TRAUMATIC BRAIN INJURY AND HYPOPITUITARISM

HIPOPITUITARISMO E TRAUMATISMO CRÂNIO-ENCEFÁLICO

David Gonçalves Nordon[1], Rodrigo Rejtman Guimarães[1], Alcinda Aranha Nigri[2]

ABSTRACT

Traumatic brain injury is a common lesion occurring during trauma, especially in young adults. Among all the complications it can cause there is hypopituitarism, an important syndrome, which can delay growth and development in children, and compromise the quality of life of anyone affected. It is usually underdiagnosed and, therefore, undertreated. Through a quick evaluation of the serum hormones involved in a head injury, it is possible to determine those which will need a more thorough investigation, and leading possibly to hormonal replacement. Treatment should be started in those who show no recovery from a severe or multiple hormonal deficiency after three months of follow-up, and those with no recovery from a light or single hormonal deficiency after one year of follow-up.

Key-words: hypopituitarism, craniocerebral trauma, brain injuries, risk.

RESUMO

Traumatismo crânio-encefálico é uma lesão comum durante o trauma, especialmente em adultos jovens. Dentre todas as complicações que ele pode causar está o hipopituitarismo, uma síndrome importante que pode atrasar o crescimento e o desenvolvimento em crianças e comprometer a qualidade de vida de qualquer indivíduo afetado. Ele é geralmente subdiagnosticado e, consequentemente, subtratado. Através de uma rápida avaliação dos hormônios séricos daqueles envolvidos em um trauma craniano, é possível determinar quais necessitarão de uma investigação mais profunda e, possivelmente, reposição hormonal. O tratamento deve ser iniciado nos que não mostrarem recuperação de uma deficiência severa ou múltipla depois de três meses de seguimento, e nos que não se recuperarem de uma deficiência leve ou única depois de um ano de seguimento.

Descritores: hipopituitarismo, traumatismos craniocerebrais, traumatismos encefálicos, risco.

TRAUMATIC BRAIN INJURY (TBI)

TBI is an external aggression to the brain, which can cause several internal lesions, such as contusion, concussion, diffuse axonal lesion, haemorrhaging (extradural, subdural, subarachnoid) and hypopituitarism.

In the USA, the incidence of TBI is higher in men, adolescents and young adults, and it is estimated to affect over 600/100.000 inhabitants per year.[1] Therefore, annually 1.4 million individuals suffer TBI, generating 50.000 deaths and direct and indirect costs of 56.3 billion dollars per year. The estimated general incidence of TBI in children, however, was of 70/100.000 children younger than 17 years old per year in the year 2000, causing a cost of 1 billion dollars, due to hospitalization.[2]

The data in Brazil is scarce, but one study shows that the hospitalization rate due to TBI in São Paulo, in 1997, was of 36/100.000 inhabitants, with an in-hospital mortality of 10% and general mortality of 26.2-39.3/100.000 inhabitants.

A higher incidence was observed in males (76.6%), younger than 10 years old, followed by those of 20 - 29 years old and those of 30 - 39 years old.[3]

HYPOPITUITARISM AFTER TBI

The most accepted theory to explain how even a mild TBI can cause a hypopituitarism is that the movement of the pituitary and its infundibulum during the trauma compromises its blood supply, due to the trauma mechanism itself (acceleration/deceleration, contusion/concussion), diminishing or even abolishing the nurturing of its cells.

As the somatotrophs and gonadotrophs are in its most external layer, their functions are the easiest to be damaged, not only by the bloody supply insufficiency, but also by a possible direct lesion to the cells. Furthermore, haemorrhages and inflammations in response to the trauma in the region may increase the lesion, resulting in an even bigger compromise of the blood supply or direct lesion to the cells by inflammatory agents.[4-6]

INCIDENCE

The incidence of acute hypopituitarism after TBI is estimated to be between 24% and 50% by several studies. Isolated hypopituitarism is the most common (21.4% to 36.9%), followed by multiple (6% to 19.6%) and rarely pan-hypopituitarism (0% to 5.7%). The most prevalent deficiency is Growth Hormone deficiency (5% to 25%), followed by central hypogonadism (17%). Other less common alterations are: hyperprolactinemia (4.2% to 10%), central hypoadrenalism (6% to 9.8%), central hypothyroidism (5-8%) and central diabetes insipidus (1-7%). The severity of trauma, evaluated by the Glasgow Coma Scale, shows no relation to the degree of hypopituitarism in most studies.[6-13]

DEVELOPMENT

There is a serious controversy surrounding the hypopituitarism development in several studies.[8,10-12]

As there are only few studies, their number of patients is generally small and their methodologies are not always alike; their results are variable and not at all reliable. However, a recovery generally occurs in a considerable number of patients (20% - 50%) even 12 months after the TBI, and an equally considerable amount (15% - 50%) develops a new deficiency after such time.11,12 Thus, hormonal changes can be transitory in the TBI and do not predict deficiencies after one year follow-up. On the other hand, the only type of hypopituitarism of worst prognosis is pan-hypopituitarism, which showed no improvement at all in any study. The follow-up for one year or longer is, therefore, recommended.

Rev. Fac. Ciênc. Méd. Sorocaba, v. 13, n. 1, p. 1 - 3, 2011

1. Acadêmico do curso de Medicina - FCMS/PUC-SP
2. Professora do Depto. de Medicina - FCMS/PUC-SP

Recebido em 15/6/2009. Aceito para publicação em 16/11/2010.

Contato: d-nordon@uol.com.br

CLINICAL IMPLICATIONS

There are several clinical implications in the disturbance of the hypothalamus-pituitary-organs axle (HPOA), especially in children.[9,14-18] Although in adults the growth hormone deficiency (GHD) may cause loss of concentration, discouragement, tiredness, muscular mass loss, decreased tolerance to physical activities, increased central body fat, premature atherosclerosis and decrease in general quality of life, in children it also compromises growth and development.

Such symptoms are usually observed after the TBI and are generally known as a "post concussion syndrome", which contributes to the underdiagnosis of their real causes.

Gonadtrophin deficiency, in women, causes menstrual alterations, infertility, loss of libido, dyspareunia, osteoporosis, premature atherosclerosis, and in men, loss of libido, sexual function difficulties, loss of muscular and bone mass and decreased erithropoesis and hair growth. In children, such deficiency delays puberty and normal sexual development.

Corticotrophic hormone deficiency, most usually diagnosed through a disturbance in cortisol secretion, acutely leads to fatigue, weakness, drowziness, nausea, vomit and circulatory collapse. Chronically, it causes tiredness, pallor, loss of weight and appetite and hypoglycemia. In children, it also compromises growth and development.

Other hormones from the HPOA produce well known clinical syndromes: thyreostimulant hormone deficiency causes central hypothireoidism; antidyuretic hormone deficiency causes central diabetes insipidus. Hyperprolactinemia itself does not generate severe changes in the organism, and more than a lesion to the pituitary, it shows a response from the organism to a stressful situation.

DIAGNOSIS AND TREATMENT

For the doctor on call, either a general practitioner, a general surgeon or a pediatrician, being able to identify a case that may need a deeper examination and a referral to the specialist is necessary.

There is no established correlation between the trauma severity and hypopituitarism; however, its incidence is undoubtedly frequent, and a hormonal examination is, therefore, important. The serum dosage of the mainly affected hormones (IGF-1, FSH, LH, testosterone (men) and estrogen/progesterone (women)) is enough for a triage in most of the times. Those, whose exams are altered, may request a more thorough research, through stimuli tests and dosage of other pituitary hormones; it is important to notice that as cortisol reaches its peak in the morning, it might not produce a trustworthy evaluation if the person is using exogenous corticoids.

As all these hormonal changes assuredly compromise the person's quality of life, apart from his/hers growth and development, when in children, a treatment in the adequate cases is mandatory.

Nowadays it is recommended that, after the three months follow-up of the hormonal deficit, if it is multiple or severe, hormonal replacement should be started as soon as possible, and a new testing one year after the trauma will show the need of a continuation in the treatment. The aim of this treatment is to allow the person to regain the normal function of his/her HPOA, which may not always happen.

If it is a single or light deficit, it is suggested an one year follow-up, to evaluate the HPOA recovery; if there is no recovery, treatment is recommended for as long as necessary. Again, this treatment may aim at a regain in the HPOA function, which may not always happen and, therefore, require a continuous treatment for the rest of the patient's life.

Nevertheless, as there is no consensus about it, the medical conduct is usually according to the experience of the responsible endocrinologist.[6,19,20]

CONCLUSION

As we take into account the high incidence of TBI nowadays and consequently the high incidence of post-traumatic hypopituitarism, the early identification of alterations of the HPOA would be extremely worthy not only for children, whose growth and development totally depends on a balanced interaction of all the hormones, but also for public health, as it would lower costs and economic losses due to these deficits, which can compromise the normal functioning and the quality of life of people who were, up until then, productive human beings.

REFERENCES

1. Cassidy JD, Carrol LJ, Peloso PM, Borg J, von Holst H, Holm L, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO collaborating centre task force on mild traumatic brain injury. J Rehabil Med. 2004; 36(43):28-60.
2. Schneler AJ, Shields BJ, Hosteler SG, Xiang H, Smith GA. Incidence of pediatric traumatic brain injury and associated hospital resource utilizations in the United States. Pediatrics. 2006; 118:483-92.
3. Koizumi MS, Lebrão ML, Mello-Jorge MHP, Primerano V. Mortalidade por traumatismo crânio-encefálico no município de São Paulo, 1997. Arq Neuropsiquiatr. 2000; 58(1):81-9.
4. Urban RJ. Hypopituitarism after acute brain injury. Growth Horm IGF Res. 2006; 16(S):25-9.
5. Poomthavorn P, Zacharin M. Traumatic brain injury-mediated hypopituitarism. Report of four cases. Eur J Pediatr, 2007; 166:1163-8.
6. Agha A, Thompson CJ. High risk of hypogonadism after traumatic brain injury: clinical implications. Pituitary. 2005; 8:245-9.
7. Tsagarakis S, Tzanela M, Dimopolou I. Diabetes insipidus, secondary hypoadrenalism and hypothyroidism after traumatic brain injury: clinical implicantions. Pituitary. 2005; 8:251-4.
8. Leal-Cerro A, Flores JM, Rincon M, Murillo F, Pujol M, Garcia-Pesquera F, et al. Prevalence of hypopituitarism and growth hormone deficiency in adults long-term after severe traumatic brain injury. Clin Endocrinol. 2005; 62:525-32.
9. Popovic V. Gh deficiency as the most common pituitary defect after TBI: Clinical implications. Pituitary. 2005; 8:239-43.
10. Tanriverdi F, Senyurek H, Unluhizarei K, Selcuklu A, Casanueva FF, Kelestimur F. High risk of hypopituitarism after traumatic brain injury: a prospective investigation of anterior pituitary function in the acute phase and 12 months after trauma. J Clin Endocrinol Metab. 2006; 91(6):2105-11.
11. Aimaretti G, Ambrosio MR, Di Somma C, Gasperi M, Cannavò S, Scaroni C, et al. Residual pituitary function after brain injury-induced hypopituitarism: a prospective 12-month study. J Clin Endocrinol Metab. 2005; 90(11):6085-92.
12. Aimaretti G, Ambrosio MR, Di Somma C, Fusco A, Cannavò S, Gasperi M, et al. Traumatic brain injury and subarachnoid haemorrhage are conditions at high risk for hypopituitarism: screening study at 3 months after the brain injury. Clin Endocrinol. 2004; 61:320-6.
13. Bavisetty S, Bavisetty S, McArthur DL, Dusick JR, Wang C, Cohan P, et al. Chronic hypopituitarism after traumatic brain injury: risk assessment and relationship to outcome.

Neurosurgery. 2008; 62(5):1080-91.
14. Aken MO, Lamberts SWJ. Diagnosis and treatment of hypopituitarism: an update. Pituitary. 2005; 8:183-91.
15. Masel BE. Traumatic brain injury induced hypopituitarism: the need and hope of rehabilitation. Pituitary. 2005; 8:263-6.
16. Popovic V, Aimaretti G, Casanueva FF, Chigo E. Hypopituitarism following traumatic brain injury. Growth Horm IGF Res. 2005; 15:177-84.
17. Lorenzo M, Peino R, Castro AI, Lage M, Popovic V, Dieguez C, et al. Hypopituitarism and growth hormone deficiency in adult subjects after traumatic brain injury: Who and when to test. Pituitary. 2005; 8:233-7.
18. Baldelli R, Bellone S, Corneli G, Savastio S, Petri A, Bona G. Traumatic brain injury-induced hypopituitarism in adolescence. Pituitary. 2005; 8:255-7.
19. Estes SM, Urban RJ. Hormonal replacement in patients with brain injury-induced hypopituitarism: who, when and how to treat? Pituitary. 2005; 8:267-70.
20. Klose M, Feldt-Ramussen U. Does the type and severity of brain injury predict hypothalamo-pituitary dysfunction? Does post-traumatic hypopituitarism predict worse outcome? Pituitary. 2008; 11:255-61.

NATUREZA EM FLOR
Liliana Alves