S100-B in patients with mild traumatic brain injury: potentially less but delayed radiology – experiences from a Swedish University Hospital

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Abstract

Mild traumatic brain injury (MTBI) is associated with a low but non-negligible risk of intracranial hemorrhage, which can be ruled out by a computed tomography (CT) scan of the head. Under some circumstances, the biomarker S100B can also be used to rule out intracranial hemorrhage and reduce CT usage. The usefulness of S100B has been questioned, however, since time loss associated with sample collection and analysis may delay the diagnosis of clinically significant hemorrhage. This study specifically investigated the lead times of urgent S100B sampling in MTBI patients with low risk of hemorrhage in a care as usual setting (n=50). 28% of patients had normal S100B levels, in line with previous reports. For samples processed according to routines for urgent lab tests (n=43), the median total time from prescription to result was 117 minutes (51-214), which was lower compared to previous reports, but still a substantial delay of diagnostic CT scans. In conclusion, we would like to raise the awareness of potential time delays associated with the implementation of S100B in the management of MTBI patients in a standard care setting. For S100B analysis to become more useful in the management of MTBI patients, we suggest the development and validation of a fast, bedside analysis method.

Background

Mild traumatic brain injury (MTBI) is a leading cause for seeking emergency care [1-3]. MTBI is associated with a low but non-negligible risk of intracranial hemorrhage, which can be ruled out by a computed tomography (CT) scan of the head [4]. Concerns about radiation exposure and costs have led to the development of clinical decision rules to reduce CT usage, but the efficiency of these rules has been questioned [5]. An alternative or potential complement to

decision rules is biomarkers. The most validated biomarker is S100B, which is expressed in glial cells and released upon central nervous system (CNS) tissue injury [6]. Prospective validation of S100B sampling in patients with MTBI has shown a sensitivity of 100% to detect clinically significant intracranial events, which makes it suitable as a negative selection marker for CT [6]. Retrospective validation of S100B sampling applied in conjunction with Scandinavian Neurotrauma Committee Guidelines (SNC) for MTBI management has indicated that S100B as a negative selection marker may reduce the use of CT by approximately 30% without increasing the risks of adverse events [7]. The usefulness of S100B has been questioned, however, since time loss associated with sample collection and analysis may delay the diagnosis of clinically significant hemorrhage. This study specifically investigated the lead times of S100B in MTBI patients with low risk of hemorrhage in a care as usual setting.

Design

50 adult patients who sought emergency care at Linköping University Hospital due to MTBI were enrolled. Inclusion- and exclusion criteria for lead time analysis are detailed in **Table 1**. The study was approved by the regional ethical review board (2013/204-31).

The time for S100B prescription, sampling and reporting, as well as CT scan findings were logged. S100B was analysed according to local routine for urgent tests by local lab using the Roche Elecsys S100B assay.

Results:

The time it took to draw, manage, and analyse the samples varied significantly, with 13 of 50 samples taken more than 15 minutes after prescription. 7 samples were not marked for urgent analysis. These samples were thus excluded from the analysis of lead time.

14 patients of 50 (28%) showed normal serum S100B levels (< 0.10 µg/l). None of these had any intracranial bleeding on CT scan. Seven patients demonstrated an intracranial hemorrhage. All these had elevated level S100B (0.12-1.9 µg/l). The overall sensitivity was 100% and the NPV 100%.

For correctly processed samples (n = 43), the median in lab time of analysis was 72 minutes (34-165). 10 samples (23%) were analysed within 60 minutes and 8 samples took more than 120 minutes to analyse. Average analysis time was 82

minutes. The median total time from prescription to result was 117 minutes for samples correctly handled (n=43) (51-214) (**Fig. 1**).

Discussion:

Limiting radiation exposure in low risk patients is an everyday concern for emergency practitioners and decision rules can potentially reduce harmful radiation exposure. Unfortunately, decision rules for MTBI suffer from a lack of specificity and/or sensitivity, leading to unnecessary scans or undetected significant injuries and indicating the need for complimentary analyses [5].

In our material, S100B was highly sensitive in identifying patients with intracranial bleeding. 28% of all patients had normal S100B levels, which is in line with previous Swedish reports [7]. With a median lead time of 117 minutes from prescription to result, the use of S100B would, however, have caused significant delays in the prescription of CT head scans in the remaining 72% of patients. The risk and cost of extended waiting times in the emergency department, therefore, has to be weighed against the potentially positive health effects of an approximately 30% reduction of CT head scans.

Interestingly, our median lead time was substantially lower compared to previous reports [6, 8]. Lead times may be reduced further by a specific protocol for sample handling, but standard analysis still requires a minimum of 20 minutes in addition to setup time, calibration and sample transport. The shortest lead time noted in this study was 51 minutes. This is probably close to the lower limit in a standard care setting using current analysis methods and still causes a significant delay of CT scans, especially in centers with dedicated ER CT scanners.

Conclusions

Implementation of S100B in the management of MTBI patients in a standard care setting is potentially associated with substantial delays in CT imaging for approximately 70% of patients. For S100B analysis to become more useful in the management of MTBI patients, we suggest the development and validation of a fast, bedside analysis method.

Contributors

JM and PBN designed the study. JM collected the data. All authors contributed to data analysis and manuscript preparation.

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Competing interests

The authors have no competing interests to declare.

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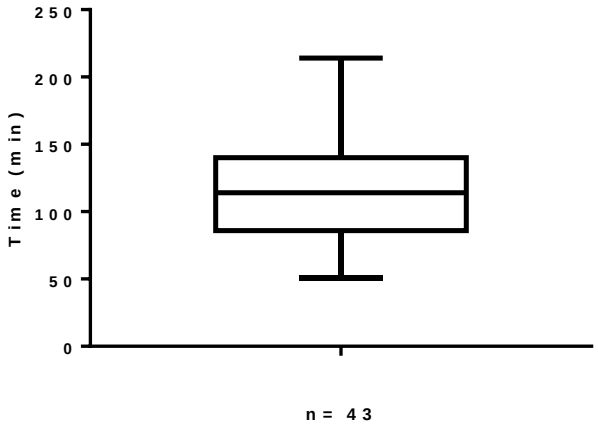
Figure 1



Legend: 43 out 50 S100B samples were correctly handled according to local routine for urgent tests and thus included in the analysis of lead time. The total lead time varied significantly (51-214 minutes) with a median time of 117 minutes.

Table 1 inclusion and exclusion criteria for lead time analysis.

Inclusion criteria	**Exclusion criteria**
Able and willing to provide informed consent	Unwilling to participate
Adults 18 years and older	Patients with multiple trauma
Minimal traumatic brain injury according to Scandinavian Neurotrauma Committee guidelines.	Intoxicated patients
Sampling possible within 3h of injury	Patients on anticoagulant treatment
	Deviation from local routines for urgent sample handling and/or analysis for any reason.

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