International Journal of Surgery 28 (2016) S103–S108

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Original research

Pituitary dysfunction and its association with quality of life in traumatic brain injury

Giulia Izzo [a], Assunta Tirelli [c], Elisabetta Angrisani [b], Giovanni Cannaviello [c], Lucio Cannaviello [c], Alessandro Puzziello [a], Alessandro Vatrella [a], Mario Vitale [a, *]

[a] Department of Medicine and Surgery, University of Salerno, Baronissi, Salerno, Italy
[b] S.C. Endocrinologia, AOU San Giovanni di Dio e Ruggi d'Aragona, Salerno, Italy
[c] S.C. Medicina Riabilitativa, AOU San Giovanni di Dio e Ruggi d'Aragona, Salerno, Italy

ARTICLE INFO

Article history:
Received 20 April 2015
Received in revised form
10 May 2015
Accepted 25 May 2015
Available online 17 December 2015

Keywords:
Traumatic brain injury
Pituitary
Quality of life
GH

ABSTRACT

Background: Traumatic brain injury (TBI) is a major cause of death and disability and may cause transient or persistent, isolated or multiple hypopituitarism in a variable percentage of cases.
Objectives: The primary aim of this study was to determine the incidence of isolated and multiple anterior pituitary hormone deficiency in subjects with TBI in a single institution. The secondary aim was to determine a correlation between pituitary deficiency and quality of life (QOL) after TBI.
Methods: Thirty-five patients, aged between 18 and 63 years, were evaluated 6months to 5 years after TBI. We evaluated the QOL by SF-12® questionnaire and measured serum basal GH, IGF1, LH, FSH, testosterone (in males), 17-β-estradiol (in women), PRL, fT4 and TSH. In patients with low IGF1, a GHRH + Arginine test was performed.
Results: Single or multiple pituitary failure was found in 13 patients (37%). Low testosterone was found in 7 males, low FSH and/or LH in 4, low IGF1 in 7 patients. Hypogonadotropic hypogonadism and GH insufficiency assessed by GHRH + Arginine test were found respectively in 3 and 2 patients. One patient displayed a concomitant GH insufficiency and low TSH level. Twenty six patients showed a reduction in QOL. A correlations between altered QOL and hormonal deficiency was not observed.
Conclusions: Isolated or multiple hypopituitarism resulting from TBI are frequent. Alterations in QOL and pituitary function resulting from TBI are not associated.

1. Introduction

Traumatic brain injury (TBI) is a major public health issue, a major cause of disability and death, and a cause of neuroendocrine dysfunction. Survey studies have demonstrated that hypopituitarism following TBI is a frequent occurrence [1,2]. Hypopituitarism due to TBI may be the direct consequence on the pituitary, the secondary effect of hypothalamus damage, or the consequence of a pituitary stalk lesion. Partial or complete pituitary dysfunction occurs in 25–50% of patients have after a TBI, a variability depending on screening methods [3,4]. Growth hormone deficiency (GHD) is the most common pituitary dysfunction, affecting approximately 20% of persons with TBI [5]. Gonadotropin, ACTH and TSH deficiency have been documented in TBI although with a lower and inconstant prevalence depending on the studies [1,2]. The correlation of the severity of the TBI with an increased risk of pituitary dysfunction has not been consistently demonstrated [6]. Another important parameter to be considered is the time elapsed from the trauma and the analysis of pituitary function. Several changes in hormone levels become apparent in the acute phase after injury [7]. However, in the following time the pituitary functionality can be partly recovered, whereas other deficits can develop [1]. TBI may cause a change in the quality of life (QOL). This can be independent from a pituitary deficiency and be correlated with the severity and the type of TBI, thus representing a marker of the risk of pituitary dysfunction. In this study, we investigated the

* Corresponding author. Department of Medicine and Surgery, University of Salerno, Via Allende 84081, Baronissi, Salerno, Italy.
E-mail addresses: giulia_izzo@hotmail.it (G. Izzo), assunta.tirelli@libero.it (A. Tirelli), e.angrisani@virgilio.it (E. Angrisani), cannaviellog@gmail.com (G. Cannaviello), lucio.cannaviello@sangiovannieruggi.it (L. Cannaviello), apuzziello@unisa.it (A. Puzziello), avatrella@unisa.it (A. Vatrella), mavitale@unisa.it (M. Vitale).

http://dx.doi.org/10.1016/j.ijsu.2015.05.056
1743-9191/

Table 1
Hormones assessed and normal reference ranges.

Hormone	Normal reference ranges
IGF-1	81–166 pg/mL (males) 101–238 pg/mL (females)
GH	0.03–0.97 ng/mL (males) 0.01–3.6 ng/mL (females)
FSH	1.40–10.1 mUI/mL (males) 2.5–10.20 mUI/mL (follicular phase) 3.40–33.40 mUI/mL (ovulatory phase)
LH	1.5–9.3 mUI/mL (males) 1.9–12.5 mUI/mL (follicular phase) 8.7–76.30 mUI/mL (ovulatory phase)
T	241–827 mUI/mL
PRL	2.1–17.7 mUI/mL (males) 2.80–29.2 mUI/mL (females)
TSH	0.35–5.50 μUI/mL
fT4	0.89–1.76 ng/dL

pituitary function and QOL in patients who suffered from mild, moderate TBI, to determine the prevalence of pituitary dysfunction and whether it correlated with a change in the QOL.

2. Patients and methods

2.1. Inclusion and exclusion criteria

Subjects with a diagnosis of traumatic brain injury (TBI) in the database of the University Hospital of Salerno antecedent of at least 6 months were invited to a screening of pituitary function and physiatrist evaluation.

The subjects enrolled were of both gender, 16–63 years old without neurological, psychiatric and medical conditions that could affect the conduct and outcome of the neuro-psyco tests, alcoholism and drug addiction, use of antidepressants, sedatives, neuroleptics, anti-epileptics, history of hypothalamic, pituitary or endocrine dysfunction, previous cranial irradiation or pregnancy. Thirty-five patients (16 females and 19 males) fulfilling inclusion and exclusion criteria were enrolled in the study. Written consent of patients and approval from the institutional review board was obtained. The patients were tested 6 months to 5 years (mean 16,1 months) after TBI.

2.2. Hormonal assessment

The following hormones were assessed in morning fasting blood sample: growth hormone (GH),insulin-like growth factor 1 (IGF1), luteinizing hormone (LH), follicle-stimulating hormone (FSH), testosterone (T, in males), 17β-estradiol (17β-E2, in women), prolactin (PRL), free *tetra-iodothyronine* (fT4), thyroid stimulating hormone (TSH). The patients with low IGF1, were requested to evaluate the GH/IGF1 axis by GHRH (Geref, Sermorelina, Serono Pharma SpA, Geneva, Switzerland) + Arginine test. The test was performed after overnight fast, at 8.00 a.m. by intravenous injection of 1 μg/kg of Geref followed by 0.5 g/kg arginine. Blood samples for GH were obtained 15 min before and immediately before the administration of Geref and then at 15, 30, 45, 60 and 90 min after the injection. Severe GH deficiency (GHD) was defined by a peek GH response <9 ng/mL during the test; GH insufficiency (GHI) by a peak of 9–16.5 ng/mL; a normal response by a peak >16.6 ng/mL.Free-T4, TSH, LH and FSH were measured by immune-radiometric assay, testosterone by radioimmunoassay, IGF-1 by enzyme-labeled chemi-luminescent immunometric assay and GH by immune-fluorometric assay. Normal reference serum hormones are reported in Table 1.

2.3. Physiatric assessment

All the patients enrolled underwent a physiatric evaluation to assess the effect of the TBI and abnormal pituitary function on quality of life using the SF 12® questionnaire [8] (Table 2). This questionnaire was self-administrated and analyzed global health, concentration, efficiency, attention and memory, depressed mood, anxiety, pain and limitations in social activities. It is made of 12 items that produce two indices: the physical component summary (PCS) and the mental component summary (MCS). The subjects were asked to answer the questions evaluating the day they fill out the questionnaire and the previous 4 weeks. A score at MCS and at PCS less than fifty is considered abnormal.

2.4. Statistical analysis

All data were compared using the chi-2 test. $P < 0.05$ was considered significant.

3. Results

Thirty-five patients, aged between 18 and 63 years (mean 44 years, median 53 years), were studied 6 months to 5 years after TBI. Road accidents were the main cause of TBI. Twenty subjects enrolled reported head trauma after car or motorcycle crash, seven after an accidental fall, three after domestic accident, two after falling from a bicycle, one after work related injury, one for assault and one for a firecracker blast.

3.1. Endocrinological assessment

According to normal reference ranges, 15 patients showed altered basal levels of one (N = 4) or more (N = 11) hormones. The most frequent hormonal alterationwasIGF1 and T below the normal reference value (N = 7), followed by LH/FSH, TSH and increased PRL (Fig. 1). One male patient showed basal GH < 0.03 ng/mL and three patients had a GH value of 0.05 ng/mL (Fig. 2A). In 3 subjects baseline GH was above the normal range. IGF1 was below the normal range in 7 patients, two of which displayed a particularly low level, ranging 50–53 pg/mL (Fig. 2B). Patients with IGF1 below the reference value were invited to submit to theGHRH + Arginine

Table 2
Hormonal abnormalities and quality of life after TBI. Quality of life was assessed by SF-12® questionnaire.

SF-12®	N	NAH	Hormonal abnormalities								
			IGF1	GH	FSH	LH	T	TSH	17β-E2	fT4	PRL
Normal	9	5	3	2	1	2	2	1	0	0	1
MCS <50	7	2	1	1	0	0	0	0	1	0	0
PCS <50	1	0	0	0	0	0	0	0	0	0	0
MCS and PCS <50	18	8	3	2	1	2	6	2	0	2	2

PCS: physical component summary; MCS: mental component summary; SF-12® questionnaire was scores 1 to 50. A score <50 was considered altered. N, number of patients; NAH, number of patients with one or more altered hormones; T, testosterone, 17β-E2, 17β Estradiol.