INFLUENCE OF INDOMETHACIN ON THE ACTIVITY OF ERYTHROCYTE GLUCOSE-6-PHOSPHATE DEHYDROGENASE AND CATALASE IN RATS

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It is well-known that prostaglandins (PG) play a role in the regulation of numerous physiological processes (4, 9). PG deficit after their synthesis inhibition by indomethacin (IM) often leads to functional disorders (12).

The influence of PG inhibition upon the activity of erythrocyte glucose-6-phosphate dehydrogenase (G-6-PD) and catalase presents a definite interest, indeed. It is known that both enzymes play an important role in the maintenance of erythrocyte integrity by ensuring the stability of restored glutathione and by preventing hemoglobin oxidation (2, 14), therefore, they are directly related to erythrocyte homeostasis maintenance.

A lot of hormonal, nutritional and other factors modulate G-6-PD activity (7, 13).

Proceeding from the data about the influence of some PGs on deformation ability of erythrocyte membrane, fragility and swelling of erythrocyte and on hemolysis (5) as well as about IM inhibitory effects on some enzymes (15) we set us the task of investigating the activity of erythrocyte G-6-PD and catalase after IM treatment; still more, in previous studies we have established erythrocyte count reduction and reticulocytosis (3).

Material and methods

Our observation was made on 40 white female rats of Wistar breed with b. w. 170—180 g. After assessing of the initial rates of erythrocytes and both enzymes the animals were divided into a control and experimental groups. Experimental animals were intraperitoneally administered IM injections twice daily of 3 mg/kg b. w. for 3 days while control ones — only solvent at the same volume (twin+alcohol diluted with saline). At the end of the experiment — on the 4th day — the erythrocytes and enzyme activity of G-6-PD and catalase were determined, too. G-6-PD activity was assessed by using of test-reagents from the firm Böhringer (GFR) and catalase one — after the method of Bach and Zubkova (cited after 1). G-6-PD activity was expressed in mE.10^9/erythrocytes but catalase one by means of the so-called catalase index (1). The data were processed by the methods of variation statistics.

Results and discussion

The data presented on table 1 demonstrate that three-day treatment with IM increases statistically significantly erythrocyte G-6-PD by 17.48 per cent ($p<0.05$) in comparison with initial rates while enzyme activity decreases by 19.44 per cent in control rats ($p<0.05$). Erythrocyte count decreases significantly (by 34.78 per cent — $p<0.001$) at the end of the trial in experimental animals while erythrocytes rise in number by 2.56 per cent in control ones. There are insignificant changes of catalase index.

Table 1

Erythrocyte catalase and G-6-PD after indomethacin treatment (dosis of 2×3.0 mg/kg)

Indexes	n	Initial levels	End of the experiment					
			n	experimental	% difference	n	control	% difference
G-6-PD activity (mE . 10^9 Er)	10	99.25±4.81	10	116.6±6.41	+17.48 p<0.05	10	83.09±3.14	−19.44 p<0.05
Catalase index	8	0.966±0.073	8	0.912±0.049	−5.92 p>0.05	8	0.994±0.061	+2.89 p>0.05
Erythrocytes (x 10^{12}/l)	22	7.447±0.264	20	5.525±0.240	−34.78 p<0.001	20	7.638±0.141	+2.56 p>0.05

Data are given as $\bar{x}$ and $S\bar{x}$. Percentage difference is calculated to initial values.

On the basis of our data we assume that PG deficit does not reflect on erythrocyte count by the way of G-6-PD and catalase commitment. Still more, erythrocyte G-6-PD is proved to be increased by 17.48 per cent ($p<0.05$) in comparison to the initial levels and by 40,32 per cent as compared with the control ones at the end of the experiment. In our opinion, this can be due to the increased reticulocyte count. As far as it is known, enzyme reduces during erythrocyte ageing (10), still more, newly-formed erythrocyte even in individuals with enzyme deficit possess practically normal erythrocyte G-6-PD activity.

In previous investigations performed in our Department of Physiology a considerable relative and absolute reticulocyte count increase after 3-day long treatment with IM has been established (3). In our opinion, erythrocyte population rejuvenation can be one of the reasons for higher erythrocyte G-6-PD activity of IM treated animals. However, G-6-PD activity reduction in control rats remains unclear yet.

The lack of significant changes of the catalase index after IM treatment excludes almost completely the influence upon catalase in the case of PG deficit. It is possible that in this respect a role is played by the proved fact that IM reacts with molecular oxygen (6) and thus prevents cell membrane destruction. By this way, catalase system dispenses with functional realization and probably because of that it does not change essentially its activity.

However, it is noteworthy that erythrocyte count decreases after IM treatment. IM stabilizes erythrocyte membrane and can in high concentrations cause hemolysis and thus induce a biphasic effect — erythrocyte stability followed by lysis (11).

Reduced erythrocyte number allows us to assume that at that IM dosis probably certain hemolytic changes occur that can stimulate erythropoiesis.

It is possble that PG deficit influences upon ineffective erythropoiesis and the augmentation of the latter can be an additional reason for the lower erythrocyte count. This presumption is based on the facts that PGs not only increase erythropoietin biogenesis but also stimulate directly erythroid cell development and maturation (8). Probably, PG lack could disturb these processes. However, additional investigations are required to prove this assumption.

We can draw the following conclusions:

1. Three-day long IM treatment increases erythrocyte G-6-PD activity but does not change catalase index. It also reduces erythrocyte number.

2. PG deficit does not influence upon erythrocyte count by means of G-6-PD and catalase commitment.

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ВЛИЯНИЕ ИНДОМЕТАЦИНА НА ЭРИТРОЦИТНУЮ Г-6-ФД И НА КАТАЛАЗУ У КРЫС

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РЕЗЮМЕ

Исследовано влияние простогландиновой ингибиции индометацином (2 по 3 мг/кг в течение трех дней) на эритроцитную каталазу и Г-6-ФД. Значение обоих энзимов для поддержания целости эритроцитов хорошо известна. Устанавливается статистически значимое увеличение Г-6-ФД в конце эксперимента по отношению к исходному уровню у животных, третированных индометацином; при этом каталазный индекс не изменяется существенно. Одна из возможных причин более высокой Г-6-ФД в эритроцитах крыс, третированных индометацином, объясняется наблюдаемым здесь ретикулоцитозом. Известно, чть молодые эритроциты являются носителями большего количества Г-6-ФД. Можно предположить, что недостаток простогландинов не отражается на число эритроцитов таким способом, который вовлекал бы в этот процесс Г-6-ФД и каталазу.