IGF-1 for Acromegaly Diagnosis

The diagnosis of acromegaly still poses a clinical challenge, and prolonged diagnostic delay is common. The most important assays for the biochemical diagnosis and management of acromegaly are growth hormone (GH) and insulin-like growth factor-1 (IGF-1) GH and IGF-1 standards are much more precise and provide more accurate tools to diagnose and monitor patients with acromegaly. However, all these biochemical tools have their limitations, and these should be taken under consideration, along with the history, clinical features and imaging studies, when assessing patients for acromegaly [1)].

Elevated IGF-1 levels, alone, are sufficient to establish a diagnosis of acromegaly in the majority of clinically suspected cases. The OGTT may be useful to obtain corroborative evidence when there is modest elevation of IGF-1 with absent or equivocal clinical features [2)]. However, in clinical practice, up to 39% of patients with discordant results are found. The patients with discordant GH and IGF-1levels, are the most difficult to manage. This review discusses the prevalence of discordant GH and IGF-1 outcomes in patients with acromegaly; factors causing this discrepancy; the impact of hormone levels on treatment outcomes. Although endocrinologists are used to dealing with this discrepancy in clinical practice for many years, discordant patients'outcome remains uncertain and undefined The optimal treatment should be individually tailored for each patient, taking into account all clinical parameters [3)]

In acromegaly IGF-I correlates well with GH activity and nadir GH on oral glucose tolerance test (OGTT) and is the most sensitive and specific test in diagnosis, where serum IGF-I is persistently seen to be elevated to a range that is distinct from that in healthy individuals. However it should not be relied on exclusively for diagnosis or used as the sole indication of disease severity and GH burden. Successful medical or surgical treatment of acromegaly is usually associated with normalisation of serum IGF-I but there is discordance between GH and IGF-I in some patients. Patients with a normal IGF-I but an abnormal GH suppression to OGTT are at risk of relapse and therefore it should not be used alone to establish disease remission. In contrast to the diagnosis of acromegaly, there is also considerable overlap in serum IGF-I with normality after primary treatment of disease, even in the presence of persisting GH excess. Gender, age and prior radiotherapy alters the relationship between GH and IGF-I and reliance on one marker of disease activity such as IGF-I is particularly precarious in certain disease states. However an elevated serum IGF-I has been shown to be associated with excess mortality and normalising IGF-I normalises mortality making it a useful marker. The tightening up of the assays means that establishing absolute concentrations as well as standard deviation scores are essential to allow cross-study comparisons. This becomes especially important in the use of Pegvisomant, where IGF-I becomes the sole biochemical marker of disease activity [4)].

The best single test for the diagnosis of acromegaly is measurement of serum Insulin-like growth factor 1 (IGF-1).

Unlike GH, serum IGF-1 concentrations do not vary from hour to hour according to food intake, exercise, or sleep, but instead they reflect integrated GH secretion during the preceding day or longer. Serum IGF-1 concentrations are elevated in virtually all patients with acromegaly and provide

excellent discrimination from normal individuals.

●An unequivocally elevated serum IGF-1 concentration in a patient with typical clinical manifestations of acromegaly confirms the diagnosis of acromegaly.

●A normal serum IGF-1 concentration is strong evidence that the patient does not have acromegaly.

●If the serum IGF-1 concentration is equivocal, serum GH should be measured after oral glucose administration. Inadequate suppression of GH after a glucose load confirms the diagnosis of acromegaly.

Both serum GH concentrations and IGF-1 concentrations are increased in virtually all patients with acromegaly. The increase in serum IGF-1 is often disproportionately greater than that in GH for two reasons: GH secretion fluctuates more, and GH stimulates the secretion of IGF-1-binding protein-3 (IGFBP-3), the major IGF-1 binding protein in serum.

The results must be interpreted, however, according to the patient's age. In normal subjects, serum IGF-1 concentrations are highest during puberty and decline gradually thereafter. Values are significantly lower in adults over the age of 60 years than in younger subjects. Thus, an apparently “normal” value in a patient aged 70 years may in fact be elevated.

In addition, there are a number of conditions that are associated with lower serum IGF-1 concentrations, including hypothyroidism, malnutrition, poorly controlled type 1 diabetes, liver failure, renal failure, and oral estrogen use. In these situations, it is possible that the diagnosis of acromegaly could be missed, and an oral glucose tolerance test (OGTT) should also be performed if the disorder is suspected.

A further caution is that values from one laboratory may not be comparable with those from another laboratory. A major cause of this finding is a difference in the calibration standards for the assay.

All patients with elevated age-adjusted IGF-1 levels should undergo testing for GH hypersecretion (eg, measurement of serum GH after oral glucose administration) [5)]

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