ORIGINAL RESEARCH

Predictors of Agitated Behavior During Inpatient Rehabilitation for Traumatic Brain Injury

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Abstract

Objective: To identify predictors of the severity of agitated behavior during inpatient traumatic brain injury (TBI) rehabilitation.

Design: Prospective, longitudinal observational study.

Setting: Inpatient rehabilitation centers.

Participants: Consecutive patients enrolled between 2008 and 2011, admitted for inpatient rehabilitation after index TBI, who exhibited agitation during their stay (n=555, N=2130).

Interventions: Not applicable.

Main Outcome Measure: Daytime Agitated Behavior Scale scores.

Results: Infection and lower FIM cognitive scores predicted more severe agitation. The medication classes associated with more severe agitation included sodium channel antagonist anticonvulsants, second-generation antipsychotics, and gamma-aminobutyric acid-A anxiolytics/hypnotics. Medication classes associated with less severe agitation included antiasthmatics, statins, and norepinephrine-dopamine-5 hydroxytryptamine (serotonin) agonist stimulants.

Conclusions: Further support is provided for the importance of careful serial monitoring of both agitation and cognition to provide early indicators of possible beneficial or adverse effects of pharmacologic interventions used for any purpose and for giving careful consideration to the effects of any intervention on underlying cognition when attempting to control agitation. Cognitive functioning was found to predict agitation, medications that have been found in previous studies to enhance cognition were associated with less agitation, and medications that can potentially suppress cognition were associated with more agitation. There could be factors other than the interventions that account for these relations. In addition, the study provides support for treatment of underlying disorders as a possible first step in management of agitation. Although the results of this study cannot be used to draw causal inferences, the associations that were found can be used to generate hypotheses about the most viable interventions that should be tested in future controlled trials.

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Approximately one third of patients receiving inpatient rehabilitation for traumatic brain injury (TBI) in the United States exhibit agitation during the stay.[1,2] When present, agitation can be distressing for the patient, family, and staff, elevating the risk of injury to self and others and posing a significant barrier to participation in rehabilitation.[3-7] Unfortunately, few well-controlled interventional studies are currently available to guide the management of agitation.[8,9]

Despite the weak evidence base, pharmacologic interventions are being used to manage agitation both directly and indirectly.[10-12] Indirect pharmacologic treatments include stabilization and regulation of the sleep-wake cycle and treatment of underlying medical disorders (eg, pain, urinary tract infection, spasms). Direct pharmacologic treatments can reduce agitation via enhancement of cognition or by suppressing behavioral output. Although pharmacologic treatment may be effective in reducing agitation, it may also lead to unintended consequences (eg, decreased arousal, increased confusion, paradoxical increases in agitation).[10,11] Research on the relation between agitation and discharge outcomes has suggested that cognitive functioning mediates the relation between agitation and outcome, underscoring the importance of using interventions that do not suppress cognition.[1]

The current observational study was designed to expand our knowledge base regarding factors associated with the severity of agitation during acute rehabilitation by using a large dataset consisting of information on a wide range of premorbid/comorbid medical conditions, injury characteristics, and pharmacologic interventions. Identification of patient characteristics associated with more severe agitation may assist with determining if there are specific patient subgroups that should be targeted for monitoring and treatment or who may differentially respond to treatment. We also sought to identify treatment factors temporally associated with agitation for the purpose of generating hypotheses about potentially effective interventions, to be tested in future studies. Therefore, we predicted the next day's agitation scores from information available about the patient and his/her treatment during the preceding 24 hours. Predictors were chosen based on the limited literature[1,13-15] and the experiences of clinicians on the study team. The team specifically questioned whether the following would be associated with severity of agitation: (1) characteristics of the injury, including an overall measure of brain injury severity (Comprehensive Severity Index [CSI]) and neuroimaging findings; (2) increased number of comorbidities and the presence of select comorbidities that can contribute to increased discomfort or confusion; (3) selected premorbid conditions associated with problems in emotional and behavioral regulation and/or cognitive impairment; (4) sleep and cognition preceding the predicted agitated behavior; and (5) medication classes used on the day prior to the measure of agitated behavior that could potentially effect agitation through direct action on central nervous system (CNS) function or through the relief of discomfort.

A number of additional predictors were considered for inclusion in the study, but they were not included if there was not consensus on their inclusion or if there were too few patients (<35) who experienced the condition or received the medication class.

List of abbreviations:

ABS   Agitated Behavior Scale
CNS   central nervous system
CSI   Comprehensive Severity Index
TBI   traumatic brain injury

Methods

Data for this study were drawn from the Traumatic Brain Injury—Practice Based Evidence study, which included a prospective cohort of 2130 participants with an acute TBI diagnosis who were >14 years of age and admitted for their first inpatient rehabilitation stay to 1 of 10 participating hospitals (9 in the United States, 1 in Canada). The study was approved by the institutional review board at each site, and informed consent was obtained for all participants. The current substudy used a portion of the full study sample that met a prespecified criterion for agitation during their rehabilitation stay. The full study sample was not used because it was beyond the scope of the current study to predict whether patients exhibited any agitation because many patients only experience agitation before their admission to rehabilitation.

Agitation was monitored each nursing shift using the Agitated Behavior Scale (ABS). Because hospitals differed in the length of their shifts (8- or 12-h shifts), for the purposes of determining the presence of agitation, scores were converted to represent 4-hour increments. Agitation was defined as the presence of 24 hours (six 4-h increments) of ABS scores >21 within a 48-hour period at some point during the inpatient rehabilitation stay. Of the sample, 26% (n=557) met the criterion for agitated behavior. No patients from the Canadian site met the criterion for agitation (admission criteria used in Canada differ from those used in the United States, with the former admitting patients in later stages of recovery). Two of the 557 subjects were excluded because of incomplete data on independent variables.

Measures

Dependent variable

Agitation was measured using the ABS,[16] an observational rating scale developed to monitor agitation over time and with treatment. The scale consists of 14 items describing a range of behaviors rated from 1 to 4, with 1 being absent and 4 being extreme, based on the extent to which the behavior interferes with functional activities and can be redirected. A total score >21 indicates the presence of agitated behavior. The ABS has been shown to have strong interrater reliability, internal consistency, and construct validity.[16-19] Sites participating in this study collected the ABS score during each shift until no scores >21 were obtained for 3 consecutive days (completion of the ABS was reinitiated if agitation was subsequently displayed). For the purposes of the current study, in the event that additional ABS data were collected outside of the data collection rule (eg, after no scores >21 were obtained), the additional data were not used. The dependent variable for the current study consisted of daytime ABS scores.

Independent variables

As described elsewhere,[20] a TBI auxiliary data module was used to capture details from the medical record about the patient, the injury and comorbidities, and progress/changes in patient status throughout the rehabilitation stay.

Independent variable: time invariant patient and injury characteristics

Severity of the TBI was summarized with the CSI brain injury index (an index that takes into account variables associated with brain injury severity[20]), and the severity of comorbid conditions present at admission was summarized with the CSI nonbrain injury index