

Thymus

4.1. Introduction

Currently, many biological response modifiers (BRM) have been identified. Examples are interleukins and cytokines. Also, the thymus plays an important role in the overall immunomodulation. One could say that the thymus is the brain of the immune system.

In 1560, Andrea Vesalius made a first description of the thymus but it took almost four centuries until in 1936, Hammar suspected that the thymus plays an important role in the immune system after birth. Today, the thymus is considered to have a key function in the development and function of the immune system and the biological defense mechanisms against cancer and chronically infected cells.

4.2. Thymus and its effects on the immune system and lymphatic tissue

Thymic tissue is responsible for selected transformation of precursor cells into different T-cells, i.e. helper (CD4+) T-lymphocytes, which aid in the differentiation of other lymphocytes, killer cells (NK cells), cytotoxic cells, and suppressor (CD8+) T-lymphocytes (1-3). Having been released into the blood stream, intestinal and peripheral tissues, the lymphocytes are characterized by well-defined antigens or activation markers on their surface. Their activities are extra thymic.

The thymus is directly innervated, thus making its role in the interaction between the immune system and the neuroendocrinal systems understandable.

In newborn mice, thymectomy causes a significant change and decrease of lymphatic tissue and a hypofunction of the Reticulo-Endothelial System (RES). In addition, the maturation of T-dependent lymphocytes is severely hampered, or even made impossible.

The thymus produces a variety of substances, including thymus-specific enzymes, proteins, peptides and steroids, which all have both central and peripheral activities. Thymus peptides have a molecular weight of about 300-100,000 Dalton. Up to now, some peptide fractions have been isolated and identified, mainly from the thymus glands of young calves or foetus.

Thymus peptides also play an important role in the development, maturation, differentiation and activation of T-lymphocytes. In addition, thymus peptides enhance proliferation of precursors of lymphoid cells in bone marrow, and their maturation into T-lymphocytes.[i],[ii],[iii]

4.3. Thymus and its effects on haematopoietic factors

There is a delicate interaction between the thymus and the active bone marrow. There is a direct and positive correlation between hypofunction of the thymus and the decline of production of colony stimulating factors (CSF). Therefore, in cases where there is insufficient production of CSF, the therapeutic application of thymus peptides can be helpful.

4.4. Clinical applications of thymus peptides

In a prospective randomized study in patients with malignant melanoma, thymus peptides caused an increased tumor-free period, a longer survival time and increased quality of life.[iv]

In a prospective, randomized study in intermediate- and high-grade Non-Hodgkins lymphoma, patients were treated with thymus peptides in addition to standard chemotherapy. The treated patients tolerated thymus peptides quite well and had a significantly higher complete response rate than those patients who did not receive thymus peptides.[v]

One prospective, randomized study in patients undergoing colorectal surgery showed that the patients who received thymus peptides in addition to Cefotetan did significantly better in lowering the rate of abdominal abscesses and upper respiratory tract infections.[vi]

One prospective, randomized study in women with advanced breast cancer could document that those women, receiving thymus peptides in addition to their chemotherapy regimen, tolerated the chemotherapy significantly better and reduced the rate of secondary infections.[vii],[viii]

One prospective, randomized study in breast cancer patients showed that thymus peptides protect the bone marrow functions against the haematological toxicities and recovery during and after high dose of Mitoxantrone.[ix]

Another study also showed significant benefit in complete response rate to therapy and prevention of myelosuppression and secondary infections when thymus peptides were added to the regimen.[x],[xi]

Therefore, in the *Cologne Model*, thymus peptides are used:

1. to enhance bone marrow function and protect the patient against myelo-suppression of standard chemotherapy;
2. to support bone marrow recovery after radiation and chemotherapy;
3. to prevent secondary infections due to immunosuppression caused by standard chemotherapy and surgical interventions;
4. to increase complete and partial response rate to anticancer therapies;
5. to improve lymphocyte function and biological defense mechanisms.

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