Impact of Secondary Insults in Brain Death After Traumatic Brain Injury

Deniz Heppekcan*, Serpil Ekin, Melek Çivi, and Demet Aydın Tok

Anesthesiology and Reanimation Department, Intensive Care Unit, Manisa Celal Bayar University Hafsa Sultan Hospital, Manisa, Turkey

ABSTRACT

In addition to primary injury in severe head trauma, secondary systemic insults that aggravate the brain injury may result in fatal neurologic outcome. We aim to evaluate the correlation between brain death and secondary systemic insults in 100 patients with severe traumatic brain injury (TBI) admitted to the intensive care unit. We collected data on hypotension and hypoxemia at the time of admission to intensive care unit and data on hypotension, hypoxemia, hypocarbia, hypercarbia, shock, anemia, hyperglycemia, and hyperthermia within the first 24 hours. In addition, we recorded the category of TBI according to computed tomography findings. Twenty-six patients (26%) who developed brain death were significantly younger than survivors. Early hypotension (odds ratio [OR], 10.24; 95% confidence interval [CI], 3.64–28.78; $P = .000$) and early shock (OR, 8.31; 95% CI, 2.65–26.01; $P = .000$) were significantly more frequent among brain-death patients. The most featured factor that independently predicted the development of brain death in patients with severe TBI was the existence of hypotension (B–2.74; 95% CI, 0.016–0.252; $P = .000$). The most common type of injury among brain death patients was a surgically evacuated mass lesion. Although all critical care principles are applied to prevent secondary systemic brain insults, when brain death occurs, the prevention of hypotension will become significant in preserving organs in better condition for procurement.

SIXTY-NINE million (95% confidence interval [CI], 64–74 million) people worldwide are estimated to sustain a traumatic brain injury (TBI) each year [1]. One of the most common causes of death in both industrialized and developing countries is TBI caused by motor vehicle accidents and falling from a height. Severe TBI treatment begins in the emergency room with resuscitation and continues with rapid diagnosis of the surgical mass lesion. Primary brain injury is the immediate physical damage acquired at the time of the injury to the brain during head trauma. Secondary injury consists of systemic brain insults such as hypoxemia, hypotension, hypo-/hypercapnia, hypo-/hyperthermia, hypo-/hyperglycemia, anemia, electrolyte imbalance, and acid-base abnormalities [2,3].

Therefore, with prevention of secondary systemic brain insults in the intensive care unit (ICU), the morbidity and mortality rate are significantly reduced. The aim of this study is to evaluate the correlation between brain death as a fatal neurologic outcome and secondary brain insults during or after admission to the ICU.

METHODS

This retrospective observational study was performed in Manisa Celal Bayar University Hafsa Sultan Hospital Anesthesiology Intensive Care Unit from January 2015 to July 2018. All patients with severe TBI were included. A series of clinical and tomography findings were collected, and data and outcomes were monitored. Patients over 15 years of age with at least 48 hours of ICU stay were eligible for inclusion in the study. Severe TBI was evaluated when the Glasgow Coma Scale score was 8 or less on admission [4]. Patients who died of a cause other than brain death were excluded. All brain death diagnoses were determined by using clinical examination and the additional confirmatory test, in which cerebral circulatory arrest is demonstrated by cerebral computed tomography angiography. Management of TBI was planned according to the

*Address correspondence to Deniz Heppekcan, Manisa Celal Bayar University Hafsa Sultan Hospital, Uncubozkoy Mahallesi, 45030, Yunusemre, Manisa. Turkey, Tel.: +905300681817; Fax: +902362321693. E-mail: denizheppekcan@yahoo.com.tr

0041-1345/19
https://doi.org/10.1016/j.transproceed.2019.01.176

© 2019 Elsevier Inc. All rights reserved.
230 Park Avenue, New York, NY 10169

recommendations of the brain trauma foundation [5,6] to prevent intracranial pressure increase.

Along with age and sex, the following systemic results were collected as the secondary systemic brain insults: admission hypotension (systolic blood pressure <90 mm Hg); admission hypoxemia (O_2 saturation measured by pulse oximeter <90%); and, within the first 24 hours after ICU admission, hypoxemia (PaO_2/FiO_2 ratio <250 mm Hg), hypotension (arterial systolic blood pressure <90 mm Hg), shock (arterial systolic blood pressure <90 mm Hg requiring resuscitation with volume replacement and/or vasoactive drugs), anemia (a hemoglobin level <10 g/dL), hyperglycemia (serum glucose value >180 mg/dL), hypothermia (body temperature <36°C), and hyperthermia (body temperature >38°C). Statistical analyses were performed using the χ^2 test to analyze percentages and the Student *t* test for continuous variables. A stepwise multiple logistic regression analysis was performed to identify the significant independent variables associated with brain death.

RESULTS

We investigated 245 patients who had experienced head trauma and considered 100 patients (40.8%) with severe TBI. The mean age of the TBI patients was 32.27 ± 13.84, and the mean Glasgow Coma Scale score was 4.20 ± 1.43. The 26 patients (26%) who developed brain death were significantly younger than survivors (age 27.34 ± 11.34 vs 34.00 ± 14.28 years, $P < .05$). Seven of 26 patients who developed brain death became donors. Admission hypotension and hypotension, shock, and hyperglycemia within the first 24 hours were significantly associated with brain death (Table 1). After a risk estimate analysis, hypotension within the first 24 hours (odds ratio [OR], 10.24; 95% confidence interval [CI], 3.64–28.78; $P = .000$) and shock within the first 24 hours (OR, 8.31; 95% CI, 2.65–26.01; $P = .000$) were significantly more frequent among the brain-death patients. With multivariate analysis, we were able to demonstrate that the factor that independently predicted the development of brain death in severe TBI patients was the existence of hypotension within the first 24 hours (B −2,74; 95% CI, 0.016- 0.252; $P = .000$). We described types of TBI patients according to the classification based on computed axial tomography [7]. The most common type of injury among the brain-death patients was surgically evacuated mass lesion (type V[7]).

Table 1. Comparison of the Main Features of Patients and Secondary Systemic Insults According to the Development of Brain Death

Variable	Brain Death (n = 26)	No Brain Death (n = 74)	*P*
Age (y)	27.34 ± 11.34	34.00 ± 14.28	< .05
Sex (male)	84.6%	90.5%	.406
GCS	3.76 ±1.39	4.35 ± 1.42	.380
Admission hypotension	46.2%	16.2%	< .05
Admission hypoxemia	30.8%	16.2%	.111
Hypotension	61.5%	13.5%	< .0001
Hypoxemia	19.2%	39.2%	.065
Hypocarbia	65.4%	44.6%	.068
Hypercarbia	42.3%	35.1%	.515
Shock	42.3%	8.1%	< .0001
Anemia	46.2%	33.8%	.261
Hyperglycemia	73.1%	41.9%	< .05
Hyperthermia	30.8%	14.9%	.075
Classification of TBI according to CT[7]			< .0001
I	0	6.8%	
II	11.5%	47.3%	
III	23.1%	21.6%	
IV	15.4%	0	
V	30.8%	24.3%	
VI	19.2%	0	

Abbreviations: CT, computed tomography; GCS, Glasgow Coma Scale; TBI, traumatic brain injury

DISCUSSION

In our study, we found that hypotension within the first 24 hours was the most important independent predictor of brain death in severe TBI. Maintaining adequate cerebral blood flow is important to prevent secondary brain injury and fatal outcome. Therefore, prevention of hypotension contributes to the continuation of cerebral blood flow and prevents exacerbation of existing injury. Control of hypotension requires immediate correction with adequate monitoring.

There has been a shift from trauma donors to donors with cardiovascular/cerebrovascular disease in developed countries over the past 10 years [8], and the donor population has become older over the years [9]. However, in developing or underdeveloped countries, trauma donors are still the majority of donors, and trauma donors are younger than others. Our trauma donor cases were younger, and comorbidities were fewer. Many studies have shown that there is an important relationship between donor age and graft outcome; older donor age is associated with worse outcomes for all organs studied [10,11].

As we have shown in our study, in the treatment of TBI, prevention of hypotension should be the most important strategy to reduce secondary brain injury and protect against a fatal outcome. If brain death occurs, the prevention of hypotension will become important for donor management to preserve organs in a better condition for deceased donor organ procurement.

REFERENCES

[1] Dewan MC, Rattani A, Gupta S, Baticulon RE, Hung YC, Punchak M, et al. Estimating the global incidence of traumatic brain injury [e-pub ahead of print]. J Neurosurg 2018 Apr 1:1–18. https://doi.org/10.3171/2017.10.JNS17352.

[2] Chesnut RM. Secondary brain insults after head injury: clinical perspectives. New Horiz 1995;3:366–75.

[3] Jeremitsky E, Omert L, Dunham CM, Protetch J, Rodriguez A. Harbingers of poor outcome the day after severe brain injury: hypothermia, hypoxia, and hypoperfusion. J Trauma 2003;54:312–9.

[4] Teasdale G, Jennett B. Assessment of coma and impaired consciousness: a practical scale. Lancet 1974;2:81–4.

[5] Bullock R. Guidelines for the management of severe traumatic brain injury. J Neurotrauma 2007;24(suppl 1).

[6] Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GWJ, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery 2017;80:6–15.

[7] Marshall LF, Marshall SB, Klauber MR, Van Berkum Clark M, Eisenberg H, Jane JA, et al. The diagnosis of head injury requires a classification based on computed axial tomography. J Neurotrauma 1992;9(suppl 1):S287–92.

[8] Saidi RF, HejazIi Kenari SK. Challenges of organ shortage for transplantation: solutions and opportunities. Int J Organ Transplant Med 2014;5:87–96.

[9] Johnson RJ, Bradbury LL, Martin K, Neuberger J. UK transplant registry organ donation and transplantation in the UK the last decade: a report from the UK national transplant registry. Transplantation 2014;97(suppl 1):S1–27.

[10] Wong G, Teixeira-Pinto A, Chapman JR, Craig JC, Pleass H, McDonald S, et al. the impact of total ischemic time, donor age and the pathway of donor death on graft outcomes after deceased donor kidney transplantation. Transplantation 2017;101: 1152–8.

[11] Dayoub JC, Cortese F, Anžič A, Grum T, de Magalhães JP. The effects of donor age on organ transplants: a review and implications for aging research. Exp Gerontol 2018;110:230–40.