The Effect of Combined Out-of-Hospital Hypotension and Hypoxia on Mortality in Major Traumatic Brain Injury

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Study objective: Survival is significantly reduced by either hypotension or hypoxia during the out-of-hospital management of major traumatic brain injury. However, only a handful of small studies have investigated the influence of the combination of both hypotension and hypoxia occurring together. In patients with major traumatic brain injury, we evaluate the associations between mortality and out-of-hospital hypotension and hypoxia separately and in combination.

Methods: All moderate or severe traumatic brain injury cases in the preimplementation cohort of the Excellence in Prehospital Injury Care study (a statewide, before/after, controlled study of the effect of implementing the out-of-hospital traumatic brain injury treatment guidelines) from January 1, 2007, to March 31, 2014, were evaluated (exclusions: <10 years, out-of-hospital oxygen saturation ≤10%, and out-of-hospital systolic blood pressure <40 or >200 mm Hg). The relationship between mortality and hypotension (systolic blood pressure <90 mm Hg) or hypoxia (saturation <90%) was assessed with multivariable logistic regression, controlling for Injury Severity Score, head region severity, injury type (blunt versus penetrating), age, sex, race, ethnicity, payer, interhospital transfer, and trauma center.

Results: Among the 13,151 patients who met inclusion criteria (median age 45 years; 68.6% men), 11,545 (87.8%) had neither hypotension nor hypoxia, 604 (4.6%) had hypotension only, 790 (6.0%) had hypoxia only, and 212 (1.6%) had both hypotension and hypoxia. Mortality for the 4 study cohorts was 5.6%, 20.7%, 28.1%, and 43.9%, respectively. The crude and adjusted odds ratios for death within the cohorts, using the patients with neither hypotension nor hypoxia as the reference, were 4.4 and 2.5, 6.6 and 3.0, and 13.2 and 6.1, respectively. Evaluation for an interaction between hypotension and hypoxia revealed that the effects were additive on the log odds of death.

Conclusion: In this statewide analysis of major traumatic brain injury, combined out-of-hospital hypotension and hypoxia were associated with significantly increased mortality. This effect on survival persisted even after controlling for multiple potential confounders. In fact, the adjusted odds of death for patients with both hypotension and hypoxia were more than 2 times greater than for those with either hypotension or hypoxia alone. These findings seem supportive of the emphasis on aggressive prevention and treatment of hypotension and hypoxia reflected in the current emergency medical services traumatic brain injury treatment guidelines but clearly reveal the need for further study to determine their influence on outcome. [Ann Emerg Med. 2017;69:62-72.]

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INTRODUCTION

Background and Importance

Traumatic brain injury is a massive public health problem, leading to more than 50,000 deaths and enormous health care expenditures each year in the United States.[1,2] The Centers for Disease Control and Prevention (CDC) estimates that at least 5.3 million Americans, approximately 2% of the US population, are living with a major, permanent, traumatic brain injury–related disability.[2,3]

During the out-of-hospital care of patients with traumatic brain injury, hypoxia occurs frequently[4-9] and significantly increases mortality.[6,7,10-16] It is independently associated with a higher risk of death even if the hypoxemic episode is reflected by only a single measurement of low

Editor's Capsule Summary

What is already known on this topic

Both hypotension and hypoxia are independently associated with higher mortality among out-of-hospital patients with traumatic brain injury.

What question this study addressed

For out-of-hospital patients with traumatic brain injury, what is the effect on survival of the combination of hypotension and hypoxia compared with either factor alone?

What this study adds to our knowledge

Among 13,151 out-of-hospital patients with traumatic brain injury during a 7-year period, only 1.6% experienced both hypotension and hypoxia. Mortality was 5.6% for patients with neither but 43.9% when the combination of hypotension and hypoxia occurred. The adjusted odds ratio for death was 6.1 (95% confidence interval [CI] 4.2 to 8.9) for the combination, 2.5 (95% CI 1.9 to 3.3) for hypotension alone, and 3.0 (95% CI 2.4 to 3.8) for hypoxia alone.

How this is relevant to clinical practice

Emphasis should be placed on avoiding hypotension and hypoxia in patients with traumatic brain injury, and additional attention should be paid to preventing their combination.

oxygen saturation.[10,12,17] Stocchetti found that the presence of out-of-hospital hypoxia more than tripled the likelihood of death among victims of severe traumatic brain injury.[6] Hypotension is also very common early in the care of traumatic brain injury[7,10,11,18] and significantly affects survival.[6,10,11,14,15,18-39] A single episode of hypotension doubles mortality, and this risk increases significantly with repeated episodes (an odds ratio [OR] of 8.1 for death in one study).[26]

Although the negative effect of hypotension and hypoxia has been well documented in the literature, little is known about their combination. Thus, it is unknown whether, together, they have no additional effect, an additive effect, or some intermediate influence on outcomes. Even though it is known that hypotension and hypoxia independently increase mortality, this is not the same as showing that the combination of the two is additive in its effect in patients who actually experience both. In fact, some authors have suggested that, because there are great similarities at the cellular level in the effect of hypoxia and hypotension (reduced oxygen delivery to the neuron), having both may add little to the risk of death because the physiologic insult may be similar with either or both.[16,22,26] With the exception of a meta-analysis that had major issues with study heterogeneity and missing data,[39] the reports that have examined the effect of hypotension combined with hypoxia in traumatic brain injury have included few cases.[6,16,22,26,28,35,40] Furthermore, even less is known about this problem in the out-of-hospital setting. To our knowledge, only 2 previous studies specifically evaluated the hypotension and hypoxia combination with out-of-hospital data.[6,16] A key reason for evaluating the effect of blood pressure and oxygenation measured before hospital arrival is because the injured brain is so highly sensitive to changes in perfusion and oxygenation and the timeframe during which neuronal damage begins is so short. It is well established that secondary brain injury is initiated by even brief periods of compromised blood flow or hypoxia.[20,22,23,28,35,40-43] Thus, decreased perfusion or hypoxia occurring during the out-of-hospital interval may have a profound effect on outcome.

Goals of This Investigation

The objective of this investigation was to evaluate the association between survival and out-of-hospital hypotension, hypoxia, or both in patients with major traumatic brain injury.[41]

In major traumatic brain injury, the combination of both out-of-hospital hypotension (systolic blood pressure <90 mm Hg) and hypoxia (oxygen saturation <90%) has additional negative influence on survival compared with either factor alone.

MATERIALS AND METHODS

The Excellence in Prehospital Injury Care (EPIC) study has been described in detail elsewhere.[41] It is funded by the National Institutes of Health, and, although not a randomized trial, it is registered at ClinicalTrials.gov (NCT01339702). Rather than reiterating the details of the parent study, here we limit the description to the design attributes relevant to this specific evaluation.

Setting

The EPIC study is evaluating the effect of implementing the out-of-hospital traumatic brain injury guidelines[42-45] in patients with moderate or severe ("major") traumatic brain injury throughout Arizona, using a before-after, controlled, multisystem, observational design. The patients in this evaluation are in the preimplementation cohort of EPIC (treated by an emergency medical services [EMS] agency between January 1, 2007, and March 31, 2014, without