REVIEW ARTICLE

The 'Natural' Growth Hormone Explosion: Fact or Fraud?

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Since the past decade there has been a rapidly growing market of natural growth hormone (GH) products based on clinical trials carried out on GH-deficient persons, using the injectable hormone, which is the FDA-approved form. Prior medical publications on the benefits of GH replacement brought about an exaggerated interest on the use of this hormone as a dietary supplement for rejuvenating purposes. This has led to the uncontrolled proliferation of all kinds of GH products advertised irresponsibly as if having extraordinary age-reversing properties without the necessary clinical trials to prove their effectiveness and safety. This review summarizes the circumstances which led to this excitement over GH therapy and provides an overview of the different types and forms in which these natural GH products are sold, giving emphasis on the possible misleading advertisements and the lack of reliable proof to their claims.

Key Words: Growth hormone therapy, Natural growth hormone, Homeopathic products, growth hormone secretagogues, IGF-1 products.

At first it was assumed that growth hormone (GH) had no physiologic relevance after the cessation of linear growth. Later, after the publication of the first two randomized placebo-controlled studies of GH replacement in GH-deficient adults in 1989 (1, 2) it became clear that lack of GH has significant clinical effects on a number of physiologic functions. The beneficial effects of GH on body composition, muscle strength, bone remodeling, cardiovascular risk and even psychological well-being have been confirmed in a series of other controlled studies that have been published since then (3-7). All of these benefits prompted the approval by the US Food and Drug Administration (USFDA) in August, 1996 of injectable GH as replacement therapy for adults with GH deficiency.

Apart from favorable surrogate endpoints, such as subjective data on quality of life, increase in bone mineral density, increase in muscle strength and improvement in body composition and lipid profile; there is only scant and not very positive information regarding GH replacement on truly clinically relevant endpoints such as fracture rate, functional status, performance on real-life events (ie. marriage, socioeconomic achievement) and rate of morbidity or mortality compared to the general population. There are a few controlled clinical trials which confirm the favorable changes in body composition brought about by the use of GH in the elderly, but without improvement in muscle strength or functional status (8,9).

One of the most cited articles on this topic is that by Rudman et al. published in the New England Journal of Medicine (NEJM) in the year 1990, on the effects of a 6-month treatment with injectable GH in 12 elderly men with low IGF-1 level (10). The trial resulted in an impressive 8.8% increase in lean body mass, a 14.4% decrease in adipose tissue mass and a 1.6% increase in lumbar bone mass. This small trial prompted the rise of what has been called the GH 'explosion' with the proliferation of 'antiaging' clinics and lay publications extolling the benefits of GH in reversing or preventing aging. Such uncontrollable frenzy promted the publication of an article "I nappropriate Advertising of Dietary Supplements" (11) by the editor-in-chief of the NEJM. The author of the editorial, published at the time of the article, reaffirmed in another article on the same issue of the journal: *"Because there are so many unanswered questions about the use of hGH in the elderly and in adults with hGH deficiency, it's general use now or in the immediate future is not justified" (12).*

To compound the problem, in 1994 the Dietary Supplement Health and Education Act (DSHEA-1994) was passed, which allows for low dose hormones to be sold and marketed as dietary supplements, falling into the category of food, not drugs. This has given way to the streaming of all sorts of 'natural' supplements which can

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include small amounts of GH in their formulations without the need of a prescription or medical surveillance. Also, this has led these companies to be able to attribute to their products the same properties and benefits achieved by the approved injectable GH replacement without the need of any rigorous, controlled clinical studies.

Since many features of normal aging resemble those of adult GH deficiency and GH secretion decreases progressively with age by approximately 14% per decade (13), popular interest has focused in the past several years on the use of GH for prevention or even regression of the normal aging process. So the GH explosion seems to have just begun.

There are two main problems with the approved form of GH therapy: first, GH is a large peptide that cannot be absorbed intact (not in tablets nor by oral spray) and must be injected subcutaneously to have any effect on the organism; and second, its cost is prohibitive to most individuals (in the range of $800-$1,500 per month). These and the above-mentioned circumstances became fertile ground for the appearance of a host of 'natural' products that claim to increase GH levels and to revert the aging process for up to 20 years.

"Natural" Forms of GH Replacement Available

These GH supplements come in diverse presentations and from multiple sources. Placing a web search on natural growth hormone therapy, it was found that these so-called natural products can be categorized into 4 main groups: homeopathic GH supplements, low-dose GH supplements, releaser GH products or a combination of any of these with IGF-1 and other growth factors.

Homeopathic GH supplements. Homeopathic GH supplements are said to use small amounts of actual synthetic GH to spur the body's natural production of its own GH. The homeopathics claim they use extremely small amounts of the hormone which is diluted in purified water and alcohol through a process of 'succussion" *(http://www.hgh-pro.com)*. The original molecule is diluted in either decimal potency, denoted by an "X", or centesimal potency, denoted by a "C". A decimal potency is prepared as 1 part GH per 10 parts purified water and alcohol, to give a 1X potency which is further diluted in 9 parts of the base solution to give a 2X potency, and so on...until a specified dilution is reached. The usual homeopathic remedies are in the 30X range which would produce 1/ 1,000,000,000,000,000,000,000,000,000,000,000th the strength of the original mother tincture. This homeopathic remedy is not likely to contain even a single molecule of GH. The homeopathy theory believes that through succussion (or specialized agitation) there is stimulation of the electrons of the active ingredient allowing the molecules to have some sort of electromagnetic imprint on the molecules of the base solution, allegedly potentiating the mixture with the strength of the original active ingredient. The concept of homeopathy states that the lower the dose the stronger the effect, so that the more diluted the better. These supplements are administered mostly by oral spray.

Regarding homeopathic GH, a single double-blind, placebo-controlled study has been reported in a journal of alternative medicine, in which GH provided wellness benefits (14).

In this trial, 69 people were given either placebo or either of two different forms of homeopathic GH, with dilutions ranging from 10^6 to 10^{400} dilution. Over the three weeks of treatment, people receiving the homeopathic remedies showed an increase in muscle mass, reduction in fat mass and improvements in various measurements of overall health and well-being compared to placebo. This study has not been reproduced. By placing a search in the Internet, I could only find the mention of one clinical study performed in Mexico which demonstrated an increase of 160% in the levels of IGF-1 in 21 patients treated with their homeopathic product ProBLEN for 5 months *(http://www.hgh-pro.com)*. But, there was no mention of the clinical benefits and the study was not found published in any medical journal.

The publicity of these companies can be so misleading as to make the public think their product is approved by the FDA by claiming it is produced in an FDA-approved laboratory. Just see an example of a deceiving affirmation by one of these companies: *"Our lab is one of the few producing Homeopathic HGH that is FDA Approved." (www.21stcenturyhgh.com)*.

Low-dose GH supplements. Low-dose GH supplements use the original hormone in very low doses so as to be considered a supplement and not a drug. These supplements claim to contain a dose of GH measured in *nanograms*, usually in the range of 300 to 2,000ng of GH per dose. The usual replacement dose of injectable GH in an adult is 0.3-0.6mg daily which is equal to 300,000-600,000 nanograms. So a supplement with 2,000 nanograms of GH provides less than one-hundredth of that normally prescribed by doctors. Making matters worse, GH is a large molecule and is not known to be absorbed orally, sublingually or even as a nasal spray, which are the forms in which these supplements are delivered. In short, there is too little GH in these products to be considered effective and it won't even be absorbed. But, there are even those who claim that their 'new patented liposome delivery system' has 200% more bioavailability than other GH products *(http://www.evitamins.com)*. This is very unlikely, but even if so, the amounts they start with are

too minute for a result to be hardly expected.

After a search through the medical literature, I found no controlled studies by independent investigators on these low-dose GH products, and most of the studies cited by these sellers are using the injectable forms of GH. I could only find tables showing a few patients demonstrating nonsubstantial increases in IGF-1 after using their product for only a few weeks. These results appeared to come from internal numbers of the sponsoring companies *(http://www.hgh-pro.com)*, but without any references to where they were published or what researchers were involved. A handful of unverifiable testimonials by alleged consumers is the main proof of efficiency of these formulations.

GH secretagogues. A third category consists of releaser GH products or secretagogues which are mixtures that may contain herbs, L-group aminoacids, plant and animal extracts and/or various vitamins and minerals that the sellers claim stimulate the anterior pituitary gland to release higher levels of GH. These oral formulations are based on the knowledge that certain aminoacids, particularly arginine, lysine and leucine, stimulate GH secretion. But, these cause only a transient increase (30-60 minutes) in serum levels of GH and taken orally the effect is less intense than when given intravenously, which is the classical method these aminoacids are used as diagnostic tools of GH deficiency. It's difficult to believe that such a short-term change in growth hormone levels could provide any real benefit. The only evidence that it actually does bring about any meaningful changes comes from two small studies conducted by a single researcher (15-16). The author claimed to find increases in strength and improvements in body composition when athletes took arginine and ornithine; however, subsequent scrutiny of the statistical analysis used in these studies found serious errors and as a result, the conclusions are not reliable. *(G:/Consumer Lab_com)*.

Many of these products are named in such a way that it appears they contain GH, but are only a mix of herbs and aminoacids. There are no studies to support the claim that they increase the release of GH nor any proof of their safety. It is not known at present if the use of GH secretagogues, assuming they are continuously stimulating GH secretion, may even cause a decrease in its production. The only mention of a clinical trial with a secretagogue in persons with chronic fatigue syndrome was on a small group of patients for only 2 months and it was not a controlled study and not published on any known medical journal *(www.ghsmax.com)*.

In April 2003 the Food and Drug Administration (FDA) announced that it had accused the maker of Nature's Youth hGH, a GH releaser, of making false and misleading claims. The company claimed that the product would "improve physical performance, speed recovery from training, increase cardiac output, and increase immune functions." The FDA had the company destroy the misbranded product and agree to change the labeling for future marketing *(G:/Consumer Lab_com)*..

IGF-1 and growth factors supplements. Another category of natural GH products is the combination of homeopathic and/or releaser products with IGF-1 and other growth factors which allegedly maximize their effectiveness. Deer antler cartilage is used in some of these products due to its high amounts of IGF-1 and anti-inflammatory properties. Even cow maternal colostrum has been marketed as an IGF-1 releaser. No published independent clinical trials were found on either the medical literature or general internet search to validate these claims.

Conclusions

During the past decade there has been an uncontrolled frenzy in the natural products market brought about by the published benefits of injectable GH treatment on individuals with GH deficiency and the liberalization in the commercialization of so-called dietetic supplements. These 'natural' GH products come in all sorts of preparations and forms of delivery, but without any hard evidence on their safety or efficacy. There are definitely proven benefits on the use of GH on deficient persons, but their use on healthy elderly people is still debatable, especially since no randomized, placebo-controlled clinical trials, with a sufficient number of subjects that would validate the results, have been performed. Many of these products are probably just fraud, but some might have a true positive effect on the organism. Responsible and trustworthy companies must carry out controlled studies with their products so that they can be reproduced by independent investigators and prove the validity of their claims.

In this article I have presented an overview of available GH products on the market and believe it is important for the medical community to start some serious research trials on those supplements that might have some scientific backup to their allegations. Fraudulence must be replaced by fact and if results are positive, there might be some promising applications for this 'so-called' hormone of youth.

Resumen

Desde la última década ha habido un crecimiento rápido en el mercado de productos naturales de hormona de crecimiento basado en estudios clínicos llevados a cabo en personas con deficiencia de hormona de crecimiento,

utilizando la hormona inyectable, que es la aprobada por la Administración de Drogas y Alimentos de los EE.UU. Las publicaciones médicas previas sobre los beneficios de reemplazo con hormona de crecimiento produjeron un interés exagerado en el uso de esta hormona como un suplemento dietético para propósitos de rejuvenecimiento. Esto ha llevado a la proliferación descontrolada de toda clase de productos de hormona de crecimiento, anunciados irresponsablemente, como si tuvieran propiedades extraordinarias de revertir el envejecimiento sin los estudios clínicos necesarios para probar su efectividad y seguridad. Este repaso resume las circunstancias que han llevado a este revuelo con la hormona de crecimiento y ofrece una vista global de los diferentes tipos y formas en que estos productos naturales de hormona de crecimiento son vendidos , enfatizando en la posible publicidad engañosa y la falta de prueba científica de sus alegaciones.

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