

Richard F Walker

International Society for Applied
Research in Aging (SARA)

Comments on “Growth hormone (GH)-releasing hormone and GH secretagogues in normal aging”

This issue of *Clinical Interventions in Aging* contains a quite interesting and informative article about a topic that is popular and also controversial among practitioners of age-management medicine. Appropriate to that controversy, Drs Hersch and Merriam (2008) have asked the question in the title of their paper, does the use of growth hormone secretagogues in age management medicine hold the promise of a fountain of youth, or that of a pool of Tantalus? While there is universal understanding of the fountain imagery, the meaning of the pool is perhaps less obvious. It derives, of course, from the Greek myth of Tantalus, who had both a hidden, divine sire and a mortal one. As the son of Zeus, he was uniquely favored among mortals and was invited to share the food of the gods. However, driven by pride, he shared the divine ambrosia with other mortals, and thus aroused the ire of the gods. As punishment, he was made to stand chin-deep in water with a variety of sweet-smelling and delicious fruit dangling just over his head. However, whenever he tried to drink or eat, the water would magically recede or the fruit would miraculously be lifted just out of his reach. Thus, it is that torment, through which something seems to be offered only to be withdrawn again, that has been called “tantalizing” in memory of its best known victim.

The authors’ comments about these images at the paper’s end indicate that they had already formed an opinion of which better represents the relationship of GH secretagogues to age management therapies. In those comments, they suggest that while beneficial, secretagogue therapy as currently employed hardly brings youthful rejuvenation and that the expectations of efficacy are more tantalizing than realizable. While most practitioners would agree that growth hormone replacement therapy (GHRT) will not restore youth, I feel that its effects are more than tantalizing since by definition the word describes that which is desired but unattainable. Thus, the description provided of the pool of Tantalus seems to define the use of secretagogues as a fantasy therapy that is ineffective in providing actual benefit. However, it should be remembered that Tantalus can also be seen as a Promethian figure. Recall that Prometheus was a Titan credited with (or blamed for) playing a pivotal role in the early history of humankind by divulging divine secrets to mortals. This alternative image of Tantalus, linked to his sharing of ambrosia with other mortals would be more positive when associated with the use of GH secretagogues in age management. In any event, without further second guessing of the authors’ intentions through symbolism, I congratulate them in providing an unbiased and comprehensive review of the current status of the subject that provides an invaluable reference guide to practitioners of age-management medicine who incorporate GHRT into their clinical practice.

Drs. Hersch and Merriam initiate the paper with a succinct review of the GH neuroendocrine axis including presumptive involvement of ghrelin. Included is a diagram proposing possible ghrelin feedback relationships within the axis and also GH independent actions of the secretagogue. The practical relevance of this information is that there are two ghrelin analogs, GHRP-2 and GHRP-6, currently being marketed as dietary supplements. A brief inspection of the dosages used and knowing that they are orally bioavailable indicates that these products are efficacious in releasing endogenous GH. In fact, I received reports from several practitioners indicating that

they elicit significant GH release and increase IGF-1. If true, this fact makes their use either alone or in conjunction with sermorelin, the only commercially available GHRH analog, practical for clinical application. Since the combination is very synergistic, its use in individuals who are relatively insensitive to GHRH alone may be of significant interest.

The authors then transition to a comparison of the clinical consequences of adult growth hormone deficiency (AGHD), a pathologic condition, and the age-associated decrease in production and secretion of somatotropin. They point out that while the etiologies of the two conditions differ significantly, they share many clinical similarities that differ basically by degree. Furthermore, replacement therapy with recombinant hGH seems to have a broader spectrum of efficacy and safety in younger individuals suffering AGHD than in the elderly. In this regard, the secretagogues which produce a more physiological profile of growth hormone secretion are more appropriate as interventions in aging than recombinant hGH because they restore function in more components of the neuroendocrine axis including feedback relationships and thus, are less likely to cause side effects. They further point out that the effects of ghrelin analogs are influenced by the same factors that modulate endogenous GHRH secretion, such as negative feedback by somatostatin providing additional

buffering against overdose. Finally, since the ghrelin analogs are smaller molecules than hGH or even the GHRH analog sermorelin, they can be administered orally, transdermally, or nasally. As mentioned above, dietary supplements for GHRP-2 and GHRP-6 are currently available and may have valuable clinical application.

In conclusion, I would agree that while there is a paucity of data on the use of secretagogues in age-management medicine, this review brings together nicely that which is currently published. As part of their professional obligations, practitioners should strive to increase this base of knowledge by measuring and reporting outcomes of treatments offered at their clinics so that the benefits and risks can be accurately assessed. In support of this effort, the Society for Applied Research in Aging is offering to create such a database with help of all practitioners willing to participate. To facilitate the effort, guidelines, data collection forms, statistical analytical services and publication of the outcomes are offered as a service to the clinical community. To learn more about this data registry go to www.ageresearchsociety.com.

Reference

Hersch EC, Merriam GR. 2008. Growth hormone (GH) – releasing hormone and GH secretagogues in normal aging: Fountain of Youth or Pool of Tantalus? *Clin Interv Aging*, 3:127–35.