ACUTE OCTREOTIDE SUPPRESSION TEST IN ACROMEGALY: PREDICTIVE VALUE IN LONG TERM RESPONSE TO LONG-ACTING SOMATOSTATIN ANALOGS

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Introduction

Long-acting somatostatin analogs (SA) are widely used in acromegaly, either as first-line or as adjuvant treatment after surgery.

In the past, acute tests have been designed for predicting long-term response of the tumoral GH secretion to short-acting somatostatin analogs. The usefulness of acute octreotide suppression test (OST) in the selection of patients with acromegaly for chronic long-acting SA treatment is still controversial.

Objective

To investigate the predictive value of OST for long-term responsiveness to long-acting SA.

Methods

Patients

Retrospective study of 25 drug-naive patients (13 males, median age 50,3 ± 16,55 years, range 25 - 88) with active acromegaly, subjected to an OST. Twelve percent of the patients had microadenoma, 32% a macroadenoma, 52% an invasive macroadenoma and 4% had no image on MRI. Twenty-two patients had undergone non-curative surgery and none had previously been treated with medical therapy.

OST protocol and follow-up

Hourly serum GH concentrations for 8 h were measured in the basal state and again after last administration of subcutaneous octreotide - 50 mcg q8h over 48h followed by 100 mcg q8h for 48h.

The mean GH achieved was used for analysis and only patients with a 20% decrease of the mean GH levels were included.

GH nadir response during OST was also evaluated.

For long-term follow-up, serum GH < 1ng/ml and normal IGF-I (both evaluated as mean of three values) were used as parameters for biochemical control during SA therapy.

Results

RESPONSE TO ACUTE OCTREOTIDE SUPRESSION TEST LONG-ACTING SOMATOSTATIN ANALOGS

On average, during OST a GH decline of 70,2±23,4% was observed in this cohort. Most patients (72%; n=18) showed a GH decrease greater than 50% during OST - **group A**, while 28% had ≤50% GH reduction - **group B**.

	Basal		OST		SA treatment				
	Mean GH	Mean IGF-1	GH<1	Mean GH reduction (%)	GH < 1	Mean GH reduction (%)	Normal IGF-1	Mean IGF-1 reduction (%)	Normal IGF-1 and/or GH
Group A (n=18)	15,6± 16	867,6± 421,9	38,9% (n=7)	82,9±11,4	7	68,2±33,3	6	54,6±22,6	11
Group B (n=7)	14,0± 14	763,3± 343,2	28,6% (n=2)	36 ±9,5	2	52,7±40,1	1	42±17,9	2
Total (n=25)	14,7± 15,2	834,8± 384,2	36% (n=9)	70,15± 23,4	9	64,3±35,6	7	50 ±22,5	13

Table 1. Pre-treatment, during OST and post-treatment hormonal profiles on two groups. GH – Growth hormone (ng/mL); IGF-1 - Insulin like growth factor 1 (ng/mL).

During SA treatment, 61,1% of group A achieved IGF-1 and/or GH normalization, with a mean reduction of 54,6% and 68,2%, respectively. In Group B, 28,5% reached IGF-1 and/or GH normalization, with a mean reduction of 42% and 52,7%, respectively. Biochemical control was observed in 11,1% of patients on group A and 14,3% on group B. In total, 36% of patients achieved a GH value<1 ng/ml during the OST. In this group 77,8%(n=7) had mean reduction >50% during OST (Table 1 and Figure 1).

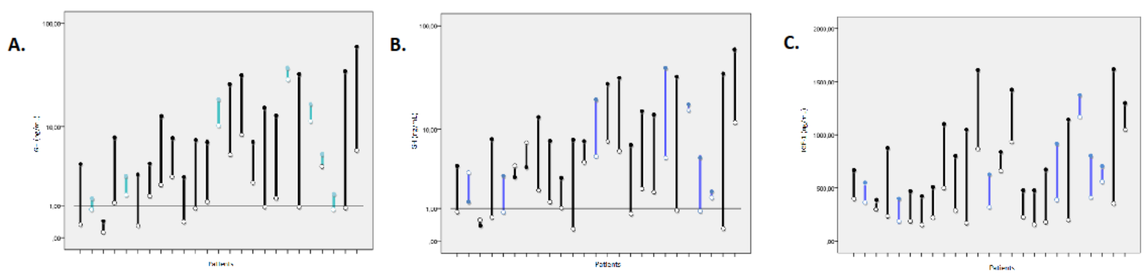

Figure 1. A. Pretreatment GH value (●) and the nadir following OST (○). B. Pretreatment GH value (●) and during SA therapy (○). The target of therapy was a mean GH of 1 mU/l (—). C. Pretreatment IGF-1 value (●) and during SA therapy (○). All values are plotted for individual patients. Group A is shown in black and Group B in blue.

RELATIONSHIP BETWEEN THE OCTREOTIDE SUPRESSION TEST AND THE RESPONSE TO LONG-ACTING SOMATOSTATIN ANALOGS THERAPY

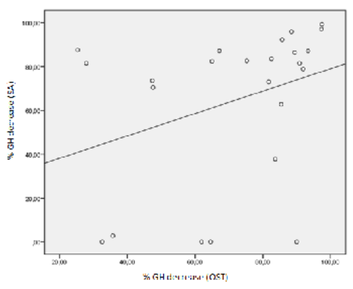

Figure 3. No significant correlation (R=0.334 e p=0.11) is seen between the percentage fall in GH during OST and the percentage fall in GH on SA treatment.

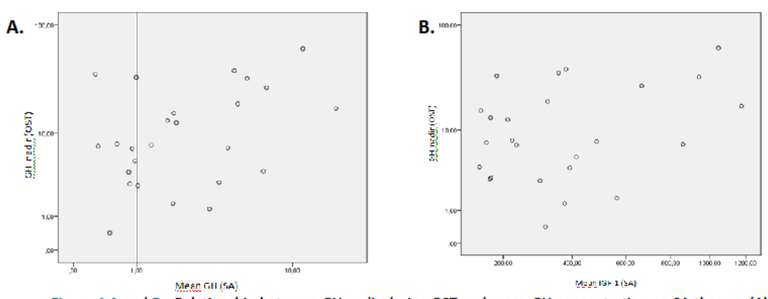

Figure 4 A and B - Relationship between GH nadir during OST and mean GH concentration on SA therapy (A) and corresponding mean IGF-I concentration (B). A significant correlation was seen between both parameters (R=0.432, p=0.031 and R=0.444, p=0,026, respectively).
The goal of therapy was a mean GH of 1 ng/ml and the optimal predictive performance of the OST was obtained with a GH nadir of 1 ng/ml.

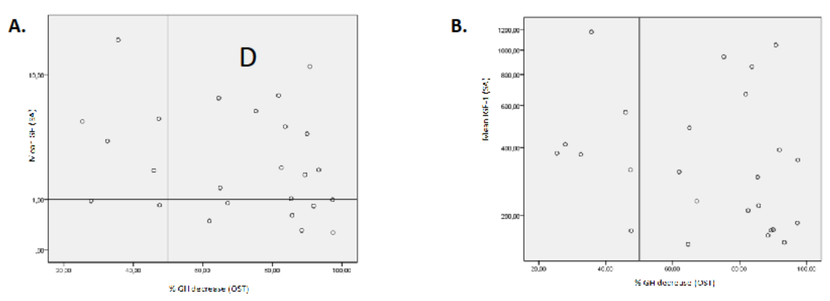

Figure 5. A and B - Relationship between percentage fall in GH after OST and mean GH concentration (A) and mean IGF-I concentration (B) during SA therapy . No significant correlations were seen between both parameters (R=0.239, p=0.251 and R=0.165, p=0.43, respectively). Despite falls in GH values following the OST of 50%, patients in quadrant D failed to normalise GH during treatment (A).

When comparing controlled and non-controlled acromegalic patients on long-acting SA, a 50% reduction and a nadir GH<1ng/ml during OST didn't show correlation with long-term normalization of serum IGF-I and/or GH (p=0.106 and p=0,271,respectively).

	OST	
	GH reduction >50%	Nadir GH level<1 ng/ml
PPV (%)	61,11	66,67
NPV(%)	71,43	56,25
Sensitivity (%)	84,62	46,15
Specificity (%)	41,67	75,0

Table 2. The positive and negative predictive value (PPV, NPV), sensitivity and specificity of achieving target GH < 1 (ng/mL) and/or normal IGF-1 for sex and age (ng/mL) on long-acting SA therapy for different OST criteria.

Conclusions

In this cohort a reduction of 50% and nadir GH<1 ng/ml following an OST weren't predictive of remission on long-term SA as defined by updated criteria.

The limitation of the test is that a poor response to a OST does not preclude a good response to long-term therapy

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