Influence of Growth Hormone Deficiency on Functional Recovery Following Brain Injury

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BACKGROUND & SIGNIFICANCE:

Patients with growth hormone (GH) deficiency secondary to brain injury have more severe deficits in attention, memory and executive functioning than patients with brain injury alone (Leon-Carrion et al, 2007). This indicates recovery from brain injury may be negatively influenced by concomitant GH deficiency. Insulin-like growth factor-1 (IGF-1) is considered the best marker of GH activity currently available (Frieda et al, 1998). Low levels of IGF-1 increase the likelihood that GH levels are also deficient. However, total IGF-1 levels in isolation do not reliably predict GH status in patients who have sustained a brain injury (Aimaretti et al, 2005). Approximately 50% of adults with GH deficiency have IGF-1 levels within the normal reference range (Lissett et al, 2003). The objective of this study was to investigate the relationship between GH and IGF-1 levels to determine if patient demographics and/or injury characteristics could reliably predict GH deficiency after brain injury. Additionally, the influence of GH/IGF-1 status on functional outcome was assessed.

METHODS:

Patients:

▪All patients admitted to Centre for Neuro Skills, a post-acute brain injury rehabilitation facility, were screened for neuroendocrine dysfunction. Patients whose Insulin-like Growth Factor-1 (IGF-1) level was less than 200 ng/ml and who had completed a glucagon stimulation test (GST) were included for analysis in this study (N=30).

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 P.M.) and Insulin-like Growth Factor 1 (IGF-1) were collected and sent to Esoterix, Inc for analysis.

▪Growth hormone (GH) levels are cyclical, making direct measurement difficult. Therefore, IGF-1 was used as a surrogate marker of GH.

▪Glucagon stimulation tests (GST) were conducted on patients whose IGF-1 levels were less than 200 ng/ml.

▪The GST provokes GH to reach its peak level within the four-hour testing period, allowing reliable GH measurements to be taken.

Outcome Measures:

•All patients were assessed at admission and discharge on the following outcome scales:

•***Disability Rating Scale (DRS):*** 30-point scale developed by Rapport et al (1982) to measure *disability* in the areas of eye opening, communication ability, motor response, feeding, toileting, grooming, level of functioning and employability. Higher scores indicate higher levels of disability.

•***Centre for Neuro Skills Scale (CNS):*** 80-point scale developed by Ashley et al (1997) to assess levels of *ability* in the areas of cognition, withdrawal, agitation & aggression, physical, occupational and speech therapy, language, education and vocation. Higher scores indicate higher levels of ability.

•***Independent Living Scale (ILS):*** 100-point scale developed by Ashley et al (2001) to assess assistance levels needed for completion of activities of daily living in a residential setting. Higher scores indicate higher levels of functional independence.

•***Living Status Scale (LSS):*** Developed by Ashley et al (1997). Ranks patient's living environment on an ordinal scale (0-10). Higher scores indicate living environments requiring a high level of supervision.

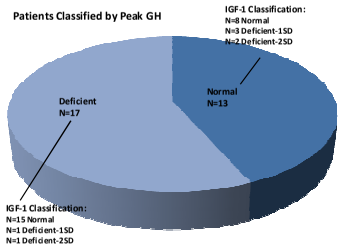
•***Occupational Status Scale (OSS):*** Developed by Ashley et al (1997). Ranks patient's vocational involvement on an ordinal scale (0-16). Lower scores indicate high levels of vocational involvement.

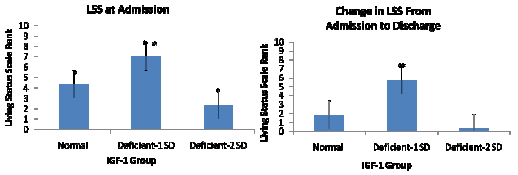
• ***Mayo-Portland Adaptability Inventory (MPAI):*** 34-item scale developed by Malec et al (2003) to assess physical, cognitive, emotional, behavior and social problems, using three subscales (Ability, Adjustment & Participation). Lower scores indicate greater ability, adjustment and participation.

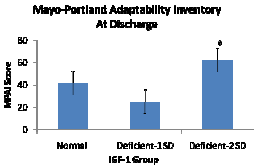
RESULTS:

Patient Demographics: N=31

Variable	Mean	Range	Std. Dev.
Age	45	23-67 years	11 yrs
Injury Chronicity	652 days	14-3987 days	1053 days
Length of Stay	163 days	43-163 days	117 days
IGF-1 value	131 ng.ml	40-188 ng/ml	39 ng/ml
Peak GH value	7 ug/L	0.05-25.0 ug/L	7 ug/L







GH Analyses:

•Peak GH levels less than 3 ug/L were considered "Deficient."

•There were no significant differences between the GH-Deficient and GH-Normal groups on any demographic variables or outcome measures.

IGF-1 Analyses:

•Patients were classified as "Deficient" (N=7) or "Normal" (N=23) based upon IGF-1 values. "Deficient" was further broken down into "Deficient—1 standard deviation" (N=4) or "Deficient--2 standard deviations" (N=3) based upon published IGF-1 reference ranges (Brabant et al, 2003). There were no significant differences between groups on any demographic variables.

Living Status Scale (LSS) Results:

•Patients in the IGF-1 Deficient-1SD group had significantly *lower admission* LSS scores than patients classified as Deficient-2SD (p=0.009) or Normal (p=0.038).

•*Change* in LSS score from admission to discharge was greatest for patients classified as Deficient-1SD when compared to Deficient-2SD (p=0.018) and Normal (p=0.017) patients.

Mayo-Portland Adaptability Inventory (MPAI) Results:

•Patients in the IGF-1 Deficient-2SD had significantly *higher discharge* scores on the MPAI than patients in the Deficient-1SD (p=0.032) group, indicating less improvement in the areas of ability, adjustment and participation.

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).

•88% of patients in this study who were classified as GH deficient via GST results were within the "normal" IGF-1 reference range for their age and gender. Published consensus statements regarding brain injury and growth hormone deficiency suggest provocative testing (i.e. GST) for patients whose IGF-1 levels fall 2 standard deviations below their mean reference range for age and gender (Ghigo et al, 2005 and Ho et al, 2007). Published reference ranges currently used may not be accurate for patients with brain injury. Reference ranges specific for patients with brain injury may need to be created.

•Although this study was limited by a small sample size, results indicated that low IGF-1 levels (independent of GH levels) can negatively influence functional recovery and should be routinely measured.