aggregation in hypertensive patients of the different age categories established the informative content of AA in the elderly patients, which exceeded significantly the similar indicator in patients of the middle age by 23,1% (p<0,05). Thereby, the aggregation process acceleration was detected by 46,7% (p<0,05) in the elderly patients compared with the middle-aged patients.
The table 1

| The indices of the spontaneous platelet aggregation in the middle-aged and the elderly patients (M±σ) |
|---|---|---|---|---|
| | I group (n=63) | II group (n=53) | III group (n=15) | IV group (n=15) | p |
| AA (%) | 2,6±1,7 | 3,2±1,7 | 1,8±0,3 | 2,5±0,2 | p<0,05, p>0,05, p>0,05 |
| TMA (min.) | 5,6±3,2 | 6,8±2,9 | 4,4±1,7 | 8,8±0,8 | p>0,05, p<0,05, p>0,05 |
| SA (%/min.) | 1,5±1,2 | 2,2±1,7 | 1,1±0,2 | 3,3±1,3 | p<0,05, p>0,05, p<0,05 |

Remark: p1 – statistical significance of difference between groups I and II, p2 – statistical significance of difference between groups I and III, p3 – statistical significance of difference between groups II and IV.

Analysis of the induced platelet aggregation with the different inductors in the middle-aged and the elderly hypertensive patients showed the greatest informative of TMA under the conditions of the adrenaline stimulation.

Thus, TMA was 6,4±2,9 min. in the elderly patients vs. 4,1±2,0 min. in the patients of the middle age. It was found the significant slowdown in terms of TMA by 56,1% in the elderly relative to the middle-aged patients (p<0,001) (tab. 2).

We found the significant increase in ADP-induced platelet aggregation activity in AA by 61,4% (p<0,01) in the elderly hypertensive patients relative to the control group.

The table 2

| The induced platelet aggregation indices in the middle-aged and the elderly patients (M±σ) |
|---|---|---|---|---|
| | The inductors | I group (n=63) | II group (n=53) | III group (n=15) | IV group (n=15) | p |
| AA (%) | ADP | 57,2±31,1 | 56,5±28,7 | 27,8±1,9 | 35,0±4,9 | p>0,05, p>0,05, p>0,05 |
| | Adrenaline | 29,0±17,3 | 35,6±32,1 | 35,2±2,6 | 42,9±5,6 | p>0,05, p>0,05, p>0,05 |
| TMA (min.) | ADP | 4,3±2,1 | 5,0±2,4 | 4,7±1,0 | 6,9±1,4 | p>0,05, p>0,05, p>0,05 |
| | Adrenaline | 4,1±2,0 | 6,4±2,9 | 4,9±0,2 | 8,2±1,8 | p<0,001, p>0,05, p>0,05 |
| SA (%/min.) | ADP | 52,3±26,9 | 53,7±21,8 | 27,4±10,7 | 49,9±11,8 | p>0,05, p>0,05, p>0,05 |
| | Adrenaline | 12,0±5,9 | 15,4±12,6 | 15,4±1,3 | 18,0±1,5 | p>0,05, p>0,05, p>0,05 |

Remark: p1 – statistical significance of difference between groups I and II, p2 – statistical significance of difference between groups I and III, p3 – statistical significance of difference between groups II and IV.

CONCLUSIONS

Therefore, there is the increase in platelet activity depending on age in the middle-aged and the elderly hypertensive patients that is manifested by adrenaline stimulation most clearly. In addition, the most significant changes are determined in the spontaneous and the adrenaline-induced aggregation namely in amplitude and slope of aggregation in the spontaneous and time of maximal aggregation in the adrenaline-induced aggregation in the patients of older age group compared with the middle-aged patients. The substantial deceleration of time of maximal aggregation
during the adrenaline stimulated aggregation in 1.6 times (p<0.001) in the elderly patients confirms the expressed thrombogenicity and sensitiveness to neurohumoral influences too. Thus, the blood plasma thrombogenicity revealed in the study of the platelet hemostasis in the elderly indicates a high probability of thrombotic complications developing in this category of the patients and this is consistent with literature [7].

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Дослідження

СОСТОЯНИЕ ТРОМБОЦИТАРНОГО ГЕМОСТАЗА У БОЛЬНЫХ ГИПЕРТОНИЧЕСКОЙ БОЛЕЗНЬЮ II СТАДИИ СРЕДНЕГО И ПОЖИЛОГО ВОЗРАСТА

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Известно, что осложнения гипертонической болезни в основном связаны с нарушениями в системе свертывания крови, а с возрастом возрастает степень абсолютного риска сердечно-сосудистых событий. Вот почему, в настоящее время большое внимание уделяется более детальному изучению механизмов тромбообразования, как составляющей осложнений гипертонической болезни, через призму гемостазиологических сдвигов. Итак, на сегодня недостаточно изученными у больных гипертонической болезнью являются регуляторные механизмы инициации тромбообразования и участия тромбоцитарного гемостаза.

Цель — выявление исходного уровня показателей тромбоцитарного гемостаза у больных среднего и пожилого возраста с гипертонической болезнью II стадии.

Материал и методы. Для выяснения этого вопроса в нашей работе мы проводили сравнительную оценку состояния тромбоцитарного гемостаза у 63 больных среднего (группа I) и 53 пожилого возраста (группа II) соответственно. Контрольную группу составили по 15 больных для каждой из обследованных категорий (соответственно III группа — обследованные среднего возраста и IV группа — обследованные пожилого возраста) с сопоставимым половым составом.

Выводы. Следовательно, у больных гипертонической болезнью II стадии среднего и пожилого возраста происходит увеличение тромбоцитарной активности и зависимости от возраста, что наиболее отчетливо проявляется при стимуляции адреналином. У больных старшей возрастной группы, кроме того, наиболее существенные изменения определяются при спонтанной и адреналин-индукцированной агрегации, а именно степени и скорости агрегации при спонтанной и временной максимальной агрегации при адреналин-индукцированной агрегации по сравнению с больными среднего возраста. Существенное замедление времени максимальной агрегации тромбоцитов, стимулированной адреналином, в 1,6 раза (р<0,001) у больных пожилого возраста также подтверждает их выраженную тромбогенность и чувствительность к нейрогуморальным воздействиям. Таким образом, обнаруженные нами тромбогенность плазмы крови при исследовании тромбоцитарного гемостаза у лиц пожилого возраста указывает на высокую вероятность развития тромботических осложнений у этой категории больных, и это согласуется с данными литературы.

Ключевые слова: артериальная гипертензия, гипертоническая болезнь, тромбоцитарный гемостаз.
Summary

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The aim of the study was to identify the baseline levels of the platelet hemostasis indices in the middle-aged and the elderly hypertensive patients.

Material and methods. We performed the comparative assessment of status of the platelet hemostasis in 63 middle-aged (group I) and 53 elderly patients (group II) respectively to clarify this issue in our work. Patients of the surveyed groups were comparable in age, sex and related pathology. The control group consisted of 15 patients for every of the surveyed groups (group III the middle-aged and group IV the elderly respectively) matched with basic by age and gender.

Conclusions. Therefore, there is the increase in platelet activity depending on age in the middle-aged and the elderly hypertensive patients that is manifested by adrenaline stimulation most clearly. In addition, the most significant changes are determined in the spontaneous and the adrenaline-induced aggregation namely in amplitude and slope of aggregation in the spontaneous and time of maximal aggregation in the adrenaline-induced aggregation in the patients of older age group compared with the middle-aged patients. The substantial deceleration of time of maximal aggregation during the adrenaline stimulated aggregation in 1,6 times (p<0,001) in the elderly patients confirms the expressed thrombogenicity and sensitiveness to neurohumoral influences too. Thus, the blood plasma thrombogenicity revealed in the study of the platelet hemostasis in the elderly indicates a high probability of thrombotic complications developing in this category of the patients and this is consistent with literature.

Keywords: arterial hypertension, essential hypertension, platelet hemostasis.