S100B in mild traumatic brain injury

A head computed tomography (CT) scan is an effective test for detecting traumatic intracranial findings after mild traumatic brain injury (mTBI). However, a head computed tomography is costly, and can only be performed in a hospital.

Today, S100B is used locally as an early screening tool in the Scandinavian Guidelines in mild traumatic brain injury and moderate TBI [1] , where low levels in serum have been shown to be able to safely exclude the presence of intracranial injury in mild TBI patients and thus obviate the needs for head computed tomography in these cases. However, it has been suggested that one of the limitations with the protein is the relatively short serum elimination half-life (suggested to be as short as 25 min in patients with no ongoing brain injury) [2]. Thus, in patients with mild/moderate TBI without pathophysiological processes to cause a sustained release in S100B, delayed sampling may be falsely reassuring and this is reflected in the guidelines, which suggest a cutoff of 6 h after trauma [3]. It is becoming increasingly clear that a specific level in serum is of little importance if in the absence of kinetic considerations.

Several potential biomarkers have been proposed for the screening of patients, but protein S100B seems now the most promising for some clinical and analytical considerations. After performing a meta-analysis of clinical trials in patients with mild head injury, Lippi et al, calculated a cumulative area under the curve of 0.753 (95% CI, 0.752-0.754), a negative predictive value of 97.7% (95% CI, 97.5-97.8 %) and positive predictive value of 23.6% (95% CI, 23.2-24.0%) for brain injury. They therefore developed a diagnostic algorithm based on the preliminary assessment of the Glasgow Coma Scale (GCS). Patients with GCS <14 are subjected to CT, those with values GCS14-15 without risk factors are discharged, whereas protein S100B is assessed stat in those with GCS 14-15 and the presence of risk factors. According to the value of the marker, patients with a concentration below the diagnostic cut-offs are discharged, whereas CT is performed in those with higher concentrations. By combining the percentage of positive CT scans in patients with mild head trauma and the negative predictive value of protein S100B, this protocol would safely abate unnecessary CT by 30-50% and costs by 28% [4].

S100B has been proposed as a putative biochemical marker in determining the extent of brain injury and corresponding prognosis in neurotrauma.

Levels of S100B below 0.105 µg/L can accurately predict normal Cranial CT findings after minor head injury (MHI) in older patients and in those treated with platelet aggregation inhibitors (PAIs). Combining conventional decision criteria with measurement of S100B can reduce the CCT scan and hospital admission rates by approximately 30% [5]

S-100B may be a promising serum marker for assessing the extent of primary injury and the time course of secondary damage after severe head injury [6]

In patients with intracranial traumatic lesions, skull fractures, as well as skull and facial bone fractures occurring together, were identified as significant additional factors for the increase in serum S100B levels ($p<0.0001$). Older age was also associated with elevated S100B serum levels ($p<0.0001$). Data show that peak S100B serum levels were found in patients with cerebral edema and brain contusions

[7].

The proportion of patients with detectable serum level was significantly ($p < 0.01$) higher among those with intracranial pathology (92%) compared to those without (34%). The negative predictive value of an undetectable S-100 serum level was 0.99. Undetectable serum level of S-100 protein predicts normal intracranial findings on CT scan. Determination of S-100 protein in serum may be used to select patients for CT scanning [8].

The dosage of S100B, an astroglial protein released after neuronal injury, is a potentially useful laboratory tool. At 24 hours from clinical onset its serum value of 1.03 mcg/L has 94% sensitivity and 83% specificity to detect massive brain edema [9].

Intraoperative stable Evoked Potentials and S100B ≤0.08 µg/l may be used as a marker to predict long-term neurological improvement, whereas EP-changes and elevated S100B levels on the 3rd postoperative day may be useful as a marker to predict long-term neurological alteration. In summary, the combined use of S100B and EPs might be helpful in the prediction of the severity of adverse spinal cord affection following surgery and guidance of patients [10].

1)
Undén J, Ingebrigtsen T, Romner B; Scandinavian Neurotrauma Committee (SNC). Scandinavian guidelines for initial management of minimal, mild and moderate head injuries in adults: an evidence and consensus-based update. BMC Med. 2013 Feb 25;11:50. doi: 10.1186/1741-7015-11-50. PubMed PMID: 23432764; PubMed Central PMCID: PMC3621842.
2)
Jönsson H, Johnsson P, Höglund P, Alling C, Blomquist S. Elimination of S100B and renal function after cardiac surgery. J Cardiothorac Vasc Anesth. 2000 Dec;14(6):698-701. PubMed PMID: 11139112.
3)
Undén J, Romner B. Can low serum levels of S100B predict normal CT findings after minor head injury in adults?: an evidence-based review and meta-analysis. J Head Trauma Rehabil. 2010 Jul-Aug;25(4):228-40. doi: 10.1097/HTR.0b013e3181e57e22. Review. PubMed PMID: 20611042.
4)
Lippi G, Cervellin G. [Diagnostic approach to the mild head trauma of the adult in Emergency Medicine: between biomarkers and imaging]. Recenti Prog Med. 2013 Mar;104(3):120-32. doi: 10.1701/1255.13861. Review. Italian. PubMed PMID:23548957.
5)
Thaler HW, Schmidsfeld J, Pusch M, Pienaar S, Wunderer J, Pittermann P, Valenta R, Gleiss A, Fialka C, Mousavi M. Evaluation of S100B in the diagnosis of suspected intracranial hemorrhage after minor head injury in patients who are receiving platelet aggregation inhibitors and in patients 65 years of age and older. J Neurosurg. 2015 Jul 7:1-7. [Epub ahead of print] PubMed PMID: 26148794.
6)
Raabe A, Grolms C, Sorge O, Zimmermann M, Seifert V. Serum S-100B protein in severe head injury. Neurosurgery. 1999 Sep;45(3):477-83. PubMed PMID: 10493369.
7)
Wolf H, Frantal S, Pajenda G, Leitgeb J, Sarahrudi K, Hajdu S. Analysis of S100 Calcium Binding Protein B Serum Levels in Different Types of Traumatic Intracranial Lesions. J Neurotrauma. 2014 Nov 3. [Epub ahead of print] PubMed PMID: 25068442.
8)
Bertil Romner, Tor Ingebrigtsen, Poul Kongstad, and Svend Erik Børgesen. Journal of Neurotrauma. August 2000, 17(8): 641-647. doi:10.1089/089771500415391.
9)
Foerch C, Otto B, Singer OC, et al. Serum S100B predicts a malignant course of infarction in patients with acute middle cerebral artery occlusion. Stroke. 2004;35(9):2160–2164.

10)
Szelényi A, Heukamp C, Seifert V, Marquardt G. S100B, intraoperative neuromonitoring findings and their relation to clinical outcome in surgically treated intradural spinal lesions. Acta Neurochir (Wien). 2014 Jan 5. [Epub ahead of print] PubMed PMID: 24390083.