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Nutritional & Herbal Support for Healthy Thyroid & Adrenal Function

Key Points at a Glance

Stress & the Thyroid and Adrenal Glands

- Prolonged stress can adversely affect the hypothalamus-pituitary-adrenal (HPA) axis and the hypothalamus-pituitary-thyroid (HPT) axis, resulting in a decreased production of thyroid hormones.
- Stress-related thyroid and adrenal dysfunction may have other wide ranging systematic effects that impact on the immune, cardiovascular and central nervous systems.

Rehmannia

- used in traditional Chinese medicine for febrile diseases, skin eruptions, nosebleed
- regarded in Western herbal medicine as an adrenal tonic (activity dmeonstrated in experimental models)
- unlike Licorice, Rehmannia is suitable fo ruse in patients with hypertension
- immune modulating effect (experimental model, uncontrolled study)

Vitamins C & E

- as antioxidants can reduce the oxidative stress, and the potential ensuing tissue damage, caused by sub-optimal thyroid function
- adrenal gland has high requirement for vitamin C
- vitamin E may also support the conversion of thyroxine to triiodothyronine

B Vitamins

- helps maintain proper cellular energy production at the mitochondrial level which is needed in conditions of low thyroid hormone activity
- can be supplied in 'activated' form (as the metabolites)

Tyrosine

- tyrosine is a critical precursor of the thyroid hormones thyroxine (T4) and triiodothyronine (T3)
- building block for norepinephine and epinephrine
- helps the body adapt to and cope with the effects of physical or psychological stress

Selenium, Iodine, Zinc

- selenium: important role in thyroid hormone homoeostasis and required by endocrine tissues including adrenal
- iodine: required for production of thyroid hormone
- zinc: essential for thyroid hormone homoeostasis

Indications & Safety

- Maintain normal thyroid and adrenal function.
- Stressful conditions, and to improve tolerance to stress.
- Fatigue, cognitive decline, lowered immune function especially during prolonged stress.
- Obesity, particularly associated with low thyroid function or slow metabolism; hypothyroidism.
- Anxiety and exhaustion associated with poor adaptation to stress.
- Conditions requiring intake of iodine, e.g. for normal basal metabolism and normal production of thyroid hormones.
- Chronic illness.
- Caution is advised for those taking monoamine oxidase inhibitors.

Thyroid Hormone Regulation

The thyroid gland is located just below the larynx in the back of the neck, and is responsible for the production and secretion of hormones that regulate the body's metabolic rate. Two significant hormones that regulate metabolism and are produced by the thyroid gland are thyroxine (T4) and triiodothyronine (T3). T3 is the active hormone that affects the metabolism of cells. The hormone secreted by the thyroid gland is primarily T4, with approximately only seven percent being the active T3 hormone. The liver and target tissues are primarily responsible for the conversion of T4 into the active T3 form. T4 consists of two tyrosine molecules each binding two iodine atoms. The enzyme, 5-monodeiodinase, found in liver and in peripheral tissues, cleaves a single iodine molecule from the outer tyrosine unit to create T3. Excess T4 is disposed of by action of a similar enzyme, which takes a single iodine molecule from the inner tyrosine, and thus creates reverse T3, which is metabolically inactive.

Adrenal Hormone Regulation

The adrenal glands can be divided into two main segments: the medulla and cortex. The adrenal medulla is responsible for the secretion of epinephrine and norepinephrine, also commonly referred to as adrenaline and noradrenaline, or the 'fight or flight' hormones. These hormones are released in potentially life threatening situations and directly impact heart rate, blood pressure and supply of blood to important organs such as the brain, heart and skeletal muscles.

The adrenal cortex is responsible for the production and release of steroid hormones, including cortisone, hydrocortisone, testosterone, oestrogen, 17-hydroxy-ketosteroids, DHEA, pregnenolone, aldosterone, progesterone, androstenedione and other intermediate hormones. The adrenal cortex is the only endogenous site for the production of aldosterone, cortisone and hydrocortisone, whilst the other steroid hormones can be manufactured elsewhere in the body.

Stress & the Neuro-endocrine System

A large body of scientific evidence suggests that the impact of stress can affect the body on multiple levels and that there is indeed a 'stress system' that is comprised of neurological, endocrinological, psychological and environmental components.[1] The adrenal and thyroid hormonal systems are intimately involved in this stress system at the neuro-endocrinological level via a cross regulation or communication system between the hypothalamus-pituitary-adrenal (HPA) axis and the hypothalamus-pituitary-thyroid (HPT) axis. Prolonged stress can adversely affect these axes, resulting in a decreased production of thyroid hormones. Glucocorticoids for example, can inhibit the peripheral conversion of T4 to T3, resulting in stress-induced decreases in serum T3 levels. Hypothyroidism is associated with a decreased corticosterone response to stress in female rats. A study has confirmed that repeated exposure to stress caused a decrease in peripheral thyroid hormone levels. Stress-induced changes in glucocorticoids and AGRP were also observed. (AGRP is hypothalamic arcuate nucleus agouti-related protein. AGRP inhibits thyrotropin-releasing hormone messenger RNA and thyroid hormone levels.)[2]

Chronic, constant low grade stress and poor nutritional status can result in a concomitant weakening of the adrenal and thyroid hormonal system via disruption of the HPA and HPT axes. In addition to the direct effects on the adrenal and thyroid glands, other endocrine glands can be affected, including the gonads and pancreas. Stress-related thyroid and adrenal dysfunction often has other wide ranging systematic effects that impact on the immune, cardiovascular and central nervous systems. Compromised immune function or autoimmune dysfunction, impaired blood glucose regulation, frequent pain and headaches further add to the feeling of constant fatigue and being run down. In a vicious cycle, normal sleep patterns may also be affected, further compromising the individual's health. A person who regularly suffers from allergies, infections, constant fatigue or lethargy may be suffering from, or have an increased risk of suffering from, adrenal and thyroid insufficiency.[3-6]

Rehmannia

Rehmannia glutinosa unprocessed root is used in traditional Chinese medicine (TCM) to reduce heat in the blood, to nourish *yin* and promote the production of body fluid. Indications for this type of Rehmannia include febrile diseases, skin eruptions and nosebleed.[7] In Western herbal medicine, Rehmannia is regarded as an adrenal tonic, due mainly to the activity demonstrated in experimental studies.

Oral administration of uncured Rehmannia (3 g/kg) for two weeks to rabbits chronically treated with a synthetic glucocorticoid (dexamethasone) significantly raised serum corticosterone levels. (This is a model of adrenal depletion.) Continuation of treatment resulted in further increases. Rehmannia treatment also prevented or reversed morphological changes in the pituitary and adrenal cortex, appearing to antagonise the suppressive effect of glucocorticoids on the hypothalamic-pituitary-adrenal axis.[8] Rehmannia may work by inhibiting the negative feedback from the glucocorticoid to the pituitary gland.[9] These results also suggest that Rehmannia supports the cells of the adrenal cortex and pituitary during times of prolonged stress.

Unlike Licorice (also an adrenal tonic), Rehmannia is suitable for use in patients with hypertension.

Rehmannia may be beneficial for the treatment of conditions that involve the immune system. Oral administration (10-500 mg/kg) of several fractions from the ethanol extract of Rehmannia had an immune modulating effect in an experimental model.[10] Therapeutic effects have been demonstrated for patients with rheumatoid arthritis.[11] Rehmannia could therefore be helpful in addressing autoimmune conditions of the adrenals and thyroid.

Tyrosine

The amino acid tyrosine plays a critical metabolic role as a precursor to several important neurotransmitters including epinephrine, norepinephrine, serotonin and dopamine. Tyrosine also aids in the production of melanin and enkephalins, and in the function of organs in the body responsible for making and regulating hormones, including the adrenal, thryroid, and pituitary glands. Low levels of tyrosine have been associated with low blood pressure, low body temperature, and an underactive thyroid.

As stated previously, tyrosine is a critical precursor of the thyroid hormones thyroxine (T4) and triiodothyronine (T3). In the thyroid gland, these hormones are synthesized from the precursor protein thyroglobulin. The thyroglobulin protein is a large protein, especially rich in tyrosine residues that are reacted with iodine to produce the respective thyroid hormones. Tyrosine, together with iodine, must be present in adequate amounts in the diet for the synthesis of T4.

Human and animal research suggests that tyrosine helps the body adapt to and cope with the effects of physical or psychological stress by minimising the symptoms brought on by stress. This is primarily due to the fact that tyrosine is a building block for norepinephine and epinephrine, two of the body's main stress-related hormones. Supplemental interventions with tyrosine may help some patients to avoid typical bodily reactions and feelings from stressful situations like surgery, emotional upset, and sleep deprivation.

The primary area where tyrosine supplementation has been studied intensely is in combat personnel who are exposed to a variety of stressful situations that include sleep deprivation, combat training and exposure to temperature extremes and loud noises. Exposure to both acute and prolonged stress has been associated with depletion of brain reserves of the catecholamine neurotransmitters norepinephrine and dopamine, and depletion of norepinephrine in particular is closely linked to stress-related inhibition of performance. This stress can in turn result in anxiety and deterioration in mood and performance. The administration of tyrosine may minimise or reverse this stress-related decrement in performance by increasing depleted brain norepinephrine levels.[12-15]

Whilst many of these experiments have used high doses of tyrosine which equate to approximately 150 mg per kilogram body weight, the recommended therapeutic daily dose of tyrosine is regarded to be anywhere between 1 and 10 grams daily for adults.[16]

An increase in blood pressure may result when tyrosine is taken by individuals taking monoamine oxidase inhibitors (MAOIs). The severity of this increase in blood pressure may vary depending on the individual and the dose of tyrosine, but is usually dose dependent. Regardless, caution is recommended for the combined use of tyrosine and MAOIs.

Selenium & Iodine

Selenium and iodine have intricate roles in enzyme formation that regulates the hormone network, particularly that of thyroid hormone homoeostasis.[17] Several selenoproteins, including glutathione peroxidase, participate in the protection of thyrocytes from oxidative damage by peroxide radicals produced for thyroid hormone biosynthesis.[18] Iodothyronine deiodinases are selenoproteins contributing to systemic or local thyroid hormone homoeostasis. A specific group of selenoproteins are the iodothyronine deiodinases, which catalyse the deiodination of thyroxine, triiodothyronine and reverse triiodothyronine and thereby regulate the concentration of the active hormone triiodothyronine.[19] In addition, the selenium content in endocrine tissues (thyroid, adrenal, pituitary, testes, ovary) is higher than in many other organs, with selenoproteins involved in endocrine functions of the adrenal glands.[18]

Iodine is required by the body to form thyroid hormone and a dietary lack of iodine can reduce thyroid hormone production and eventually result in goitre as the thyroid gland enlarges. Iodine supplementation can be an effective method for correcting iodine deficiency hypothyroidism and can halt the development of goitre if the cause is not complicated by malnutrition or environmental and dietary goitrogens.

The combined deficiency of both iodine and selenium may particularly affect the thyroid gland. In one study, the combination of both iodine and selenium deficiency was particularly detrimental to the thyroid gland by increasing inflammation and resulting in necrosis of thyroid tissue.[20]

Zinc

Zinc is essential for thyroid hormone homoeostasis, with one particular role being the synthesis of thyrotropin releasing hormone (TRH). Zinc deficiency may lower 5-deiodinase activity, thereby contributing to lower T4 to T3 conversion. Zinc may also play a role in healthy genetic expression of thyroid hormone by influencing transcription factors that affect T3 nuclear receptor interactions.[17,21]

B Vitamins

The B vitamins are required as coenzymes essential for cellular function and have a fundamental role in maintaining proper cellular energy production at the mitochondrial level. A deficiency of any B vitamin will compromise mitochondrial function. Thiamine (B1) is essential for the oxidative decarboxylation of the multienzyme branched-chain ketoacid dehydrogenase complexes of the citric acid cycle. Riboflavine (B2) is required for the flavoenzymes of the respiratory chain, while NADH is synthesised from niacin (B3) and is required to supply protons for oxidative phosphorylation. Pantothenic acid (B5) is required for coenzyme A formation and is also essential for alpha-ketoglutarate and pyruvate dehydrogenase complexes as well as fatty acid oxidation. B vitamins may also have an antioxidant role in terms of cellular energy metabolism.[22] Vitamins B6 and folate are involved in the metabolic conversion of L-tyrosine into neurotransmitters. Thyroid hormone regulates mitochondrial action and needs to be supported, since low thyroid hormone activity is associated with poor mitochondrial energy production.

Recent research highlights the importance of the active metabolites of B vitamins also called activated B vitamins or vitamers. Activated B vitamins may be important in people with DNA polymorphisms that encode less active forms of enzymes involved in B vitamin metabolism.[23-26]

- Riboflavin sodium phosphate (flavin mononucleotide or FMN) is an active metabolite of riboflavin (B2). FMN is itself a vital coenzyme in metabolism of both pyridoxine (B6) and folate, and converts to flavin adenine dinucleotide (FAD). FAD functions as a cofactor for the enzyme MTHFR (methylene tetrahydrofolate reductase) which is involved in folate metabolism.[27]
- Pyridoxal 5-phosphate is an active metabolite of pyridoxine (B6),[25] and is an important coenzyme in many amino acid related reactions.[28]
- Calcium folinate is rapidly and extensively converted to 5-methyl tetrahydrofolate (5-methylTHF) in the body.[29] 5-methylTHF is the major transport form of folate.[27] A crossover study in a small number of volunteers has confirmed that the intestine is efficiently able to convert folinate to 5-methylTHF but poorly able to convert folic acid to 5-methylTHF.[30]

Vitamins C & E

Recent research has suggested that antioxidant vitamins, such as vitamin C and vitamin E, can reduce the oxidative stress caused by sub-optimal thyroid function. Also the adrenal gland is among the organs with the highest concentration of vitamin C in the body. Ascorbic acid is a cofactor required both in catecholamine biosynthesis and adrenal steroidogenesis.[31] Vitamin C is a required co-factor in the conversion of dopamine to norepinephrine and therefore deficiency of this nutrient may be associated with depleted catecholamine levels.

Vitamin C and E combined also can help reduce oxidative stress caused by hypothyroidism.[32] Vitamin E may additionally support the conversion of T4 to T3 by influencing hepatic 5-deiodinase activity, most likely via antioxidant support to cell membranes in which 5-deiodinase exists. In one animal study, vitamin E was shown to protect animals from increased oxidation and thyroid cell damage and support liver and kidney glutathione levels.[33] Another study found that hypothyroidism induces cell and auto-antibody proliferation resulting in goitre. However, supplemental vitamin E was found to inhibit the development of this proliferation.[34]

Supportive Formulation

These nutrients and Rehmannia would complement each other in a very potent formulation with the following actions:

- stimulating thyroid function,
- anti-inflammatory,
- adaptogenic,
- relieve nervous tension and mild anxiety.

Indications

- Maintaining normal thyroid and adrenal function.
- Fatigue and cognitive decline, especially during periods of prolonged stress.
- Poor tolerance to extremes of temperature or loud noises.
- Lowered immune function, especially in those under stress.
- Improving physical tolerance to stress.
- Hypothyroidism; chronic illness.
- Obesity, particularly associated with low thyroid function or slow metabolism.
- Anxiety and exhaustion associated with stress.
- Conditions requiring intake of iodine, e.g. to assist normal basal metabolism and normal production of thyroid hormones.

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