

Preoperative octreotide therapy in acromegaly: Associations between effects on glucose homeostasis and biochemical cure

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BACKGROUND AND OBJECTIVE

In acromegaly, high GH/IGF-1 levels are associated with abnormal glucose metabolism. Treatment with somatostatin analogues (SSAs) reduces the GH and IGF-1 levels. However, SSAs may worsen glucose homeostasis despite this, due to concomitant inhibition of insulin secretion.

The objective of this study was to analyse the possible association between glucose homeostasis, SSA treatment and biochemical cure in *de novo* patients with acromegaly.

DESIGN

Post hoc analysis from a randomised controlled trial of newly diagnosed patients with acromegaly in Norway during 1999 - 2004 (the POTA study, ref 1).

METHODS

Of the 62 *de novo* patients included in the POTA study, seven subjects (11 %) had impaired glucose tolerance and 12 subjects (19 %) had overt diabetes mellitus.

The 55 patients with acromegaly not using antidiabetic medication were included in the present analyses. Of them, 26 received SSA for 6 months preoperatively. HbA1c and an oral glucose tolerance test (OGTT) were performed at diagnosis, before surgery and 3 months postoperatively. Area under curve of glucose (AUCglucose) was calculated. Indices of glucose homeostasis were compared between cured and non-cured patients.

RESULTS

No associations between basal IGF-1/GH levels and fasting glucose, AUCglucose or HbA1c were found.

After SSA treatment, the percentage reduction in both mean GH and IGF-1 correlated positively with reduction in HbA1c levels (Table 1).

	Mean GH reduction		IGF-1 reduction	
	r	p	r	p
Fasting glucose (% reduction)	0.00	0.99	0.03	0.91
HbA1c (% reduction)	0.50	0.021*	0.64	0.001*
AUCglucose (% reduction)	0.13	0.56	0.050	0.82

Table 1. After 6 months SSA pretreatment. Correlations between changes in hormone levels and changes in glucose homeostasis.

RESULTS cont.

Biochemical cure by IGF-1 and nadir GH, or IGF-1/nadir GH alone after SSA treatment were also associated with larger reduction in HbA1c but not to AUCglucose or fasting glucose (Table 2, figure 1).

	Cured by both nadir GH and IGF-1		Cured by nadir GH	Cured by IGF-1
	Yes	No	p	p
Fasting glucose (% reduct.)	0.0	-3.9	0.18	0.93
HbA1c (% reduction)	5.3	-5.1	0.003*	0.009*
AUCglucose (% reduction)	-13.6	-12.3	0.89	0.49

Table 2. Percentage reduction in glucose indices (median value) and correlation to biochemical cure after 6 months octreotide treatment. Mann-Whitney test.

Table 3 (below). Correlation to biochemical cure 3 months after surgery.

	Cured by both nadir GH and IGF-1		
	Yes	No	p
Fasting glucose (% reduct.)	10.7	11.1	0.595
HbA1c (% reduction)	5.5	2.4	0.065
AUCglucose (% reduction)	20.0	15.2	0.118

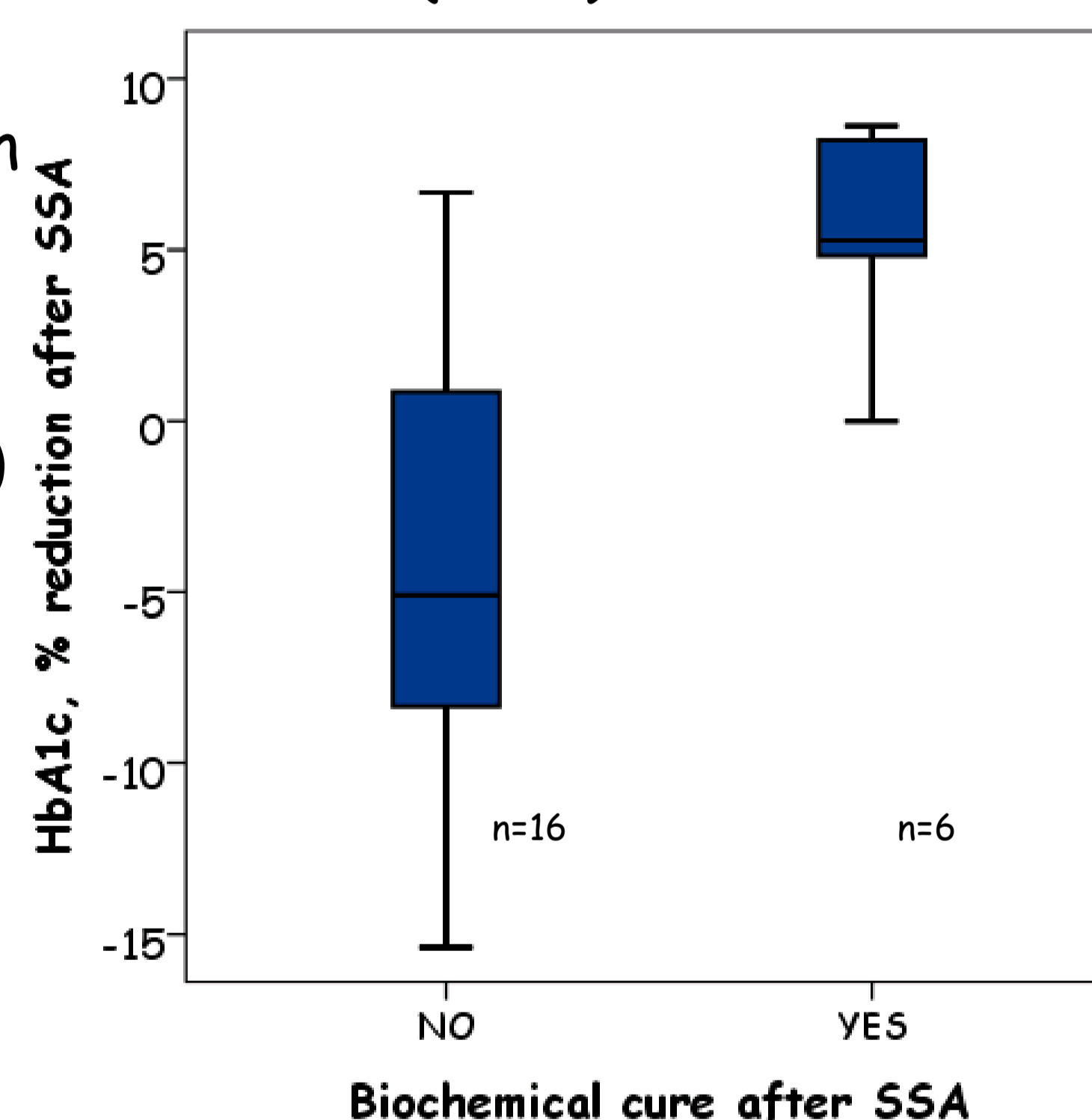


Figure 1. After SSA pretreatment. Percentage reduction in HbA1c in patients with and without achieved biochemical cure.

Three months postoperatively, biochemical cure by IGF-1 and nadir GH associated with lower AUC-glucose (p=0.041) but not with fasting glucose or the reduction from baseline in both variables.

For HbA1c, a possible trend towards larger reduction from baseline in patients cured after surgery, can be claimed (Table 3).

CONCLUSION

In *de novo* patients with acromegaly, disease activity do not correspond to glucose homeostasis indices.

However, hormonal control of GH and IGF-1 after SSA treatment is associated with reduction in HbA1c.