Pregnenolone for brain and pain

written by Dr. Ronald Hoffman | October 8, 2021

I've long been a fan of DHEA (dehydroepiandrosterone), available as an over-the-counter supplement. It's a weak androgen, like testosterone, but more unisex; unlike testosterone, of which men have around twenty times as much as women, DHEA is normally only two to three times as high in men.

Thus, when supplementing DHEA, it's less likely to cause undesirable side effects like body hair, alopecia, or acne when taken by women.

It has a host of benefits, including enhancing libido, mood, bone density, and body composition; some studies have shown it curbs autoimmunity, and it may even boost the efficacy of IVF for infertility.

But lately, I've been intrigued by another natural steroid hormone, which is also available over-the-counter: pregnenolone.

Pregnenolone is a "mother hormone"—one of the most ubiquitous hormones produced by the body. Until recently it was thought not to have particular attributes of its own; rather, it is a precursor to other steroid hormones like estrogen, progesterone, testosterone, DHEA, cortisol and mineralocorticoids.

But lately, its role as a "neurosteroid" has been appreciated. It's found in high concentrations in the brain. A review claims, "Neurosteroids are endogenous regulators of neuronal excitability, and therefore provide tremendous opportunities for developing therapeutic approaches."

Pregnenolone is an endocannabinoid, akin to CBD (cannabidiol) in its action, hence its application for mood and pain. It's been said to have the potential to improve memory function. It may support myelinization, offering the prospect of slowing multiple sclerosis nerve deterioration.

Pregnenolone was used briefly in the 1950s as an alternative anti-inflammatory for treatment of arthritis. Its poor bioavailability via the oral route caused it to be abandoned as a medication. Plus, pregnenolone is natural and not subject to patent protection, unlike synthetic designer drugs, so it fell by the wayside.

Pregnenolone levels are known to decrease with aging. It's the first biotransformation step after cholesterol, so overzealous efforts to lower cholesterol may inadvertently result in accelerated pregnenolone depletion. Alternatively, might a paucity of dietary cholesterol pose a risk of neurosteroid insufficiency in strict vegans, who, incidentally, are known to suffer from higher rates of depression?

The symptoms of low pregnenolone may include:

- Poor memory
- Declining concentration and attention
- Fatigue
- Dry skin
- Joint and muscle pain
- Decreased sex drive

Less is known about the effects of pregnenolone than of DHEA, so for a long time I shied away from its use. Occasionally, I would timidly apply 5, 10, or at most 25 milligrams of pregnenolone to patients with only "meh" results.

But, according to recent studies, maybe I was using *too little?*

What caught my eye recently was a double-blind placebo-controlled trial at the VA hospital in Chapel Hill, North Carolina on 94 vets suffering from chronic low back pain. Researchers gradually ramped up dosages to 500 mg per day.

After just 4 weeks of treatment, there were significant improvements in pain scores and mobility. Side effects were negligible. The study authors concluded: "Pregnenolone may represent a novel, safe, and potentially efficacious treatment for the alleviation of chronic low back pain . . ."

Pregnenolone has also been studied for depression. In a 2014 study, 500 mg/day was used for 12 weeks in patients suffering from bipolar depression. Depression remission rates were greater in the pregnenolone group (61%) compared with the placebo group (37%). The treatment was well-tolerated. The authors concluded: "The results suggest that pregnenolone may improve depressive symptoms in patients with bipolar depression and can be safely administered."

Similarly, a group of women suffering from menopausal depression will be treated with pregnenolone at Massachusetts General Hospital as part of a new pilot study.

Women who suffer from menstrual migraines were found to have low levels of pregnenolone, opening up a treatment option with replacement. The researchers state: "Consequently, restoring low endogenous neurosteroid levels could exhibit therapeutic potential in migraine management."

Investigators are also exploring pregnenolone as a treatment for

neuroinflammatory disorders like multiple sclerosis. In an animal model of the disease, allopregnenolone, a metabolite of pregnenolone, blocked inflammatory responses.

Pregnenolone has shown effectiveness in clinical studies of traumatic brain injury, schizophrenia, alcoholism, and other disorders.

As for its safety, it’s noteworthy that pregnenolone, unlike many anabolic steroids, has not been banned by the US Anti-Doping Association. But if you live in California, you’ll be assailed by dire warnings about cancer risk on labels of pregnenolone products; that’s due to Proposition 65’s insistence that even remote or negligible risks be declared.

The science tells us that, although pregnenolone is a precursor to many sex hormones, its consumption results in very minimal increases in potentially cancer-promoting estrogen, testosterone, or DHEA. Moreover, its anti-inflammatory effects are probably not due to boosting cortisol, which in excess, like popular corticosteroid drugs, can accelerate bone loss, ulcers, glaucoma, cataracts, muscle-wasting and diabetes. Therefore, there’s less concern over steroid-like side effects with pregnenolone than with long-term prednisone use.

A word of caution: I believe that pregnenolone supplementation, like DHEA, should be undertaken under the supervision of a health practitioner acquainted with its use. A baseline blood level of pregnenolone and its metabolites can be obtained, and subsequent serial measurements can assess its impact on downstream hormones. Prescribing for patients with hormonal cancers—breast, ovary, uterus and prostate—may require special caution because, while likely safe, its long-term effects haven’t been thoroughly studied.

BOTTOM LINE: Pregnenolone’s wide range of benefits, its relative freedom from side effects, the reassuring fact that it’s one of the body’s most prevalent natural hormones, and its ubiquity as an over-the-counter supplement warrant its investigation for a wide range of ailments for which there exist few safe and effective options.