BIOMARKERS IN MILD TRAUMATIC BRAIN INJURY: A SYSTEMATIC REVIEW
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Introduction: Mild traumatic brain injury (TBI) is responsible for the majority of pediatric head injuries. Diagnosis and evaluating the severity of mil TBI are difficult especially in non-verbal children; however, even mild TBI may be associated with the development of cognitive and behavioral conditions later in life. Thus, sensitive and specific biomarkers would greatly improve our capacity to pursue clinical management and research.

Objectives: The purpose of our systematic review was to evaluate the diagnostic and prognostic value of biomarkers of children with mild TBI.

Methods: A systematic search of the literature was performed with MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials databases using terminology selected for biomarkers, TBI and children (< 18 years) from inception to July 2013. Articles were excluded if they did not include children with mild TBI and biomarkers measured within 24 hours of injury. Qualitative assessment was performed by independent reviewers using standard procedures designed for observational studies (QUADAS-2) and prognostic studies (REMARK).

Results: Of 5978 articles identified, all abstracts were screened, and 461 full text articles were selected for review; 20 articles met inclusion criteria and 9 articles were found from bibliographies. Among 29 studies, only 7 focused exclusively on children. The median sample size was 99 [range 16-1560]. Of 55 biomarkers examined, 22 studies (76%) examined S100B. Comparing the serum of mild TBI to that of controls, there were 7 biomarkers increased and 8 biomarkers decreased in mild TBI. Glasgow coma scale and symptoms on admission were examined in association with biomarkers; however, the results were controversial. 11 studies evaluated the association between biomarkers and anomalies visible on computed tomography (CT) scans. S100B was increased in CT positive group; high sensitivity (83-100%) but low specificity (12-65%). Outcomes, such as post concussion syndrome, functional impairment, or return to work/activities, were studied; however, the heterogeneity of studies and the limited sample size did not allow summary conclusions to be generated for prognostic biomarkers. The over all quality of the studies was relatively low and may have contained a lot of potential bias.