PLASMA THROMBOCYTOPOIETIN ACTIVITY IN PATIENTS WITH CHANGED THROMBOCYTE COUNT

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It is know that thrombocytopoietin is a specific humoral thrombocytopoiesis regulator (8). It is supposed that it presents a glucoproteide (4) and it is synthesized in kidney (9). Concerning its place and mechanism of action it is known that it stimulates the development of committed precursors of megakaryocytes and of megakaryocytes themselves as well (7, 12). There are single investigations of plasma thrombocytopoietin activity (PTA) in healthy persons and patients with different blood diseases (1, 5).

The aim of the present study is to follow-up PTA in patients with changed thrombocyte count.

Material and Methods

We determined PTA in 22 females of which 10 healthy controls and 12 patients with the following diseases: 3 – with idiopathic thrombocytopenic purpura (ITP), 8 – with symptomatic thrombocytopenia (ST) and one with essential thrombocytemia (ET). Plasma was injected to a total of 112 male mice (72 experimental and 40 control). PTA level was evaluated according to changes of ^{75}selenomethionine (^{75}Se-M) incorporation in newly-formed thrombocytes as well as to thrombocyte count in peripheral blood of recipient mice. The percentage of the incorporated ^{75}Se-M was determined after widely used radioisotope Penington's method (10) in our modification. To this purpose we used as recipients instead of C_{57}-non-thoroughbred white male mice only mice with initial thrombocyte count between 200 and 380.10^9/l. Plasma was injected subcutaneously at dosis 1 ml on two consecutive days. All the mice were intraperioneally injected 2 Ci ^{75}Se-M each one hour after the second injection. 72 hours after that we aspirated by means of cardiac puncture 0.5 ml blood from all the mice each under ether narcosis in order to determine the percentage of isotope incorporated. We apprehended to determine ^{75}Se-M incorporation instead on the 24th hour (as proposed by Penington) on the 72nd one because this period coincided with the peak of thrombocyte count increase and most manifested changes of isotope incorporation as well. Further sample processing and calculation of ^{75}Se-M incorporation into thrombocytes was carried out completely after Penington's method.

Initial thrombocyte levels were determined with all the mice at the end of experiment after Feissly and Lüdin (cited after 3), too.

All the animals were divided into 4 groups, namely: 1st group – injected with plasma from ITP patients; 2nd – with plasma from ST ones; 3rd – with plasma from ET patients, and 4th – with plasma from healthy individuals (controls).

Data obtained were processed by the methods of variation analysis.

Results and Discussion

On fig. 1 and 2 one can see the data about PTA determined by the percentage of ^{75}Se-M incorporated in newly-formed thrombocytes as well as thrombocyte count changes. It has to be noted that plasma from ITP and ST patients does not cause one and the same kind of changes in the parameters studied in all the patients of one and the same group. More concretely, plasma of one female ITP patient causes a strong isotope incorporation increase (with 46.37 per cent, $p < 0.025$) and thrombocyte count one (with 32.96 per cent, $p < 0.05$) although there is a normal thrombocyte count in this patient. However, plasma injection from the rest two patients of this group reduces ^{75}Se-M incorporation with 73.41 per cent ($p < 0.001$) and thrombocyte count with 42.50 per cent ($p < 0.001$) in recipient mice. Thrombocyte number is below 80.10^9/l in both patients.

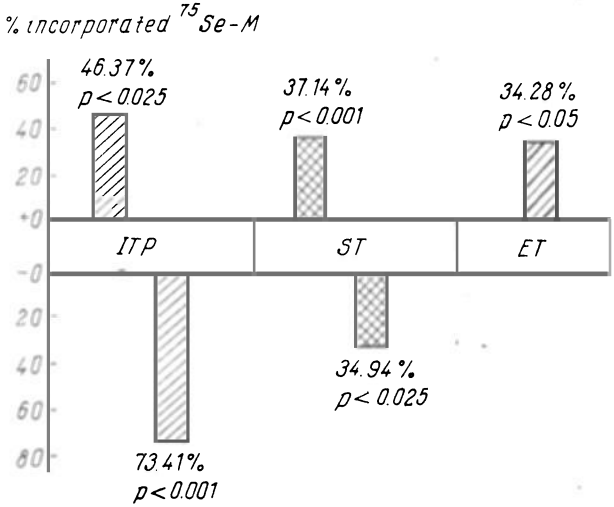

Fig. 1. PTA determined by the percentage of ^{75}-Se-M incorporated in newly-formed thrombocytes of recipient mouse. Percentage deviation is determined in relation to the control level accepted for "0". Sign (+) indicates an increase and sign (-) a decrease.

ST patients show also contrary results. Plasma induces isotope incorporation increase in 62.50 per cent of them with 37.14 per cent ($p < 0.001$) and thrombocyte count one with 45.26 per cent ($p < 0.001$). There is a considerable reduction in the rest patients (36.50 per cent) of ^{75}Se-M incorporation (with 34.94 per cent. $p < 0.025$) and of thrombocyte count (with 41.09 per cent, $p < 0.001$) as well. The mean thrombocyte number of the patients of the whole group is below 50.10^9/l.

Thrombocytemic plasma injection is followed by ^{75}Se-M incorporation increase in newly formed thrombocytes of recipient mice with 34.28 per cent ($p < 0.05$) and by thrombocyte count one with 35.66 per cent ($p < 0.025$). Patient's thrombocyte number is between 700 and 1000.10^9/l.

In our opinion, increased PTA of some ITP patients and ST ones results from a realized negative feed-back mechanism induced by their thrombocytopenia (2). Besides we accept that strongly reduced PTA of the rest patients with the same diseases provides an indirect evidence for probably increased plasma inhibitory properties. This fact coincides with data reported by

other authors (1, 6). It can not be excluded that in this case reduced PTA is due to insufficient thrombocytopoietin production.

Our data concerning PTA increase in ET cases could be explained to a certain extent by the present evidences for an increased thrombocytopoietin activity in chronic myeloid leukemia and in other diseases as well (11). According to our opinion, that is confirmation of the idea that production of specific humoral thrombocytopoiesis regulator is not regulated only by circulating thrombocyte number but also by bone-marrow megakaryocyte count and other factors as well (2).

Having in mind that ^{75}Se-M incorporation and thrombocyte count are basic indexes for PTA determination (1, 12) our results obtained allow us to draw the following conclusions:

1. ITP, ST, and ET are diseases accompanied by contrary changes of thrombocytopoietin activity;

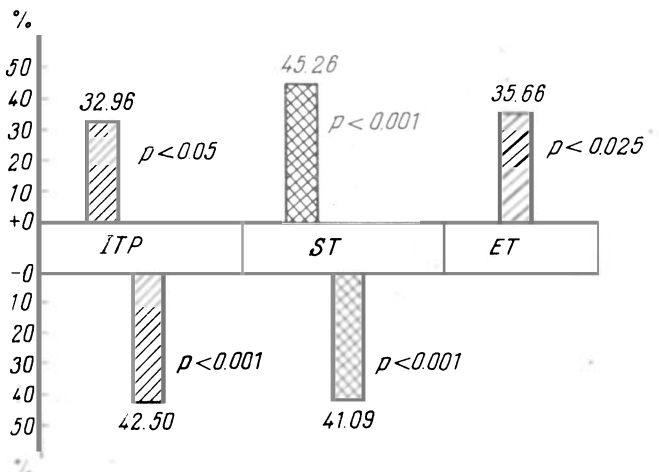

Fig. 2. PTA determined by thrombocyte count changes of recipient mouse. Values are presented as percentage deviation in relation to the control level accepted for "0". Sign (+) indicates an increase and sign (–) a decrease.

2. These contrary changes of thrombocytopoietin activity allow the suggestion that pathogenetic mechanisms different to a great extent are involved in these diseases.

We consider PTA determination a possible additional differential-diagnostic criterion at this stage, mainly when patients with ET and to a lower extent when ST patient are concerned.

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ТРОМБОЦИТОПОЭТИНОВАЯ АКТИВНОСТЬ ПЛАЗМЫ У БОЛЬНЫХ С ИЗМЕНЕНИЕМ ЧИСЛА ТРОМБОЦИТОВ

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РЕЗЮМЕ

Исследована тромбоцитопоэтиновая активность плазмы у больных с изменением числа тромбоцитов по модифицированному авторами радиоизотопному методу Penington (1970). Тромбоцитопоэтиновая активность плазмы устанавливалась посредством процента включенного 75 селенометионина в новообразованные тромбоциты и при учете числа тромбоцитов у тест-мышей под влиянием испытуемой плазмы. При эссенциальной тромбоцитемии устанавливается значимое повышение тромбоцитопоэтиновой активности. У некоторых из больных с идеопатической тромбоцитопенической пурпурой и симптоматической тромбоцитопенией устанавливается достоверное увеличение тромбоцитопоэтиновой активности плазмы, а у остальных – достоверное уменьшение. Возможно использование этого показателя в качестве дополнительного дифференциально-диагностического критерия.