Cerebral Autoregulation Monitoring and Online Arden Syntax Clinical Decision Support for the Treatment of Intracranial Hypertension in Children With Traumatic Brain Injury

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Abstract. Background: Intracranial hypertension is a serious complication in the intensive care of children with severe traumatic brain injury (STBI). Objective: The goal was to create a computer system for simultaneous neuromonitoring of cerebral parameters and Arden-Syntax-based clinical decision support (CDS) in children with STBI undergoing intensive care treatment. Methods: Intensive care of these patients is based on internationally accepted guidelines. Arden Syntax, which is an HL7 medical knowledge representation and processing standard for CDS systems, was used to develop digital algorithms for these guidelines. Results: Comparison of a group of 37 conventionally treated patients with a second group (84 patients) monitored and treated with the combined CDS system yielded statistically significant differences. Conclusion: A combination of cerebral autoregulation monitoring with Arden-Syntax-based CDS in accordance with guidelines for the treatment of intracranial hypertension in children with STBI provides markedly better treatment outcomes. It opens up new options for the use of standards to formalize and process medical knowledge in neuromonitoring.

Keywords. severe traumatic brain injury (STBI), cerebral perfusion pressure (CPP), intracranial pressure (ICP), clinical decision support (CDS), Arden Syntax

1. Introduction

Severe traumatic brain injury (STBI) is one of the main causes of death and severe disability, especially among children [1]. Unfavorable outcomes are usually caused by intracranial hypertension (ICH) and traumatic brain edema. According to many authors,

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ICH occurs in 40–80% of patients with traumatic brain injury (TBI), and a third of them develop uncontrolled ICH, which often leads to unfavorable outcomes [2].

Usually patients with STBI require multimodal monitoring in intensive care units (ICUs), online monitoring of intracranial pressure (ICP), and invasive monitoring of central hemodynamics including continuous measurement of arterial blood pressure. Increased ICP is liable to cause cerebral ischemia and impair cerebral autoregulation mechanisms.

Cerebral autoregulation of blood flow and brain metabolism is a fundamental ability of the brain to maintain stable energy expenditure when external conditions change [3]. Cerebral autoregulation can be monitored by many approaches. The best known and most widely used approach is the so-called pressure-reactivity index (PRx), first proposed by the Cambridge School of Neurosurgery [4]. PRx is determined as a linear Pearson's correlation coefficient between mean arterial pressure (MAP) and ICP. It varies from −1 to +1; a negative zone expresses preserved autoregulation while a positive one signifies its violation.

The treatment of ICH is based on internationally accepted guidelines [5] and their local adaptations. A local Russian edition of guidelines for the treatment of ICH in children was developed in 2015 at the Clinical and Research Institute for Emergency Pediatric Surgery and Trauma (CRIEPST), Moscow, and is known as "Step therapy for the treatment of intracranial hypertension in children" [6]. This clinical protocol is an algorithmic diagram sequence of steps to normalize ICP and maintain safe levels of cerebral perfusion pressure (CPP), and is specially adapted to the intensive care of children with STBI.

Clinical guidelines provide valuable knowledge that can be implemented in clinical decision support (CDS) systems. One of the instruments for building CDS is Arden Syntax, which is a medical knowledge representation and processing standard for CDS systems, defined and supported by Health Level Seven International [7]. It defines the way clinical and scientific knowledge can be represented, computerized, and processed. Arden Syntax was first approved as a standard by the American Society for Testing and Materials in 1992 [8]. Several extensions followed. The current version (v2.10) was released in November 2014 [9].

The goal of this work was to develop a combined computer system for simultaneous online monitoring of cerebral autoregulation and an online CDS (ICPCDS: intracranial pressure clinical decision support) system based on Arden Syntax as a computerized digital version of "Step therapy for the treatment of ICH in children" guideline.

2. Material and Methods

2.1 General information landscape

The children's ICU at CRIEPST is equipped with a monitoring system known as Philips IntelliVue [10]. Bedside monitors have hardware interface modules for integrating on-line data from devices of other vendors (ventilators, ICP monitors, and others) into a single information stream. All bedside monitors along with the Philips Information Center are physically organized as a dedicated Philips Virtual Local Area Network (VLAN). Over the HL7 bridge, the data from all ICU bedside monitors are redirected to the hospital network, then parsed and saved into an ICU monitoring database (MDB). The MDB is also synchronized with the hospital information system (HIS) via HL7

protocols. This mechanism provides end-to-end patient identification across all information sources.

2.2 ICPCDS system architecture

The architecture of the ICPCDS system is shown in Figure 1. It was developed using the public Java Eclipse Oxygen Environment [11] and the ArdenSuite software, which is a commercial CDS authoring and processing platform based on Arden Syntax developed by Medexter Healthcare, Vienna, Austria [12]. It consists of four main blocks:

- Sources: patient's data, monitoring data, knowledge and simulation
- Development: Eclipse Oxygen and ArdenSuite Integrated Development Environment (IDE)
- Processing: Server modules for Java and Arden Syntax executable programs on the ArdenSuite Server. There is also a local database for controlling users and their rights and properties.
- Interface: Web graphical user interface (GUI) and messenger services (SMS, WhatsApp, and others) for sending alarm and notification messages.

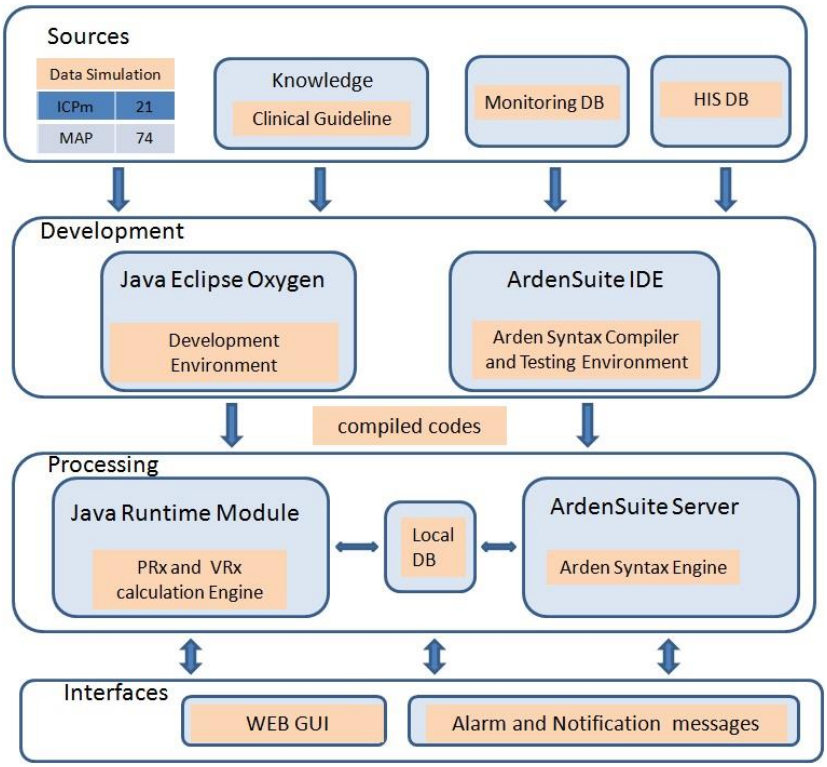

Figure 1. Architecture of the ICPCDS system.

2.3 Calculation of cerebral autoregulation indices

Two calculated indices for monitoring cerebral autoregulation were used: a) Classical Cambridge PRx, as already described, and b) the variation reactivity index (VRx) developed at CRIEPST. VRx is defined as Pearson's correlation between variations of mean ICP and MAP in contrast to their average values. A 40-point moving window of MAP and a mean ICP with five seconds of sampling and a five-second shift were used for calculating PRx and VRx.

The visualization method of PRx and VRx trends (now in the patenting stage) is based on averaging algorithms, which provide pseudo real time display mode and suppress noise factors. Along with cerebral autoregulation indices, several additional parameters were calculated: average ICP and MAP for the last five and 30 minutes. These parameters were calculated in moving window with a five-second shift and used as input trigger signals to activate the corresponding chains of step therapy for ICH.

2.4 Clinical protocol of ICH therapy

Clinical guidelines (step protocol) for the treatment of ICH in children with STBI consist of seven clinical actions (steps) aimed at reducing ICP and maintaining safe levels of intracranial perfusion pressure. These clinical steps are:

1. body position control
2. sedation
3. drainage of cerebral fluids
4. introduction of osmodiuretics
5. controlled hyperventilation
6. barbiturate coma
7. decompressive craniotomy.

The steps are usually performed sequentially, but some may be repeated or skipped. An example of the step diagram is shown in Figure 2.

2.5 Clinical study

The clinical study included two groups of patients. The protocol group consisted of patients who had been treated since 2017 with the step therapy protocol using the developed ICPCDS system (84 patients). The reference group was collected retrospectively (37 patients) and consisted of patients who had undergone conventional ICH therapy. The groups did not differ statistically in terms of the severity of trauma and clinical stage, age, gender and duration of stay at the ICU. A 6-month Glasgow Outcome Scale (GOS) was available for each patient [13,14]. Based on the GOS, the outcomes were divided into three groups: Moderate disability or good recovery was noted in 63 patients (75.00%) in the protocol group and 18 patients (48.65%) in the reference group. Severe disability or a vegetative state was noted in 14 (16.67%) and 7 (18.92%), respectively; and fatal outcomes (death) were observed in 7 (8.33%) and 12 (32.43%), respectively. Statistical analysis was performed using the STATISTICA 8 package [15].

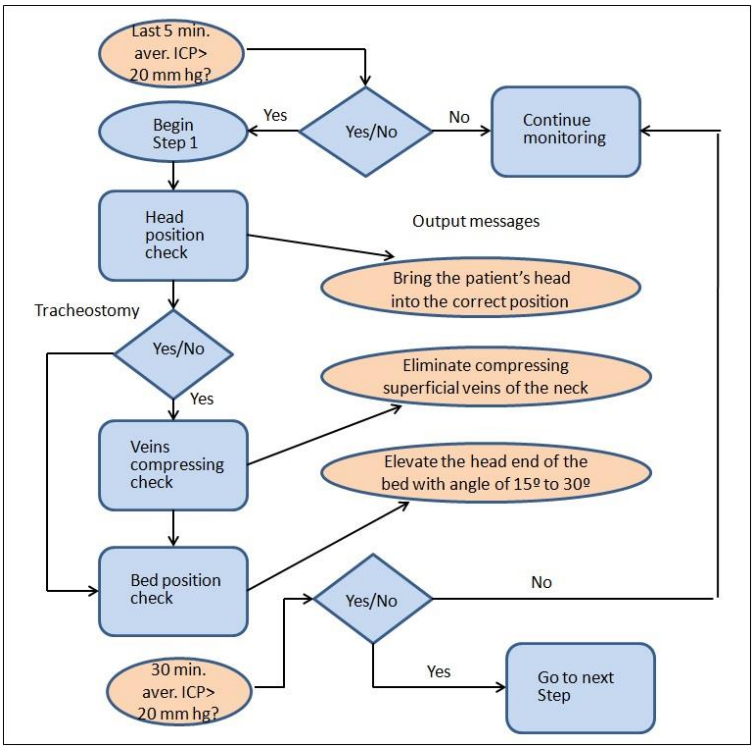

Figure 2. An example of the step protocol diagram.

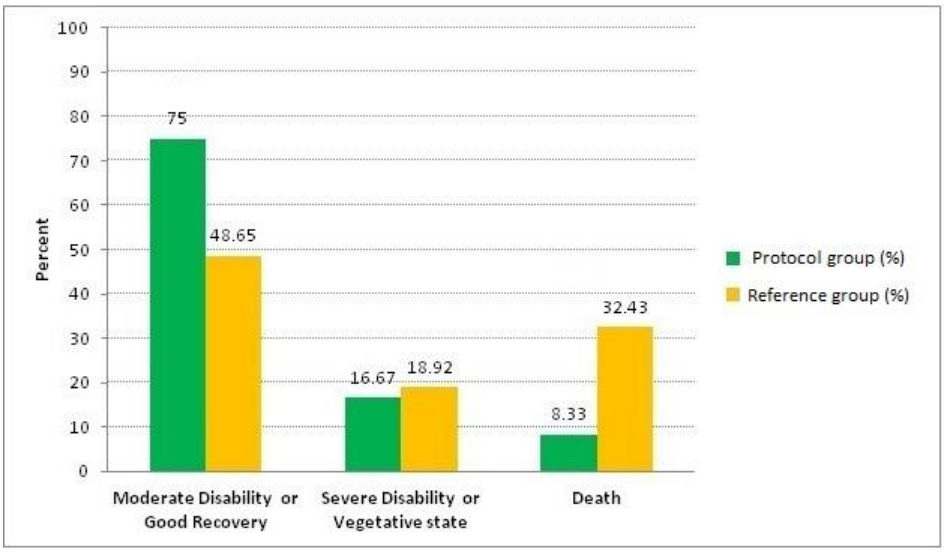

Figure 3. Comparison of outcomes for protocol (with ICPCDS) and reference groups.
Pearson's Chi-square =12.24, df=2, p=0.0022, p<0.05

3. Results

Statistical analysis of combined frequencies revealed significant difference between groups in respect of GOS (Figure 3). A significant decrease (24.1%) in deaths was noted in the ICPCDS group of patients, and an increase was registered in the number of favorable outcomes (26.35%) compared to the reference group.

The graphical user interface of the ICPCDS system (Figure 4) is based on Web access and is platform independent. The information is updated every five seconds, which is practically a “live” display of the clinical picture of cerebral monitoring and brain autoregulation. The output messages from the CDS system express an alarm situation or carry some notification. The notification messages require confirmation by the clinical user. All events and actions are stored in the system’s local database along with cerebral monitoring and autoregulation data.

Figure 4. ICPCDS system’s Web interface. 1 – Digital table of monitoring parameters. 2 – Autoregulation indices PRx and VRx presented as “living” circular diagrams updated every five seconds; the green sector expresses good cerebral autoregulation, the red sector marks the zone of lost autoregulation, the yellow sector is the zone of uncertainty. 3 – Linear graphical trends of circular diagram sectors. 4 – Synchronized trends of ICP CPP charts. 5 – Window for displaying messages from the step protocol of the Arden Syntax CDS system.

4. Discussion

It is impossible to isolate the effect of the electronic ICH treatment protocol on clinical results. However, the combination of cerebral autoregulation monitoring with an Arden-Syntax-based CDS system whose clinical knowledge is based on the step protocol of treatment of ICH in children with STBI provides doctors with a convenient and reliable tool for choosing clinical actions and measuring their effectiveness. The use of Arden Syntax creates a unified platform for building compatible systems to support clinical decisions and is expected to accelerate the process of their certification.

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References

[1] M. Peden, R. Scurfield, D. Sleet, D. Mohan, A.A. Hyder, E. Jarawan, C. Mathers (Eds), *World Report on Road Traffic Injury Prevention*, World Health Organization, Geneva, 2004.

[2] M. Balestreri, M. Czosnyka, P. Hutchinson, L.A. Steiner, M. Hiler, P. Smielewski, J.D. Pickard, Impact of intracranial pressure and cerebral perfusion pressure on severe disability and mortality after head injury, *Neurocritical Care* **4**(1) (2006), 8–13.

[3] O.B. Paulson, S. Strandgaard, L. Edvinsson, Cerebral autoregulation, *Cerebrovascular and Brain Metabolism Reviews* **2**(2) (1990), 161–192.

[4] M. Czosnyka, Z. Czosnyka, P. Smielewski, Pressure reactivity index: journey through the past 20 years, *Acta Neurochirurgica* **159**(11) (2017), 2063–2065.

[5] P.M. Kochanek, N. Carney, P.D. Adelson, S. Ashwal, M.J: Bell, S. Bratton, S. Carson, R.M. Chesnut, J. Ghajar, B. Goldstein, G.A. Grant, N. Kissoon, K. Peterson, N.R. Selden, R.C.Tasker, K.A. Tong, M.S. Vavilala, M.S. Wainwright, C.R. Warden. Guidelines for the acute medical management of severe traumatic brain injury in infants, children and adolescents – second edition, *Pediatric Critical Care Medicine* **13**(Suppl 1) (2012), S1–S82.

[6] I.Kolykhalkina, T. Chernishova, V. Amcheslavsky, O. Karaseva, T. Ivanova, V. Bagaev,Y. Berezhnoy, S. Arseniev, E. Grigorenko.I., Prevention and treatment of intracranial hypertension in children with severe traumatic brain injury, *Neotlozhnaya medicina 1. Meditzinsky alfavit* **5**(221) (2014), 16–21.

[7] M. Samwald, K. Fehre, J. de Bruin, K.-P. Adlassnig, The Arden Syntax standard for clinical decision support: Experiences and directions, *Journal of Biomedical Informatics* **45**(4) (2012), 711–718.

[8] Health Level Seven International, Health Level Seven International – Homepage, http://www.hl7.org/index.cfm, last access: 27.1.2020.

[9] Health Level Seven International, *Health Level Seven Arden Syntax for Medical Logic Systems, Version 2.10, November 2014*, Health Level Seven International, Ann Arbor, 2014. Available at: http://www.hl7.org/implement/standards/product_brief.cfm?product_id=372.

[10] Philips Healthcare, Critical Care, www.philips.ru/healthcare/medical-specialties/critical-care, last access: 27.1.2020.

[11] Eclipse Foundation, Oxygen, https://www.eclipse.org/oxygen/, last access: 27.1.2020.

[12] Medexter Healthcare GmbH, ArdenSuite CDS Platform, https://www.medexter.com/products-and-services/ardensuite, last access: 27.1.2020.

[13] B. Jennett, M. Bond, Assessment of outcome after severe brain damage. *Lancet* **1**(7905) (1975), 480–484.

[14] S.R. Beers, S.R. Wisniewski, P. Darcia-Filion, Y. Tian, T. Hahner, R.P. Berger, M.J. Bell, P.D. Adelson, Validity of a pediatric version of the Glasgow Outcome Scale–Extended. *Journal of Neurotrauma* **29**(6) (2012), 1126–1139.

[15] TIBCO Software Inc., STATISTICA Product Features, http://www.statsoft.com/Products/STATISTICA-Features, last access: 27.1.2020.