L-Ornithine Aspartate – a Rationale for Its Use in Combination with Chemotherapy, Radiation, and Hyperthermia in Oncology

L-ornithine aspartate has been widely used in hepatology for its well-known effects on lowering blood ammonia concentrations by increasing urea synthesis [1]. Moreover, accumulating evidence suggests that L-ornithine aspartate restores muscle protein synthesis, an effect which can be exploited in patients suffering from cancer or HIV infections [2].

Other studies showed significant improvements of clinical values and liver function in patients undergoing radiation therapy receiving L-ornithine aspartate [3]. Furthermore, L-ornithine aspartate increased the tolerance towards cytostatic drugs in patients receiving chemotherapy [4]. In this study with 157 patients the chemotherapy-induced increase in liver transaminases could be limited, whereas the production of cholinesterase as parameter for liver function could be increased in patients receiving L-ornithine aspartate parallel to chemotherapy with antimetabolites, platinum derivatives, alkylating agents, anthracyclines, and mitosis-inhibiting substances. Chemotherapy is known to induce transient states of hyperammonemia [5].

The hypothesis is put forth that L-ornithine aspartate also may have a protective effect on proliferation kinetics of tumor cells. Recently, ammonium cholate has been shown to accelerate the growth of the MCF-7 cell line in vitro, an effect which may be blocked by the administration of L-ornithine aspartate [6]. Ammonia has been shown to be associated with increased metastasis [7] as well as anorexia and showed a rise in activity, following the ad-

ministration of intravenous injections of ^{13}N -labelled ammonia in different tumor types. Ammonia also is involved in the regulation of protein turnover in tumor cells. L-asparagine synthetase has been suggested as a marker for metastases. Moreover, in multiple myeloma growth has been allied with hyperammonemia [8]. This hyperammonemia could be demonstrated not to be due to liver dysfunction but to increased production of ammonia by myeloma cells. Furthermore, progressive malignant growth in tumor-bearing animals correlated with increased ammoniogenesis and increased glutamine uptake in other tumor tissues and the liver [9].

The hyperthermic treatment of cancer also induces high levels of ammonia in the tumor environment [10], indicating increased proteolysis reflected in the rise in urea.

Taken together these findings indicate that conventional cancer treatments such as chemotherapy and radiation together with hyperthermia are associated with a rise in the levels of ammonia both in the blood stream and the tumor microenvironment. On the other side, ammonia may function as a mediator for local tumor growth and metastasis. Hence, further experimental and clinical studies are indicated to investigate the potential of the administration of L-ornithine aspartate as an adjunct to standard cancer treatment regimens.

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