

HUMAN CHORIONIC GONADOTROPIN: EMERGING USE IN PAIN TREATMENT

By

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Introduction

Thanks to the revelation that Dodger baseball star, Manny Ramirez, used and is now suspended for the use of human chorionic gonadotropin (HCG), this compound is now known to the general public.

They now realize that it can enhance athletic performance.

HCG is a new, emerging treatment that appears to have great potential as an adjunct to opioid pain treatment. Adverse publicity involving anabolic steroids has already caused most of them to be removed from the commercial market depriving physicians and patients of beneficial treatment options. Unfortunately the Ramirez fiasco has the potential to tarnish the image of HCG and cause it to be restricted for medical uses.

Due to the HCG sports controversy, and despite very early clinical experience, we want to let practitioners know that HCG, is starting to be used as an adjunct in severe, chronic pain patients. Use in pain patients is a far cry from its use to enhance athletic performance. To alert practitioners to HCG's potential, some of my preliminary experiences with HCG are reported here. To date it appears quite beneficial, safe, and easy to administer. Some females with low testosterone serum levels have greatly benefited from it.

WHY HAS HCG ENTERED PAIN PRACTICE?

Over a year ago, Practical Pain Management published articles about the emerging use of hormonal treatments, including HCG, in pain practice.¹ Hormone therapy in pain patients is now being used for replacement particularly of testosterone and cortisol. HCG stimulates the production of testosterone, progesterone, estradiol, and thyroid, which should bring obvious benefits to some pain patients.²⁻⁴

HCG may also achieve pain reduction through neurogenesis and tissue healing.

WHAT IS HCG?

The name "Human Chorionic Gonadotropin" 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 HCG in female urine. It is now known, however, that it is additionally produced in the pituitary of males and females of all ages.²⁻⁴ 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 thyroid stimulating hormone (TSH).² Consequently, HCG, when given, stimulates the testes, ovary, thyroid, and adrenal to produce testosterone, thyroid, estradiol, progesterone, and related compounds. It is this pro-hormone stimulation that gives HCG multiple clinical uses. 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).⁴ cAMP is known to be a critical element in tissue production and growth. 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.⁴

Although considerable mystery about the physiologic effects of HCG remain, it is clear that the combined effects of hormonal stimulation and enhanced tissue growth through cAMP and NO production make HCG a compelling compound for clinical trials in severe, chronic pain patients.

HOW IS IT PRODUCED?

One of the myths about HCG is that commercial products come from animal urine. The most commonly used HCG product in the United States is produced and distributed by Abraxis Pharmaceutical Products. The only HCG product listed in the 2009 Physician's Desk Reference (PDR) is Ovidrel® produced by EMD Serona Inc. Ovidrel® is in a prefilled syringe. The former is marketed in a 10cc vial containing 10,000 USP units, and its package insert lists the production source as urine from pregnant women. The latter obtains its HCG from a cell line which comes from hamster ovaries. Both products are FDA approved and are marketed only after high level, scientific straining and sterilization techniques have been used. It is highly recommended that pain practitioners only obtain or prescribe American manufactured HCG that is distributed through, local American pharmacies and suppliers and refrain from purchasing any product from unknown internet sources or from out of the country. There is a large underground, clandestine, Mexico-Canada trade comprised of so-called HCG products which are unknown, non-standard, and which have questionable sterility and potency issues. HCG must be injected since it apparently is digested if taken orally.

MEDICAL USES

The popular press refers to HCG as a female fertility drug. This is only partially correct.

The fact is that it has multiple US Food and Drug Administration (FDA) approved indications. The HCG insert from Abraxis Pharmaceutical Products lists three indications:

1. Prepubertal cryptorchidism;
2. Hypogonadotropin (pituitary deficiency) hypogonadism;
3. Induction of ovulation and pregnancy in anovulatory women.

Patients who require high dose opioid therapy and who develop hypogonadism as evidenced by a low testosterone serum level qualify for indication No. 2. Opioids are known to suppress the pituitary gland producing a hypogonadotropin state.¹ It was this indication that first attracted the author to its possible benefit in pain patients.

In addition to the package insert indications, HCG is used "off-label" for other purposes. (See Table One) It is emphasized that there are few clinical studies or reports involving HCG. Its most widespread use has probably been weight control. This has been controversial. Some observers don't believe there is much weight loss with HCG, but it is reputed to cause slimming apparently due to muscle building at the expense of fat reduction. This belief is unproven.

<p style="text-align: center;"><u>TABLE ONE</u></p> <p style="text-align: center;"><u>USES OF HCG</u></p> <p style="text-align: center;">Undescended Testicle in Boys*</p> <p style="text-align: center;">Menstrual Regulation</p> <p style="text-align: center;">Infertility in Females*</p> <p style="text-align: center;">Hypotesteronemia*</p> <p style="text-align: center;">Weight Control</p> <p style="text-align: center;">Pain Relief/Neurogenesis</p> <p>*Labeled Indications</p>

LESSONS FORM THE SPORT'S WORLD

HCG has been used by athletes to enhance performance since at least the early 1980's. Manny Ramirez is hardly the first to use HCG, and his widespread publicity will likely encourage other athletes to seek it. Some states now classify HCG as an anabolic steroid and/or classify it as a

controlled substance in an attempt to limit its non-medical use. Ethical pain practitioners must guard against any attempts by teen-agers or other athletes to obtain it for non-medical purpose.

A common misunderstanding is that athletes only use HCG at the end of a steroid cycle to up-regulate their natural testosterone production and libido, since a high dose cycle of anabolic steroids will suppress testicular function and libido.

While end-of-cycle use of HCG is common, it is used by itself or with other anabolic steroids to bolster performance. It is highly instructive to read the 1982 handbook entitled, "The Practical Use of Anabolic Steroids With Athletes". This book, now a valued underground manual, is about the last treatise on the use of anabolic steroids written by a knowledgeable physician. This handbook was written by Robert Kerr MD who was an orthopedic surgeon practicing in Los Angeles County in the 1970's and early 80's when it was fundamentally considered ethical medical practice to prescribe anabolic steroids to athletes. Dr. Kerr specialized in body builders and power lifters, and rumor has it that his clientele contained many of the famous athletes and body builders who supposedly took anabolic steroids. Today, the recommendations of Dr. Kerr, if followed, would likely be considered grounds for delicensure or criminal prosecution. He certainly could not have written his handbook of which this author is fortunate enough to have a copy and which I consider to be the first and last "bible" of what anabolic steroids really do. Consequently, I pass on these quotes from Dr. Kerr's chapter on "Human Chorionic Gonadotropin", and my comments.

To quote Kerr, "Many body builders have the feeling that HCG is used for "cutting up" claiming that it rids the body of the subcutaneous fat needed to show cuts and vascularity", and "HCG will add more endogenous testosterone to the body for its anabolic effect. When this is combined with the exogenously taken oral or injected testosterone product, the effect will bring on a renewed "pumping

effect" that will increase the muscle size and this "pump" will, in turn, better show the muscle divisions, fibers, and striations. "The increase in blood vessel size or "vascularity" so desired by body builders".

My Comment

Now that we understand that HCG has anabolic or growth affects due to CAMP and NO production, it makes sense that muscle will grow and blood vessels will increase blood flow.

Kerr well relates that HCG will neutralize the sexual suppressing effects of anabolic steroids.

To quote Kerr, "HCG will continue the endogenous production of testosterone, and the athlete will usually not notice any decrease in libido functioning to the relief of all concerned."

My Comment

This statement clearly indicates that HCG will continue to bolster libido even when testicular- ovarian suppression may be taking place. Opioid drugs also cause pituitary-adrenal-testicular suppression, so HCG should help neutralize these complications.

The dosages used by Kerr were 1000 to 2000 units given three times, a week which is higher than most dosages recommended for treatment of hypogonadism. In general athletes use much higher dosages of performance enhancing drugs that the dosages used for legitimate medical needs. I use 500 to 1000 units given 1 to 3 times a week.

Clinical Uses in Pain Practice

The author has begun using HCG in severe chronic pain patients who required high dose opioids which are known to suppress testosterone and other hormones. Patients are given one or two trial dosages of 500 or 1000 USP units. If patients believe they experience positive effects with libido, energy, or pain relief, they are given a 90-day course of 1 to 3 weekly injections. They sign an "off-label" consent agreement. While my experience to date is limited, some patients report extraordinary results. Others report no effects. Acne, in some females, has occurred which necessitated stopping HCG or reducing the dosage. No other side effects have been observed. The following are illustrative cases.

Case Reports

A. A 68 year old female has intractable pain due to severe spine degeneration. She has had a cervical neck fusion and has lumbar spinal stenosis. Her daily opioid intake is approximately 1300mg of morphine equivalence. Her serum testosterone was less than 20ng/dl. She takes 1000 units of HCG once a week, and she reports the following: (1) increased energy, libido, sleep; (2) decreased pain, depression, and house-bounding.

B. A 65 year old female developed severe fibromyalgia in 1997 following a severe auto accident. She progressively worsened despite multiple treatments and numerous physician consultants. In March 2008 she had deteriorated with constant, severe pain to the point of being bed or house bound, tachycardia over 100 per minute, insomnia, anorexia, extreme lethargy and progressive wasting despite a daily morphine dose equivalence of approximately 3500mg. Serum testosterone concentration was less than 12ng/dl. As a last option, she was started on HCG, 500 to 1000 units three times a week. Within a week she began to have more energy, appetite, lowered pulse rate, and less pain. Over a

year's treatment she states her pain is approximately 50% improved and her daily opioid intake has dropped to 1400mg morphine equivalence.

As the above two cases indicate, HCG trials have primarily been initiated to deal with the problem of hypotesterism in females and patients who have progressively deteriorated. Patients who appear to benefit, report improvements in libido, energy, mobility, and pain control. Patients who report pain relief are an intriguing group because it may be that HCG causes neurogenesis or permanent healing. HCG has anabolic or tissue healing capabilities due to its anabolic powers resulting from hormonal stimulation and up-regulation of CAMP and NO. Although the author's experience is quite limited and preliminary, HCG is simple to administer, and short course trials appear to be quite safe.

Conclusion

The recent use of HCG by baseball star Manny Ramirez has put this compound in the public spot light. While publicity has its merits, the zealous desire to "clean up" sports could cause an overreach and limit HCG's legitimate medical uses. Recent research shows that HCG has potent hormonal and tissue growth capabilities. Consequently, HCG has great potential as an adjunct in the treatment of severe, chronic pain patients particularly in those who demonstrate hormonal deficiencies or who show progressive wasting and deterioration. To date it appears simple and safe to use in pain practice, and physicians are encouraged to try it.

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