Posttraumatic hypopituitarism epidemiology

The objective of this study is to systematically review clinical studies that have reported on the prevalence of chronic post-traumatic brain injury anterior pituitary dysfunction (PTPD) 12 months or more following traumatic brain injury (TBI). Emelifeonwu et al., searched Medline, Embase and Pubmed up to April 2017 and consulted bibliographies of narrative reviews. They included cohort, case-control, cross-sectional studies enrolling at least five adults with primary TBI in whom at least one anterior pituitary axis was assessed at least 12 months following TBI. They excluded studies in which other brain injuries were indistinguishable from TBI. Study quality was assessed using the Newcastle-Ottawa Scale (NOS) score. They also considered studies that determined growth hormone deficiency (GHD) and adrenocorticotrophic hormone (ACTH) reserve using provocation test to be at low risk of bias. Data were extracted by four independent reviewers and assessed for risk of bias using a data extraction form. We performed meta-analyses using random effect models and assessed heterogeneity using the I2 index. We identified 58 publications, of which 29 (2,756 participants) were selected for meta-analysis. Twelve of these were deemed to be at low risk of bias and therefore 'high quality' as they had NOS scores greater than 8 and had used provocation tests. The overall prevalence of at least one anterior pituitary hormone dysfunction for all 29 studies was 32% [95% CI 25 - 38%]. The overall prevalence in the 12 'high-quality' studies was 34% [95% CI 27 - 42%]. We observed significant heterogeneity that was not solely explained by the risk of bias. Studies with a higher proportion of participants with mild TBI had a lower prevalence of PTPD. Our results show that approximately one-third of TBI sufferers have persistent anterior pituitary dysfunction 12 months or more following trauma. Future research on PTPD should differentiate between mild and moderate/severe TBI [1)].

Traumatic brain injury most commonly affects young adults under the age of 35 and frequently results in reduced quality of life, disability, and death. In long-term survivors, hypopituitarism is a common complication.

Pituitary dysfunction occurs in approximately 20-40% of patients diagnosed with moderate and severe traumatic brain injury giving rise to growth hormone deficiency, hypogonadism, hypothyroidism, hypocortisolism, and central diabetes insipidus. Varying degrees of hypopituitarism have been identified in patients during both the acute and chronic phase. Anterior pituitary hormone deficiency has been shown to cause morbidity and increase mortality in TBI patients, already encumbered by other complications. Hypopituitarism after childhood traumatic brain injury may cause treatable morbidity in those survivors. Prospective studies indicate that the incidence rate of hypopituitarism may be ten-fold higher than assumed; factors altering reports include case definition, geographic location, variable hospital coding, and lost notes. While the precise pathophysiology of post traumatic hypopituitarism has not yet been elucidated, it has been hypothesized that, apart from the primary mechanical event, secondary insults such as hypotension, hypoxia, increased intracranial pressure, as well as changes in cerebral flow and metabolism may contribute to hypothalamic-pituitary damage. A number of mechanisms have been proposed to clarify the causes of primary mechanical events giving rise to ischemic adenohypophysial infarction and the ensuing development of hypopituitarism.

Future research should focus more on experimental and clinical studies to elucidate the exact mechanisms behind post-traumatic pituitary damage. The use of preventive medical measures to limit possible damage in the pituitary gland and hypothalamic pituitary axis in order to maintain or re-

establish near normal physiologic functions are crucial to minimize the effects of TBI [2].

May be significantly underdiagnosed in people with previous traumatic brain injury.

Although, there is now increasing awareness of and investigations into such post-traumatic hypopituitarism (PTHP), the exact prevalence and incidence remain uncertain.

1)
Emelifeonwu JA, Flower H, Loan J, McGivern K, Andrews PJ. Prevalence of Anterior Pituitary Dysfunction 12 months or more following Traumatic Brain Injury in Adults - A Systematic review and Meta-analysis. J Neurotrauma. 2019 May 21. doi: 10.1089/neu.2018.6349. [Epub ahead of print] PubMed PMID: 31111791.
2)
Sav A, Rotondo F, Syro LV, Serna CA, Kovacs K. Pituitary pathology in traumatic brain injury: a review. Pituitary. 2019 Mar 29. doi: 10.1007/s11102-019-00958-8. [Epub ahead of print] Review. PubMed PMID: 30927184.