The Prevalence of Adult-Onset Growth Hormone Deficiency in Uncomplicated Mild Traumatic Brain Injury

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INTRODUCTION

- Following traumatic brain injury (TBI) hypothalamic-pituitary deficiencies are a major cause of morbidity.
- Growth hormone deficiency (GHD) is the most common post-traumatic pituitary deficiency in adults (1) with a prevalence of 12-27% across all TBI severities (2-5).

RESEARCH NEED

- Few studies report the prevalence of GHD following mild TBI.
- Few studies differentiate complicated and uncomplicated mild TBI (6).
- Prior prevalence studies are influenced by heterogeneity of dynamic endocrine testing procedures and diagnostic cut-points.
- Using retrospective clinical and research data we sought to clarify the **prevalence of adult-onset GHD** in patients with histories of **uncomplicated mild TBI** and persistent, post-concussion symptoms ≥ 12 months post-injury.

METHODS

- Retrospective analysis of fixed-dose glucagon stimulation tests (FD-GST) in 144 patients from two endocrine centers (Center A, n=76; Center B, n=68).
- Patients a had history of uncomplicated mild TBI and presented with persistent post-concussion symptoms ≥ 12 month post-injury.
- Patients with comorbidities (e.g. diabetes mellitus, organic hypothalamic-pituitary disease) were excluded.
- Fixed-dose glucagon stimulation test (FD-GST)-
  - ≤ 90 kg = 1 mg glucagon IM injection
  - > 90 kg = 1.5 mg glucagon IM injection
- GST procedures
  - Center A conducted 240 minute FD-GSTs
  - Center B conducted 180 minute FD-GSTs
- BMI-adjusted cut-points were used to define growth hormone deficiency
  - Peak GH ≤ 3.0 ng/mL (BMI < 25 kg/m^2)
  - Peak GH ≤ 1.0 ng/mL (BMI ≥ 25 kg/m^2)
- The cut-point of 1.0 ng/mL was chosen for patients with BMI 25-30, based on the assumption of lower pre-test probability in order to avoid over-estimating the prevalence of GHD.

Uncomplicated Mild TBI (GCS 13-15)

All subjects in this study sustained an uncomplicated mild TBI

1. Meets diagnostic criteria for concussion/mild TBI
2. Absence of criteria for complicated mild TBI (1-4)

GCS = Glasgow Coma Scale

Complicated Mild TBI (GCS 13-15)

One or more of the following:

1. Need for hospitalization for more than 24 hours
2. Need of ICU monitoring and/or neurosurgical intervention
3. Presence of acute pituitary hormone changes in the first 2 weeks following TBI
4. Any anatomical changes on initial CT or MRI

RESULTS

- Prevalence of GHD was 18.4% at Center A and 17.6% at Center B with a combined average of 18.1% (Table 1).
- Prevalence of GHD was similar between centers despite differences in GST test duration (240 vs.180 minutes respectively)(Fig. 1).
- BMI was negatively correlated with peak GH.
- Age was not significantly correlated with peak GH.

	Center A	Center B	Centers A & B
N	76	68	144
GHD Positive	14 (18.4%)	12 (17.6%)	26 (18.1%)
Age (years)	45 (13.3) [18-71]	47.2 (11.1) [23-66]	46 (12.3) [18-71]
Sex (M/F)	37/39	45/23	62/82
BMI kg/m^2	28.7 (6.6) [18.8-53.4]	28.7 (5.7) [19.5-43.2]	28.7 (6.2) [18.8-53.4]

*Mean (SD) [Range]

Table 1. Demographic information of clinical patients and research participants with a history of mild TBI and persistent post-concussion symptoms.

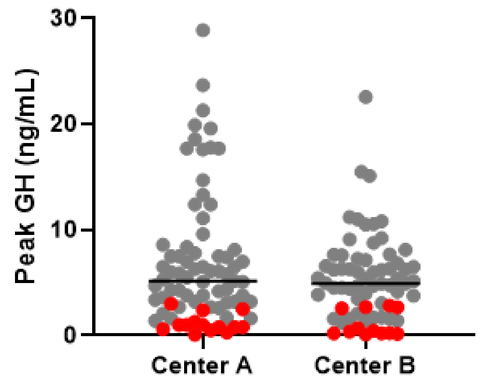

Fig. 1. Peak plasma growth hormone levels following glucagon stimulation testing in adults with a history of mild TBI and persistent post-concussion symptoms. Data was collected at two different facilities. Red symbols indicate individuals with growth hormone deficiency.

CONCLUSIONS

- Post-traumatic GHD is common in symptomatic patients in the chronic phase following uncomplicated mild TBI.
- This is the first study the authors are aware of that has established the prevalence of GHD in this population via fixed-dose glucagon stimulation test in accordance with recent clinical practice guideline recommendations and utilizing strict BMI-adjusted cut-points (7).
- Limitations include sample size and potential over-estimation of GHD when utilizing a 180 minute FD-GST. This is likely balanced due to a conservative application of BMI-adjusted diagnostic cut-points for individuals with BMI 25-30 kg/m^2.

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