Chapter 16

GHRELIN: IMPLICATIONS IN PEDIATRIC ENDOCRINOLOGY

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Abstract: Ghrelin, a 28 amino-acid acylated peptide predominantly produced by the stomach, displays strong growth hormone (GH)-releasing activity mediated by the hypothalamus-pituitary GH Secretagogue (GHS) receptors which had been shown to be specific for a family of synthetic, orally active GHS. Ghrelin and GHS show other endocrine and nonendocrine actions including orexigenic effects and influence on gastro-entero-pancreatic functions. Ghrelin manages the neuroendocrine and metabolic response to starvation. The study of ghrelin secretion as function of age and gender as well as the study of the endocrine and nonendocrine effects of ghrelin and its analogues in physiological and pathological conditions will likely provide critical information about the role of ghrelin and the potential perspectives of its analogues in clinical practice. This point is of particular interest in the field of pediatric endocrinology and metabolism because the ghrelin story started focusing on GH deficiency and is now extending to aspects that once again are of major relevance such as obesity and eating disorders, regulation of the hypothalamus-pituitary-adrenal and gonadal axis. GHS analogues acting as agonists or antagonists on appetite could represent new drug intervention in eating disorders. GHS could therefore represent a reliable provocative test for the diagnosis of GH deficiency but as orally active growth-promoting agents they are not comparable with rhGH in terms of efficacy.

Key words: GH, IGF-I, genetic, GH deficiency, obesity
1. INTRODUCTION

Ghrelin, a 28 amino-acid peptide predominantly produced by the stomach, displays strong growth hormone (GH)-releasing activity mediated by the activation of the GH Secretagogues (GHS) receptors (GHS-R) type 1α which is specific for synthetic, peptidyl and non peptidyl GHS (1-4). GHS were invented more than 20 years ago and their strong GH-releasing activity even after oral administration suggested potential clinical usefulness for diagnosis and treatment of GH deficiency (GHD) in childhood as well as for treatment of other conditions of GH insufficiency including aging (2,4). Ghrelin and synthetic GHS act via receptors concentrated in the hypothalamus-pituitary unit but are also distributed in other central and peripheral tissues (2,5). While hypothalamus-pituitary receptors explain the stimulatory effect of GHS on GH and also on prolactin and adrenocorticotropic hormone secretion as well as the inhibitory influence on gonadal axis, other central and peripheral specific binding sites explain other activities (1,4,6-9). Among these, the orexant activity coupled with control of energy expenditure is receiving particular interest because of the potential therapeutic implications for ghrelin analogues acting as agonists and antagonists.

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Aim of this chapter is to consider the knowledge accumulated so far about ghrelin secretion and actions in childhood and meantime to review the potential clinical pediatric implications of ghrelin analogues.

2. GHRELIN SECRETION: FROM NEWBORNS TO ADULTHOOD

Ghrelin secretion, mostly represented in its acylated form, occurs in pulsatile manner. It is noteworthy that there is no strict correlation between ghrelin and GH levels while ghrelin pulses are correlated with food intake episodes and sleep cycles in rats (10). Particularly, in humans it has been shown that peaks in ghrelin levels anticipate food intake suggesting the latter is triggered by ghrelin discharge (11).