Impact of gsp mutations in somatotroph pituitary adenomas on growth horAmone response to somatostatin analogues: a meta-analysis


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Introduction

Somatic mutations in the GNAS1 gene, which encodes the alpha-subunit of the Gi stimulatory protein (gsp) complex coupled to GHRH receptor, are detected in about 40% of somatotroph pituitary tumors.

Gsp mutations have been associated with specific clinical and histopathological characteristics such as:
- smaller, less invasive tumors occurring in older patients and
- densely granulated adenomas.

Methods

The aim of the present study was to investigate whether the presence of a gsp mutation in sporadic somatotroph adenomas is a prognostic factor of the response to somatostatin analog (SSA) treatment.

Following a literature search in MEDLINE and SCOPUS for a period up to January 2014, a meta-analysis was performed, including 8 eligible studies (Figure 1 & Table 1), in order to estimate the effect of gsp mutation on the percent reduction of growth hormone (GH) levels during an acute octreotide suppression test (OST).

OST was selected as the outcome measure because it was the test used most widely in the studies, with consistently available data. Furthermore, it has been validated as accurate predictor of the long term response of GH-secreting adenomas to SSAs.

No study addressing the research question in a prospective manner, with long term results of SSA treatment on GH and IGF 1 levels was found. A total of 310 patients with acromegaly (128 gsp (+) and 184 gsp (-)) were included in the analysis.

Results

The presence of the gsp mutation was related with a greater reduction in GH levels on OST [Weighted Mean Difference (WMD): 9.08% (95% CI, 2.73, 15.42; p=0.005; random effects model).

There was significant heterogeneity for this effect estimate (I²= 56%, p value for heterogeneity= 0.02) (Forest plot 1).

A sensitivity analysis after exclusion of a study with different methodology of OST provided similar estimates [WMD: 6.93% (95% CI, 1.40, 12.46); p=0.01], albeit with no significant heterogeneity (I²= 35%, p value for heterogeneity= 0.16) (Forest plot 2).

Conclusions

The present meta-analysis suggests a role for gsp mutations as a predictive factor of somatostatin analog treatment response in acromegaly.

In order to further clarify this position, studies evaluating the long term effect of treatment, using the combination of GH and IGF-1 measurements are needed.

References