

Thymus : No more a Vestigeal Organ - Review Article

Aliya Zahid

Department of Anatomy, Allama Iqbal Medical College, Lahore.

SUMMARY

The thymus is one of our major immune system glands. It is composed of two soft pinkish-gray lobes lying in bib-like fashion just below the thyroid gland and above the heart. The thymus, increases in size and activity until adolescence, but decreases thereafter. For that reason it was thought, until as late as 1964, that the thymus was inactive in adults. More recent research, however, has shown the thymus to play an important role in the body's response to disease invasion. To a large extent, the health of the thymus determines the health of the immune system. The thymus seeds the body with immature T-cells, the white blood cells responsible for "cell-mediated immunity". This gland secretes special chemicals called cytokines (i.e interferon, interleukins) that influence the specialization and migration of T-lymphocytes throughout the body. The thymus also releases hormones that regulate immune function. These thymic hormones help immune cells to mature, "programming" them to recognize tissues as either self or invader. Recognizing the enemy is the first and likely most important step in the immune response. Discovered in the early 1960s, thymic factors and hormones isolated from thymus tissue have proven to be of great therapeutic value in the treatment of a multitude of chronic and degenerative conditions. In addition to their efficacy in the treatment of compromised immune function (cancer, AIDS, allergies, and viral infections), thymus extracts are now being used in the prevention of osteoporosis, biomembrane damage and as a natural immune-enhancer for the aging population. The available research is impressive, and future clinical trials will prove beneficial in further evaluating the clinical efficacy and safety of thymus extract administration.

Key words: Thymus, thymic extracts indications

INTRODUCTION

People in earlier centuries regarded the thymus as one of the many useless organs in the human anatomy. Located around the upper chest area behind the sternum, many early scientists believed that this organ was vestigial because it was not connected to anything else within the body aside from it's main articulation. Furthermore, due to it's change in form from a large, healthy looking gland during childhood into a shrivelled, disappearing mass of tissue as one matures in age, many even ventured to conclude that this organ was a hazard to people's health .

Early in the history of science however many other scientists speculated on the importance of the thymus. Galen, a Greek physician from the 2nd Century A.D., was perhaps the first to venture a

published guess. According to him, this irregularly shaped mass found above the heart was the "seat of courage". Some ancient philosophers even argued that such an organ was the "abode of the soul." Even the name Thymus itself is believed to be named after the Greek plant called thyme. Incidentally, this word was also synonymous to the notion of spirit. Although quite prosaic, these people had the right idea regarding the true importance of this small mass of cells^{1,2}.

During the Renaissance, the speculations regarding the function of the thymus were still quite diverse. Some thought that this organ was important for blood formation during fetal development or even metabolism. Many even believed that it was a sort of "shock absorber" for the heart to prevent its damage. During the 1950's, however, the purpose of the thymus was finally revealed. Although not

precisely decided what its exact function was, the thymus was unequivocally identified as a lymphoid organ. The thymus gland is the heart of the immune system. Its role is vital, but often overlooked³. The thymus is responsible for many immune system functions, including the production of T lymphocytes, a type of white blood cell responsible for "cell-mediated immunity." Cell-mediated immunity refers to immune mechanisms not controlled or mediated by antibodies. It is responsible for vigilance against chronic viruses, fungi, yeast, and parasitic infections as well as neoplasms and aging. Thymus extracts have been used clinically in a variety of ways involving some of these conditions. They have been used orally and as injectables; by themselves and in combination with other therapeutics⁴⁻⁶.

Thymus extracts have been used to treat severe and chronic allergies involving the respiratory tract and skin as well as in severe acute and chronic infectious diseases. The extracts have also been shown to reduce post surgical infections, decrease the damage of chemotherapy and radiation and have been used as adjuncts to mainstream therapy for treatment of neoplasms. The thymus gland also releases several hormones, such as thymosin, thymopoietin, and serum thymic factor, that regulate many immune functions. The epithelial cells of the thymus synthesize at least 30 different polypeptides: the thymic hormones. Numerous studies have confirmed high clinico-immunological efficiency of natural and synthetic thymus preparations: tactivin, thymalin, thymoptin, thymogen, thymomodulin, thymovocal, thymostimulin, thymopentin TP-5 and others⁷⁻¹⁰.

Indications of thymus extracts:

The most striking features of therapy using thymus extracts is the wide variety of conditions in which these extracts have been successfully employed.

1) Allergic Conditions:

The thymus contains the most effective tissue for producing lymphocytes, with the greatest lymphopoietic activity and is a key regulator of immunocompetence potential. Thymic factors are said to be immune modulators. Thymic

extracts have been shown to normalize the ratio of T-helper cells to suppressor cells whether the ratio is low as in AIDS, chronic infections and cancer, or high as found with allergies. In other words, thymic factors appear to influence the immune response up or down as needed! Perennial allergic rhinitis, bronchial asthma and atopic dermatitis are all known to result primarily from a defect in cellular immunity. All have shown benefit from using oral administration of thymus extracts¹¹. The oral administration of Thymomodulin has been shown in preliminary and double-blind clinical trials to improve the symptoms and course of hay fever, allergic rhinitis, asthma, eczema, and food allergies (in conjunction with an allergy elimination diet)¹²⁻¹⁵.

2) Angina & bronchitis

Eighty-six patients with angina and concomitant bronchitis received antibiotics, splenin (a spleen extract) and vilozen (a thymus extract) in a clinical trial. They were compared to 52 controls who received routine treatment. The results revealed that a combination of splenin and vilozen produced a pronounced fortification of the immune response in the treated group, consequently improving their clinical status. Immuno-modulators (thymus and spleen extracts) are indicated in the treatment of repeat and relapsing angina, especially in the presence of concomitant bronchitis¹⁶⁻¹⁸.

3) Tuberculosis:

Thirty patients with active tuberculosis were given the thymus extract t-activin (tactivin) as part of a multimodal therapeutic regimen. The results showed an elevation of T helper cells, enhancement of lymphocyte activity and increased IL-2 synthesis. Enhancement of natural killer cell activity and IL-1 synthesis by macrophages were also observed. This normalization of specific and nonspecific immune responsiveness paralleled clinical improvement¹⁹⁻²².

4) Hepatitis :

The use of thymus extracts to normalize the

aberrant immune responses seen in hepatitis B is a logical treatment choice. Consistent with this line of reasoning, 18 patients with biopsy proven chronic active hepatitis B and a lowered T4/T8 ratio received thymic extract TFX for 6 and 12 months in two different groups²³. Improvement in the T4/T8 ratio was seen beginning 14 days after treatment had begun, followed by a decrease in the abnormally high NK cell count. As the NK cell count decreased, NK cell migration and killing activity increased to normal in both the 6 and 12 month groups. Normalization of biochemical and immunological parameters occurred within 5-6 months of beginning of treatment. A two year follow up showed continued clinical remission with normal immunological and biochemical panels in both groups. The thymus extract had an immunostimulatory action of lasting duration. In another study, significant decrease was seen in total bilirubin and iron levels in conjunction with more rapid clinical improvement and shorter hospitalization time in a group of 15 patients with laboratory confirmed acute hepatitis B. Patients were given 15 injections of the thymus extract, TFX, beginning the day of diagnosis and followed over the course of the disease until recovery²⁴⁻²⁷.

5) As Antiaging Agent:

Current data reveals that the cells of the thymic endocrine subcapsular zone produce hormones such as oxytocin, vasopressin, beta-endorphin and calcitonin. The implications of using thymus extract as an **anti-aging** modality are profound when one reviews the role of calcitonin production and bone loss in the aging population, and particularly in postmenopausal women. There is an exponential rise in the occurrence of osteoporosis with age that is hormonally controlled. Calcitonin production by the thymus gland is incorporated in the regulatory mechanism of bone tissue metabolism, and administration of crude thymus tissue, which increases calcitonin production and inhibits parathyroid hormone (PTH), has been shown to prevent bone loss in

postmenopausal women suffering with osteoporosis. While synthetic estrogen and sometimes progesterone have been the standard treatment for the prevention of postmenopausal osteoporosis, this therapy increases a woman's risk of endometrial and breast cancer. It appears that the administration of thymus extract in the prevention and treatment of postmenopausal and senile osteoporosis is an appropriate line of therapy, given its ability to increase calcitonin production and inhibit the release of PTH²⁸⁻³¹. Thymic extracts have also been implicated for their antioxidant effects in the control of intensive lipid peroxidation caused by age-related cellular reactions, trauma, shock and burns. Decreased cellular immunity is directly associated with increased aging. The use of thymus extracts may be an important, but overlooked, option in treating and possibly preventing many clinical conditions of the aging person. Thymic extracts have ability to normalize the basic functions of the human organism, i.e. to improve the indices of the cardiovascular, endocrine, immune, and nervous systems, homeostasis, and metabolism. In a study, the restoration of homeostasis in the patients receiving thymic extracts was accompanied by a 2.0-2.4-fold decrease in acute respiratory disease incidence, reduced incidence ischemic heart disease clinical manifestations, hypertension, deforming osteoarthritis, and osteoporosis, as compared to the control group. Such a significant improvement in the somatic state of the patients corresponded to a decrease in their mortality rate during the observation period: 2.0-2.1-fold among the Thymalin-treated patients³²⁻³⁶.

6) Rheumatoid arthritis:

Several studies have shown the effectiveness of thymus extracts in treating this disease. TFX thymus extract was used in a trial in which 20 subjects received daily injections for 3 months. Eighty percent of those involved showed clinical improvement as evidenced by decreased joint swelling and tenderness and an increase in muscle strength. Forty percent

showed a decrease in rheumatoid factor alpha 2 and serum IgG levels as well as an increase in hemoglobin and serum iron levels³⁷. It was concluded that TFX was of therapeutic value in the management of RA patients either alone or in combination with anti-inflammatory or basic anti-rheumatic drugs³⁸.

7) Preeclampsia and eclampsia:

Progressive immune depression accompanied by a parallel drop in parathyroid hormone level to critical values has been demonstrated in patients with eclampsia. Patients with preeclampsia delivered by cesarean section were treated post-operatively with the thymus extract, t-activin. Cellular immunity was compared with patients receiving no t-activin. A marked immuno-stimulatory effect of the thymus extract on T-lymphocytes and especially on theophylline-resistant T-lymphocyte subpopulations was observed. The effect of t-activin was most marked on the 3rd to 5th day of the postoperative period³⁹.

8) AIDS:

Evidence that the thymus gland suffers extensive damage during HIV infection has led to research on using thymus hormone replacement therapy as a means to counteract the damage. Thymus hormones are proteins that affect the development of immune system T-cells in the thymus gland. They also enhance immune function in mature T-cells in the blood and lymph. While their exact role in AIDS therapy is unclear, various experiments suggest that injecting thymus hormones can increase the numbers of the various T-cell subpopulations. By enhancing the activity of the immune system's killer cells, they may increase these cells' ability to seek out and destroy cells infected by HIV.

In one of the best designed studies, AIDS patients were treated with liquid thymus extract orally. The results showed significant increases in T cells, T helpers and in T4/T8 ratios. These indices play an important role in the pathogenesis of AIDS. Clinically, the number

of patients demonstrating chronic lymphadenopathy decreased by 2/3rds, fever disappeared in all subjects and the incidence of thrush decreased remarkably during and after treatment⁴⁰⁻⁴⁷.

9) Skin disorders:

Thymus extract was useful in modulating IgE disregulation in atopic children. Many studies have shown a general improvement in the overall condition of atopic children receiving thymus extracts⁴⁸. Thymic extract proved beneficial in psoriasis⁴⁹, systemic lupus erythematosus^{50,51} etc.

10) Neoplasms:

Cancer is typically treated with chemotherapy, radiotherapy and/or surgery. One difficulty with these treatments is that all three significantly decrease the ability of the system to adequately function. Yet an adequately functioning immune system is essential for any sustained recovery. Impaired cell-mediated immunity, in particular, is involved not only in the growth but also in the spread of cancer. In most instances, thymus extracts helped restore immune function or decreased impairment and, in some cases, appeared to prolong the life of the patients. Newer therapies are typically tried on the most advanced cases with the poorest prognoses. Thymic extracts administration diminished the chemotherapy-related toxicity in metastatic colorectal cancer patients treated with chemotherapy and folinic acid⁵², increased the T-lymphocyte counts and improved skin response to DNCB in chemotherapy-treated patients with gastrointestinal cancer⁵³, reduced the number and severity of infectious episodes in small-cell lung cancer patients treated with chemotherapy⁵⁴ and reduced the incidence of infections in chemotherapy-treated breast cancer patients⁵⁵. In some studies, thymus extracts were used as the only therapy. However, more frequently, the thymus extracts were used as an adjunct to conventional therapy in an effort to help restore the immune system or prevent its profound depression and the immune related complications typically

associated with conventional treatment. In most instances, thymus extracts helped restore immune function or decreased impairment and, in some cases, appeared to prolong the life of the patients⁵⁶⁻⁶⁸.

11) Burns:

Opportunistic micro-organisms causing infections in burn patients are often acquired in hospitals. These infections commonly involve Gram-positive organisms which may be resistant to several antibiotics. Teicoplanin, alone and in combination with additional antibacterial drugs, proved effective in the treatment of Gram-positive infections of various types in hospitalized burn patients. In another study the thymus extract t-activin was used in combination with sodium nucleinate plus lidocaine to restore phagocytic function of peripheral blood lymphocytes and increase humoral immunity in severely burned animals. Treatment decreased colonization of pseudomonas aeruginosa and candida pathogens and decreased the death rate⁶⁹.

12) Miscellaneous:

Thymic extracts proved beneficial in conditions like post operative sepsis⁷⁰, suppurative surgical infections^{71,72}, cirrhosis of liver⁷³, duodenal ulcer⁷⁴, multiple sclerosis⁷⁵, goiter⁷⁶, diabetes mellitus in children⁷⁷, peritonitis⁷⁸, nonspecific lung disease⁷⁹, trauma⁸⁰, sarcoidosis⁸¹, respiratory tract infections⁸², ophthalmic herpes⁸³, etc.

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The Author:

Aliya Zahid
Assistant Professor of Anatomy
Allama Iqbal Medical College
Lahore.

Address for correspondence:

Aliya Zahid
27 A1 , Johar town
Lahore.
E mail Address:
aliyaimtiaz@hotmail.com

Phone: 5173869
Mobile: 0333-4219025