"CRITERIA FOR DISEASE CONTROL IN ACROMEGALY UNDER SSA TREATMENT: MEAN GH PROFILE (GHP) OR GH RANDOM (GHR)?"

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N. Prencipe, C. Bona, I. Karamouzis, A. Berton, S. Di Giacomo, F. Guaraldi, V. Gasco, M. Maccario, E. Ghigo, S. Grottoli
Divisione di Endocrinologia, Diabetologia e Metabolismo, AOU Città della Salute e della Scienza di Torino, Università di Torino

BACKGROUND:

Acromegaly is a rare disease that is most often caused by a growth hormone (GH) secreting benign pituitary tumor. The pathological GH hypersecretion increased insulin-like growth factor -I (IGF-I) concentration and both cause signs and symptoms. Mean acromegaly features are soft tissue enlargement, excessive skeletal growth with characteristic acral enlargement and coarse facial features as well as multiple comorbidities such as diabetes mellitus, cardiomyopathy and sleep apnea syndrome. Growth hormone and IGF-I are the biochemical parameters used to diagnose acromegaly and to assess disease activity during treatment.
Several studies have related control of acromegaly, defined by a normal IGF-I and/or a particular GH concentration, to an improved mortality risk and to prevalence of several co-morbidities. Acromegaly threefold increased mortality. Last GH and IGF-I levels are fundamental mortality prognostic determinants.

CRITERIA FOR CONTROLLED ACROMEGALY – BEFORE AND AFTER 2010

First-line therapy of acromegaly: A statement of the A.L.I.C.E. (Acromegaly primary medical treatment Learning and Improvement with Continuous Medical Education) Study Group

A. Colao*, E. Martino[2], P. Cappabianca[3], R. Cozzi[4], M. Scanarini[5], E. Ghigo[6], and the participants of the A.L.I.C.E. (Acromegaly primary medical treatment Learning and Improvement with Continuous Medical Education) Study Group

CRITERIA OF CURE

Despite evidence that the cure criteria proposed by the Consensus Statement in 2000 (1) should be amended in accordance with a more recent statement (2), the group came to the conclusion that criteria for controlled or cured acromegaly are based on GH levels <2.5 µg/l or suppressed GH levels <1 µg/l after glucose load in the presence of normal IGF-I levels for age and gender, as acceptable.

BEFORE — ANNO 2010 — AFTER

EXPERT CONSENSUS DOCUMENT

A consensus on the medical treatment of acromegaly

Andrea Giustina, Philippe Chanson, David Kleinberg, Marcello D. Bronstein, David R. Clemmons, Anne Klibanski, Aart J. van der Lely, Christian J. Strasburger, Steven W. Lamberts, Ken K. Y. Ho, Felipe F. Casanueva and Shlomo Melmed

Treatment goals
Biochemical outcomes
Elevated GH and IGF-I levels are predictors of mortality in patients with acromegaly (HQ).[10] and lowering GH and normalizing IGF-I levels in patients with acromegaly results in mortality rates similar to those expected in the general population (MQ).[11] However, the definition of a safe GH level (in terms of normalizing mortality rates) is likely to be outdated because the data were collected retrospectively using less sensitive assays than those in routine use nowadays. Using sensitive and specific assays the cut-off for GH levels is likely to be <1 µg/l (MQ).

OBJECTIVE:

Aim of our study was to compare reliability of different "safe GH cut-off" in acromegaly patients under somatostatin receptor ligands (SSA).

METHODS:

In an observational and retrospective study, we enrolled 34 responsive to SSA treatment acromegalic patients (25 F, 33-86 years). Responsiveness is defined by normal IGF-I levels and no clinical activity. In all subjects the dose of SSA was stable in last 2-5 years. In all subjects in phase 1 (before 2010) mean GH Profile (GHP), IGF-I and IGF-BP3 (at least 2 evaluations) and in phase 2 (after 2010) GH Random value (GHR), IGF-I and IGF-BP3 (3 evaluations) were evaluated.
Statistical analysis was performed using Wilcoxon's test for the comparison of GH profile and GH random, while the correlation between GH and IGF-I and IGF-BP3 levels was analyzed by Spearman test.

RESULTS:

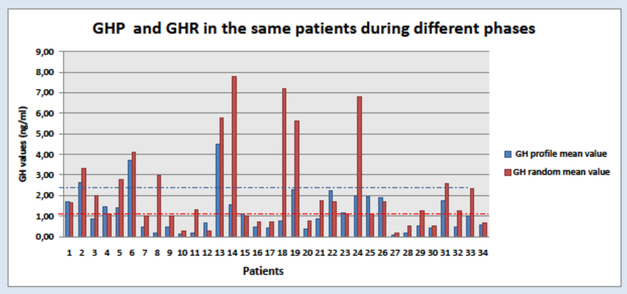
In all subjects in both phases of the study IGF-I and IGF-BP3 levels were normal for age.

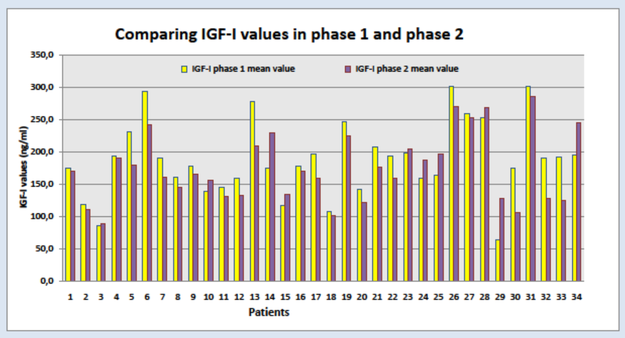
- IGF-I (phase 1: 186.8 ± 10.0; phase 2: 175.0 ± 37.3 ng/ml)
- IGF-BP3 (phase 1: 2.7 ± 0.1; phase 2: 2.5 ± 0.1 µg/ml).

GHR (2.2 ± 0.48 ng/ml) levels are higher (p = 0.1) than GHP (1.17±0.57 ng/ml).

Concordance between GHP < 2.5 ng/ml and normal IGF-I was demonstrated in 85.3% of patients.

Concordance between GHR < 1 ng/ml and normal IGF-I in 29.4% (p < 0.01).





CONCLUSIONS:

Our study shows that in responsive to SSA acromegalic patients, mean GH profile < 2.5 ng/ml better than GH Random < 1 ng/ml correlate with normal IGF-I levels. Thus seems to indicate that evaluation by GH profile would more reliably reflect an appropriate disease control.

GH profile (even a 3-hours profile as in our case) can be uncomfortable and expensive.
Considering these results, we believe it is necessary to select patients in which IGF-I values and clinical acromegalic pattern are discordant performing a GH profile only in these ones.
No additional benefit seems to be in performing GH random.

Our study is a preliminary one. Further informations are definitely needed. Our next step will be:

- to increase the sample size;
- To also consider not controlled during SSA patients to evaluate correlation GHP and GHR with somatotroph secretion in these patients;
- To consider glycometabolic profile and quality of life (in addition to IGF-I values) as markers of disease activity.

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