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ADRENERGIC INFLUENCES ON ERYTHROCYTE DEFORMABILITY IN RATS

T. Ganchev, N. Negrev, R. Zaharieva

Department of Physiology, Higher Institute of Medicine, Varna

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It is known that erythrocyte deformability is one of their most important properties - to change their configuration when passing through the critical points of microcirculation [2]. The state of spectrin-actin system in erythrocyte membrane plays an important role in this aspect thus enabling the cell to adapt to the intensity of blood flow in the vascular bed. Loss of this property reduces their half-life "in vivo". It is indicated that spectrin really plays an essential role in the formation of covalent-bound parts of erythrocyte membrane. It is supposed that these regions of bilayers can move in the membrane structure and diminish its deformability [5].

A series of pharmacological agents change erythrocyte deformability such as adrenalin, isoprenalin, prostaglandins, pyracetam [4,9] under conditions "in vitro" and "in vivo" as well.

The purpose of the present study is to follow-up these changes setting in this significant functional parameter of erythrocytes under "in vivo" conditions under the influence of adrenergic agents varying in their mechanism of action and influencing on the adrenergic neurone or on alpha- and beta-adrenoreceptors. We proceed mainly from two considerations: the lack of systemic literature data available on this topic, and, second, the established fact that stimulation of the adrenergic system has a positive reflection on erythropoiesis. Data obtained will enable us to throw certain light on the adrenergic dependence of this important property of the single erythrocyte influencing upon rheological peculiarities of circulating blood.

MATERIAL AND METHODS

Our observation covered a total of 169 white male rats of Wistar breed with body weight of 170-180 g. There were 85 control and 84 experimental animals divided into 6 control and 6 experimental groups. Group one - treated with reserpine (R)-Fluka (Switzerland) in a dose of 2 mg/kg b.w. s.c. daily; control animals were injected vehicle only; group two - treated with phenoxybenzamine (PBA)-Koch-Light (England) in a dose of 5 mg/kg b.w. intraperitoneally daily; group three - injected with isoprenaline (IP)-Koch-Light (England) twice in a dose of 5 mg/kg b.w. intraperitoneally; group four - treated with propranolol (PR)-ICI (England) twice in a dose of 5 mg/kg b.w. intraperitoneally; group five - treated with dobutamine (DB)-Lilly Res. (England) twice in a dose of 3 mg/kg b.w. s.c., and group six - treated with salbutamol (SB)-Polfa (Poland) in a dose of 5 mg/kg b.w. s.c. daily. Controls from the rest five groups were treated with physiological saline (PS). Experiment duration was 3 days for all groups.

Erythrocyte deformability was estimated after the method of Tannert-Lux [12] in a modification of Zaharova et al. [2]. The essence of the method consists in the comparison of diameters of a spot from an isotonic buffer (D_1) and of a spot from threefold washed-up erythrocyte suspension with hematocrit of 0,60 (D_2) on filter paper Filtrak 390 (GDR). When erythrocyte spot diameter D_2 is larger D_1/D_2 index will be smaller, i.e. there is an increased erythrocyte deformability. The smaller diameter of erythrocyte spot will increase this index what means a reduced deformability. Representative error of this method according to our data was delta = 0,017, i.e. an index of 3,35 +/- 0,017.

Results were processed by the methods of variation statistics by using of Student-Fisher's t-criterion.

RESULTS AND DISCUSSION

Erythrocyte deformability changes are presented on table 1. It is evident that erythrocyte deformability does not change in R-treated rats although postreserpine adrenergic blockade setting in as results from exhaustion of noradrenalin storages of impounding vesicles [10] suppresses erythropoiesis [1]. Despite the reduction of reticulocyte count and of 59-Fe incorporated into erythrocytes (indexes of inhibited bone-marrow erythropoiesis) it does not influence upon functional properties of the erythrocyte as a whole and on its membrane in particular.

Table 1

Erythrocyte deformability

Treatment	n	Erythrocyte deformability index	Real difference in %
I. Peserpine	15	3,06+\-0,10	+0,32
controls	15	3,07+\-0,06	-
II. Phenoxybenzamine	14	3,78\-0,08	-29,45
controls	15	2,92+\-0,10	p<0,001
III. Isoprenaline	10	3,06+\-0,06	+18,18
controls	10	3,74+\-0,11	p<0,001
IV. Propranolol	15	3,20+\-0,08	-3,90
controls	15	3,08+\-0,09	-
V. Dobutamine	15	3,22+\-0,11	+16,58
controls	15	3,86+\-0,16	p<0,01
VI. Salbutamol	15	3,67+\-0,13	-3,08
controls	15	3,56+\-0,14	-

Data are presented as x +/- Sx. Percentage difference is calculated towards controls. Sign (+) means increase, sign (-) - decrease, n is number of animals. Index increase means erythrocyte deformability reduction (see "Methods").

Non-selective alpha-adrenoceptor blockade by PBA reduces by 29,45 per cent ($p<0,001$) erythrocyte deformability in comparison with that of controls. This finding is contrary to a certain extent to the increased reticulocyte number [7] as far as it is known that metabolically active cells possess better functional characteristics. It seems possible that deformability reduction is due not only to alpha-adrenergic receptor blockade and noradrenalin elevation but also to the extrareceptor PBA action proved concerning other systems [14]. It is known that adrenalin diminishes this erythrocyte property [4].

Analysis of data obtained after non-selective and selective influences on beta-adrenoceptors demonstrates that IP stimulates erythrocyte deformability by 18,18 per cent ($p<0,001$) while PR (a non-selective beta-blocker) does not change significantly this function. This suggests a definite beta-adrenergic dependence of this functional erythrocytic property. The fact that treatment with DB, a $beta_1$-adrenoceptor stimulant, almost repeats IP effect confirms the idea of $beta_1$-adrenergic dependence of the property of erythrocyte deformability. Precizing of an eventual beta2-

receptor participation in this erythrocyte function does not show such a dependence (table 1-VI).

Stimulating effect of IP and DB on erythrocyte deformability is in accordance with rejuvenation of erythrocyte population (enhanced reticulocyte count)[1] and contrary to data of other authors [4] obtained in an "in vitro" system in a dose of IP of 10^{-7} M. As far as it is known that erythrocyte deformability depends on age, metabolic cellular state and viscose-elastic properties of erythrocyte membrane [3] our data are confirmed by the known facts concerning stimulation of cellular metabolic processes after treatment with IP and DB [6,11,13].It is probable that the presence of younger erythrocytes with enhanced metabolic processes as result from beta-adrenostimulation determines the changed into a positive direction erythrocyte deformability.

We can conclude that suppression of functions of the neuronal link of the adrenergic mediator unit does not change erythrocyte deformability. This essential erythrocyte function depends on the functional state of receptor components of the adrenergic system: it is inhibited in case of alpha1,2-adrenoceptor blockades which is probably due to noradrenalin enhancement, and it is elevated in case of beta1-adrenostimulation which possibly depends on the stimulated cellular metabolism, too.

The aforementioned changes should be considered with a view to their influence upon blood rheological properties especially when certain anomalies are present.

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АДРЕНЕРГИЧЕСКИЕ ВЛИЯНИЯ НА ЭРИТРОЦИТАРНУЮ ДЕФОРМАБИЛЬНОСТЬ У КРЫС

Т. Ганчев, Н. Негрев, Р. Захариева

РЕЗЮМЕ

Изучается влияние различных механизмов действия адренеергических агентов на эритроцитарную деформабильность в условиях "ин виво".

Устанавливается, что блокада неврального звена адренергической медиаторной единицы резерпином не вызывает изменения эритроцитной деформабильности, в то время как феноксибензамин, неселективный альфа-адреноблокер, значительно ее понижает (29,45 %, $p < 0,001$). Неселективная бета-адренорецепторная стимуляция изопреналином повышает эритроцитную деформабильность на 18,18 % ($p < 0,001$), а блокада этих рецепторов пропранололом не приводит к существенным изменениям. Добутамин как бета1-адренорецепторный стимулянт повторяет стимулирующий эффект изопреналина.

В заключение можно принять утверждение о том, что эритроцитная деформабильность у крыс выявляет определенную зависимость от функционального состояния адренергических рецепторов и связанных с этим обменных процессов. Она заторможена при блокаде альфа1,2-адренорецепторов и повышена при бета1-адреностимуляции.