IS ASPARTIC ACID A REGULATOR OF HEMATOPOIESIS?

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UDC 615.31:547.466.63/.015.4:612.119

KEY WORDS: aspartic acid; bone marrow

Recent years have seen an upsurge of interest in the study of endogenous regulators of hematopoiesis. Amino acids can also claim to play the role of regulators of this kind. It has been shown that some of them (aspartic and glutamic acids, for example) can accelerate recovery of hematopoietic tissue after posthemorrhagic anemia [6]. However, the mechanisms of the regulatory effects of this group of metabolites on hematopoiesis are by no means completely clear.

The aim of this investigation was to study the action of aspartic acid on committed precursor cells of myelopoiesis.

EXPERIMENTAL METHOD

Experiments were carried out on male Wistar rats weighing 120-150 g, kept under ordinary animal house conditions. The animals were given intramuscular injections of DL-aspartic acid (from "Reanal," Hungary) in a dose of 100 μg/kg daily for 5 days. Control animals were given the corresponding volume of physiological saline. Before the experiment and 3 days after the last injection, the usual hematologic parameters were studied (red and white cell counts, hemoglobin concentration, number of myelokaryocytes in the femur, and calculation of the leukocyte formula and myelogram). To assess the state of committed precursor cells of myelopoiesis, bone marrow was cultured in diffusion chambers (DC) [5], as the writers described previously [2]. The experimental results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

Injection of aspartic acid caused no changes in the peripheral blood of the animals, and there were no significant abnormalities of bone marrow morphology, as reflected in the myelogram. To evaluate the state of the precursor cells, bone marrow cultures were set up in DC. Colony-forming units under those conditions have been shown to be analogous to precursors found in agar cultures [7]. Analysis of the cloning efficiency of the hematopoietic cells gave the following results (Table 1). The composition of the earliest (cluster- and colony-forming units of granulocyto- and monocytopoiesis (ClFU/CFU-GMdc) had a tendency to be inhibited. The level of monocyte/macrophage precursor cells remained unchanged after injection of aspartic acid. Meanwhile the cloning efficiency of the granulocytic precursors was increased by 24%. It can be postulated that the fall in the level of ClFU/CFU-GMdc took place through stimulation of the differentiation of these cells in the granulocytic direction. A similar effect was demonstrated by the writers previously for tactivin also [2].

Ekaterinburg Branch of the All-Union Kurgan "Restorative Traumatology and Orthopedics" Research Center. Presented by Academician of the Russian Academy of Medical Sciences E. D. Gol'dberg.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 114, No. 9, pp. 293-294, September, 1992. Original article submitted March 13, 1992.

0007-4888/92/0009-1323$12.50

TABLE 1. Cloning Efficiency of Bone Marrow Cells in Response to Injection of Aspartic Acid (10^5 cells)

Type of cluster and colony	Control	Aspartic acid
ClFU/CFU-GMdc	53,4±2,0	36,7±2,5*
ClFU/CFU-Mdc	328,4±14,3	301,2±17,8
ClFU/CFU-Gdc	253,4±10,1	314,9±13,9
ClFU/CFU-Fdc	74,1±4,1	100,4±4,0*

Legend. *$p < 0.05$.

The role of aspartic acid in the regulation of hematopoiesis is probably not confined to its action on myelopoiesis. For example, incorporation of this amino acid into the combination treatment of iron-deficiency anemia led to optimization of restoration of the erythron [1]. It must be emphasized that the effect of aspartic acid is manifested when it is used in quite low concentrations (10^{-7} M). In this dose it can change the content of cyclic nucleotides and modify DNA synthesis in hematopoietic and thymic cells [3]. During bone culture in DC clusters and colonies of fibroblastlike cells (ClFU/CFU-Fdc) also appear [4, 5]. These are probably precursors of stromal mechanocytes, which define the hematopoiesis-inducing microenvironment and the osteogenic powers of the bone marrow [8]. It is interesting to note that under the influence of aspartic acid the cloning efficiency of the ClFU/CFU-Fdc was increased. It therefore seems possible that aspartic acid may act on hematopoiesis through the hematopoiesis-inducing microenvirnoment. The results are also evidence that this metabolite possesses definite osteogenesis-stimulating properties, at least at the level of osteogenic precursor cells.

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