

W O N D E R W H Y ?

The Use of Hormones for Chronic Pain

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ABSTRACT

Anabolic hormone therapies and Prolotherapy are innovative approaches to treating chronic pain. They are complimentary and can be simultaneously administered.

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KEYWORDS: adrenal, corticoid hormones, DHEA, gonadal, HCG, HGH, human chorionic gonadotropin, human growth hormone, iontophoresis, pituitary, pregnenolone, testosterone.

Hyperalgesia - an increased sensitivity to pain.

system receptors.^{2,3} The claims and concerns about “hyperalgesia” are probably related to hormonal deficiencies that could be easily corrected. The androgenic compounds testosterone, androstenedione, and dehydroepiandrosterone (DHEA) promote tissue growth and help regulate opioid receptors.⁵⁻⁷ Pregnenolone, the precursor of all adrenal and gonadal steroids, is critical for pain control mechanisms, but poorly recognized as essential to pain control. (See Figure 1.) It is ubiquitous in brain and nervous tissue and interacts with gamma-amino-butyric acid and N-methyl-D-aspartate (NMDA) receptors to help regulate neurogenic processes.⁸⁻¹² The tissue building hormones, human growth hormone (HGH) and human chorionic gonadotropin (HCG) are emerging as true breakthroughs in some pain patients.¹³⁻¹⁵ In particular, HCG is a relatively inexpensive compound that appears to permanently lower pain intensity in some pain patients.¹ Besides hormone administration, the understanding of pain’s affects on the endocrine system, particularly the pituitary-adrenal-gonadal axis, is critical to help guide pain management. Excess pain causes catecholamine release resulting in tachycardia and hypertension. Pituitary, adrenal, or gonadal hypofunction may occur with unabated, uncontrolled, and undertreated pain, requiring a need for hormone replacement.¹⁶

INTRODUCTION

Hormone administration is progressively becoming more and more important in treatment of chronic pain.^{1,2} Some specific hormonal therapies offer the patient real opportunities to greatly reduce and even eliminate pain and suffering.^{2,3} They can be simultaneously administered to patients who participate in Prolotherapy or take opioids which is the standard symptomatic medication now used by about 10 million Americans. In some cases hormone treatments are necessary to save a life or prevent incapacitation and suffering.¹ This report reviews the hormone treatment and replacement needs that may exist in chronic pain patients. Many of these treatments can be simply and inexpensively incorporated as adjunctive measures to a practitioner’s current regimens.

WHY HORMONES?

Proper pain treatment may require specific hormone administration. Adrenal corticoid hormones are long known to resolve inflammation and allow healing of injured and inflamed tissue sites. Proper blood levels of adrenal corticoids are also necessary to effectively treat patients with opioids and other pharmacologic agents that must cross the blood brain barrier and affect central nervous

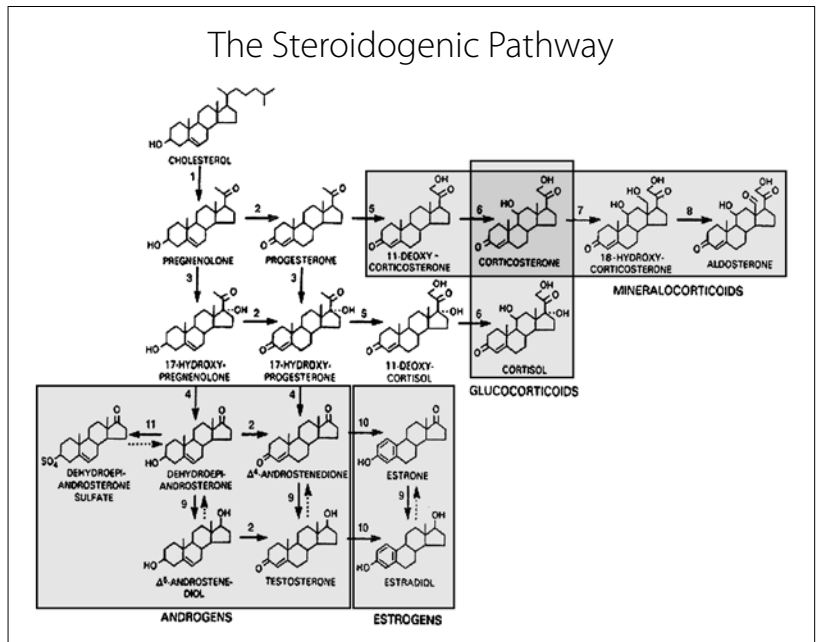


Figure 1. The steroidogenic pathway is the major metabolic pathway in the adrenals and gonads. It is incorrect to state some hormones are “male or female.”

CORTICOID HORMONES

Intralesional and oral adrenal corticoids have been a mainstay in pain treatment for about six decades. Over the years there has been steady improvement in formulation and potency of corticoids. There is no effective substitute for oral corticoids in such painful, inflammatory conditions as acute flares of rheumatoid arthritis. Injections of a corticoid into a “trigger point,” painful joint, or epidural space are routine measures in pain treatment. The new development in corticoid hormone treatment is the administration of high potency adrenal corticoids under an electromagnetic instrument. This technique is generically termed iontophoresis which means to “transport an ion through tissue.” While iontophoresis is an old technique, it has never been widely accepted. Old methods tried to administer metals, salicylates, or weak corticoids by ineffective electric current instruments that were cumbersome, utilized low electric intensity and frequency, and applied medication under small skin contact pads.

HIGH POTENCY CORTICOID HORMONES UNDER ELECTROMAGNETIC INSTRUMENTS

There are many electromagnetic instruments that can effectively drive high potency adrenal corticoid hormones into a pain site. Known generally as “iontophoresis”, any of the electric current devices on the market can be used if it has skin contact pads capable of putting hormone cream on the skin under them. Infrared, laser, ultrasound, and radiofrequency instruments deliver electromagnetic energy in waves of various lengths, and these waves, like an electric current, will cause hormones to diffuse through tissue from the skin surface into a pain site. There are inexpensive, ultrasound and infrared devices that are very suitable for at-home use by patients. Some in-office instruments are extremely effective iontophoretic devices in that they deliver a pulsed electric current or electromagnetic energy, and have skin contact pads or plates that are 2 to 8 inches on a side. If an electromagnetic device is not available, high potency corticoid hormones can usually reach and enter a pain site from the skin surface if heat, massage, or a vibrator is used to promote tissue diffusion.

The author has systematically attempted to administer through the skin a number of androgenic and corticoid hormones at various dosages by a variety of electromagnetic instruments. These trials have led to the



Pulsed radiofrequency used as iontophoretic instrument to drive hormones into pain site.

identification of these two adrenal corticoid analogues: Prednisone and Medroxyprogesterone, 40mg in one ounce of a base cream. (See Table 1.)

Iontophoretic delivery of high potency hormones

Recommended Hormones	Dosage
<ul style="list-style-type: none"> • Prednisone • Medroxyprogesterone 	<ul style="list-style-type: none"> • 40mg in one ounce of soluble base cream
Delivery Instruments	
<ul style="list-style-type: none"> • Electric Current Devices • Ultrasound 	<ul style="list-style-type: none"> • Infrared • Radiofrequency • Laser

Table 1. Iontophoretic delivery of high potency hormones.

The requirements for a cream base are simply that the cream must dissolve crushed hormone tablets and then dissolve the cream mixture through the skin over a pain site. Treatment sessions with a high potency corticoid under a electromagnetic device range from 10 to 30 minutes. Not enough corticoid enters the blood by this technique to produce hyperadrenalism symptoms, but caution is given to avoid this theoretical complication by avoiding daily use.

THE CRITICAL KNOWLEDGE ABOUT HORMONES AND PAIN

Every pain practitioner must have a basic understanding of how uncontrolled pain affects the pituitary-adrenal-

gonadal axis. (See Figure 2.) If pain is severe and goes uncontrolled for even a few days or weeks, profound and deleterious hormonal changes occur.^{4, 16, 17} It is the disturbance of this axis that fundamentally incapacitates a pain patient, thrusts them into a vegetative, non-functional, bed or house bound state, and produces immense suffering, and shortened life.

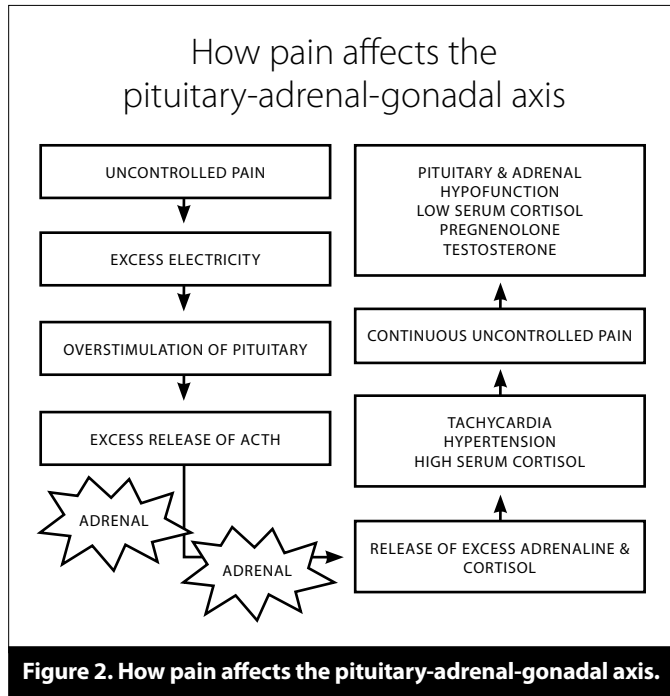


Figure 2. How pain affects the pituitary-adrenal-gonadal axis.

Chronic, severe, uncontrolled pain will initially overstimulate the axis to cause high serum levels of corticoids (e.g. cortisol, pregnenolone), and catecholamines (e.g. adrenaline, noradrenaline). If over-stimulation continues, pituitary, adrenal and gonadal exhaustion and hypofunction will occur resulting in low serum corticoids, catecholamines, testosterone, and other compounds in the steroidogenic pathway.^{4, 16, 17}

BLOOD SCREENING FOR PITUITARY-ADRENAL-GONADAL FUNCTION

Not every pain patient needs to be tested for serum levels of pituitary-adrenal-gonadal hormones. Only those patients that claim constant, chronic, persistent, or intractable pain for a few weeks or more and require regular opioid medication are candidates for hormone screening. (See Table 2.) I recommend a simple, short screening panel: cortisol, pregnenolone, and testosterone. This screening panel can be done by any licensed clinical laboratory on an 8:00am, fasting, whole blood specimen.

Recommended screening panel for pituitary-adrenal-gonadal function

- Pregnenolone
- Cortisol
- Testosterone

Table 2. Recommended screening panel for pituitary-adrenal-gonadal function.

These three serum hormone levels give a pain practitioner enough information to know if pituitary-adrenal-gonadal overstimulation or hypofunction is present.

I recommend a total serum testosterone rather than any free or sub-total test. Testosterone is critical for pain control, libido, energy, motivation, and mental function. (See Table 3.) Although some of testosterone’s functions (e.g. libido) may rely on the non-protein bound, serum fraction, testosterone has other functions critical to pain management that may require the protein-bound component.⁵⁻⁷

Recommended screening panel for pituitary-adrenal-gonadal function

- | | |
|-------------------|------------------------------|
| 1. Lack of energy | 5. Diminished opioid affects |
| 2. Loss of libido | 6. Loss of motivation |
| 3. Depression | 7. Apathy |
| 4. Poor healing | |

Table 3. Symptoms of testosterone deficiency in males and females.

MANAGEMENT OF LOW SERUM CORTISOL LEVELS

Some severe chronic pain patients may demonstrate serum cortisol levels that range 2 to 3 times above the upper normal level of about 20-25ug/dl.¹⁸ A high cortisol level simply means that pain is uncontrolled and aggressive opioid administration will need to be instituted. If the patient has pituitary or adrenal hypofunction, serum cortisol levels will be under 5ug/dl. The key to normalizing high or low serum cortisol levels is opioid management which stabilizes the pituitary-adrenal-gonadal axis. Opioid dosage should be raised from any current daily dosage or initiated if the patient is not taking opioids. Normalization of serum cortisol will almost always take place within 4 to 6 weeks.¹⁷

Cortisol replacement is seldom necessary. I recommend plain hydrocortisone or prednisone administration for 2 to 4 weeks if the serum cortisol is below 2ug/dl. This is a precautionary measure done as a potential, life-saving procedure as serum cortisol levels this low pose grave danger to the patient. Levels this low do not provide immunologic protection against infections or maintain adequate blood pressure or glucose levels.

MANAGEMENT OF LOW SERUM PREGNENOLONE LEVELS

Few physicians are even aware of pregnenolone and its numerous biologic roles.⁸⁻¹² Pregnenolone is the primary precursor of all hormones produced in the steroidogenic pathway. A low serum pregnenolone represents a potential, problematic situation in that there may not be enough substrate for the steroidogenic pathway.

Pregnenolone is, itself, a critical hormone. It is probably the most plentiful hormone in human brain. Normal levels are necessary for gamma amino butyric acid (GABA) neurotransmission.⁸⁻¹⁰ It also helps stabilize the NMDA receptor.^{11, 12} If serum concentrations are below 20ng/dl, I recommend a daily, oral dosage of 100 to 200mg. At this time, pregnenolone, due to its high safety and non-abuse profile, is available over-the-counter without prescription.

MANAGEMENT OF LOW SERUM TESTOSTERONE

Commercial laboratories now report normal levels for males and females making it easy for the practitioner to make a diagnosis of hypotestosteronemia. Patients with low serum testosterone usually voice a number of symptoms which are outlined in *Table Three*. Low testosterone in females produces significant symptomatology just as in males.^{18, 19}

If the serum testosterone is low, several testosterone products are available including injectable, patch, buccal tablet, and gel formulations. I recommend a female starting dose of about 20 to 25% of the male dose.¹⁸ In addition to plain testosterone, the use of progesterone, androstenedione or DHEA may assist or enhance testosterone activity.²⁰⁻²²

THE PROBLEM OF OPIOID SUPPRESSION OF HORMONES

When pain is severe enough to require regular, treatment with opioids, the practitioner must be aware that opioids may suppress one or more hormones of the pituitary-adrenal-gonadal axis. It is clear that hormone suppression

is a major opioid complication.²³⁻²⁶ Opioids are probably more likely to suppress hormone production if an opioid is constantly in the blood rather than present on an intermittent basis.

The hormone most commonly suppressed by opioids appears to be testosterone in males and females.^{18, 24} The suppression is primarily due to suppression of follicle stimulation hormone (FSH) and luteinizing hormone (LH) in the pituitary. Intrathecal opioids do not enter the general blood circulation to reach the adrenals or gonads, but they suppress testosterone production in the pituitary.²⁶

It is known that opioids may, in a few patients, suppress ACTH or directly impact adrenal metabolism.^{23, 25} In these cases it may be necessary to replace pregnenolone, cortisol, and possibly other compounds. One common suppression may be aldosterone which is a diuresis and fluid retention hormone. This is apparently the cause of opioid edema.²³ It can usually be relieved by a corticoid injection since cortisone converts to aldosterone.

The author highly recommends that pain patients who require opioids take pregnenolone and DHEA as dietary supplements. Although no published data is available, pregnenolone and DHEA are very active hormones, as well as the metabolic precursors of all corticoids, androgens, and estrogens. Dosage ranges from 50 to 100mg a day. These compounds are non-prescription and can be inexpensively obtained over-the-counter. It is the author's observation that supplementation with these hormones prevents hyperalgesia, helps retain opioid potency, and aids adrenal and gonadal functions.²⁰⁻²²

THE INTRIGUE OF HUMAN CHORIONIC GONADOTROPIN (HCG)

A most intriguing discovery relative to pain treatment and hormones in recent times is that HCG, in some patients, provides short-term and/or long-term pain reduction.²⁷ Its cousin, human growth hormone (HGH) may also reduce pain when given over several weeks. This is understandable since HGH is well known to produce bone, cartilage, and muscle growth.¹³⁻¹⁵ Just how effective HGH may be in pain treatment is unclear, since the hormone is so expensive that there is very limited clinical experience with it. To date, its use in the author's hands has been inconsistent. On the other hand HCG elicits a positive pain reduction response in about 75% of pain patients.²⁷

Human chorionic gonadotropin (HCG) derives its name from the fact that it was originally believed to be only produced in the placenta during pregnancy. Indeed, the common at-home pregnancy test is based on the finding of elevated HCG levels in female urine. It is now known, however, that it is also produced in the pituitary of males and females of all ages.^{28, 29} Chemically, it is made up of two amino acid sub-units. One of the units contains amino acid sequences that are essentially identical to FSH (follicle stimulating hormone), LH (luteinizing hormone), and TSH (thyroid stimulating hormone).^{28, 29} Consequently, HCG, when given, stimulates the testes, ovary, thyroid, and adrenal to elevate serum levels of testosterone, thyroid, estradiol, progesterone and related compounds.^{28, 29} It is this pro-hormone stimulation that undoubtedly gives HCG a role in pain treatment. Severe chronic pain patients who must take opioids develop multiple hormonal deficiencies that may be ameliorated by HCG's hormone-stimulating properties.

The other sub-unit of HCG has some biologic activities that may also assist pain patients. It increases cyclic adenosine monophosphate (cAMP) and nitric oxide (NO). cAMP is known to be a critical element in tissue production and growth while NO has important intracellular and intercellular regulatory functions. NO is known to increase blood flow. HCG receptors are found throughout the body, so this finding validates that HCG has a much greater biologic role than simply maintaining a placenta in pregnancy.

Clinicians have observed that pain patients during pregnancy require fewer opioids. Apparently, the rise of HCG in pregnancy is responsible. Indeed, after a single injection of HCG, some pain patients report pain relief within hours. Others report significant and progressive pain reduction during a course of HCG treatment which is 2 to 3 injections a week for 6 to 8 weeks. Each dosage is .5 to 1.0ml of injectable HCG (10,000 units in 10ml).

Case Reports: The Use of Hormones in Chronic Pain

CASE #1

A 44 year-old male suffered three lumbar, herniated discs which required fusion and placement of metal rods. He was started on multiple opioids but did poorly and was

referred for medical evaluation and management. His serum testosterone was 154mg/dl (Normal 241-827mg/dl). Within days of starting a testosterone gel of 50mg a day, his pain dramatically decreased and his energy, motivation, and libido increased. An addition of oral medroxyprogesterone 10mg, twice a day considerably improved his libido and physical abilities. With testosterone and a precursor, progesterone, he has gone from a bed/house-bound state to one in which he is active each day and can work part-time.

CASE #2

A 68 year-old female has multiple cervical and lumbar fusions. She was treated with multiple spinal corticosteroid interventions including epidural and facet injections. She was referred in a bed-bound state despite taking a daily, extended release oxycodone dosage of 160mg. Admission serum cortisol was 27.2mcg/dl (Normal 4.0-22.0mcg/dl) indicating overstimulation of the pituitary-adrenal axis. Her oxycodone extended release dosage was increased to 700 to 800mg a day, and she was given a trial of HCG, 0.5ml twice a week. These injections were associated with a decrease in pain and oxycodone dosage. This dosage was later increased to 1.0ml three times a week, and she believes she is incapacitated if she misses HCG injections, and she credits it for control of her pain and ability to function. The patient now has serum cortisol levels under 20mcg/dl and is no longer bed-bound. She attends to all her activities of daily living and is able to drive and visit grand children.

CASE #3

A 58 year-old female registered nurse was diagnosed with degenerative cervical spine disease with bulging discs. She subsequently developed fibromyalgia with temporal mandibular joint (TMJ) disease, migraine headaches, and radiating pain into the legs causing her physician to refer her for evaluation and management. Her opioid medication consisted of hydrocodone, 40mg a day. To better control her pain, her opioid dosage was increased by adding hydromorphone, 16mg a day. She was started on HCG, 1.0ml twice weekly. Within 4 hours after starting HCG she felt pain relief and increased energy, motivation, and libido. After 4 weeks of HCG, all TMJ and migraine headaches stopped. She has continued on HCG for over 6 months, and she reports that her pain has progressively and permanently decreased and that her physical activities are increasing.

SUMMARY

Corticoid hormones for interlesional use and oral administration have been and remain a mainstay in pain treatment. High potency adrenal corticoids such as topical prednisone and medroxyprogesterone in a dosage of 40mg per ounce of base cream can be administered iontophoretically under a number of electromagnetic devices. Patients can use inexpensive infrared, ultrasound, or vibrators to self-treat at home with high potency corticoids. Severe, uncontrolled pain may overstimulate the pituitary-adrenal-gonadal axis to release excess corticoids and catecholamines which increase heart rate and blood pressure. If severe pain continues unabated, the pituitary and adrenal may exhaust, deplete hormonal reserves, and demonstrate low serum levels of cortisol, testosterone, or pregnenolone. Hormone replacement may be necessary. Opioid treatment may suppress some hormones, particularly testosterone, in females as well as males. Testosterone is required for libido, energy and opioid activity, and it has to be replaced should serum testing show low levels. HCG is a most intriguing hormone that apparently reduces pain by multiple, physiologic mechanisms. It is quite void of side-effects and is worthy of therapeutic trials to treat pain. Pregnenolone and DHEA are themselves active as well as precursor compounds in the steroidogenic pathway. They are safe, inexpensive and classified as dietary supplements, and sold over-the-counter. They are recommended as preventive measures in chronic pain patients who take opioids. ■

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