ANABOLIC THERAPY FOR COMBINED ADHESIVE ARACHNOIDITIS AND EHLERS-DANLOS SYNDROME

SPECIAL REPORT

Precis: Some adhesive arachnoiditis (AA) patients who seek treatment for this condition will also have an Ehlers-Danlos/Hypermobility Syndrome. In order to provide comfort, maintain stability and retard connective tissue complications, we found it necessary to administer anabolic hormones.

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INTRODUCTION

The basic components of adhesive arachnoiditis (AA) treatment consist of medication and physiologic measures with the necessity of patient participation in lifestyle changes in order to facilitate efficacy. Goals are to normalize spinal fluid flow and prevent adhesions of nerves and tendons, and contractures of muscles. Medication treatment includes: (1) suppression of neuroinflammation; (2) promotion of neuroregeneration; and (3) pain control. As we clinically initiated specific treatment for AA patients, a surprising and unexpected number were found to also have an Ehlers-Danlos/Hypermobility Syndrome (EDS). Initially we were not aware that these two diseases closely coincide. Our initial treatment evaluations of AA patients uncovered diagnostic criteria indicating the presence of EDS. In many instances, patients were not aware that they had EDS.[1] These patients, like typical AA patients, sought help for chronic pain and other neurologic symptoms, because they didn't respond well to the usual and standard, symptomatic pain treatments.[2-6] Their treatment histories generally included a myriad of treatments including anti-inflammatories, opioids, antidepressants, muscle relaxants and neuropathic (anti-seizure) medications as well as such measures as corticoid injections both epidural and paraspinal , physical therapies, medically suggested noninvasive treatments, electrical stimulators, and spinal surgical interventions. The EDS patients who sought treatment for AA also had a high prevalence of other spinal cord disorders which have been previously reported by others.[7-11] Included are Tarlov Cysts, tethered cord, syringomyelia, syringobulbia and Chiari malformations.[7-11] All of our patients also had other known complications of EDS such as dysautonomia, cardiac arrythmias, arthritis, ruptured or prolapsed organs, dental decay, unexplained neuropathies, and bowel disorders among others.[12-24]

Patients with the combined diseases of EDS and AA as well as their family all recognized a progressive deterioration in the patient. Families often expressed a desperate and increased emphasis on unusual histories and sought some treatment that would stop the deterioration or at least explain this disorder. It should also be noted that these patients have often suffered greatly with pain and other impairments and had a constant fear that additional connective tissue complications and/or early death would occur. To treat patients with combined AA and EDS, we found that we have had to prescribe anabolic hormones to achieve comfort, maintain physical functions, and retard progression of EDS and its' complications. Hormone therapy is the core of our anabolic therapy, but we have also added to it the adjunctive measures of specific exercises, diet, and electromagnetic therapy to hopefully potentiate the anabolic effects of hormone administration. We explain and share our approach as we have, in the utilization of this approach, observed significant benefits and improvements in these tragic, severely compromised patients. In addition, we know of no alternative treatment for EDS other than symptomatic drugs.

THE THEORY BEHIND ANABOLIC THERAPY

Anabolic means tissue growth or physiologic utilization of energy to create metabolic generation. Catabolic means tissue dissolution or degeneration. EDS patients are genetically programmed to have connective tissue catabolism or deterioration.[1,11,24] Most, but not all, develop this occurrence in childhood and teenage years.[25-29] The tissues most affected are the soft (non-bone) connective tissues found in blood vessels, small nerves, intestine, and spinal

cord.[7,9,10] They progressively dissolve, degenerate, and even disappear, or worse, disassociate from their original location and lodge in a location where symptomatic impingement occurs upon nerves and joints, due to collagen breakdown. Collagen deterioration is followed by micro-tears, inflammation, and pain. Degeneration and dissolution of the connective tissues of the brain and spinal cord are very common in EDS patients as some are quite thin and fragile such as pia mater.[7,9,10] Serious, painful complications, therefore, including tethered cords, syringomyelia, Chiari malformations, Tarlov cysts, and AA are quite common in EDS patients.[7-11] Our basic theory is that catabolism and connective tissue degeneration must be countered with anabolic measures (particularly medical agents, that may rebuild tissue). This can be achieved utilizing the most appropriate medical agents with the intention of enabling the body to rebuild and generate tissue.[3-6] Symptomatic medications for pain and inflammation may provide temporary comfort, but they do not counteract progressive connective tissue dissolution and destruction.

***The public is somewhat knowledgeable about this terminology, because athletes have used high doses of "anabolic steroids" to grow tissue and excel in a sport. While the public may be familiar with athletes "bulking up", be clearly apprised that the dosages, formulations, and gross tissue growth in athletes is hardly the situation when anabolic steroids are used as medically labeled with standard dosages.**

OUR CLINICAL UTILIZATION OF BASIC ANABOLIC THERAPY

The core of anabolic therapy is the use of hormones that have tissue protective and regenerative effects.[30-35] With properly dosed therapy, the anabolic process can increase the patient's own healing process, as the origin of these medications are produced by the body itself in a healthy state. Our initial motivation and guidance in attempting this approach was based on the recent and profound discovery that within the central nervous system (CNS consists of the brain and spinal cord), a set of hormones is made that the CNS uses to protect and regenerate nerve cells.[30-38] This set of hormones is collectively called "neurosteroids", because they are hormones that contain the steroid chemical structure.[34,36,37] Some of the neurosteroids are known to the public as they are also produced in the gonads (ovary and testicles) and include estradiol, progesterone, and testosterone. Other lesser-known neurosteroids include pregnenolone, allopregnanolone, and dehydroepiandrosterone (DHEA). Our reasoning is simple. If the CNS naturally makes neurosteroids for nerve cell protection and regeneration, shouldn't we be administering them for painful, spinal cord conditions such as AA?

Besides the neurosteroids, basic science research has also shown that human chorionic gonadotropin (HCG), human growth hormone (HGH), and oxytocin have essential anabolic functions in the human body.[39-43] These three hormones are made and stored in the brain's pituitary gland. They are periodically is released and activated to protect and regenerate tissue. Again, our fundamental reasoning has been, "if the body naturally makes these hormones for tissue protection and regeneration, shouldn't we be administering them to AA and EDS patients?"

Oxytocin is released during child birth and stimulates the release of the body's natural opioids, endorphins and enkephalins.[42,43] We have used oxytocin in doses of 20-40mcg as a sublingual tablet or solution, troche, or nasal spray. Oxytocin is available commercially as a powder for injection; but many pharmacies compound this medication for non-injection in order to meet a specific patient need. Oxytocin is an excellent pain reliever in some EDS patients in addition to its anabolic properties.[42,43]. An unexpected benefit of oxytocin is that it may prevent anticipatory anxiety, which we have found tends to decrease the experience of actual pain.

BLOOD TESTING AND HORMONE REPLENISHMENT

We begin anabolic therapy with a hormone blood profile since severe chronic pain can deplete some hormones that are essential for healing.[44,45] Now that science has clearly shown that certain hormones protect and regenerate tissue, common sense dictates that we first know if the body has enough hormones to get the job done.[30-33] We recommend that every EDS/AA patient have a blood profile consisting of the following 6 hormones: (1) cortisol; (2) dehydroepiandrosterone (DHEA); (3) estradiol; (4) pregnenolone; (5) progesterone, and (6) testosterone. If any of the 6 show a blood deficiency, that specific hormone should be replenished by taking a low dose supplement to bring the hormone blood level up into normal range. Long-term supplementation may be necessary to maintain normal blood levels. Supplements of hormones don't need to be taken each day. We recommend that a hormone blood profile be obtained in AA/EDS patients about every 3-4 months.

ANABOLIC HORMONE ADMINISTRATION

In patients with combined AA and EDS, we routinely prescribe one or more of the following:

1. Dehydroepiandrosterone (DHEA)[38] – The dosage is 200 to 400 mg a day. DHEA is a neurosteroid that, at a 200 mg dosage, will metabolize to estradiol, progesterone, and testosterone.

2. Pregnenolone[38] – The dosage is 100 to 300 mg a day. At this dosage pregnenolone has direct spinal cord and nerve root anabolic effects. It also metabolizes to allopregnanolone which is a potent neurosteroid with anabolic effects.

3. Human Chorionic Gonadotropin (HCG) – This is one of the so-called "pregnancy" hormones. It goes up in pregnant women as it is THE HORMONE that grows the CNS in the embryo and fetus. When given to animals and humans, it has a direct healing effect on spinal cord and nerve roots.[40-41] In addition, it raises body levels of thyroid, progesterone, estradiol, and testosterone. Dosage is 250 to 500 units on 2 to 3 days a week. It can be taken as an injection, sublingual tablet, or buccal (cheek) troche.

4. Nandrolone[46-50] – This is a synthetic testosterone derivative that is FDA labeled for wasting and deteriorating disease. EDS/AA patients qualify. EDS patients who are deteriorating and have serious complications should most assuredly give this hormone a trial as it has generalized anabolic effects. It will regenerate tissue inside and outside of the CNS. Nandrolone can be taken as a weekly injection (25 to 50 mg), or it can be compounded as a troche to be taken (25 mg) on 2 to 3 days a week.

5. Human Growth Hormone – Although we have less experience with this hormone than the others listed here, some patients have responded in a very positive way. Given its expense and less predictability, it is not our first choice. Patients who have benefitted from it have all simultaneously used one of the other anabolic hormones listed here.

It is to be noted that anabolic hormone administration is considered "adjunctive" to symptomatic pain care. Standard analgesics, anti-inflammatory, and neuropathic agents are simultaneously administered to the patient.

THERAPEUTIC TRIALS

We highly recommend therapeutic trials with the anabolic hormones listed here to determine clinical safety and effectiveness. This is particularly necessary since there are no long-term, controlled studies to guide drug, dosage, and frequency of administration. The minimal length of time necessary to experience positive effects is roughly 2 to 4 weeks. Unless there is positive clinical benefit of an anabolic hormone after about 8 weeks, we recommend the hormone be discontinued.

DOSING AND ROTATION: START INTERMITTENT AND LOW

We recommend that anabolic hormones be given 2 to 5 times a week. Intermittent use reduces the likelihood of any complications. Hormones can also be rotated and/or different hormones can be taken on different days. (Example: HCG and nandrolone rotated each week.) AA/EDS patients may require anabolic hormones for a long period if not a life-time. Our dosing motto for safety is "start intermittent, low, and go slow".

HORMONAL SUPPLEMENTS – NON-PRESCRIPTION

Recently AA/EDS patients have informed us of some non-prescription, hormonal products that they perceive to be effective. They can be taken with other hormones or by themselves. Since they are non-prescription, no guarantees can be made for their effectiveness. If taken, they should be viewed as ancillary to other measures given here.

Gonadal Extracts (Orchex® or Other)

These extracts contain low levels of DHEA, estradiol, progesterone, and testosterone.

Colostrum

This is a milky hormonal substance secreted by primates (humans, animals with a spine and extremities) for a few hours after a female delivers an offspring. Colostrum supports and sustains newborns as it contains a number of anabolic compounds including insulin and epidermal growth factors and growth hormone**.**

Deer Antler Velvet Extract

Although new to the commercial market, it is hardly new. Deer Antler Velvet is a "velvet" type substance in the interior lining of the antlers of a deer. It secretes hormones that nourish and grow antlers and other tissues. Historically, deer antler velvet was known as the medicine for "royalty". At this time, only a few patients have taken it, so we don't have reports to share. Deer antler velvet contains several hormones that are known to grow tissue which include insulin growth factor and epidermal growth hormone.

It is to be noted that some patients who have EDS but have not developed serious complications such as AA or organ rupture may find these non-prescription hormonal supplements quite adequate. It needs to be recognized, however, that an EDS patient with AA

or other neurologic complication is probably too serious to rely on non-prescription, hormonal compounds.

TOPICAL HORMONES

Topical (skin application) of medications for pain relief are primarily anti-inflammatory (i. e. corticoid) or anesthetic (i.e. lidocaine). We have begun using progesterone and estradiol creams over painful joints and soft tissue areas in EDS/AA.[31] We believe that we see a positive, clinical response in some cases. This attempt is reported here to encourage topical anabolic therapy in EDS/AA patients, and could be extremely efficacious to those with less severe cases taking less medications.

ELECTROMAGNETIC THERAPY

There are commercial devices that deliver electromagnetic energy to painful and degenerated tissues.[51] Electromagnetic energy is 50% magnetic and 50% electric. This ratio roughly equates to the body's electromagnetic energy. There are three classes of devices that deliver electromagnetic energy to tissues. They vary in potency and clinical applicability by the length and frequency of the energy waves they deliver. Laser has a very short, frequent wave. Radiofrequency has a long, infrequent wave. Infrared is in the middle of these devices.[51] We recommend electromagnetic therapy in EDS/AA patients because several studies indicate that these devices reduce edema and inflammation as well as provide an anabolic tissue effect. We believe we see a positive effect when these devices are used over the painful joints and neuropathies of EDS/AA patients. All three classes of electromagnetic devices: (1) laser; (2) infrared; and (3) radiofrequency are now available for in-clinic and at-home use. Pulsed electromagnetic field therapy (Provant® or others) is an emerging technology that is being made more available to the general public. When the energy wave is pulsed, it penetrates deep into tissue to decrease inflammation and create analgesic and anabolic effects. Pulsed electromagnetic energy goes in deep enough to affect paraspinal tissues and possibly even inter-spinal tissues.

NUTRITION

To give EDS/AA patients the best chance to succeed we recommend a high-protein, anti-inflammatory diet and some specific dietary supplements. Although EDS is a genetically programmed disease, some nutritional measures may be anabolic and able to retard connective tissue catabolism. Protein is recommended as tissue growth requires the amino acids that are found in protein. The diet we recommend to patients is attached. Besides a daily intake of protein (fish, poultry, beef, cottage cheese, eggs) we recommend vegetables and fruits that are reputed to have anti-inflammatory effects. We also recommend weight control by carbohydrate restriction as excess weight can aggravate joints that are affected by EDS. Often it is not what one may eat, but what they leave out of the diet that can help the most.

EXERCISES - WEIGHT LIFTING, STRETCHING, AND WALKING

To possibly enhance anabolism and prevent falls we recommend 3 basic categories of exercise: (1) weight lifting; (2) stretching "range of motion"; and (3) mobility.[18]

Here is our general guide to our daily exercise recommendations:

1. Weight lifting: Use light weights of 5 to 10 pounds in the form of bar bells or other. Lift with arms only as high as to not cause pain.
2. Stretching: Raise and stretch arms and legs to their maximal reach without pain.
3. Mobility: Walk daily. Walking in water is highly encouraged. Stationary bicycling and trampoline walking are recommended.

TREATMENT OUTCOMES

Although every EDS/AA patient doesn't participate in our entire program, we have used this program in over three dozen EDS/AA patients. Specific data on each patient will be published elsewhere, but clinical improvement in pain and function has been observed in all patients. HCG and nandrolone are the most potent anabolic agents and are used for those patients who have had Chiari malformations, ruptured organs, or other serious EDS complications in addition to AA. Although no claim of cure or near-cure are made, we believe that all EDS/AA patients, and their families and medical practitioners should consider that EDS/AA is a serious catabolic, disease combination that must be countered with anabolic hormones.

SUMMARY

We have recently encountered AA patients who also have EDS which apparently contributes to their spinal cord disease. EDS is just now being recognized by primary medical practitioners and pain management specialists.[1] Many of these patients presented to us with AA without knowing they have EDS. In fact, the association of AA and EDS has been so striking that we believe all AA patients should be screened for EDS.[53] Our standard protocol for AA treatment consists of medication and physiologic measures designed to enhance spinal fluid flow and prevent neuromuscular contractures and limb paralysis. The medication regimen consists of 3 components: (1) anti-neuroinflammation; (2) neuroregeneration; and (3) pain control. We have learned that patients with combined AA and EDS require an anabolic approach to protect and regenerate connective tissue in and outside the spinal canal. To this end, we have initiated the use of anabolic hormones in these patients. To date we believe we have seen positive results in amelioration of not only pain and neurologic impairments, but a salient effect on connective tissue complications outside the spinal canal. Given that there is no recognized medical treatment except symptomatic drugs for EDS, we highly recommend anabolic hormones for patients who have both AA and EDS. We have noticed that some physicians have some reservations about utilizing this kind of therapy. By writing this report, we hope to present anabolic therapy in such a manner that provides increased awareness and the reality that treatment options in these tragic patients are very limited.

The patients that we have seen with these two combined serious and tragic conditions had all experienced other complications of EDS such as organ rupture and prolapse, Chiari malformations, dental decay, dysautonomia, and multiple neuropathies. This special report has been written to call attention to the combined disorders of AA and EDS and to suggest that potent anabolic hormones may likely be needed to prevent, minimize, and possibly reverse the tragic complications of connective tissue degeneration.

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ATTACHMENT

DIET FOR COMBINED EDS/AA PATIENTS

PROTEIN

IT PROVIDES THE AMINO ACID BUILDING BLOCKS THAT ARE NECESSARY FOR THE PRODUCTION OF NEUROTRANSMITTERS AND TISSUE HEALING.

You must eat some of the following EACH DAY:

FISH	CHICKEN	TURKEY	BEEF
PORK	EGGS	COTTAGE CHEESE	

Spirulina and chlorella algae, black beans, and pumpkin seeds are as high in protein as meat. If you can't or won't eat any of the above, you must obtain protein powder drinks and/or protein bars from the health food store.

Vegetables and Fruits

Some vegetables and fruits have anti-inflammatory activity. Eat some of these EACH DAY.

CARROT	CELERY	BEETS	TOMATOES	BROCCOLI
BRUSSEL SPROUTS	SPINACH	CUCUMBERS	RADISH	ONION
LETTUCE	WATERMELON	BERRIES	APPLE	

Drinks: (Only use dietary sugars if weight is a problem): Coffee, Tea, Dietary Sodas, Water

Low dose, occasional alcoholic drinks are acceptable.

Restricted for Weight Control: Milk, Regular Sodas, Fruit Juice, Bread, Rolls, Buns

Highly Restricted for Control Weight (Eat these very sparingly): Potatoes, Corn, Cakes/Pies, Pasta/Pizza

Gluten Restriction (If Needed): bread, pasta, rolls, noodles

DIETARY SUPPLEMENTS

Vitamins: C, D, B_{12}

Minerals: Calcium and Magnesium

PROTEIN SUPPLEMENTS

Whey

Bone Broth

Amino Acid Powders, Drinks, Bars