

Efficacy of sedative drugs on intracranial pressure in traumatic brain injury patients: a CENTER-TBI study

Marco Carbonara¹, Benjamin Gravesteijn², Tatiana Birg¹, Fabrizio Ortolano¹, Tommaso Zoerle¹, Giuseppe Citerio³, Raimund Helbok⁴, Arturo Chiaregato⁵, Nino Stocchetti¹, Hester Lingsma²

¹ Neurointensive Care, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy

² Center for medical decision sciences, department of public health, Erasmus University Medical Center, Rotterdam, Netherlands

³ School of medicine and surgery, University of Milano-Bicocca, Monza, Italy

⁴ Department of neurology, University of Innsbruck, Innsbruck, Austria

⁵ Neurointensive care, ASST Great Metropolitan Niguarda, Milano, Italy

Introduction: Sedation is a first-line therapy used in intensive care unit (ICU) to control raised intracranial pressure in severe traumatic brain injury (TBI) patients. However, it remains unclear what the effect of different sedative drugs is on intracranial pressure (ICP) and therapeutic intensity level. This analysis of the CENTER-TBI study uses comparative effectiveness research to fill this knowledge gap. Methods: The CENTER-TBI study (clinicaltrials.gov registration NCT02210221) is a prospective observational longitudinal cohort study including patients with TBI from 65 centers across Europe. Data were extracted from the CENTER-TBI database v1.1 with Neurobot v2.6. We included all patient who were admitted to the ICU with ICP monitoring and who had more than one day of mechanical ventilation. For every patient, the primary sedative (the sedative that the patient received most of the days) was selected. We focused on midazolam and propofol, since these were the most frequently used. Results: 4509 patients were included in the CENTER-TBI study: we selected 611 patients who received propofol, and 451 patients who received midazolam. There was large variation between centers in choice of sedative drugs and length of sedation. Number of ICP observations above 20 mmHg were not different between two groups but area under curve of ICP above 20 mmHg were larger for midazolam, without any difference for cerebral perfusion pressure. The OR of "propofol" patients to receive extreme ICP treatment (decompression, barbiturates, hypothermia) was 0.60 (95% CI: 0.42 - 0.87) before adjustment, and 0.67 (95% CI: 0.46 - 0.99) after adjustment compared to "midazolam" patients. Conclusion: There is sedation policy large variation among European neurotrauma centers. ICP values are similar in patients sedated with propofol or midazolam, but use of propofol is associated with less extreme ICP treatments.