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MELATONIN ACTIVATES THROMBOCYTOPOIESIS IN RATS

N. Negrev, Yu. Nyagolov, Z. Dimitrov
Department of Physiology, Varna

Melation (M) is a pineal hormone attracting attention with its endocrine and antineoplastic effects. It penetrates all biomembranes, easily reaches cell nucleus and may influence directly on mitotic activity.

Recently it is proven that inhibition of M synthesis depresses megakaryocytopoiesis. Having in mind all this we formulated our aim to study M effects on thrombocytopoiesis and plasma thrombocytopoietin activity (TPA) in rats.

The trial covered 60 white male Wistar rats and 30 male mice of Swiss breed. Rats were divided into 2 main groups. Effects of M on some basic parameters of thrombocytopoiesis - thrombocyte count, percentage of ^{75}Selenomethionine (^{75}Se-M) incorporation in newly-formed platelets and bone marrow megakaryocytes (MKC) was investigated in the first main group, divided into two subgroups. Melatonin (Merck, Germany) was applied in a dose 2 mg/kg b.m. twice daily, s.c. for 3 consecutive days at 12 h dark/light exposure. TPA of the 2nd main group of rats was determined after Penington's method - our modification. TPA level was estimated according to the shifts of platelet count and percentage of isotope incorporation in recipient mice. Data were processed by the methods of variation analysis. Influence of M on thrombocytopoiesis is shown on fig.1-ab. It is obvious that M increases significantly not only thrombocyte count (fig.1-a) - by 80,23% ($p<0.001$) but also percentage of

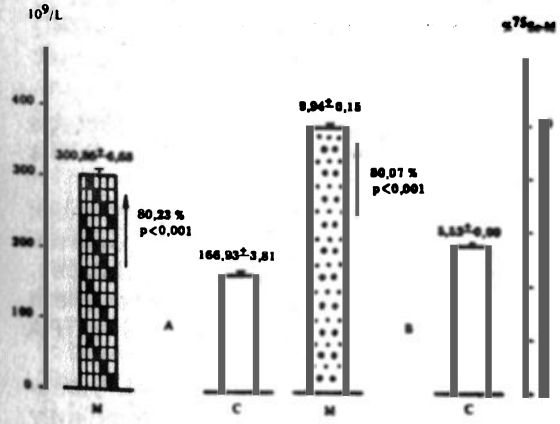

Fig. 1-a: Changes in thrombocyte count; Fig. 1-b: Percentage of ^{75}Se-M incorporation in newly-formed thrombocytes

^{75}Se-M incorporation in newly-formed platelets (fig.1-b) - by 80,07% ($p < 0,001$).

Bone marrow MKC show significant increase not only of their total count by 83,73% ($p < 0,001$) but also of all cell stages: I - by 61,66% ($p < 0,001$); II - by 74,35% ($p < 0,001$); III - by 118,18% ($p < 0,001$) and IV stage - by 150,00% ($p < 0,001$). TPA obtained from M treated donors is illustrated on fig.2-ab. It is evident that both thrombocyte count (fig.2-a) and percentage of ^{75}Se-M incorporation (fig.2-b) are increased by 120,75% ($p < 0,001$) and 70,12% ($p < 0,001$), respectively. Data analysis shows that M elevates significantly all examined parameters of thrombocytopoiesis - thrombocyte count, percentage of ^{75}Se-M incorporation (fig.1-ab) and bone marrow MKC and this is a valid criterion of its stimulation.

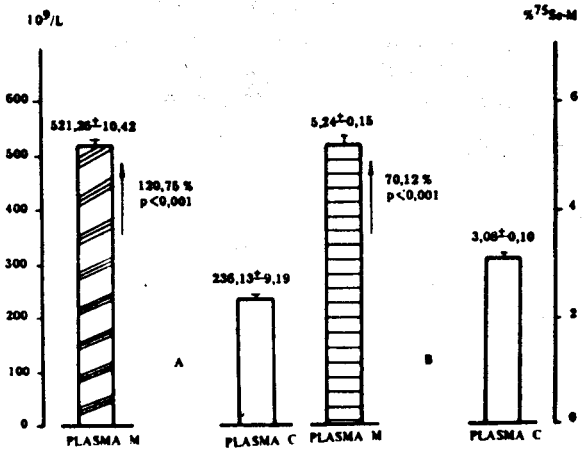

Fig. 2-a: Changes in thrombocyte count; Fig. 2-b: Percentage of ^{75}Se-M incorporation in newly-formed thrombocytes in recipient-mice. Plasma M - plasma of M treated donors; Plasma C - controls

Having in mind that the total count of MKC and stages I and II characterise the level of proliferation and stages III and IV - diferentiation of these cells, it is obvious that M activates these processes. The increase of platelet count and ^{75}Se-M incorporation in recipient mice (fig.2-ab) by plasma from M treated donors shows higher TPA level.

For this reason it could be assumed that most probably M stimulated thrombocytopoiesis is predominantly a result of a significantly enhanced biosynthesis of the specific humoral regulator of this process - thrombocytopoietin.