Abstract title

An outlier analysis for acute blood biomarkers of moderate and severe traumatic brain injury

Abstract text (incl. figure legends and references)

BACKGROUND: Blood biomarkers have been studied to improve the clinical assessment and prognostication of patients with moderate – severe traumatic brain injury (mo/sTBI). To assess their clinical usability, one needs to know potential factors that might cause abnormal values and affect clinical decision-making.

MATERIALS AND METHODS: In a prospective study we recruited patients with mo/sTBI (n = 85) and measured the blood levels of eight protein biomarkers (GFAP, S100B, NFL, H-FABP, IL-10, t-tau, amyloid B40, and amyloid B42) within 24 hrs of admission. Similar analyses were conducted for controls (n = 40) with an acute orthopaedic injury in absence of head trauma. The patients with TBI were divided into subgroups of normal vs. abnormal (n = 10/75) head CT and favourable (Glasgow Outcome Scale extended = GOSe 5-8) vs. unfavourable (GOSe < 5) (n = 42/38, 5 missing) outcome. Biomarker levels outside +/- 1.5 IQR were considered as outliers. The medical records of each outlier patient were gone through in a team meeting to determine possible reasons for abnormal values.

RESULTS: In the CT subgroups, 21 patients (25%), and in the outcome subgroups, 23 patients (27%) showed abnormal values in at least one biomarker. Among the controls 12 (30%) showed abnormal values. Several patients had abnormal values in more than one biomarker (up to 4) in all subgroups. All abnormal values were higher than +1.5 IQR. A logical explanation was found for almost all cases, with the exception of amyloids and tau. Explanations for high values included extremely severe injury, esp. for GFAP and S100B all outliers in the CT subgroups died because of the injury. In case of H-FABP and IL-10 the explanation was extracranial injuries (thoracic injuries for H-FABP and multi-trauma for IL-10), in some cases these also associated with abnormally high S100B. Sampling related factors and demographic factors such as earlier head injuries or neurological conditions and old age explained some of the abnormally high values (esp. for NFL). Similar explanations also emerged in controls, where the abnormal values were caused especially by pre-existing neurological diseases.

CONCLUSION: In order to utilize blood-based biomarkers in clinical assessment of mo/sTBI, pre-existing health issues, extremely severe injuries, multi-trauma, and temporal factors must be taken into consideration. Very high levels seem to be often associated with poor prognosis and mortality (GFAP and S100B). This information is important for decision-making in clinical settings.

Authors

Otto Korhonen[1-3], Malla Mononen[1-3], Mehrbod Mohammadian[1-2], Jussi P. Posti[1-3], Iftakher Hossain[1-4], David Menon[4], Virginia Newcombe[4], David Menon[4], Peter Hutchinson[5], Henrik Zetterberg[6], Kaj Blennow[6], Jean-Charles Sanchez[7], Leire Azurmendi[7], Linnéa Lagerstedt[7], Riikka Takala[8], Ari Katila[8], Jussi Tallus[9], Olli Tenovuo[1-2]

[1]Turku Brain Injury Center, Turku University Hospital, Turku, Finland, [2]Department of Neurology, University of Turku, Turku, Finland, [3]Neurocenter, Department of Neurosurgery, Turku University Hospital, Turku, [4]Division of Anesthesia, Department of Medicine,, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom, [5]Division of Neurosurgery, Department of Clinical Neurosciences, University of Cambridge, Addenbrooke's Hospital, Cambridge, United Kingdom, [6]Istitute of Neuroscience and Physiology, Department of Psychiatry and Neurochemistry, Shalgrenska Academy at the University of Gothenburg, Mölndal, Sweden, [7]Department of Specialities of Internal Medicine, Faculty of Medicine, University of Geneva, Geneva, Switzerland, [8]Perioperative Services, Intensive Care Medicine and Pain Management, Department of Anesthesiology and Intensive Care, Turku University Hospital, University of Turku, Turku Finland, [9]Department of Radiology, , Turku University Hospital, University of Turku, Turku Finland