ORIGINAL RESEARCH PAPER

Volume-8 | Issue-5 | May-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ANTICOAGULATION IS ASSOCIATED WITH INCREASED MORBIDITY AND MORTALITY IN CONCUSSIVE INJURY AMONG ELDERLY TRAUMA PATIENTS

Surgery

Krishna Akella DO, Stonybrook Southampton Hospital, South Hampton, NY

Samer Ibrahim* DO, Stonybrook Southampton Hospital, South Hampton, NY *Corresponding Author

Brian Boden DO, Stonybrook Southampton Hospital, South Hampton, NY

Akella Chendrasekhar Richmond University Medical Center, Staten Island, NY. SUNY Downstate Medical Center, Brooklyn, NY.

ABSTRACT

To study the association between concussive injury in elderly patients on anticoagulation and development of non-bleeding complication.

A retrospective data analysis was performed comparing elderly trauma patients with concussion on antiplatelet therapy, anticoagulation or both. Data obtained included age, ISS, likelihood of development mental status alteration, change in CT scan, hospital length of stay, and survival.

1000 patients patients age > 65 years [elderly] with concussion were enrolled, 622 women and 378 men, all on either antiplatelet therapy, anticoagulation or dual therapy. Patients had an average age of 80 years with average ISS of 1.4. Between the 3 groups (antiplatelet, anticoagulation and dual therapy), notable differences were found in alteration of mental status requiring the obtaining of a repeat CT scan (44% vs. 63% vs. 85%, $p < .0001$), changes noted in CT scan at 24 hours (8% vs. 19% vs. 56%, $p< .0001$), hospital length of stay (days) (4.5 vs. 5.1 vs. 6.0, $p < .0001$), and survival (100% vs. 94% vs. 85%, $p < .0001$). We also noted a significant difference between patients on aspirin or clopidogrel with regard to hospital length of stay (days) (4.2 vs. 5.4, $p < .0001$).

Elderly patients on antiplatelet therapy with concussive injury were less prone to develop morbidity such mental status changes, changes in CT at 24 hours and prolonged hospital length of stay when compared to patients on anticoagulation or dual therapy. With 100% survival and hospital length of stay ranging between 4.2 to 5.4 days, raises questions with regard to resource allocation in concussed patients on only antiplatelet therapy.

In patients on anticoagulation with or without antiplatelet therapy, changes in CT scan were unrelated to bleeding but more commonly found to be due to worsening of chronic conditions -- edema and prior infarction - possibly related to withholding of anticoagulation or antiplatelet therapy.

Concussive injury in patients on anticoagulation is associated with a higher morbidity and mortality than patients with similar injury only on antiplatelet therapy. The change in mental status even with antiplatelet therapy would suggest observing these patients for at least 24 hours.

KEYWORDS

Antiplatelet Therapy, CT scan, Traumatic brain injury (TBI)

INTRODUCTION:

Traumatic brain injury (TBI) is the most common cause of death in trauma patients - having an estimated economic cost of $76.5 billion dollars in 2010.[1] Despite a significant medical, social and economic burden, the complex management of TBI is poorly understood and can be highly variable. At our level 1 trauma center, we noted a significant clinical difference in elderly patients with concussive injury on anticoagulation and antiplatelet therapy unrelated to bleeding events and sought to characterize this difference in outcomes.

MATERIALS AND METHODS:

We performed a retrospective cohort study using elderly patients admitted to our trauma service. As this was a retrospective data analysis using de-identified data, we sought and obtained exemption from our institutional review board for the study of human subjects. Data obtained included age, gender, injury severity score (ISS), incidence of delirium prompting repeat computed tomography (CT), change in brain CT imaging at 24 hours, hospital length of stay (HLOS), and survival. One way analysis of variance (ANOVA) was then performed using JMP Statistical Software ©.

RESULTS:

Our study enrolled 1000 patients patients of age 65 years and older with concussion consisting of 622 women and 378 men. All patients enrolled were on antiplatelet therapy, anticoagulation or dual therapy. The average of the population was 80 years. Average ISS was 1.4. Patients on antiplatelet therapy were found to have a significant reduction ($p < 0.0001$) in incidence of delirium prompting repeat CT (44%) in comparison to patients on anticoagulation (63%) and dual therapy (85%). Additionally, significant changes on repeat CT at 24 hours were less frequently found in patients on antiplatelet therapy (8%), in comparison to anticoagulation (19%), and dual therapy (56%) (Figure 1). With regard to clinical outcomes, patients on antiplatelet therapy or anticoagulation (4.5 days vs. 5.1 days vs. 6.0 days, $p < 0.0001$). and worse survival to discharge in comparison to patients on antiplatelet therapy alone (Figures 2A and 2B). We also noted a significant difference in HLOS between patients on aspirin (4.2 days) or clopidogrel (5.4 days) (Figure 3).

Figure 1: Computed Tomography Outcomes in TBI

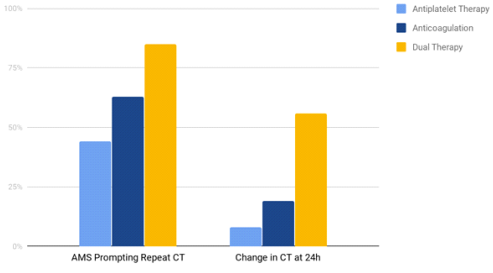


Figure 2A: Anti-thrombotic Agents in TBI vs. HLOS

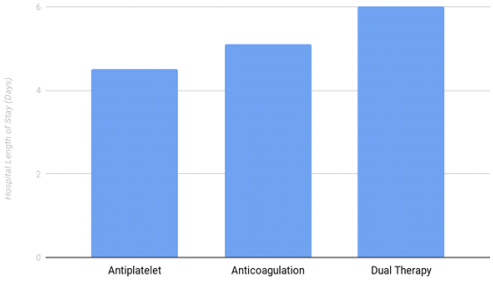


Figure 2B: Anti-thrombotic Agents in TBI vs. Survival to Discharge

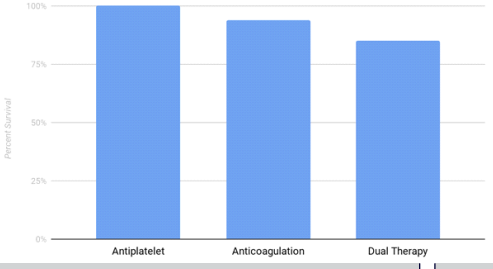
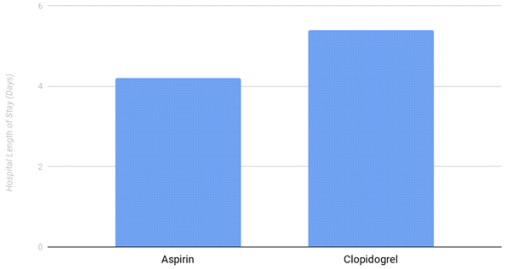


Figure 3: Anti-platelet Agent vs. HLOS



DISCUSSION:

Traumatic brain injury (TBI) is the most common cause of death in trauma with a estimated economic of $76.5 billion dollars.[1] Even independent of concurrent injury, patients with TBI are complex to manage as sequela of neurologic injury often involves multiple organ systems. TBI is differentiated into primary injury, the initial insult, and secondary injury, all subsequent complications that can develop in the setting of an acute trauma.[2] The mainstay of management revolves around prevention of secondary injury induced by hypotension, hypoxia, and dysregulation of normal cerebral protection mechanisms.[3]

Understanding nuances of management strategy in the TBI patient requires a thorough appreciation of the fundamental pathophysiology, which is multifocal in nature. Additionally an understanding of the Monro-Kellie Doctrine (which states that cerebrospinal fluid, blood and brain tissue collectively has a constant volume) plays a key role in management strategy.[4] Normal cerebral protection mechanisms are complex including:

1. Cerebral autoregulation, which maintains a constant blood flow despite variation in mean arterial pressure (MAP) from a range of 60-160 mmHg.[5]
2. Blood brain barrier, which provides isolation from toxin exposure, infection, and metabolic sequela of physiologic processes including hypercarbia and acidosis.
3. Endocrine system control via the pituitary gland and hypothalamus.
4. Thermoregulation
5. Vagal and catecholamine response.[2]

The pathophysiology of TBI involves disruption of these fundamental physiologic control and protection mechanisms as a result of primary injury. The sequela of this disruption results in secondary injury. In the acute phase of TBI, cerebral protection mechanisms are impaired due to direct tissue damage, edema and secondary hypoxia as expanding brain tissue displaces blood volume. The loss of cerebral autoregulation compounds tissue hypoxia and lactic acidosis ensues.[2] The subsequent catecholamine response and cytokine upregulation typically affect the cardiovascular, respiratory and endocrine systems, which tend to be dysregulated in TBI patients and are the foci of management in secondary injury prevention strategy.[3]

The neurologic assessment of TBI patients is classically performed using the Glasgow Coma Scale (GCS). Despite ubiquitous use, there is limited prognostic value and a high degree of interobserver variability.[6] As a recent addition to the neurologic assessment, the Rancho Los Amigos Score, which scales patients from I (non-responsive) to X (demonstrating purposeful movement), is commonly used to track clinical progression of patients and has demonstrable prognostic value.[7] A major concern after the acute phase of TBI is maintenance and monitoring of intracerebral pressure as a high intracranial pressure (ICP) can reduce cerebral perfusion. Maintenance of cerebral perfusion pressure (CPP) is a primary concern in TBI patients as loss of autoregulation can predispose patients to further ischemic injury.[8] Strategies to maintain CPP focus on managing contributors:

CPP = MAP - ICP

By maintaining MAP and reducing ICP, adequate CPP can be obtained preventing further damage to the penumbra (the area surrounding primary tissue damage which is particularly vulnerable to ischemia and hypoxia). The Brain Trauma Foundation (BTF) guidelines recommend monitoring for ICP greater than 22 mmHg with a goal CPP of 60-70 mmHg.[9] The American College of Surgeons (ACS) recommends a tiered approach to patients with ICP of 20-25 mmHg.[10]

1. Tier 1 - head elevation of 30 degrees, sedation, and ICP monitoring. Proceed to tier 2 if ICP is unchanged.
2. Tier 2 - Osmotherapy, testing cerebral autoregulation, ICP monitoring and "test dose" for neuromuscular paralysis. Proceed to tier 3 if ICP is unchanged.
3. Tier 3 - Salvage therapy using neuromuscular paralysis, barbiturate/propofol coma, hypothermia and craniectomy.

The gold standard strategy for ICP monitoring is currently external ventricular drain (EVD) method where a catheter is placed into the ventricles via burr hole.[11] Device infections are relatively common from 1-27% incidence.[12] Current guidelines recommend use of antibiotic impregnated catheters and empiric antibiotic therapy for 7-14 days in penetrating TBI.[13] Alternative complementary monitoring strategies include cerebral microdialysis, measurement of focal brain tissue oxygen tension (PbO2), and jugular venous oxygen saturation (SjvO2).[14] Osmotherapy aims to expand blood volume while concurrently reducing cerebral edema using a hyperosmotic solution. Hypertonic saline has demonstrated greater efficacy of ICP reduction than mannitol (0.25-1 g/kg), however the relationship of degree of ICP reduction to difference in outcomes remains unclear.[11] Approximately 20% of patients with TBI develop seizures during course of hospitalization and associated with worse prognosis.[15,16] Maximal benefit for seizure prophylaxis is obtained by 1 week post initial insult.[17] Although data has demonstrated no clinical difference between efficacy of phenytoin and levetiracetam,[18] levetiracetam is commonly used as there is a wide therapeutic window, relatively mild side effect profile, and simple dosing strategy. Patients who require further suppression and continue to maintain elevated ICP refractory to initial therapy may benefit from coma induction using propofol or barbiturates.[10] This strategy is geared towards reduction of cerebral metabolic oxygen requirement with subsequent reduction in blood flow and ICP.[19] For similar reasons, refractory therapy additionally includes hypothermia. However, prolonged hypothermia can potentially be detrimental as patients have an increased incidence of infection. In refractory cases to medical therapy, the use of decompressive craniotomy can rapidly reduce ICP.[20] In comparison to medical therapy, however, patients demonstrated reduction in mortality but increase in vegetative states and disability.[21]

In review of outcomes literature specifically in regard to anti-thrombotic therapy in the setting of TBI, we noted a paucity of available literature - specifically in the setting of concussive injury. Our findings seem to suggest that in elderly patients with concussive injury on antiplatelet therapy with or without anticoagulation, patients had worse outcomes independent of bleeding when medications were held. This was commonly found to be due to worsening of chronic conditions - specifically edema and prior infarction. Even among different antiplatelet agents, differences were noted likely related to severity of chronic illness. Our data suggests that withholding therapy within this patient population may be detrimental and medical therapy should be aimed at restarting these medications within a shorter time-frame to reduce iatrogenesis. The resumption of antiplatelet or anticoagulation medication would logically suggest these patients be observed in a hospital setting.

REFERENCES

1. Coronado, V.G., Faul, M., McGuire, L.C., Sugerman, D. & Pearson, W.S. (2012). Epidemiology of TBI. Brain Injury Medicine. Principles and Practice, 2nd edition.
2. Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery 2017; 80: 6-15.
3. Bhagat H, Narang R, Sharma D, Dash HH, Chauhan H. ST elevation--an indication of reversible neurogenic myocardial dysfunction in patients with head injury. Ann Card Anaesth 2009; 12: 149-51.
4. Mokri B. The Monro-Kellie hypothesis: Applications in CSF volume depletion. Neurology. 2001. doi:10.1212/WNL.56.12.1746
5. Armagan Dagal, Arthur M Lam Cerebral autoregulation and anesthesia. Curr Opin Anaesthesiol: 2009, 22(5);547-52
6. Wijdicks EF, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. Ann Neurol 2005; 58: 585-93.
7. Lin K, Dulebohn SC. Ranchos Los Amigos. Treasure Island (FL), StatPearls Publishing. 2017.
8. Sharshar T, Citerio G, Andrews PJ, Chieregato A, Latronico N, Menon DK, et al. Neurological examination of critically ill patients: a pragmatic approach. Report of an ESICM expert panel. Intensive Care Med 2014; 40: 484-95.
9. Carney N, Totten AM, Reilly CO, et al. Guidelines for the Management of Severe Traumatic Brain Injury 4th Edition. J Neurotrauma. 2016.
10. Nathens AB, Cryer HG, Fildes J. The American college of surgeons trauma quality improvement program. Surg Clin North Am 2012; 92: 441-54.
11. Dash HH, Chavali S. Management of traumatic brain injury patients. Korean J Anesthesiol. 2018. doi:10.4097/kjae.2018.71.1.12
12. Rebuck JA, Murry KR, Rhoney DH, Michael DB, Coplin WM. Infection related to intracranial pressure monitors in adults: analysis of risk factors and antibiotic prophylaxis. J Neurol Neurosurg Psychiatry 2000; 69: 381-4.

13. Wang X, Dong Y, Qi XQ, Li YM, Huang CG, Hou LJ. Clinical review: efficacy of antimicrobial-impregnated catheters in external ventricular drainage–a systematic review and meta-analysis. Crit Care 2013; 17: 234.
14. Tisdall MM, Smith M. Multimodal monitoring in traumatic brain injury: current status and future directions. Br J Anaesth 2007; 99: 61-7.
15. Clausen T, Alves OL, Reinert M, Doppenberg E, Zauner A, Bullock R. Association between elevated brain tissue glycerol levels and poor outcome following severe traumatic brain injury. J Neurosurg 2005; 103: 233-8.
16. Vespa PM, Nuwer MR, Nenov V, Ronne-Engstrom E, Hovda DA, Bergsneider M, et al. Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring. J Neurosurg 1999; 91:750-60.
17. Temkin NR, Dikmen SS, Wilensky AJ, Keihm J, Chabal S, Winn HR. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. A randomized, double-blind study of phenytoin for the prevention of post-traumatic seizures. N Engl J Med 1990; 323: 497-502.
18. Yang Y, Zheng F, Xu X, Wang X. Levetiracetam versus phenytoin for seizure prophylaxis following traumatic brain injury: a systematic review and meta-analysis. CNS Drugs 2016; 30: 677-88.
19. Bhalla T, Dewhirst E, Sawardekar A, Dairo O, Tobias JD. Perioperative management of the pediatric patient with traumatic brain injury. Paediatr Anaesth 2012; 22: 627-40.
20. Cooper DJ, Rosenfeld JV, Murray L, Arabi YM, Davies AR, D'Urso P, et al. Decompressive craniectomy in diffuse traumatic brain injury. N Engl J Med 2011; 364: 1493-502.
21. Hutchinson PJ, Kolias AG, Timofeev IS, Corteen EA, Czosnyka M, Timothy J. Trial of decompressive craniectomy for traumatic intracranial hypertension. N Engl J Med 2016; 375: 1119-30.