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Can a single growth hormone level be used to assess disease activity after treatment of acromegaly?

Original article Jayasena CN *et al.* (2007) Measurement of basal growth hormone (GH) is a useful test of disease activity in treated acromegalic patients. *Clin Endocrinol (Oxf)* [doi:10.1111/j.1365-2265.2007.02996.x]

SYNOPSIS

KEYWORDS acromegaly, basal growth hormone, insulin-like growth factor I, nadir growth hormone, oral glucose tolerance test

BACKGROUND

Measurement of the nadir growth hormone (GH) level during an oral glucose tolerance test (OGTT) is conventionally used to monitor disease activity after treatment of acromegaly. Nonetheless, the need to collect multiple blood samples represents a potential drawback of this test.

OBJECTIVE

To determine whether measurement of the GH level in a basal blood sample taken before administration of oral glucose can be used as a surrogate for the nadir GH level.

DESIGN AND INTERVENTION

This study enrolled patients who were treated for acromegaly at a single UK tertiary endocrine center between 1998 and 2005. Acromegaly was diagnosed from the clinical features and an inability to suppress GH to <1 µg/l during an OGTT. Basal GH was defined as the fasting serum GH level before administration of a 75 g glucose load. The levels of GH were measured every 30 min for a 2 h period during the OGTT, and the nadir GH level was defined as the lowest serum GH measurement during this time.

OUTCOME MEASURES

The main outcome measures were the basal GH, nadir GH, and insulin-like growth factor I (IGF-I) levels.

RESULTS

The study enrolled a total of 76 patients, with a mean age at diagnosis of 40.8 years. The OGTT was performed on 226 occasions: 121 after surgery (39 patients) and 162 after radiotherapy (57 patients). Medical therapy was received by 52 patients. The OGTT was performed during somatostatin treatment on 91 occasions and during dopamine agonist treatment on 27 occasions. Hydrocortisone replacement therapy was received by 53 patients (48 of whom had undergone radiotherapy). A strong association was found between the basal GH level and the nadir GH level (Pearson correlation coefficient = 0.955, P <0.01). This relationship was unaffected by prior radiotherapy: the correlation coefficient was 0.957 for patients who received radiotherapy and 0.985 for those who did not receive radiotherapy. Basal GH levels <1 µg/l and >2 µg/l reliably predicted the nadir GH level. By contrast, only 25 of the 46 basal GH levels of 1–2 µg/l (54%) corresponded to a nadir GH level >1 µg/l. When disease activity was considered, a basal or nadir GH <1 µg/l was predictive of a normal IGF-I level, whereas a basal GH >2 µg/l or a nadir GH level >1 µg/l was predictive of a high IGF-I level.

CONCLUSION

Basal GH levels <1 µg/l and >2 µg/l reliably predicted the nadir GH level, with each measure showing concordance with inactive and active disease in patients with treated acromegaly. By contrast, the predictive value of basal GH levels of 1–2 µg/l is uncertain, and suggests that an OGTT should be performed in such cases.

COMMENTARY

Ken KY Ho

The study of Jayasena *et al.* addresses the relative utility of a single random GH measurement and post-glucose GH measurement as an indicator of disease activity in acromegaly.

GH secretion in normal individuals is episodic, and is characterized by minimal basal activity interspersed with highly regulated secretory bursts. In patients with acromegaly, however, there is increased and dysregulated secretion of GH from a pituitary adenoma.[1] A continuous pattern of GH secretion is observed in acromegaly, with blunted pulses and impaired responses to metabolic cues such as glucose. The tonic secretory profile renders a random GH measurement a good approximation of hormone output in acromegaly. The correlation coefficient between such a measurement and 24 h integrated GH secretion is >0.8.[2]

Although overall GH output predicts 67–80% of the IGF-I level in acromegaly, it is the constant rather than the pulsatile component of the GH signal that exerts the predominant influence on IGF-I.[2,3] This tonic level of GH secretion can be estimated by measuring the nadir GH level in response to an oral glucose load.[4] In their study, Jayasena *et al.* observed a very tight relationship between basal (preglucose) and nadir (postglucose) GH concentrations and advocated a random GH measurement as a "test of disease activity" without the need to resort to an OGTT.

The authors' conclusion requires qualification. First, the study was conducted in a group of patients of whom about half had received medical treatment (mostly with somatostatin analogs). The GH-suppressive effects of these medications are likely to constrain variability and bias the outcome to a tight relationship between basal and postglucose GH values. Second, as the OGTT is not a quantitative measure of overall GH secretion, GH measurements must be complemented with simultaneous measurement of IGF-I, which is the most robust biochemical indicator of GH status.[1] Even with basal or nadir GH levels of <1 μg/l, approximately a quarter of patients in the study had an elevated IGF-I level.

An issue not addressed by Jayasena *et al.* is the value of an OGTT as a test for neuroregulation of GH after successful surgery. Freda *et al.*[5] observed that, among patients who achieved remission (defined as a normal IGF-I level), the nadir GH level did not suppress to within the normal range during an OGTT in several patients. These patients were subsequently found to have a higher level of both spontaneous and stimulated GH secretion, which points towards persistence of subclinical disease. These results indicate, therefore, that even when GH output is returned to normal, an OGTT could uncover persistent neuroendocrine abnormality, which might increase the risk of disease recurrence.

To conclude, in the evaluation of treatment outcome, a random GH measurement gives a quantitative indication of residual output whereas the nadir GH level (obtained after an OGTT) gives additional information as to whether neuroregulation has been restored as a true indication of cure.

References

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Competing interests
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PRACTICE POINT
A random GH measurement is a reliable indicator of GH output in patients with treated acromegaly; however, an IGF-I measurement is required to determine persistence of active disease