CNI609 6/98
CLINICAL NUTRITION INSIGHTS

Vol.6, No. 9

Herbal Support for Adrenal Function

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The adrenal glands, which are composed of the adrenal cortex and the adrenal medulla, are involved in many physiological processes such as blood pressure regulation, steroid hormone synthesis, and the body's stress response mechanism. The adrenal cortex produces androgens (eg, DHEA), glucocorticoids (eg, cortisol) and mineralcorticoids (eg, aldosterone), while the adrenal medulla produces epinephrine and norepinephrine. The glucocorticoids play a critical role in the body's response or resistance to stress and the mineralcorticoids serve to regulate electrolyte and water balance. Epinephrine and norepinephrine also participate in the body's stress response. Generally, compromised adrenal function will negatively impact one's blood pressure, energy level, and resistance to infection.

From a conventional medicine standpoint, the concept of compromised adrenal function refers primarily to adrenal insufficiency due to adrenocortical disease. However, in the naturopathic or functional medicine model, and from the perspective of traditional Chinese medicine, a gradual loss of adrenal function is widely recognized as a contributor to a decline in health and is considered to be both an indirect cause as well as a side effect of many acute and chronic illnesses. In addition to vitamins such as pantothenic acid and vitamin C, a number of botanicals are known to support adrenal function and may provide therapeutic support for individuals with compromised or diminished adrenal function.

CONDITIONS ASSOCIATED WITH HYPOADRENAL FUNCTION

The most recognized medical condition associated with diminished adrenal function is Addison's disease, a life-threatening condition characterized primarily by a chronic deficiency of the glucocorticoid cortisol. The effects of cortisol deficiency include fatigue, hypotension, and weakness as a result of deficient neuromuscular function. Resistance to infection, trauma, and other types of stress is also diminished because of reduced adrenal output. Individuals with Addison's disease require glucocorticoid replacement, with hydrocortizone being the drug of choice.

More commonly, a general decline in adrenal function is also thought to occur as a result of physiological stress as with acute or chronic illness, or even with normal physiological changes such as menopause. It also appears that certain chronic illnesses particularly asthma and chronic fatigue syndrome (CFS) are exacerbated by insufficient adrenal hormone secretion. Patients with CFS were found to have significantly reduced basal evening glucocorticoid levels and low 24-hour urinary free cortisol excretion.[1] Low levels of adrenocortical hormones have also been reported in asthmatic children suffering from severe or persistent attacks.[3] During an attack, the concentration of cortisol appears to increase in proportion to the severity of an attack but subsequently decreases with time. It is speculated that the inability to sustain an elevated cortisol level leads to the development of chronic asthma. Additionally, suppressed adrenocortical function has been implicated in the development of nocturnal worsening of asthma.[4]

Adrenal hypofunction can sometimes be the result of impaired activation of adrenocorticotropin hormone (ACTH) release. ACTH is responsible for stimulating the release of cortisol via the hypothalamus-anterior pituitary system. Some research suggests that the depressed cortisol levels seen in CFS patients may be due to impaired ACTH release.[5,6] Also, a lack of ACTH may occur in patients receiving corticosteroids, or for a time following therapy.[7] In the absence of ACTH, the adrenal cortex atrophies and secretion of cortisol is greatly reduced.

LICORICE ROOT

Of the many herbs available, licorice root (*Glycyrrhiza glabra or G. uralensis*) is one of the most highly regarded herbs used to treat conditions associated with diminished adrenal function. Licorice is known to have multiple pharmacological actions including adrenocorticoid-like activity.[8,9]

In addition, licorice has antiinflammatory, antiallergy, antitussive, antiviral, antiulcer, and estrogen balancing properties.[8-12] Its antiviral and adrenocorticoid properties make it a good candidate for chronic fatigue syndrome. Licorice is also recommended for Addison's disease, asthma and allergies, coughs, peptic ulcer, arthritis, and following steroid therapy.[8,13,14] Resent research suggests that licorice may also be useful in the treatment of AIDS and chronic hepatitis.[15-18,10]

The adrenocorticoid activity of licorice is associated with two active components glycyrrhizin and glycyrrhetinic acid. Glycyrrhizin and glycyrrhetinic acid have been reported to bind to both glucocorticoid and mineralcorticoid receptors, possibly displacing endogenous steroids thus contributing to an increase in availability of free cortisol within the body.[19] Additionally, research suggests that glycyrrhizin and/or glycyrrhetinic acid increases the half-life of circulating cortisol in the body by inhibiting its metabolism or breakdown.[20] In one clinical study, glycyrrhizin was shown to significantly increase the concentrations of total and free prednisolone in men given intravenous prednisolone hemisuccinate together with glycyrhizin.[21] In another study, glycyrrhetinic acid was shown to delay the clearance of cortisol in patients with adrenocortical insufficiency and in patients who had been taking oral prednisolone medication for at least 3 months.[22]

It is important to note that due to the mineralcorticoid effect of glycyrrhizin and glycyrrhetinic acid, excessive or prolonged licorice intake can cause sodium and water retention with resultant hypertension and hypokalaemia. The mineralcorticoid effect of glycyrrhizin is attributed to its ability to inhibit 11-beta-hydroxysteroid dehydrogenase, an enzyme that catalyses the conversion of cortisol to cortisone.[23] Inhibition of this enzyme leads to increases in free cortisol. Cortisol possesses mineralcorticoid activity whereas cortisone does not, thus, a hypermineralcorticoid effect can occur. It is reported that this effect does not seem to occur in patients or animals with adrenal insufficiency.[23] Also, there appears to be great individual variation in the susceptibility to the adverse reactions to

licorice. Highly sensitive individuals may react to as little as 100 mg of glycyrrhizic acid, while others may be able to tolerate much more.[24] Patients therefore need to be regularly evaluated for signs of pseudoaldosteronism when taking licorice preparations. A safe guideline is to not exceed 3 grams of licorice root per day for more than six weeks. It has been suggested that a high potassium, low sodium diet may help to counteract the potential adverse effect of licorice, although no formal trial has been performed. Pregnant women and individuals with hypertension or high blood pressure should avoid licorice supplementation.

HERBAL ADAPTOGENS

The term "adaptogen" has been given to botanicals that appear to have a beneficial influence on the body's adaptive response mechanism associated with stress. Herbs such as ginseng (*Eleutherococcus senticosus*) and the Ayurvedic herb ashwagandha (*Withania somnifera*), also known as Indian ginseng, are especially noted for their adaptogenic properties and their ability to support adrenal function. Both herbs have been traditionally used for convalescence, nervous exhaustion, fatigue, geriatric debility, physical and mental stress, and insomnia.[8,13,25] Few adverse side effects have been reported with prolonged ginseng use while no side effects have been reported with ashwagandha.[26]

It has been suggested that ginseng and ashwagandha may influence adrenal hormone activity by helping to support normal hypothalamic-pituitary-adrenal axis (HPA) function.[13] Ashwagandha in particular is believed to interact with areas of the brain, spinal cord, and central nervous system. Recent research suggests that ashwagandha enhances cholinergic activity in the brain, which helps to explain the reported memory and cognition enhancing effects of ashwagandha extracts.[27] This activity may be of potential benefit for the treatment of Alzheimer's disease, which is associated with cortical cholinergic dysfunction. Other research suggests that ashwaganda also has GABA-mimetic activity which could contribute to the herb's antianxiety and CNS inhibitory effects.[28]

Other reported activities of ashwagandha include antiinflammatory, antiarthritic, antitumor, and immunomodulatory.[29-32] Research also suggests that ashwagandha may be useful as an adjuvant during cancer chemotherapy and radiosensitization.[33,34] Additionally, ashwagandha has been shown to prevent stress-related disorders such as ulcers, and prevent stress-induced depletion of vitamin C and cortisol in laboratory animals.[35]

HERBS THAT TONIFY

In Chinese herbology, there are a number of herbs that are classified as "tonifying herbs," a category that can be likened to that of an adaptogen. Tonifying herbs include both licorice and ginseng, as well as Chinese yam (*Dioscorea opposita*), rhemannia (*Rhemannia glutinosa*), cordyceps (*Cordyceps sinsensis*), and others. Many of these "tonic" herbs contain constituents, such as steroidal saponins, that may act as precursors to adrenal hormones. In general, most of the herbs that fall under this category appear to have broad therapeutic effects, presumably via an ability to influence the endocrine system.

According to traditional Chinese herbology, licorice, ginseng, and Chinese yam are said to promote energy by tonifying "chi," or "vital force," while rehmannia and cordyceps are said to tonify the blood.[8] As with licorice, Chinese yam and cordyceps are recommended for asthma, coughs, and female complaints. Rehmannia, which is often used in herbal formulas as a complementary herb, is said to help regulate the activity of the adrenal cortex by promoting the function of the hypothalamus-pituitary-adrenal axis and the release of steroid hormones.[36] Rehmannia is traditionally used for general debility, sexual dysfunction in males, and menopause and menstrual irregularities. Preliminary research also suggests that the aqueous extract of rehmannia contains immunologically active polysaccharides that may help to increase resistance to infection.[37-38]

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