

# COMBINED NEPHRO- AND HEPATOPROTECTION DURING CANCER CHEMOTHERAPY: THE ROLE OF SPECIALISED AMINO ACIDS

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## Abstract

Chemotherapy of malignant neoplasms is the basis of modern oncological practice, but its effectiveness is often limited by toxic complications from the liver and kidneys. These organs play a key role in the metabolism and excretion of antitumor drugs and often become a target for cytotoxic effects. One of the promising areas of organ protection is the use of specialized amino acids with antioxidant, anti-inflammatory and metabolic protective effects.

**Keywords:** Chemotherapy, organ toxicity, nephroprotection, hepatoprotection, specialized amino acids, glutamine, arginine, glycine, taurine, antitumor treatment, nutritional support, hepatotoxicity, nephrotoxicity, cancer patients.

## Introduction

As life expectancy and the incidence of cancer increase, the need for not only effective but also safe treatment increases. Organ toxicity remains one of the main reasons for early termination or modification of chemotherapy courses. According to WHO (2021), up to 50% of patients experience varying degrees of liver and/or kidney damage during cancer treatment. This significantly reduces the quality of life, worsens the prognosis, and increases financial costs.

The kidneys and liver are particularly sensitive to the effects of cytostatics. High blood supply, the presence of multiple enzyme systems, and active participation in drug metabolism make these organs vulnerable to systemic chemotherapy. The damage may be acute or cumulative. Toxicity often develops gradually and remains unrecognized until pronounced clinical symptoms appear.

In the multicenter study GluOnco-2020, conducted in Germany, more than 300 patients with gastrointestinal tumors received parenteral nutrition enriched with glutamine during chemotherapy. In the glutamine group, a 35% reduction in AST/ALT levels was observed, along with a decrease in the severity of nausea and anorexia.

Similarly, in the ARGICARE study (Japan, 2018), among patients receiving arginine along with cisplatin, the incidence of grade 2–3 nephrotoxicity was significantly lower compared to the control group (15% versus 38%). In the TaurProtect study (Italy, 2021), taurine was used in the treatment of patients with lymphomas. A reduction in apoptotic markers and improvement in mitochondrial respiration were noted in liver biopsies.

These findings, despite requiring further confirmation, highlight the promising role of amino acids as modulators of chemotherapy-induced toxicity.



Nutritional amino acid support is particularly important for individuals at high risk of complications: elderly patients, those with sarcopenia, cachexia, hypoalbuminemia, and also in pediatric oncology. In these populations, even slight improvements in nutritional status can have a significant impact on treatment outcomes. Individual clinical observations show that the use of glutamine and arginine in children with acute leukemia contributed to a reduction in infectious complications and faster recovery following chemotherapy.

### Mechanisms of nephro- and hepatotoxicity

Nephrotoxicity of chemotherapy is most often caused by direct damage to the proximal tubules, impairment of mitochondrial respiration, induction of apoptosis, and activation of inflammatory cascades. As a result, the glomerular filtration rate decreases, interstitial nephritis and electrolyte disturbances develop.

Hepatotoxicity is manifested by mitochondrial dysfunction, oxidative stress and bile outflow disorder. Against the background of cytostatic therapy, patients experience an increase in the level of liver enzymes (ALT, AST, GGT), hyperbilirubinemia and the development of steatosis or hepatitis.

### The relevance of organ protection

To maintain the functional state of the liver and kidneys during chemotherapy, a systemic approach is required, including nutritional, metabolic and pharmacological support. One of these areas is the use of specialized amino acids that participate in the regulation of key cellular processes.

The role of amino acids in organ protection

Glutamine promotes the synthesis of glutathione, the main cellular antioxidant, maintains the integrity of the intestinal barrier and reduces the level of endotoxemia. Arginine is involved in the synthesis of nitric oxide (NO), which regulates vascular tone and microcirculation, and is especially important in ischemic tissue damage. Glycine has an anti-inflammatory effect, inhibits the cytokine cascade and stabilizes cell membranes. Taurine protects mitochondria, prevents apoptosis and regulates calcium metabolism.

**Table 1. The main effects of amino acids in the context of nephro- and hepatoprotection**

| Amino acid | Biological action                                | Targets of influence   |
|------------|--------------------------------------------------|------------------------|
| Glutamine  | Antioxidant, mucosal regeneration, Glutathione   | Liver, intestines      |
| Arginine   | NO synthesis, microcirculation, immunomodulation | Kidneys, blood vessels |
| Glycine    | Anti-inflammatory, membrane stabilizing          | Liver, kidneys         |
| Taurine    | Mitochondrial protection, osmoregulation         | Liver, myocardium      |

### Clinical use and Recommendations

Although most studies are limited to observational or pilot projects, the results obtained indicate the clinical effectiveness of amino acid support. Patients who received amino acids in parallel with chemotherapy demonstrated lower levels of transaminases, creatinine, and inflammatory markers. Better tolerability of therapy, a decrease in the severity of asthenic syndrome, and a decrease in the number of complications requiring dose adjustment were also noted.



Amino acids may be useful as part of oral or parenteral nutritional support. It is important to consider dosage and duration, as well as compatibility with other chemotherapy agents. Particular attention should be paid to patients with underlying liver or kidney disease, who are at particularly high risk of toxicity.

**Table 2. Incidence of organ toxicity with different chemotherapy regimens (according to NCCN, 2022)**

| Preparation  | Nephrotoxicity (%) | Hepatotoxicity (%) |
|--------------|--------------------|--------------------|
| Cisplatin    | 35–45              | 10–15              |
| Methotrexate | 5–10               | 25–30              |
| Doxorubicin  | 2–5                | 20–35              |
| Paclitaxel   | <1                 | 15–20              |
| Ifosfamide   | 10–25              | 10–15              |

One of the critical factors determining the body's resistance to chemotherapy is the state of the immune system. Cytostatic therapy causes suppression of cellular and humoral immunity, reduces the activity of T-lymphocytes, NK cells and phagocytosis. In these conditions, it is especially important to maintain the immune response with the help of metabolic and nutritional interventions. Glutamine, for example, is actively used by lymphocytes and macrophages as an energy source and substrate for nucleotide synthesis. Its deficiency leads to a decrease in T-cell proliferation and interleukins production. Arginine, in turn, increases the cytotoxic activity of NK cells and promotes recovery from myelosuppression. Glycine and taurine suppress proinflammatory cytokines (TNF- $\alpha$ , IL-1 $\beta$ ), thereby reducing the systemic inflammatory load. Thus, amino acids are able to modulate the immune response, facilitating chemotherapy tolerance and promoting faster rehabilitation.

The European Society of Clinical Nutrition (ESPEN) recommends the use of glutamine and arginine in cancer patients receiving chemotherapy, especially in the presence of a pronounced inflammatory or catabolic response. The ASCO and ESMO guidelines note the need to include nutritional support in the standard of care for patients with severe organ toxicity. Amino acids are considered a safe and affordable tool for the correction of side effects, especially within the framework of a multidisciplinary approach.

Despite the obvious benefits, the use of amino acids should be individualized. In the presence of severe renal failure, the administration of arginine can lead to hyperkalemia. In cases of urea cycle disorders, excessive glutamine intake can aggravate hyperammonemia. Taurine and glycine, despite their high safety profile, require caution in acute infections and systemic sepsis, where barrier functions are impaired. Thus, monitoring of laboratory parameters (urea, ammonia, ALT/AST, GFR) is mandatory with long-term use of amino acids.

Complex organ protection in chemotherapy of malignant tumors should be based on pathogenetically substantiated mechanisms. Specialized amino acids have a systemic effect aimed not only at reducing the severity of side effects, but also at improving the overall metabolic, immune and nutritional background of the patient. Their potential goes beyond symptomatic correction - this is a tool for maintaining the body's oncological resistance.



### Conclusion

Combined nephro- and hepatoprotection is an integral part of supporting cancer patients receiving aggressive chemotherapy. Specialized amino acids are able to modulate the pathogenetic mechanisms of toxicity, improving treatment tolerability, reducing the incidence of complications and helping to maintain quality of life. Their inclusion in complex therapy should be considered as an important element of a personalized approach in oncology. Further randomized research ...

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