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Pituitary dysfunction due to sports-related traumatic brain injury

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Abstract

Purpose After traumatic brain injury was accepted as an important etiologic factor of pituitary dysfunction (PD), awareness of risk of developing PD following sports-related traumatic brain injury (SR-TBI) has also increased. However there are not many studies investigating PD following SR-TBIs yet. We aimed to summarize the data reported so far and to discuss screening algorithms and treatment strategies.

Methods Recent data on pituitary dysfunction after SR-TBIs is reviewed on basis of diagnosis, clinical perspectives, therapy, screening and possible prevention strategies.

Results Pituitary dysfunction is reported to occur in a range of 15–46.6% following SR-TBIs depending on the study design. Growth hormone is the most commonly reported pituitary hormone deficiency in athletes. Pituitary hormone deficiencies may occur during acute phase after head trauma, may improve with time or new deficiencies may develop during follow-up. Central adrenal insufficiency is the only and most critical impairment that requires urgent detection and replacement during acute phase. Decision on replacement of growth hormone and gonadal deficiencies should be individualized. Moreover these two hormones are abused by many athletes and a therapeutic use exemption from the league's drug policy may be required.

Conclusions Even mild and forgotten SR-TBIs may cause PD that may have distressing consequences in some cases if remain undiagnosed. More studies are needed to elucidate epidemiology and pathophysiology of PD after SR-TBIs. Also studies to establish screening algorithms for PD as well as strategies for prevention of SR-TBIs are urgently required.

Keywords Sports-related traumatic brain injury · Pituitary dysfunction · Growth hormone deficiency · Central hypogonadism

Introduction

The first case reporting hypopituitarism caused by traumatic brain injury (TBI) was in 1918 [1]. Since then increasing number of studies have been published and TBIs have turned to be one of the major etiologic factors for pituitary dysfunction [2]. However it is not until recent years that sports-related traumatic brain injuries (SR-TBIs) are also accepted as an important cause for hypopituitarism.

A population based study reported that 21% of all traumatic brain injuries were sports-related and that the estimated incidence rate was 170:100,000 of the general population [3]. However this data may be underestimating the exact incidence since many SR-TBIs remain unreported due to motivation to remain in the team, lack of awareness of the concussion or considering the injury unimportant [3–5].

Sports-related traumatic brain injuries not only concern professional athletes but also a whole community that is involved in recreational activities or amateur sporting, though at different rates. It was reported that traumatic brain injuries during sports or recreational activities stand for 7% of all injuries among patients treated in emergency departments but for 52.5% among professional kickboxers [6, 7]. The patients younger than 19 years constitute 70% of the cases and the incidence of SR-TBIs is increasing with time, a fact explained by increased awareness though exact reason is not known [6]. Males are reported to experience SR-TBIs twice the rate than females though there is conflicting data regarding gender differences [6, 8].

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Concussion, defined as rapid and reversible impairment of neurological functions following a direct blow or a transmitted impulsive force to the head, face or neck is the major injury occuring during sports [9]. A meta-analysis reported that rugby, American football and hockey were the sports with highest incidence rate of concussion, while volleyball, baseball and cheerleading had the lowest incidence among children and adolescents younger than 18 years [10]. Combative sports like boxing, kickboxing are particularly associated with repetitive head traumas. Brain damage, neuropsychological disorders are more frequent among these athletes [11].

Sports-related traumatic brain injuries may be subdivided on basis of continuity as acute or chronic. Acute SR-TBIs are similar to TBIs characterized by a single bout like traffic accidents or falls. Chronic SR-TBIs can happen as unforeseen multiple injuries like heading during football or as regularly occuring repetitive traumas like during boxing [2].

Pituitary dysfunction (PD) was reported to occur in a range of 15–45% after SR-TBIs depending on the study design [12, 13]. The rate of PD also depends on severity and chronicity of the trauma which are related to the type of sporting activity [14]. Pituitary dysfunction may develop after a single bout or multiple, repetitive traumas. The symptoms of hypopituitarism may be subtle and non-specific, thus easily attributed to other concomittant disorders occuring secondary to TBIs, raising the question of routine screening in patients that suffered SR-TBIs.

Keeping in mind that most of SR-TBIs occur among young or middle aged athletes, undiagnosed pituitary deficiency in this population with normal life expectancy may have distressing consequences. Moreover PD after SR-TBIs gain more importance considering the fact that even mild and forgotten TBIs may be the cause [15, 16]. We aimed to review recent data on PD after SR-TBIs and to discuss requirements of routine screening as well as possible prevention strategies.

Epidemiology

We identified 7 studies that investigated PD after SR-TBIs so far and the reported incidence varied grossly [12–14, 17–20]. Heterogeneity of the studies regarding severity of the trauma, hormonal analysis, stimulation tests, evaluation times and included populations resulted in a range of 15–46.6% of PD following SR-TBIs [12–14, 17–20]. The studies evaluating the PD after SR-TBIs were presented in Table 1.

The rate of developing PD after SR-TBI depends on severity of the trauma that is mainly evaluated with Glasgow Coma Scale [21]. Schneider evaluated studies that included all grades of TBI in chronic phase and reported the pooled prevalences of PD as 35.5%, 10.9% and 16.8% after severe, moderate and mild TBIs, respectively [22]. We were not able to find studies presenting frequency of PD based on severity of SR-TBIs, but studies generally included athletes that suffered brain injuries of multiple or repetitive nature which could be considered as mild TBIs (Table 1).

Growth hormone deficiency (GHD) is the most common pituitary hormone deficiency reported to occur in athletes after SR-TBIs. Studies evaluated growth hormone (GH) axis using various methods, some measured baseline IGF-1 levels while some performed GHRH-GHRP-6 test, glucagone stimulation test or insulin tolerance tests. The prevalence of GHD in boxers was reported as 45% by Kelestimur et al. using GHRH + GHRP-6 [14]. Tanriverdi diagnosed 22.7% of kickboxers and 15% of boxers as GH deficient by GST in addition to GHRH + GHRP-6 using the same cut-off values [12, 17]. Kelly et al. used GST with BMI-adjusted peak cut-off points and reported GHD in 19% of retired football players [18]. In a recent study Lithgow et al. reported GHD as 57% among athletes evaluated by GST and ITT using a higher cut-off value (5 µg/L), nevertheless the rate was 43% with a lower cut-off (3 µg/L) [13]. In a study that used only baseline IGF-1 levels for the diagnosis, none of the athletes had GHD [20]. Contrary to previous studies Roser et al. performed GST in professional soccer players and reported no increase in GHD [19].

Based on baseline gonadotropin and testosterone levels 8.8% of retired football players who had repetitive head traumas had central hypogonadism with normal prolactin levels [18]. A prospective study reported that 23.5% of women had menstrual irregularities following a sports related concussion, a significantly higher rate than control group (OR 5.85, 95% CI 1.61–21.22) [23].

Two studies reported similar rates of central adrenal insufficiency among athletes that suffered repetitive head trauma. The prevalence was 9.1% and 8% based on GST among kickboxers and boxers, respectively [12, 17]. However none of the retired football players had adrenal insufficiency with 250 µg ACTH stimulation testing [18].

Development of central hypothyroidism or central diabetes insipidus following SR-TBIs were presented in case reports [15, 24] but in none of the studies that included athletes with history of repetitive head traumas [12, 14, 18, 19].

Pathogenesis

There are several pathophysiological mechanisms proposed to play role in developing pituitary deficiency after TBIs. Mechanisms that involve direct trauma like sella turcica fractures, gland hemorrhage, compression of the gland by intracranial hemorrhage or edema, increased intracranial pressure or shear type injuries can cause PD [25–27].

Table 1 Studies reporting frequency of pituitary dysfunction after SR-TBIs

First author, year	Study design	Study population	Hormonal evaluation	GH (%)	ACTH (%)	FSH, LH (%)	TSH (%)	Comment
Kelestimur et al., 2004 [14]	Cross-sectional	Active or retired boxers n = 11 (male: 11) Age: 38 years (mean)	IGF-1, cortisol, total and free testosterone, FSH, LH, PRL, fT3, fT4, TSH Stimulation tests: GHRH + GHRP-6	45	0	0	0	Negative correlation was reported between boxing duration, number of bouts and peak GH levels
Tanriverdi et al., 2007 [17]	Cross-sectional	Kickboxers n = 22(male: 16) Age: 27.3 years (mean)	IGF-1, cortisol, total and free testosterone, FSH, LH, PRL, fT3, fT4, TSH Stimulation tests: GHRH + GHRP-6, Glucagon stimulation test	22.7	9.1	0	0	Negative correlation was observed between IGF-I levels and age, duration of sports and number of bouts
Tanriverdi et al., 2008 [12]	Cross-sectional	Active or retired boxers n = 61(male: 11) Retired boxers n = 17 Age: 42 years (mean) Active boxers n = 44 Age: 20 years (mean)	IGF-1, cortisol, total and free testosterone, FSH, LH, PRL, fT3, fT4, TSH Stimulation tests: GHRH + GHRP-6, Glucagon stimulation test	15	8	0	0	Retired boxers with GH deficiency had significantly lower pituitary volume
Kelly et al., 2014 [18]	Prospective	Retired football players n = 68 (male: 27) Age: 47.3 years (mean)	IGF-1, cortisol, ACTH, total and free testosterone, FSH, LH, PRL, TT4, fT4, TSH, serum&urine Na&osm, urine gravity Stimulation tests: Glucagon stimulation test, ACTH stimulation test (250 µg)	19.1	0	8.8	0	GH deficiency and hypogonadism may contribute to poor QoL, erectile dysfunction, and metabolic syndrome
Kovacs et al., 2016 [20]	Cross-sectional	Professional retired football players n = 27(male: 27) (9 had TBI) Age: 48 years (median)	IGF-1 LH Total testosterone Stimulation tests: NA	0	0	0	0	Players with a history of SR-TBI had lower LH levels No evidence of an increased prevalence of central hypogonadism or GH deficiency
Lithgow et al., 2018 [13]	Cross-sectional	All group(TBI) n = 62(male: 29) Age: 43 years (median) Subanalysis of SR-TBI Various sports[a] n = 15 Gender: NA Age: NA	IGF-1 Stimulation tests: Glucagon stimulation test, insulin tolerance test	46.6	0	No exact data	No exact data	Baseline IGF-1 level has no value in predicting GH deficiency in patients that had TBI Two patients developed GH deficiency following a single SR-TBI

Table 1 (continued)

First author, year	Study design	Study population	Hormonal evaluation	GH (%)	ACTH (%)	FSH, LH (%)	TSH (%)	Comment
Roser et al., 2018 [19]	Cross-sectional	Professional soccer players n = 15(male: 15) Age: 31 years (mean)	Stimulation tests: Glucagon stimulation test	0	0	0	0	Playing soccer is not a risk factor for GH deficiency

ACTH adrenocorticotropic hormone, *FSH* follicle stimulating hormone, *fT4* free thyroxine, *GH* growth hormone, *IGF-1* insulin like growth factor-1, *LH* luteinizing hormone, *NA* not available, *PRL* prolactin, *QoL* quality of life, *SR-TBI* sports-related traumatic brain injury, *TBI* traumatic brain injury, *TT4* total thyroxine

[a]Hockey (n = 4), cycling (n = 2), basketball (n = 2), soccer (n = 2), football (n = 2), dirt biking (n = 1), wrestling (n = 1), equestrian (n = 1)

Vascular injuries of the hypothalamo-hypophysial portal vessels with or without transection of the stalk can lead to cessation of blood supply and result in pituitary infarction [28]. Also secondary insults like hypotension, hypoxia and anemia can cause ischemia of the gland [29]. Such insults can reasonably be expected after acute and severe head traumas occuring during sports too.

Persistant neuroinflammation is another mechanism reported to be responsible for post-traumatic hypopituitarism. Dynamic hormonal changes may be observed even years after TBIs and it was suggested that concussion may trigger autoimmunity leading to development of PD over time [2, 30]. Tanriverdi et al. reported high titers of antipituitary antibodies (APAs) and antihypothalamus antibodies (AHAs) in amateur boxers and AHAs were associated with PD [31].

It was demonstrated that Apolipoprotein E (Apo E) polymorphism is related to development of PD in patients that suffered TBIs, including boxers and kickboxers [32]. Apolipoprotein E is synthesized in central nervous system and plays role in cholesterol transport to neurons as well as in downregulation of inflammatory cytokines [33, 34]. It has three isoforms and it is known that people carrying Apo E4 allelle are prone to diseases like Alzheimer's disease and amyloid angiopathy [35, 36]. Apolipoprotein E was detected abundantly in hypothalamus and an association between Apo E polymorphism and susceptibility to head trauma was proposed [34, 37]. Recent studies proved that a relationship exists between Apo E3/E3 genotype and a decreased risk of PD in patients that suffered TBIs [32].

Pathological analysis of post-mortem brain tissues of boxers revealed perivascular accumulation of pathologic tau protein, a condition called chronic traumatic encephalopathy (CTE) [38]. Some other proteins like amyloid precursor protein, neurofilament, amyloid β, α-synuclein are also reported to accumulate in axons after head traumas [39]. There are no studies reporting frequency of PD in patients suspected to have CTE or investigating the relationship between accumulation of the pathologic proteins and hypopituitarism. Some of these proteins like glial fibrillary acidic protein, amyloid β and tau protein are discovered to be increased in blood after TBIs and that the increase was correlated with severity of the trauma [40]. It has also been reported that neuron-specific enolase and tau protein were increased after concussions in boxers and ice-hockey players, respectively [41, 42]. Considering that PD is more prevalent after severe head traumas it may be hypothesized that a relationship may exist between accumulation of these proteins and PD.

LaFountaine et al. hypothesized in their interesting study that prolactin may be a marker after SR-TBIs to determine adequate time for athletes to return to play [43]. They proposed that concussion will cause dopaminergic activation during subacute period causing decrease in prolactine levels.

They observed decrease in prolactine levels in four athletes during first 48 h after concussion and then increase after 14 days accompanying the resolution of symptoms [43].

There is need for more studies to elucidate mechanisms leading to PD especially after multiple and repetitive SR-TBIs in order to develop strategies for prevention and detect novel markers that would predict PD.

Diagnosis and screening strategies of pituitary dysfunction after sports-related traumatic brain injuries

Pituitary hormone deficiencies may occur during acute phase following trauma or new deficiencies may develop during chronic phase. It was also observed that some hormonal deficiencies improve with time [30, 44]. Symptomatology of pituitary hormone insufficiencies may be subtle and non-specific but also may cause serious life threatening conditions like hypotension or electrolyte imbalances. Considering the dynamic changes regarding pituitary function after head trauma and possible dramatic outcomes, hormone analyses and stimulation tests as well as timing of the evaluation is of utmost importance and some screening algorithms have been proposed for diagnosis of PD after TBIs [2, 45–48]. Although there are no prospective studies and well-established algorithms for screening PD after SR-TBIs, it seems reasonable to follow recommendations made for PD after TBIs. Studies are also needed to develop screening algorithms for PD after sports-related repetitive head traumas like in boxing.

American Association of Clinical Endocrinologists offered that all patients with moderate or severe TBIs and also symptomatic patients with mild TBIs should be screened for PD during acute and chronic phase [47]. Tanriverdi et al. suggested that all patients that were hospitalized for at least 24 h or monitored in intensive care unit, patients that had an abnormality on initial computed tomography (CT), ACTH deficiency or central diabetes insipidus during acute phase or those with signs and symptoms of PD at any time after the event should be evaluated for pituitary dysfunction [2, 46]. According to suggested algorithm ACTH deficiency should be tested during acute phase and then all pituitary hormones should be re-evaluated at sixth month, at first year and then yearly until fifth year post TBI [2, 45, 48].

Somatotropic axis is evaluated with baseline IGF-1 levels and stimulation tests. However baseline IGF-1 levels are not always concordant with the peak GH levels after stimulation tests and the diagnosis solely based on IGF-1 levels may be misleading in this patient group [13]. Patients with three or more pituitary hormone deficiencies and low IGF-1 levels can be diagnosed as GH deficient without a stimulation test [49], but in cases of isolated GH deficiencies it is suggested to confirm GHD with a dynamic test unless IGF-1 level is below 2 SD [48]. Insulin tolerance test may be risky in these patients that may have accompanying central nervous system pathologies and glucagon stimulation test, GHRH-arginine or GHRH-GHRP-6 stimulation tests seem more appropriate for evaluation of GHD during follow-up. Diagnostic cut-off levels for mentioned tests are as determined previously in related guidelines [49].

Gonadotropin deficiency is diagnosed with repeatedly low morning testosterone levels with accompanying low or normal gonadotropin levels in men. Regular menstrual cycles in women are suggestive of intact hypothalamo-pituitary gonadal axis and no further evaluation is needed but low gonadotropin levels in post-menopausal women indicates PD.

Assessment of somatotropic and gonadal axes should be performed several months after TBI because of transient suppression during acute phase [50]. Dynamic testing for GHD may be deferred until 12th month due to significant rate of recovery and lack of evidence on beneficial effects of early replacement [45].

Athletes that had an acute and severe SR-TBI and are hospitalized due to critically ill condition should be followed for signs of central adrenal insufficiency and if it is suspected they should be screened with baseline cortisol measurements. Synacthen stimulation test is not sensitive enough and is not recommended during acute phase [51]. Morning cortisol levels of less than 7.2 µg/dL or levels between 7.2 and 18 µg/dL in the presence of signs and symptoms attributable to adrenal insufficiency are considered inappropriately low that should deserve treatment [22]. Functionality of adrenal axis should be re-tested with ACTH stimulation test during follow up period.

Thyroid axis is evaluated with baseline hormonal measurements (TSH, free T4) and low free T4 levels in the presence of low or normal TSH levels is suggestive of central hypothyroidism. It is suggested that thyroid hormones are evaluated in acute phase only when the patient is stable before hospital discharge and then reassessed at regular intervals as mentioned before [2, 46].

Patients that developed PD should undergo pituitary imaging for exclusion of any sellar masses. Specific lesions with pituitary gland enlargement were detected in 30% of patients during acute phase after moderate or severe TBIs [52]. However a study evaluated pituitary volume during chronic phase and reported that retired boxers who were GH deficient had significantly lower pituitary volume than boxers with intact pituitary functions [12]. Also another study reported pituitary gland atrophy in 14% of boxers and mixed marital art fighters [53].

Besides implementing proposed algorithms for diagnosing and screening athletes that suffered TBIs, informing the patient regarding pituitary dysfunction and its symptoms

may help in early diagnosis. In case of suspicious complaints tests may be performed at any time.

Clinical perspectives of pituitary dysfunction after sports-related traumatic brain injuries

Pituitary dysfunction following TBIs may masquerade clinical picture of post-TBI period itself and clinicians should be aware of possibility of hypopituitarism in patients presenting with non-specific symptoms like fatigue, depression and cognitive disorders [54].

Growth hormone deficiency may cause complaints like lack of energy, memory and concentration problems, being easily irritated and difficulty in coping with stressful conditions [55]. Amateur boxers and kickboxers that had GH deficiency secondary to SR-TBIs had significantly lower P300 amplitudes compared with GH-sufficient athletes indicating impaired cognitive performance [56].

Growth hormone has metabolic effects and deficiency was reported to be associated with a higher body mass index and waist circumference, lipid disturbances and higher fasting blood glucose [57]. Tanriverdi et al. presented for the first time the relationship between low IGF-1 levels and impaired body composition parameters like high waist circumference, fat ratio, abdominal fat mass and increased serum leptin levels in retired boxers. They speculated that this condition may constitute a risk for cardiovascular complications [58].

Patients with GHD generally had lower scores on surveys questioning quality of life [59]. Kelly et al. reported GHD as 19% among retired football players who had poor quality of life scores and suggested contribution of hormone deficiencies [18].

Patients that developed GHD after TBI had reduced aerobic and endurance capacity compared to those without GHD [60]. It was also reported that patients with GHD had significantly lower evaporative heat loss and impaired thermoregulation during exercise suggesting that athletes with GHD may be at increased risk of hypertermia especially in hot environments [61].

Multiple head traumas may be the cause of loss of libido like in a 27-year old male professional soccer player who was diagnosed with isolated central hypogonadism. His complaints improved after replacement therapy [16]. Also there is a case report presenting a kickboxer that experienced transient central hypogonadism after an acute bout [62]. Kelly et al. reported that retired professional football players with low testosterone levels had significantly lower erectile function and orgasmic function compared to the eugonadal group, suggesting contribution to lower quality of life. Moreover metabolic syndrome and obesity rates in this group were significantly higher [18]. There are many studies reporting decreased semen quality and ejaculatory dysfunction in athletes secondary to several mechanisms but none of them reported a relationship to SR-TBIs [63].

Pre-menopausal women that had SR-TBIs may experience menstrual irregularities or amenorrhea. A prospective study reported that 23.5% of women had menstrual irregularities following a sports related concussion, a significantly higher rate than among control group (OR 5.85, 95% CI 1.61–21.22). The fact was explained by mechanisms like ischemic damage, acute hyperprolactinemia or activation of HPA axis secondary to stress response [23].

There are not many cases emphasizing TSH deficiency following SR-TBIs. One case report presented a 14-year old athlete complaining of low energy levels and failure to grow. He had suffered four head traumas that first three were unreported. Tests revealed that he had developed central hypothyroidism together with central adrenal insufficiency and GH deficiency. His complaints improved following replacement therapy [15]. Non-specific symptoms like fatigue, exercise intolerance, cognitive dysfunction should be warning the clinicians about central hypothyroidism.

Polyuria and polydipsia with low urinary osmolarity indicating diabetes insipidus, electrolyte imbalances suggestive of inappropriate ADH syndrome or cerebral salt wasting are among TBI complications that may be seen during acute phase. These disturbances might be expected also following acute and severe SR-TBIs. There is a case report presenting a swimmer that developed isolated diabetes insipidus following a mild head trauma [24]. Central diabetes insipidus may recover over time but is likely to be persistant after severe TBIs [64].

Treatment

Central adrenal insufficiency is the most critical impairment that requires urgent detection and replacement during acute phase after all TBIs as well as sport related ones. There is not enough evidence that replacement of somatotropic, gonadal and thyroid axis insufficiencies improves outcome during acute phase and it is not recommended [22].

However cortisol and thyroid hormone deficiencies should be replaced in all patients thereafter but treatment of GHD and hypogonadism is not essential in every case and the decision on replacement should be individualized. Moreover growth hormone and testosterone are two hormones that are abused by many athletes for the sake of a better performance and are prohibited by sports leagues [65]. Treatment of an athlete with pituitary dysfunction may require application for a therapeutic use exemption (TUE) from the league's drug policy.

Growth hormone replacement has many favourable effects on cognition, metabolism and body composition [66, 67]. It has lipolytic effects on adipose tissue and replacement leads

to decrease in fat tissue and improvement in lipid parameters [66]. Growth hormone replacement also induces increase in lean body mass and bone mineral contents [66, 68]. Tanriverdi et al. reported improvement in body composition parameters, lipid profiles and quality of life scores in two GH-deficient retired amateur boxers after GH therapy [69]. Also improvement in pulmonary parameters, cardiac output and exercise capacity is observed in patients with GHD after replacement [70, 71]. However there is not enough evidence on the effect of muscle strength [72].

Growth hormone use by healthy recreational athletes significantly increased sprint capacity and the effect doubled when applied with testosterone but other performance measures (endurance, strength, power) did not change [73]. A meta-analysis evaluated effects of GH on athletic performance in healthy young adults and reported that even lean body mass is increased, strength was not increased and that exercise capacity may be even decreased. Also soft tissue edema and fatigue were experienced by GH treated participants [74]. Another meta-analysis did not report increase in muscle strength or aerobic exercise capacity in healthy participants [75].

Athletes that are GH deficient with severe symptoms should be considered for replacement. The dosage is the same as for other GH-deficient adults. There is no scientific evidence that benefits expected to be observed in this GH-deficiency group will also be obtained in healthy athletes, who aim to reach supraphysiologic levels of GH.

Treatment protocol of gonadotropin deficiencies that persist during chronic phase after SR-TBI is the same as any other etiologies of central hypogonadism.

Prevention

Centers for Disease Control and Prevention (CDC) suggested primary and secondary strategies for prevention of SR-TBIs. Using protective equipment, coaching appropriate sport-specific skills, adhering to rules of play and attention to strength and conditioning were among primary strategies. Secondary strategies were increasing awareness of the signs and symptoms of TBI and responding appropriately if suspected TBI occurs. Also it is stated that return to play should only be allowed after evaluation and permission by an experienced health-care provider [76].

A most recent study reported that professional fighters had dramatic lack of knowledge regarding concussion symptoms. Nearly half of them returned to play the same day they had a head injury and many of them concealed symptoms of the concussion [77]. The Association of Ringside Physicians reported a consensus statement on concussion management. They recommended that all combat sports athletes and their trainers should be educated about signs and symptoms of concussion and that an athlete who experienced a concussion should be removed from the activity [78].

Besides these common recommendations prevention strategies should also be specified to each sport and recreational activity.

Development of pituitary dysfunction itself may be a useful marker to prevent further SR-TBIs and more severe consequences but there have been no studies investigating this issue so far and clinical studies are needed.

Conclusion

Sports-related traumatic brain injury is a public health problem concerning both professional athletes and the whole population involved in sports and recreational activities. Increasing number of studies turned attention to the risk of developing PD after SR-TBIs. Pituitary deficiency may cause morbidity, decreased quality of life and even mortality if remain undiagnosed in this young and healthy population. It gains more importance considering the fact that even mild and forgotten TBIs may be the cause. More studies are needed to elucidate epidemiology and pathophysiology of PD following SR-TBIs. Also studies to establish screening algorithms for PD are urgently required. Besides the common recommendations to prevent SR-TBIs, strategies for prevention should be specified to each sport and recreational activity.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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