Growth Hormone Response to GHRH During Lifespan

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SYNOPSIS

Recent evidence has shown that growth hormone-releasing hormone (GHRH) enables investigation of the pathophysiology of GH secretion in a variety of different states, but it cannot be used as a test for probing pituitary somatotrophic function, due to the extreme inter- and intra-subject variability in normal subjects. This task is better accomplished when compounds which deprive the pituitary of inhibitory (somatostatinergic) influences, e.g. pyridostigmine, arginine, etc., are given in combination with GHRH.

Administration of GHRH in both animals and humans reveals a state of GH hyperresponsiveness in the immediate postnatal period, which is likely to be due to a reduced pituitary sensitivity to somatostatin. GH responses to GHRH are relatively constant throughout the different stages of pubertal development, though further studies are needed to confirm these findings, and decline after the third-fourth decade in men, after menopause in women. It is apparent that during aging the releasable pool of GH is preserved and that impaired GH secretion is due to defective hypothalamic GHRH function and a relative predominance of somatostatinergic function.

INTRODUCTION

The isolation and characterization of growth hormone releasing hormone (GHRH) in 1982 /1/, i.e., a factor whose action is directed at the somatotrophs, has enabled considerable exploration of the pathophysiology of GH secretion in a variety of different states /1/, but has been followed by a limited and discouraging use of GHRH in the clinical setting. It has become apparent, in fact, that the ability of GHRH to affect somatotroph function cannot be used as a test for identifying patients with inadequate spontaneous GH secretion (see below). Consideration of other factors affecting GH secretion is mandatory for a proper evaluation of the GH response to GHRH occurring in subjects of different ages, which is the topic of this contribution.

GHRH

The ability of GHRH to elicit GH release has to be evaluated in the context of the many influences which, acting in *in vivo* conditions at the pituitary and/or the hypothalamus, may modulate somatotroph responsiveness to the neurohormone /2/. Among these influences those played by the inhibitory hypothalamic peptide, somatostatin (SS), appear crucial for dictating the endogenous GH secretory pattern. It is well known that GH secretion in mammals is not a continuous event but is episodic in nature /3/, due to the interaction between GHRH and SS secretion; it has been shown in rats that the GH-releasing ability of a GRF peptide varies markedly according to the time of injection, the GH response being significantly greater when the peptide is administered during peak than during trough periods /4/. Moreover, proof has been given that the weak GHRH-induced GH response observed during trough periods is due to antagonism by secreted SS, since immunoneutralization of SS permits marked GH release even during the trough period /4/. These results obtained in rats have been essentially confirmed in humans where it has been demonstrated that