

HPA-D Treatment Therapies and Supplements Review

ADJUNCTIVE THERAPIES

MINDFULNESS-BASED COGNITIVE THERAPY

When we talk about perceived stress, there are four key factors that determine how stress is perceived (acronym NUTS):

- Novelty
- Unpredictability
- Perceived threat to body or ego, and
- Sense of loss of control

The first two aren't particularly modifiable, but the second two can be influenced by how we frame the event in our mind.

For example, job loss. You perceive that event as a sign of your worthlessness and an indicator that you'll never be successful, or you can perceive the loss of your job as an opportunity to pursue a long-time dream that you've ignored or a chance for a fresh start.

Reframing can be a powerful ally in stressful situations, but it depends on your capacity to stay present in a difficult situation. A mindfulness practice helps here.

Mindfulness-based cognitive therapy, or MBCT, is one methodology for doing this. It combines the ideas of cognitive behavioral therapy with meditative practices and attitudes based on the cultivation of mindfulness.

MASSAGE

Massage is another modality shown to reduce cortisol and regulate the HPA axis.

ACUPUNCTURE

- Has been shown to reduce subjective markers of stress, and most people who receive acupuncture report feeling a deep sense of relaxation.
- Also has been shown to regulate the HPA axis in both animal and human studies.
- Historically developed in China to be done as often as every day, but certainly two to five times a week.

- New model in the U.S. called community acupuncture, where treatments are offered on a sliding scale of \$15 to \$45. This allows for better results as the patient attends more frequently.

BASIC NUTRIENTS

Nutrients that play an important role in HPA axis function include vitamin C, B vitamins, potassium, sodium, calcium, zinc, and magnesium can be obtained from a high-quality multivitamin. However, studies have shown that long-term calcium supplementation increased risk for cardiovascular disease in both men and women.

Calcium should be in the hard tissues such as the bones and the teeth, and it should stay out of the soft tissues. The problem with longer-term calcium supplementation is that the calcium likely gets into the soft tissues, so consider a multivitamin that does not contain calcium for longer term use.

Vitamin C 2 grams/d in liposomal form	Magnesium 400-600 mg/d in glycinate form	Pantethine 450-900 mg/d
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Remember that glycemic dysregulation, circadian disruption, and inflammatory signaling are three of the four drivers of HPA-D, so below are some supplements to address those issues.

GLYCEMIC CONTROL

1. Diet, exercise, sleep.
2. Metabolic Synergy and GlucoSupreme from Designs for Health.
3. Soluble fibers such as PGX or glucomannan and resistant starch such as potato starch can also be helpful.
4. Patients with advanced blood sugar issues may require medication such as metformin

INFLAMMATION

Consider curcumin, boswellia, skullcap, EPA, and DHA.

- Curcumin reduces inflammation, promotes T-regulatory cell production and differentiation, is a COX-2 inhibitor, and it reduces oxidative stress.
 - Bioavailability of curcumin varies widely.
 - I currently prefer:
 - Longvida form, particularly in cases of neurodegenerative disease
 - Liposomal form
- Boswellia

- Inhibits tumor necrosis factor α , interleukin-1 β , nitric oxide, and mitogen-activated protein kinases, or MAP kinases.
- Standard dose is 400 mg per day.
- More concentrated or isolated Boswellia AKBA dose is 100 mg per day.

There is some logic to taking curcumin and boswellia together because they work with complementary mechanisms/pathways.

CHINESE SKULLCAP

- Reduces the expression of nitric oxide;
- Is a COX-2 inhibitor, as well as inhibiting other inflammatory cytokines.
- Reduces neuroinflammation, supports memory and learning, reduces anxiety, and can improve blood glucose.
- I like the tincture form of Chinese skullcap from Woodland Essence, and the dose would be one full dropper twice a day.

EPA AND DHA

Have been found to reduce inflammatory markers in a wide variety of conditions such as rheumatoid arthritis, diabetes, and pain conditions.

1. Recommend eating a pound of coldwater, low-mercury, fatty fish per week.
2. An alternative is cod liver oil or wild salmon oil supplement.

CIRCADIAN DISRUPTION

- Botanicals such as valerian, passionflower, jujube, and hops.
- Best taken in low to medium doses, particularly valerian, which can be really sedating and cause a hangover effect.
- Bedtime Tea from Yogi Tea is a great blend.
- Tranquility from Natura Health Products is also a good supplement blend.

GABA

- Major inhibitory neurotransmitter, the off switch for the nervous system.
- Kavince, blend of taurine and 4-amino 3-phenylbutyric acid.
 - For those with difficulty staying asleep, take one to two capsules before bed.
 - For those who have trouble falling asleep, take Kavince an hour or two before the time the patient would like to go to bed
- Dependence on Kavince may be possible with higher doses, such as two capsules three times a day.

- I have not seen dependence when Kavince is used at lower doses such as one to three capsules before bed. I have seen patients successfully stop cold turkey.
- If the patient is concerned, you can pulse it, so they could take it four or five days on and two to three days off, or maybe two weeks on and a week off.

PHOSPHATIDYLSERINE (PS)

- Naturally occurring phospholipid essential for the membranes of all cells, especially in the central nervous system.
- Studies have shown it to reduce cortisol levels.
- Dose used for therapeutic effect of PS ranges from 400 to 800 mg a day, though some have shown benefits at 200 to 300 mg per day.
- Integrative Therapeutics has a good brand of phosphatidylserine that is soy-free.

TAURINE

- Supports sleep and is the second-most abundant amino acid in the central nervous system.
- I don't typically prescribe it on its own, as it is in Kavince.
- If used on it's own, I suggest a dose of 2 to 3 g taken before bedtime.

FIVE-HYDROXYTRYPTOPHAN (5-HTP)

- Naturally occurring in seed pods of Griffonia simplicifolia, a West African medicinal plant.
- In humans, 5-HTP is the immediate nutrient precursor to serotonin.
- 5-HTP increases serotonin levels in the brain, and supplementing with 5-HTP has been shown to help reestablish healthy sleep patterns in people with chronic sleep disturbances.
- If you increase serotonin, you increase melatonin because one of serotonin's metabolic pathways leads directly to melatonin.
- Dose for 5-HTP is 50 to 100 mg taken in the evening at dinnertime or before bed.

MELATONIN

- Hormone secreted by the pineal gland in the brain that helps regulate other hormones and maintains the body's circadian rhythm.
- For sleep-onset insomnia, use sublingual form of melatonin.
- Oral form is best for sleep-maintenance insomnia, 30 to 60 minutes prior to bed.
- Some evidence suggests that lower doses from 250 mcg to 1 mg may be more sedating than higher doses, which are used for treating neuroinflammation and cancer.
- Special considerations:
 - Contraindicated in young children and pregnant and nursing women.

- May reduce effectiveness of antidepressant drugs and/or worsen depression.
- Melatonin has quite a few potential drug interactions, use with caution.

L-THEANINE

- Unique amino acid found only in green tea and certain mushrooms.
- At higher doses, it can have a calming and focusing effect.
- It improves natural sleeps at night but does not cause sedation during the day.

Nutrients that support cholinergic system may help to reset the circadian clock and can be useful when the diurnal cortisol rhythm is disrupted.

Nutrient	Dosage
Alpha-GPC	200–300 mg/d
N-acetyl L-carnitine	50–100 mg/d
Huperzine A	150–300 mcg/d
Pantothenic acid	High dose, up to 1 gram/d

SUMMARY OF NUTRIENTS FOR HPA-D

Category	Dosage/Comments
Basic HPA axis support	Vitamin C, B vitamins, potassium, sodium, calcium, zinc, magnesium; take in multivitamin (without calcium), or individually
Glycemic control	Chromium, zinc, manganese, vanadium, gymnema, bacopa, etc. Metabolic Synergy & GlucoSupreme from DFH good options (no need for multi if you use Metabolic Synergy)
Inflammatory signaling	Curcumin, boswellia, skullcap, EPA/DHA
Circadian disruption	Botanicals (valerian, passionflower, jujube, hops), GABA, PS, taurine, 5-HTP, melatonin, L-theanine, pantothenic acid, alpha-GPC, huperzine A, N-acetyl L-carnitine

ADAPTOGENS

- Are botanicals that should increase resilience in metabolic reserve and improve stress tolerance and recovery.
- Recognized to have a balancing effect.
- Reduce stress-induced damage, so they are anti-fatigue, anti-infectious, antidepressant, and restorative.

ADAPTOGEN MECHANISMS

- Modulation of heat shock protein expression
- Manage folding, affinity, nuclear transport, genomic signaling, and half-life of cortisol receptors
- Increase in neuropeptide Y expression and release
- Promotion of genomic signaling of genes

SIBERIAN GINSENG

- Improves mental performance under stress and helps with exercise recovery.
- Studies have shown measurable improvements in chronic fatigue or quality of life.
- Also shown to relieve depression in bipolar teens.
- Safe in both high- or low-cortisol states.

SCHISANDRA CHINENSIS

- Shown to protect against stress and support energy production, cardiovascular, immune, respiratory, endocrine, and GI systems.
- Can be used in both high- and low-cortisol states.

RHODIOLA

- Studies show improvements in fatigue, burnout, and saliva cortisol awakening response.

ASHWAGANDHA

- Has shown some benefit in neurodegenerative conditions such as Alzheimer's.
- Sensoril ashwagandha is the most potent form available, eight times the strength of standard ashwagandha.
- A therapeutic dose of Sensoril, is 450 mg per day, standardized to 10 percent withanolides, which are other compounds in ashwagandha. A lot of other ashwagandha contains lower levels of withanolides of 2 to 3 percent.
- Note that ashwagandha contains iron, and some sources recommend avoiding it in people who have hemochromatosis. However, most plant-based forms of iron are not very well absorbed, so that may not be necessary.

CORDYCEPS

- Long history of use in China and Tibet as a remedy for weakness and fatigue.
- Also believed to enhance athletic performance and improve aerobic capacity.
- Dose for cordyceps is 5 to 10 g per day. Note that there is a really wide variety in the quality of cordyceps preparations, so make sure to get it from a reputable source. The highest quality you can afford is the best quality to get, which can get expensive.

PANAX GINSENG (ALSO KNOWN AS KOREAN OR ASIAN GINSENG)

- More stimulating, thus I don't recommend it for nonspecific HPA-D or high cortisol.
- May be useful as tonics or for their stimulating effects in hypocortisolism, but use cautiously and over the short term.
- If you don't have any experience with ginsengs, it is best to learn more about them before you use them extensively because they can be quite potent.

LICORICE

- Active compound in licorice is glycyrrhizin, the structure of which is similar to corticosteroids.
- Its metabolites have been shown to block 11- β HSD2, which is the enzyme that converts cortisol to cortisone. This results in increased levels of circulating cortisol. Understand that it doesn't actually raise or increase cortisol production, but it increases the circulating half-life of cortisol.

- Be aware that chronic high intake of licorice can raise blood pressure.
- With low cortisol, licorice can be helpful in maintaining adequate cortisol levels.
- European studies caution against consuming more than 100 mg/d per day.
- Studies have shown that a very safe upper limit for glycyrrhizin is 0.23 mg/kg per day for all people, including those with higher cortisol.
- Licorice is contraindicated with high blood pressure, blood sugar medication, corticosteroid use, insulin, laxatives, oral contraceptives, and digoxin.

MAGNOLIA OFFICINALIS AND PHELLODENDRON AMURENSE

- Magnolia officinalis is one of the other few natural substances along with phosphatidylserine and GABA that has been shown to decrease cortisol.
- Magnolia and phellodendron are combined in a product called Relora, which has been shown to reduce sleep latency, increase overall well-being, and prevent weight gain by reducing cortisol that contributes to belly fat.
- Dose of Relora is typically 500 mg a day taken in two divided doses, though up to 750 mg per day has been shown to be safe for shorter durations of a few weeks or months.

CANNABIDIOL (CBD)

- One of the 85 active compounds found in the marijuana plant, cannabis.
- Has a number of medicinal properties that could help to reverse HPA-D. In fact, it addresses all four primary triggers of HPA-D: perceived stress, inflammation, dysglycemia, and circadian disruption.
- CBD is not psychoactive, so it can be sold over the counter and shipped to all 50 states.
- Delivery format of CBD is important. Water-soluble forms tend to be more bioavailable.
- If any of your patients work in an environment where they are drug tested, it is possible for CBD use to result in a positive THC test.
- For the water-soluble form, I suggest a starting dose of 5 to 20 mg per day. You can increase to a maximum of 50 mg.
- If using fat-soluble standard preparations, start at 50 to 100 mg per day, with a maximum dose of 400 to 600 mg per day.
- I typically start with other interventions that we've talked about earlier such as adaptogens and supplemental nutrients first, and then if not successful, add CBD.
- Consider using CBD initially in cases of a lot of inflammation and anxiety.

SUMMARY OF BOTANICALS FOR HPA-D

Botanical	Dosage/Comments
Eleuthero	Whole herb/powder: 1-6 grams per day; as tincture, 20-40 drops BID/TID; look for 2:1 or 1:1 extract
Schisandra	Whole herb/powder: 1-3g daily; as tincture, 20-40 drops BID/TID
Rhodiola	Whole herb/powder: 300-700 mg/d; as tincture, 20-40 drops BID/TID
Ashwagandha (Sensoril)	Whole herb/powder: lowest effective dose 300-500 mg/d, up to 6g/d has been used; Sensoril preferred (standardized to 10% withanolides)
Cordyceps	Whole herb/powder: 1,000-3,000 mg/d; as tincture, 20-40 drops BID/TID; dose depends on quality of preparation
Ginseng	5-20 drops BID/TID; use with caution, only in hypocortisolism
Licorice	1 drop = approx 0.75 mg of glycyrrhizin; 10-20 drops in 2 oz. of water BID/TID; only in hypocortisolism
Magnolia & Phellodendron (Relora)	500 mg daily; can be taken on its own or as part of a formula
CBD	5-50 mg daily (water-soluble); 50-100 mg daily (standard)

ADRENAL GLANDULARS

- Drawback: In most cases, desiccated organ products are not standardized for any peptides or hormones, and none that I know of have been clinically tested for HPA-related function in humans using modern research techniques.
- However, they appear to be safe after many years of clinical use.
- I have found them helpful in patients in both hypercortisol and hypocortisol states.
- When taken in the morning they have a stabilizing (calming but also energizing) effect.
- I like the Dr. Ron's brand of adrenal glandulars because he uses desiccated adrenal glands from pasture-raised animals in New Zealand.

HORMONES

BIOIDENTICAL FORMS OF DHEA AND PREGNENOLONE

- Shown to improve bone mineral density in elderly women; increase the DHEA-to-cortisol ratio and blunt cortisol's catabolic effects; and improve cardiovascular, sexual, and cerebral functions, especially in the elderly.

- Newer studies show that DHEA benefits autoimmune disease, specifically in lupus, rheumatoid arthritis, and IBD, at higher doses around 200 mg per day.
- For HPA axis dysfunction, the dose tends to range from 25 to 100 mg a day and up to 200 mg per day for autoimmune conditions.

SUBLINGUAL VERSUS ORAL DHEA

- Micronized forms are more bioavailable and should be preferred.
- 10 mg sublingual DHEA more likely to increase serum DHEA than equivalent oral dose.
- 25 to 50 mg of oral DHEA increases saliva and serum DHEA much more than 10 mg of sublingual DHEA.
- Topical or intravaginal DHEA administration is not recommended.
- Some patients are able to tolerate much higher doses of oral DHEA than sublingual.

Side effects of DHEA include agitation, painful skin breakouts (most common side effect I see), and sleep disturbances.

PREGNENOLONE

Less data than on DHEA; however, there are some studies suggesting that pregnenolone supplementation may provide benefits for the HPA axis.

SUMMARY OF DHEA AND PREGNENOLONE

Hormone	Dosage/Comments
DHEA	<p>Dose ranges from 25-200 mg. Higher dose of 200 mg may be appropriate for autoimmune disease.</p> <p><i>For HPA-D, start with lower dose (25 mg/d orally, or 8-9 drops of sublingual) and increase to 50-100 mg/d as necessary. Short-term use recommended.</i></p>
Schisandra	<p>Dose varies widely, from 5-400 mg/d.</p> <p><i>For HPA-D, start with 25 mg/d orally, or 8-9 drops of sublingual) and increase to 50 mg/d as necessary. Short-term use recommended.</i></p>

See HPA-D protocol matrix handout for a summary of treatment protocols based on DUTCH hormone test results.