

Clinical Practice Management Guidelines

Head Injury in Anticoagulated Patients

I. Purpose

A recent review of the state of Arkansas trauma performance improvement data has revealed that up to one-third of the preventable trauma related deaths occur in patients on chronic anticoagulation with head injury. Frequently, these patients will present neurologically intact following seemingly minor head trauma, only to progressively deteriorate and die due to expanding intracranial hemorrhage (ICH). The intent of this practice guideline is to provide a means for rapid triage, evaluation and reversal of anticoagulation in order to reduce the associated morbidity and mortality.

II. Background/Summary

Currently, it is estimated that over six million patients in the US are treated with warfarin, with an increasing number being treated with an antiplatelet drug (APD), most commonly clopidogrel, or one of the newer anticoagulants, dabigatran, rivaroxaban or apixaban. This, coupled with the fact that the population over the age of 65 years (the group most likely to be treated with one of these agents) is expected to double to 20% of the total U.S. population by the year 2030, suggests that the issue of head trauma in the chronically anticoagulated patient will continue to become more prevalent. Moreover, it has been demonstrated that patients older than 65 years are at increased risk for ICH with resulting increased morbidity and mortality. This fact is presumed to be related to intracerebral changes associated with aging. Additionally, because of cerebral atrophy, significant ICH can occur without early ICP elevation and the associated mental status changes typically seen in the younger population. These injuries can go undetected if the usual criteria for determining the need for head CT are used in the elderly, particularly those on anticoagulation. Many groups advocate liberal criteria for determining the need for head CT scanning in the elderly, including those that present with a GCS of 14 to 15, and no LOC, amnesia, vomiting or diffuse headache (Moore et al 2012).

III. Study Datum

In order to illustrate the significance of head injury in the chronically anticoagulated patient, a review of the recent outcome literature was performed. The majority of the studies that looked at outcome in head injured patients taking ASA or clopidogrel were typically retrospective and limited by small sample size. They suggested that the increase in morbidity and mortality in patients taking ASA, and probably clopidogrel, was related to cardiovascular co-morbidities and not to worsening CNS injury (Mina et al 2002, Spektor et al 2003, Ohm et al 2005, Jones et al 2006 and Ferraris et al 2012). The same was not found to be true of patients taking warfarin. A number of retrospective studies and several prospective cohort studies suggested a positive correlation between wafarin use and mortality related to expanding intracranial hemorrhage (Franko et al 2006, Pierracci

et al 2007, Bonville et al 2011). Additionally, the degree of anticoagulation appears to be associated with an increased incidence of intracranial hemorrhage and mortality (Pierracci et al 2007). Few outcome studies are available involving CHI in patients taking dabigatran, rivaroxaban or apixaban. One retrospective study looked at patients presenting with CHI after a single level fall and compared outcomes between those on no anticoagulation (NAC) vs those on warfarin or dabigatran. The warfarin patients were reversed using a standardized protocol employing FFP and Vitamin K. Reversal was attempted by a variety of methods including FFP, platelets, rFVIIa and hemodialysis in the dabigatran patients. There was no significant difference in outcome between the NAC and warfarin groups. The dabigatran group demonstrated statistically significant progression of ICH on follow up CT and mortality (40% vs 0%) when compared to the NAC and warfarin groups. It should be noted that this study was limited by its retrospective nature and small sample sizes (Parra et al 2013).

A. Recommendations

1. Question #1: Should patients on warfarin with seemingly minor head trauma be considered at risk for the development of ICH?
 - Level I data – no level I data
 - Level II data – no level II data
 - Level III data – patients presenting with a GCS of 14-15 should be considered at risk for ICH, particularly those with higher INR's.

The risk of intracranial hemorrhage with minor head trauma, patients presenting with GCS of 14-15, is significant in the presence of warfarin anticoagulation. An incidence of intracranial hemorrhage between 7% to 29% has been noted in this setting and it may be higher in elderly patients and those with higher INR's (Li et al 2001, Reynolds et al 2003, Claudia et al 2011 and Brewer et al 2011). Loss of consciousness may be predictive of intracranial hemorrhage but a significant number of patients will present without LOC.

2. Question #2: Does the risk of delayed ICH in patients taking anticoagulation warrant follow up head CT scanning or admission?
 - Level I data – no level I data
 - Level II data – no level II data
 - Level III data – The risk of delayed ICH in patients on warfarin appears to be low enough to not warrant follow up head CT's without changes in the neurological exam except for possibly those patients with supratherapeutic INR's.

The risk of delayed intracranial hemorrhage in patients on warfarin appears to be low but may be increased in those with higher INR's. The rate of delayed ICH in those patients taking warfarin with mild CHI (GCS 14 – 15) ranged from 0 to 1.4% with one study reporting a rate of 6% in those patients with INR's over 3 (Kaen et al 2010, Peck et al 2011, Menditto et al 2011, and Nishijima et al 2012). Repeat

head CT in those patients with a negative initial CT was not felt to be warranted; however admission with serial neurological exams, particularly in those patients with INR's >3, was thought to be reasonable.

3. Question #3: Does the use of a triage and reversal protocol improve outcomes in head injured patients on anticoagulation?

- Level I data – no level I data
- Level II data – no level II data
- Level III data – use of a triage and reversal protocol improves outcome in head injured patients on anticoagulation.

Ivascu et al. demonstrated in 2005 and 2006 that institution of a formal protocol to triage anticoagulated patients with head injury decreased time to evaluation, time to obtain head CT results and time to begin INR reversal as compared to historic controls. No improvement in mortality was noted initially. The protocol was further revised and they were able to demonstrate continued improvement in the time to initial evaluation, time to obtain head CT results, and time to begin INR reversal (1.9 vs 4.3 hours). Improvement in limiting ICH progression (11% vs 40%) and mortality (10% vs 37%) were realized with the revised protocol.

IV. Protocol

Based on the above information, the following protocol for the triage, evaluation and management of chronically anticoagulated patients with closed head injury is suggested. Each institution should modify the protocol to fit their resources and need. The following recommendations are considered to be Level III recommendations.

A. Inclusion Criteria

1. Any patient on anticoagulation or antiplatelet therapy (warfarin, clopidogrel, dabigatran, rivaroxaban or apixaban) who presents with a blunt trauma mechanism including a single level fall (i.e. fall from standing) and has at least one of the following:
 - a. History of loss of consciousness
 - b. History of mental status changes (i.e. GCS < 15)
 - c. Any sign of external injury to the head or neck
 - d. Any history of trauma to the head or neck

B. Triage

1. Each facility should develop a mechanism for rapid identification and triage of these patients that is integrated with their current triage process
2. Prompt identification by the triage RN of anticoagulation use in patients meeting the above inclusion criteria.

3. Patients should be triaged directly to a treatment area with immediate notification of ED physician.
4. Stat blood draw for PT/INR and Type & Screen with initiation of adequate peripheral IV access
5. Initiation of emergent head CT. These patients need to receive equal prioritization with trauma and stroke activation patients and there should be a written protocol where the triage RN can initiate the initial blood work and head CT scan.
6. Immediate interpretation of head CT by Radiology with direct call back to the ED physician. The recommended time interval between ordering the head CT and interpretation resulting to the ED physician should be no more than 30 minutes.
7. Initiation of treatment (see below).
8. Given the presentation of the patient, other lifesaving interventions such as endotracheal intubation, volume resuscitation, and initiation of appropriate transfer should supersede this protocol.
9. Emergent neurosurgical consultation or initiation of transfer to a higher level of care in those facilities without neurosurgical coverage upon CT documentation of ICH.
10. Patients should be admitted to an ICU setting for continued monitoring.

C. Treatment of Patients Receiving Warfarin Anticoagulation

1. Patients identified with CT confirmed ICH should have abnormal PT/INR's initially corrected with 10 – 15 ml/kg (or 4u in the average Pt) FFP.
2. Depending on the size of the facility and their FFP use, the initial 2u FFP could be ABO Type A FFP that is pre-thawed, thawed on initial triage of the patient, or thawed at the time of CT documented ICH. The subsequent 2u FFP would be ABO compatible. The mechanism should be tailored to minimize the time for the facility blood bank to issue FFP.
3. Subsequent FFP transfusion would be guided by serial PT/INR assays with the goal to return the INR to normal. In those facilities having access to thromboelastogram (TEG), this modality could be used to guide correction of anticoagulation.
4. Vitamin K 10mg IVPB over 30 minutes should be concurrently administered at the time of the initial FFP administration. Consider repeat dosing in 12 hours.

5. Prothrombin Complex Concentrate (PCC)

- a. If available, PCC would be preferred to FFP to correct warfarin coagulopathy due to quicker availability, lower infused volume, and minimal risk of infectious complications and pulmonary injury.
- b. Both three factor (II, IX, and X) and four factor (II, VII, IX, and X) PCC are commercially available.
- c. Three factor PCC is administered as 25-50 mcg/kg with low dose rFVIIa (30 mcg/kg).
- d. Four factor PCC is administered as 25 IU/kg for therapeutic INR and 35-50 IU/kg for supratherapeutic INR.

D. Treatment of Patients Receiving Antiplatelet Therapy

1. No information available to support the routine use of platelets in patients on APD's with ICH. Transfused platelets may be inhibited by APD still in circulation.
2. Although there is no information available to support the routine use of DDAVP in patients on APD's with ICH, results from other study populations suggest that DDAVP (0.3 mcg/kg with repeat dosing in 8 hours) should be considered.
3. There is no information available to support the routine use of rFVIIa in patients on APD's with ICH.

E. Treatment of Patients Receiving Dabigatran

1. No antidotes currently available.
2. Administration of activated charcoal if ingested within two to three hours of presentation.
3. Emergent HD or CVVHD depending on HD stability to correct to ECT or rTEG ACT to < 150sec.

F. Treatment of Patients Taking Rivaroxaban or Apixaban

1. No antidotes currently available.
2. Administration of activated charcoal of ingested within two to three hours of presentation.
3. Hemodialysis unhelpful due to protein binding.
4. Consider use of four factor PCC 50 IU/kg.

G. Treatment of Patients with a Normal Head CT

1. Admission for 24 hour observation with serial neurological exams should be considered in patients taking warfarin (particularly those patients with INR's > 3), dabigatran, rivaroxaban or apixaban.
2. Unless indicated for other injuries, correction of therapeutic INR's in the face of a normal head CT is probably not necessary. Consideration should be given to correction of supratherapeutic INR's.
3. In patients taking ASA or clopidogrel, a shorter period of observation or discharge with a reliable caretaker would be considered reasonable.
4. Repeat head CT is not indicated without changes in neurological exam.

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