

enrolled patients by applying a systematic selection algorithm to minimize selection bias, and physicians and pharmacists evaluated patients prospectively to evaluate the causal associations between the drug regimens and patient presentations. Subsequently, a research pharmacist and physician independently reviewed the charts of ADE patients from these cohorts, abstracting data using electronic forms. Reviewers recorded patient, provider and system factors that contributed to the development of ADEs. The main outcome was the presence of at least one contributing factor in the development of an ADE. We used descriptive statistics with appropriate measures of variance. The sample size was determined by enrolment into the primary studies. **Results:** We reviewed the charts of 670 patients diagnosed with 725 ADEs. We identified ≥ 1 contributing factors in 62% (95%CI 58-65%) of ADEs. Multiple contributing factors were present in 17% of ADEs (95%CI 13-20%). The most common contributing factors were inadequate patient counseling or instructions about medication use (15%), insufficient laboratory monitoring or follow-up of monitoring tests (12%), lack of staff education (7%), lack of provider adherence with recommended treatment guidelines (7%), and delayed or inadequate clinical reassessment after a medication change (6%). Provider errors in drug administration contributed to 0.3% of ADEs (95%CI 0.0-0.7). **Conclusion:** Contributing factors were identified for most ADEs. They were often related to inadequate counseling and follow-up, and were rarely the result of errors. Further research is required to understand how communication of medication instructions can be improved. Investments in technologies to reduce provider errors may not significantly reduce the numbers of ADE patients presenting to EDs. **Keywords:** adverse drug event, patient safety, prevention

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Prognostic value of S-100B protein for prediction of post-concussion symptoms following a mild traumatic brain injury: systematic review and meta-analysis

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Introduction: Mild traumatic brain injury (mTBI) is a major cause of morbidity but there are no validated tools to help clinicians predict post-concussion symptoms. This systematic review and meta-analysis aimed to determine the prognostic value of S-100B protein to predict post-concussion symptoms following a mTBI in adults. **Methods:** The protocol of this systematic review was registered with the PROSPERO database (CRD42016032578). A search strategy was performed on seven databases (CINAHL, Cochrane CENTRAL, EMBASE, MEDLINE, Web of Knowledge, PsycBITE, PsycINFO) from their inception to October 2016. Studies evaluating the association between S-100B protein level and post-concussion symptoms assessed at least seven days after the mTBI were eligible. Individual patient data were requested. Studies eligibility assessment, data extraction and risk of bias assessment were performed independently by two researchers. Analyses were done following the *meta-analysis using individual participant data or summary aggregate data guidelines* from the Cochrane Methodology Review Group. **Results:** Outcomes were dichotomised as persistent (≥ 3 months) or early (≥ 7 days < 3 months). Our search strategy yielded 23,298 citations of which 29 studies presenting between seven and 223 patients ($n = 2505$) were included. Post-concussion syndrome (PCS) (16 studies), neuropsychological symptoms (9 studies) and health-related quality of life (4 studies) were the most frequently presented outcomes. The S-100B

protein serum level of patients with no PCS was similar to that of patients experiencing persistent PCS (mean difference 0.00 [-0.05, 0.04]) or early PCS (mean difference 0.03 [-0.02, 0.08]). The odds of having persistent PCS (OR 0.56 (95% CI: 0.29-1.10) or early PCS (OR 1.67 (95% CI: 0.98-2.85) in patients with an elevated S-100B protein serum level was not significantly different from that of patients with normal values. No meta-analysis was performed for other outcomes than PCS due to heterogeneity and small samples. Studies' overall risk of bias was considered moderate. **Conclusion:** Results suggest that the prognostic value of S-100B protein serum level to predict persistent and early post-concussion symptoms is limited. Variability in injury to S-100B protein sample time and outcomes assessed could potentially explain the lack of association and needs further evaluation.

Keywords: traumatic brain injury, post-concussion symptom, meta-analysis

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Prognostic value of neuron-specific enolase (NSE) for prediction of post-concussion symptoms following a mild traumatic brain injury: a systematic review

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Introduction: Mild traumatic brain injury (mTBI) is an understudied worldwide health problem and a socio-economic burden that remains a major cause of morbidity. However, there is no prognostication tool to help clinicians predict the occurrence of post-concussion symptoms. This systematic review aimed to determine the prognostic value of neuron-specific enolase (NSE) to predict post-concussion symptoms following a mTBI in adults. **Methods:** The protocol of this systematic review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) database (registration number CRD42016033683). Seven databases (CINAHL, Cochrane CENTRAL, EMBASE, MEDLINE, PsycBITE, PsycINFO, Web of Knowledge/Biosis) were searched for cohort studies evaluating the association between NSE levels and post-concussion symptoms assessed at least seven days after the mild TBI. Grey literature was also screened using databases on dissertations and theses as well as abstracts from relevant congresses. Two researchers independently screened studies for inclusion, extracted data, and appraised their quality using the Quality in Prognostic Studies (QUIPS) tool from the Cochrane Collaboration Group. **Results:** Our search strategy yielded a total of 23,298 citations from which eight cohorts presented in 10 studies were included. Studies included between 45 and 141 patients (total = 608 patients). The most frequently assessed outcomes were post-concussion syndrome (PCS) (13 assessments), neuropsychological disorders (10 assessments), return to work or sick leave (2 assessments) and Glasgow Outcome Scale (GOS) (2 assessments). No association was found between an elevated NSE serum level and the occurrence of PCS. Of the 33 outcomes assessments performed, only three showed an association between a higher level of serum NSE and a post-concussion symptom (alteration of at least three cognitive domains at 2 weeks, standardised physician assessment at 6 weeks and headache at 6 months following a mild TBI). Included studies' overall risk of bias was considered moderate. **Conclusion:** Results of this systematic review conclude that based on current levels of evidence, serum NSE levels alone do not provide prognostic information on persistent or early post-concussion symptoms after a mTBI.

Keywords: traumatic brain injury, post-concussion symptom, systematic review