

Incidence of Neuroendocrine Dysfunction Post-Stroke

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BACKGROUND & SIGNIFICANCE:

Cerebrovascular disease is prevalent in the general population and frequently leads to permanent disability and decreased quality of life (Nedeitchev et al 2005). Insulin-like growth factor-1 (IGF-1) and growth hormone (GH) are hormones implicated in the development of vascular disease (Frystyk et al 2002; Bondanelli et al 2003). IGF-1 levels in the low normal range may be associated with increased morbidity and mortality from stroke (Juul et al 2002; Scwab et al 1997). Growth hormone deficiency (GHD) in adults may lead to increased cardiovascular risk and increased mortality from cerebrovascular disease. Studies estimate the incidence of GHD in patients with brain injury to be 15-37% (Agha et al 2006; Lieberman et al 2001), but less is known about the incidence of GHD in patients with stroke.

The objective of the present study was to examine the incidence of neuroendocrine dysfunction, specifically in the IGF-GH axis, in patients receiving post-acute rehabilitation following stroke.

METHODS:

Patients:

All patients admitted to Centre for Neuro Skills, a post-acute brain injury rehabilitation facility, were screened for neuroendocrine dysfunction via a hormone lab panel. Adult patients with a documented history of ischemic (N=22) or hemorrhagic (N=14) stroke and who had both an IGF-1 level and who completed a glucagon stimulation test (GST) were included for analysis in this study (total N=36).

Procedures:

Hormone Assays:

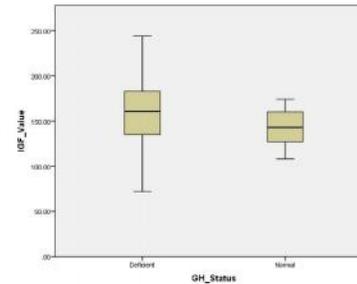
- After an overnight fast, venous blood levels of Thyroid stimulating hormone (TSH), Triiodothyronine (T3), Thyroxine (T4), Follicle stimulating hormone (FSH), Luteinizing hormone (LH), Estradiol (females only), Free and Total Testosterone (males only), Prolactin, Cortisol (A.M.) and Insulin-like Growth Factor 1 (IGF-1) were drawn (~0600h) and sent to an independent laboratory (Esoterix, Inc) for analysis of anterior pituitary function.
- Growth hormone (GH) levels are cyclical, making direct measurement difficult. IGF-1 has been used as a surrogate marker of GH status; however, 50% of adults with GHD have IGF-1 levels within the normal reference range (Lissett et al, 2003). The only "true" assay of GH levels is through provocative testing, such as the glucagon stimulation test (GST). For this reason, GSTs were conducted on all patients, regardless of IGF-1 level.
- The GST was performed after an initial blood draw. Glucagon was given (1 mg IM) and blood was sampled at 90, 120, 150 and 180 minutes for GH. Patients with a peak GH of <10 ug/L were considered growth hormone deficient (GHD).

DISCUSSION & CONCLUSIONS:

Results provide further support that total IGF-1 levels in isolation do not reliably predict GH status in patients with brain injury (Aimaretti et al, 2005) or stroke.

64% of patients in this study who were classified as GHD via GST results were within the "normal" IGF-1 reference range for their age and gender. Published reference ranges currently used may not be accurate for patients with brain injury. Reference ranges specific for patients with traumatic brain injury and for stroke need to be established and verified.

Variable	Mean	Range	Std. Dev
Age at injury	53 years	32-69 years	10 years
Injury Chronicity	276 days	9-4253 days	764 days
IGF-1 Value	155 ng/ml	72-244 ng/ml	41 ng/ml
Peak GH level	4.6 ug/L	0.10-14.70 ug/L	3.82 ug/L



	IGF Deficient	IGF Normal
GH Deficient	7 Hit	23 False Negative
GH Normal	1 False Positive	5 Hit

Reference range based on age and gender: N=36

	IGF Deficient	IGF Normal
GH Deficient	21 Hit	9 False Negative
GH Normal	6 False Positive	0 Hit

Reference range based on age and gender: N=36

	IGF Deficient	IGF Normal
GH Deficient	8 Hit	19 False Negative
GH Normal	0 False Positive	9 Hit

RESULTS:

Deficient GH Group:

Mean IGF-1 Level: 157.90 Std. Dev.: 43.06
Mean Injury Latency (days): 175.50 Std. Dev.: 374.92

Normal GH Group:

Mean IGF-1 Level: 142.50 Std. Dev.: 24.21
Mean Injury Chronicity (days): 777.00 Std. Dev: 1704.58

No significant differences existed between the groups on type of stroke, age at the time of injury, severity of injury at admission and discharge, injury chronicity or IGF-1 value.

Reference Ranges Can Be Misleading:

64% of patients with stroke whose IGF-1 level falls within the *normal* reference range for their age and gender were GHD.

Using a cutoff of ≤ 175 ng/ml to indicate IGF-1 deficiency, (Zgaljardic et al, 2011) 25% of patients who had *normal* levels of IGF-1 were GHD.

Using a cutoff of ≤ 200 ng/ml to indicate IGF-1 deficiency, 14% of patients who had *normal* levels of IGF-1 were GHD.