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Special Article - Human Chorionic Gonadotropin

Multiple Non-Traditional Promising Therapies with Human Chorionic Gonadotropin

Rao CV*

Departments Molecular and Human Genetics and Obstetrics and Gynecology, Florida International University, USA

***Corresponding author:** Rao CV, Departments of Cellular Biology and Pharmacology, Molecular and Human Genetics and Obstetrics and Gynecology, Reproduction and Development Program, Herbert Wertheim College of Medicine, Florida International University, Miami, Florida, USA

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Letter to the Editor

Human Chorionic Gonadotropin (HCG), popularly known as pregnancy hormone, is a member of glycoprotein hormone and cystine-knot growth factor families. It is a structural and a functional homolog of Luteinizing Hormone (LH), which is derived from the anterior pituitary glands. In contrast, hCG is primarily made by trophoblasts. Both hormones bind to the same G-protein coupled cell surface receptors. These receptors are widely distributed, which explains why these hormones have pleiotropic actions in the body. The findings, which are a paradigm shift, have faced several obstacles in the beginning to convince many investigators that hCG/LH had broad regulatory actions in the body1. However, there are many lacunae and only further research can fill these scientific gaps.

The traditional (gonadal) hCG/LH actions have led to the hCG use in an induction of follicular maturation and ovulation and in the treatment of male hypogonadotropic hypogonadism. The non-traditional actions, on the other hand, have a promise of bringing much greater number of therapies. They are listed in Table 1 with the references that will provide detailed scientific and clinical basis for these indications.

Some of these diseases can be fatal, If not intervened early. Others will have troublesome long-term health consequences, debilitating, come with chronic pain and suffering, sleep deprivation, depression, anxiety, social isolation and stigma, loss of sexual intimacy, productivity in the work place, job and health insurance, among others. They place high emotional and economic burden on affected family members and friends. The cost to the U.S. economy runs into millions to billions of health care dollars per year.

Current therapies are either not effective or have devastating side effects. Many are quite expensive and a few have a low tolerability. Clearly, there is an unmet need for the cost effective and safer therapies for all these diseases. HCG therapy could be one of them. Anecdotal evidence, studies on animal models, cells and tissues and on human subjects supports that hCG therapy most likely will work for these diseases. To capture this promise, randomized, double blind, placebo controlled clinical trials have to be performed with optimal hCG doses, route and frequency of administration and an appropriate patients selection, etc. The optimal treatment conditions could vary with the disease.

It is important to keep the expectations low, as no therapy will work for everyone and initial failures are common, which should be considered as only temporary setbacks. Scale on demand can meet an increased market for hCG. Since the clinical trials are not patentable, and the pharmaceutical companies are primarily the ones to benefit from an increased demand for hCG, perhaps they should be the ones to share substantial financial burden to conduct the clinical trials.

The hCG therapies will have a minor to tolerable side effects and cost effective. The effectiveness can be further enhanced by making much more active analogs than regular hCG that can be non-invasively administered and in ways that can keep its levels high for a longer periods of time. Such technologies do exist and can be made to work for hCG. One such technology is oral “hCG Pills”. Perhaps they can be developed for hCG, employing the procedures that are being used for developing insulin pills. The technology allows encapsulating hCG in neutral spheres of lipid molecules that prevent the hCG destruction by stomach acids. The availability of hCG pill will have a huge worldwide impact on its use even in the remote areas of the world.

Combination therapies could be another way to increase the effectiveness. For example, hCG combination therapies could lower the toxicity of currently used drugs, reduce the cost, while preserving their desirable properties. Moreover, the combination therapies could be more active than single therapies because of the differences

Table 1: Non-traditional hCG therapies [1].

Indication	References
Breast cancers [2]	[2,3]
Chronic pain [3]	[1,4]
HIV/AIDS	[5,6]
Tubal infection with *Neisseria Gonorrhoeae*	[7]
Rheumatoid arthritis, Sjogren’s Syndrome and the other autoimmune diseases that ameliorate during pregnancy [4]	[8]
Pre-term births [5]	[9]
Overactive bladder	[10]
Painful bladder syndrome/interstitial cystitis	[11]

May also include therapies for injury and inflammation of other target tissues including, central and peripheral nervous systems [1].
Includes decreasing breast risk in young women, who plan to delay their first childbirth [2].
Includes chronic pain due to many different illnesses [3].
Includes Lupus erythematosus; type 1 diabetes; ankylosing spondylitis; multiple sclerosis; thyroiditis; Crohn disease; Hepatitis [4].
May also include several other pregnancy complications [5].

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in their mechanisms of action. The potential hCG therapies should not be considered as panacea and may not completely replace the current therapies. Instead, they can complement them and become an important part of a physician's toolbox. So what do we have to lose by exploring these promising therapies? This is a call for action by pharmaceutical companies around the world.

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