Original Article

'TIME IS BRAIN' for Haemorrhagic Stroke Secondary to Warfarin Therapy in the Elderly

Shabir A[1]

Abstract

Intra-cerebral haemorrhage (ICH) is a rare complication of warfarin that is life-threatening and requires emergent treatment. Also, as ICH is unpredictable, large cohort studies are not possible especially in elderly patients. Treatment will continue to be based on case series and clinical experience. We present observational study of 4 cases of elderly patients with haemorrhagic stroke secondary to warfarin therapy with supratherapeutic INR. All patients received 10mg IV Vitamin K and 4 factor Human Prothrombin Complex Concentrate (Octaplex) for warfarin reversal. Of the 4 patients, 2 patients had good clinical outcome due to prompt reversal of INR with octaplex, while the other 2 patients had fatal outcome due to delay in warfarin reversal. Our study though small reiterates, as 'Time is Brain' in ischaemic strokes, likewise it holds true for haemorrhagic strokes. Larger trials are required to assess time for "door to reversal" similar to "door to needle" in stroke thrombolysis.

Keywords: Haemorrhage, stroke, warfarin, elderly

(Journal of The Indian Academy of Geriatrics, 2016; 12:169-171)

INTRODUCTION

Intra-cerebral haemorrhage (ICH) is a rare complication of warfarin that is life- threatening and requires emergent treatment. The increased use of anticoagulants for the prevention and treatment of thromboembolic diseases has led to a rising incidence of anticoagulant-related intracranial haemorrhage (AICH) in the elderly people in the West. AICH has high mortality and significant and debilitating long-term consequences.[1]

We present observational study of 4 cases with haemorrhagic stroke secondary to warfarin therapy.

METHOD

Prospective data collection of 4 patients who were admitted with ICH secondary to warfarin therapy with High INR. All patients received 10mg IV Vitamin K and 4 factor Human Prothrombin Complex Concentrate (Octaplex) in a dose of 50 units/ kg as per Guidelines from British Society for Haematology

Case 1 –Unfavourable outcome

79 year old man presented to Emergency Department at 15:53 hrs. with headache, vomiting, right sided weakness and slurred speech. Patient was seen immediately by Stroke Team. Initial vital signs were normal. GCS-15/15. Examination-right sided facial droop, hemi attention, hemi paresis, right homonymous hemianopia and cerebellar signs. NIHSS score 6. Past medical history: Cerebellar stroke, Atrial Fibrillation, Type 2 DM, Hypertension, duodenitis. Drug History: Digoxin, Gliclazide, Warfarin, Omeprazole, Metformin. Social History-Independent with ADLs. Urgent CT Head scan done at 16:04hrs showed small 2.9x2.2 (cm) acute intraparenchymal bleed within left

*Address for Correspondence Department of Stroke Medicine, University Hospital of North Staffordshire, and Keele University, Stoke on Trent, UK

cerebellar hemisphere with old right cerebellar infarct. Bloods for INR sent. Case discussed with Neuro-Surgical Team at 17:00hrs who advised not for neurosurgical intervention. Blood results at 1730 hrs.-INR 2.5. Case discussed with Haematologist for Octaplex. Vitamin K 10 mg given. GCS was E3 M6 V5 (14/15). Octaplex issued by Lab at 17:50hrs. GCS dropped to E1 M5 V1 (7/15) at 18:30hrs. Octaplex given to patient at 18:50hrs. At 19:00 hrs, patient's airway was compromised and case rediscussed with Neurosurgeons who advised not for surgical intervention and palliative approach. Patient passed away next morning (Octaplex given after 2 hrs 50 mins).

Case 2 –Unfavourable outcome

78 year old male admitted to A&E department with reduced GCS and no details about his past medical history. Onset of symptoms at 15:15hrs. At 1540 hrs, reviewed by Stroke Team on arrival to A&E, GCS E2 M3 V1 (7/15). Urgent CT-Head done at 1550 hrs showed large left sided intra-cerebral bleed with midline shift. At 1650 hrs GCS dropped to 3. After discussion with Stroke Consultant, it was decided patient is not for neurosurgical intervention and family were informed. At 1730 hrs, 10mg vitamin K given as doctors were informed by family that patient was on warfarin for AF, previous embolic stroke and right carotid endarter-ectomy. At 1745hrs, INR 2.1 and Octaplex reques-ted. Commenced Octaplex at 1800 hrs. No clinical improvement in GCS. Patient died at 2320 hrs. (Octaplex given after 2hr 45 min)

Case 3 –Favourable outcome

75 year old male admitted at 0425hrs to A&E with blurred vision, slurred speech, vomiting and facial droop. Past medical history: Atrial Fibrillation, Ischaemic stroke on warfarin, Hypertension, Polymyalgia Rheumatica on Steroids. Seen by A&E Team immediately. On initial assessment BP >200 mmHg, GCS 15/15 and NIHSS score 5. Cerebellar signs and left sided facial weakness was noted. CT-Head done at 0445 hrs showed right cerebellar intraparenchymal bleed 3 x 1.5cm extending into 4th ventricle with minor surrounding oedema and old right MCA territory infarct. At 0500 hrs INR 2.9, 10mg Vitamin K IV given and Octaplex requested. At 0600 hrs GCS 15/15, Octaplex given and GTN infusion commenced as BP >220/120. Repeat INR sent at 0730 hrs 1.1. Repeat NIHSS score 3 and Neurology improved (Octaplex given within 1 hr. 35 mins).

Case 4 –Favourable Outcome

79 year old female admitted to AE at 1205 hrs with reduced GCS and right sided weakness after being found by carers on the floor. Vital signs on presentation and glucose were normal. Seen immediately by AE Team. Past medical history: Vascular dementia, Warfarin for DVT, high cholesterol. Drug History: warfarin, simvastatin, furosemide. Social History: Lived in warden controlled home, reasonably independent. Examination: GCS-E3 V1 M6 (10/15), right arm and leg weakness. NIHSS score 24. CT head scan done at 1215 hrs showed a large intraparenchymal haematoma with areas of active bleeding measuring 4.2x 3.3 (cm) left basal ganglia and left thalamus with intra-ventricular extension and midline shift. At 1250 hrs blood results were available and INR was not processed as bottle was under filled. Last INR done 1 week ago was 3.2, so patient was given 10mg IV Vitamin K at 12:55hrs. Case discussed with Neurosurgical Team at 1300hrs advised not for surgical intervention. NIHSS score 29. After discussing with Haematologist patient was given Octaplex at 1335 hrs. Repeat INR at 1430 hrs was 1.1 and patient was admitted to Stroke Ward. GCS remained at 10 and neurology improved. Patient when stable was discharged to rehabilitation hospital (Octaplex given within 1 hr. 30 mins)

RESULTS

Of the 4 patients, 2 patients had good clinical outcome due to prompt reversal of INR with octaplex, mean time of 1 hour 30 minutes, while the other 2 patients had fatal outcome due to delay in warfarin reversal with mean time of 2 hours 45 minutes.

DISSCUSSION

The use of anticoagulants has increased exponentially over the last two decades along with the incidence of atrial fibrillation in aging western populations.[2,3,4] 5.6 million patients in the USA will be on anticoagulation for atrial fibrillation by 2050.[5] With this increased use, the incidence of AICH has risen. It carries 0.3 to 3.7% annual risk of warfarin-related intracerebral haemorrhage (WRICH) when the International Normalized Ratio (INR) ranges from 2 to 4.5.[6]

Early and aggressive treatment after presentation to the A&E department can make a difference, particularly given the neurological deterioration because of early haemorrhage expansion and its long term outcomes.[7,8] Haematoma enlargement

within first 24-48 hrs. of admission is associated with poor outcome.[9]

The present consensus is that life-threatening bleeding such as ICH requires rapid warfarin reversal to correct warfarin associated coagulopathy as soon as possible.[10] In 2005 survey, only 30% of hospitals had protocols/critical care pathways for management of ICH which included reversal of anticoagulation.[11] Preventative measures to mitigate WRICH are relatively inefficient and the cornerstone is on rapid reversal of coagulopathy.[12] The same probably holds true for AICH related to newer anticoagulants.

Given the emergent nature of AICH and their unpredictability, randomized clinical trials and large cohort studies especially in the elderly population are unlikely and hence, recommendations regarding treatment strategies will continue to be based on case series and anecdotal experience.[13]

CONCLUSION

Intra-cerebral haemorrhage (ICH) is a rare complication of warfarin which is life-threatening and requires emergent treatment. Also, as ICH is unpredictable, large cohort studies are not possible especially in elderly patients. Treatment will continue to be based on case series and clinical experience. Our observational study though small reiterates that 'Time is Brain' in the management of haemorrhagic stroke secondary to warfarin therapy similar to management of ischaemic stroke. Close collaboration between treating Physician, A&E Team, Haematology Team, Neurosurgeons is of utmost importance. Prompt assessment of haemorrhagic stroke patients in A&E and urgent CT-Head needs to be emphasized. In our two cases with fatal outcome, non-availability of finger prick INR testing machine and octaplex in A&E were the main reasons for delay in reversal of warfarin. Larger trials are required to assess time for "door to reversal" similar to "door to needle" in stroke thrombolysis. More robust pathways on rapid reversal are needed particularly with newer anticoagulants on the market.

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