



Research paper

Early neurological wake-up test in intubated brain-injured patients: A long-term, single-centre experience



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ABSTRACT

Background: In prehospital setting, a severe traumatic brain injury (TBI) requires tracheal intubation, sedation and mechanical ventilation pending the initial imagery. An early neurological wake-up test (ENWT), soon after the initial imaging assessment, allows a rapid neurological reassessment. This strategy authorises an initial clinical examination of reference with which will be compared the later examinations. The main objective of this study was to describe the characteristics of the patients who underwent an ENWT, and to determine its causes of failure.

Methods: We conducted a retrospective, observational, single-centre study including all intubated TBI admitted in the trauma centre. An ENWT was defined as cessation of sedation within 24 h after TBI. Data concerning patient characteristics, CT-scan results, and outcomes were extracted from a prospective register of all intubated TBI admitted in the ICU. Characteristic of ENWT and causes of failure were retrieved from patient files. A multivariate logistic regression model was developed to determine the risk factors of ENWT failure.

Results: During 7 years, 242 patients with intubated TBI were included. An ENWT was started in 96 patients, for an overall rate at 40%. The ENWT was stopped in 38 patients (39.5%), mostly due to neurological deterioration in 27 cases (71%) or respiratory distress in 10 cases (26%). Significant predictors of ENWT failure were: the presence of subdural hematoma with a thickness >5 mm on first imagery (OR = 3.2; 95%CI [1.01–10.28]), and an initial GCS score <5 (OR = 7.4; 95%CI [1.92–28.43]). Prevalence of poor outcome at 1 year was lesser in patients with successful ENWT compared to those with failure or absence of ENWT: 4% vs. 48% and 49% ($p < 0.0001$).

Conclusions: The ENWT is achieved in 40% of patients, with a success rate of 60.5%. In presence of a subdural hematoma with a thickness >5 mm or an initial GCS score <5, an ENWT failure may be expected.

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1. Introduction

Traumatic brain injury (TBI) presents a major public health challenge worldwide, affecting predominately young people.¹ In

developed country, TBI is a leading cause for premature death and disability with a huge socioeconomic impact.^{1,2} The annual incidence of TBI is estimated at 500/100 000 in the United States and Europe.^{1,3} Severe TBI is defined by a Glasgow Coma Scale (GCS) ≤ 8 after initial resuscitation.⁴ In prehospital setting, it requires tracheal intubation, sedation and mechanical ventilation pending the initial imagery, which will specify the primary lesions.¹ Meanwhile, sedation allows a decrease of the intracranial pressure as well as the cerebral metabolic rate of oxygen consumption, limiting the risk of secondary ischemic lesions.⁵ An early neurological wake-up test

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(ENWT), soon after the initial imaging assessment, allows a rapid neurological reassessment, after the stabilization or the analgesia of a painful associated injury. This strategy authorises an initial clinical examination of reference with which will be compared the later examinations. Indeed, clinical examination still remains the gold standard for monitoring brain-injured patients.⁶ Neither the brain imaging nor the paraclinical monitoring can replace this clinical evaluation.⁷ Furthermore, if the patient wakes up correctly, it limits the aggressiveness of the resuscitation (duration of mechanical ventilation, invasive monitoring, . . .). However, to our knowledge, the literature on this topic is very limited.

The main objective of this study was to describe the characteristics of the patients who underwent an early neurological wake-up test, and to determine its causes of failure.

2. Patient and methods

2.1. Study design and patients selection

We conducted a 7-year retrospective, observational, single-centre study at the Sainte Anne Military Hospital of Toulon (France). Between January 2007 and December 2013, all intubated traumatic-brain injured patients admitted to the intensive care unit (ICU) were eligible. Inclusion criteria were as follows: patients with age over 18, severe TBI defined as a GCS ≤ 8 , and mild/or moderate TBI (GCS 9–15) with significant abnormalities at initial CT scan (Marshall scores ≥ 2).⁸

Before ENWT, all patients were sedated, intubated and mechanically ventilated in accordance with the international guidelines and with the following objectives: head elevation (30°), PaO₂ > 85 mmHg, PaCO₂ between 35 mmHg and 45 mmHg, natremia between 140 mEq/L and 145 mEq/L, targeted temperature < 37.5 °C, intracranial pressure (ICP) < 20 mmHg in case of invasive monitoring, and cerebral perfusion pressure (CPP) > 60 mmHg. If ICP increased, the protocol included moderate hypocapnia (PaCO₂ between 30 mmHg and 35 mmHg), increase of sedation with propofol, muscle paralysis with cisatracurium and moderate hypothermia (34–35 °C). Third line therapy included barbiturates infusion and/or unilateral craniectomy.^{9–14} An intraparenchymal ICP sensor was inserted into the frontal lobe at the discretion of the physician in charge.

The institutional review board approved the study and waived the requirement for informed consent from the patients or patient's kin given the retrospective nature of the study.

2.2. Early neurological wake-up test (ENWT)

An ENWT was defined as cessation of sedation within 24 h after TBI. The initiation of an ENWT test was at the discretion of the physician in charge, while respecting the benefit–risk ratio. The institutional protocol allows an ENWT in the following cases: hemodynamic and respiratory stability with a Marshall score ≤ 2 , or GCS minimal before sedation and intubation ≥ 8 , or isolated epidural hematoma surgically evacuated. An initial Transcranial Doppler (TCD) had to be normal before the test. An intraparenchymal ICP sensor was inserted into the frontal lobe before the ENWT at the discretion of the physician in charge. During the test, GCS score and pupillary analysis were checked hourly. TCD for monitoring of ICP was used regularly in patients without invasive sensor.¹⁵ The failure criteria for the ENWT were the following ones: absence of improvement or degradation of the GCS score, occurrence of pupillary abnormality, ICP > 20 mmHg during more than 5 min or abnormal TCD, and/or respiratory distress. In case of failure of the wake-up test, the sedation was reintroduced for at least 48 h, and an invasive monitoring of ICP was established.⁵ An ENWT success

was defined as an improvement of the clinical examination without signs of intracranial hypertension allowing a complete withdrawal of sedation.

2.3. Data collected and definition

Data concerning patient characteristics, mechanisms of injury, results of imagery and Marshall classification, in-hospital mortality and outcome with Glasgow Outcome Scale (GOS) at 6 months and 1 year were extracted from a prospective register of all intubated TBI admitted in the ICU. Characteristics of the ENWT and causes of failure were retrieved from patient files.

The GOS score is a five-point scale: death, persistent vegetative state, severe disability, moderate disability, and good recovery.

A poor outcome at 6 months or 1 year was defined as a GOS score between 1 and 3. A good outcome at 6 months and 1 year was defined as a GOS score at 4 or 5.

2.4. Endpoints

The primary endpoint of this study was to describe the characteristic of the patients having an ENWT. Secondary endpoints were to determine the rate, causes, and the risk factors of test failure.

2.5. Statistical analysis

Statistical analysis was performed with XLSTAT version 2015.3.01 (Addinsoft, Paris, France). Continuous data were reported as the mean \pm standard deviation or median with interquartile ranges [25–75th] when not normally distributed. Nominal variables are reported as numbers and proportions (%).

A univariate analysis was conducted using the Chi-square test or Fisher's exact test to compare categorical variables and the Mann–Whitney test or Student's *t*-test to compare groups for continuous variables (respectively for comparison of medians and comparison of means). Independent factors associated with wake-up test failure were identified using a logistic regression model. All parameters with *p* value < 0.1 on univariate analysis and clinically relevant were included in the multivariate regression model. The Hosmer–Lemeshow goodness-of-fit test and the area under the receiver operating characteristic (ROC) curve were used to evaluate the overall fit of the final model. The final model expressed the odds ratio (OR) and 95% confidence intervals (CI). For all tests, *p* < 0.05 was considered statistically significant.

3. Results

3.1. Study population

During the 7-year study period, 242 intubated patients with TBI were admitted to our ICU. There were 232 severe TBI (96%) and 10 mild or moderate TBI (4%). The most common mechanism of injury was motorcycle crash (29%) (Fig. 1). Four patients had penetrating trauma (2%) and 238 suffered from blunt trauma (98%). Isolated TBI concerned 81 patients (33%). The median age of the population was 38 [23–56] years, the median ISS score was 22 [16–34], and the median initial GCS score was 7 [4–9]. The sex ratio was 3.7M/1F.

3.2. Early neurological wake-up test

An ENWT was started in 96 patients, for an overall rate at 40%. Comparisons of patients with and without ENWT are displayed in Table 1. Notably, patients with ENWT were less severely injured with a SAPS 2 score at 38 [28–46] vs. 46 [35–59] (*p* < 0.0001) and an ISS score at 16 [9–24] vs. 26 [16–38] (*p* < 0.0001). The velocity of crash was also different with less high-speed crash in the

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