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Case Report

Acenocoumarol induced intra cerebral haemorrhage

Jyotsna Allamsetty[1], Syam Prashanth Pedada[1], Dr. Allu Hari Krishna[2], Dr.G.V.Nagaraju[3].

[1] Department of Pharmacy Practice, Avanthi Institute of Pharmaceutical Sciences, Near Tagarapuvalasa Bridge,Vizayanaragam,AP,India

[2] Associate professor, Department of Pharmacy Practice, Avanthi Institute of Pharmaceutical Sciences, Near Tagarapuvalasa Bridge,Vizayanaragam,AP,India

[3] Assistant Professor, Department of Pharmacy Practice, QIS College of Pharmacy, Ongole, AP, India.

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***Corresponding Author**

Jyotsna Allamsetty
Email: jyotsnabittu@gmail.com

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Abstract

Life threatening intra cerebral haemorrhage (ICH) is the most serious complication of oral anti-coagulation therapy (OAT) with mortality in excess of 50%.early intervention focuses on rapid correction of coagulopathy in order to prevent continued bleeding. Although management guidelines for such haemorrhages are available for the older generation anticoagulants, they are still lacking for newer agents, which are becoming popular among physicians. Supportive care, including blood pressure control, and reversal of anticoagulation remain the cornerstone of acute management of AICH. A case report of young lady of age 29yrs old came with chief compliant of headache, vomiting and involuntary maturation, sudden loss of vision both eyes .she had history of CRHD(chronic rheumatic heart disease) with severe mitral valve stenosis and of post Operative MVR(mitral valve replacement). Altered sensorium after surgery .past medication history was using Acenocoumarol (acenocoumaral) 3mg for 15 days .while observing the patient. Patient was irritable nd abdomen was soft, neck was stiff. Acenocoumarol has been induced intra cerebral haemorrhage in patient and also lead to sub dural haemorrhage infract temporal parietal region

Introduction

Intracranial haemorrhage (ICH) is an inclusive term referring to several different conditions, including hemorrhagic stroke, subdural hematoma, and epidural hematoma, and is characterized by the extra vascular accumulation of blood within the skull. Approximately 20% of all strokes are due to ICH. Of these, most consist of intracerebral haemorrhage and subarachnoid haemorrhage [1,2]. Moreover, it is also important to remember two other, less common, pathological entities: subdural and epidural hematoma, which are both frequently associated with head trauma, especially in the elderly [3-5].These bleeding events
are a growing cause of death and disability worldwide due to the increasing number of elderly people, and the Increasing use of oral anticoagulants (OACs) and anti platelet agents. 6 In particular, ICH is the most serious complication of oral anticoagulant therapy (OAT), with

mortality rates in excess of 50%, and three times higher than that of ischemic stroke[7].The use of Warfarin and other vitamin K antagonists (VKAs) in patients with Atrial fibrillation (AF) for prevention of ischemic stroke has considerably increased after the publication of several studies proving their efficacy [8, 9]. Although more effective than aspirin in preventing ischemic stroke in patients at risk for ischemic stroke, VKAs are, however, associated with a higher risk of ICH [10]. In the 1990' s, the use of warfarin in the US quadrupled and, during the same period, an increase was seen in the incidence of hemorrhagic stroke [11]. Important evidence suggests that even a perfectly conducted VKA treatment, with international normalized ratio (INR) between 2 and 3 in AF patients, doubles the risk of ICH [12]. Use of anticoagulation therapy among the population for varied thromboembolic diseases potentially places them at risk of developing anticoagulant-related intracranial haemorrhage (AICH). The indications for use of anticoagulants are published in a guideline statement by the American College of Chest Physicians [17], to which readers are referred. AICH can be spontaneous or traumatic, and can occur in different intracranial compartments (for example, subdural haemorrhage, and epidural haemorrhage. Most clinical data on AICH are related to ICH, while extra parenchymal haemorrhages are reported but data on these are sparse. In the absence of clinical evidence, definitive guidelines, and proven therapies, clinicians are left scrambling for rapid correction of the coagulopathy and maintaining homeostasis to prevent secondary brain injury. The present review will primarily focus on the importance and impact of AICH, and, where available, the evidence-based management of this mostly iatrogenic disease.

Principles And Interpretation Of Monitoring Anticoagulant Therapy

Evaluating and monitoring blood coagulation parameters is imperative after AICH. This is particularly true when obtaining history is difficult, thus precluding knowledge of the culprit anticoagulant, information that is crucial to guide therapy. Although coagulation tests are mere surrogate markers for hemostasis, the effect of different anticoagulants on the coagulation system is important knowledge for the treating clinician to have. Some of these tests are quantitative, and others provide only qualitative information. Moreover, it is important to understand that testing techniques and their sensitivities vary widely especially with newer anticoagulants [18]. Routine and commonly used ex vivo coagulation tests are the prothrombin time (PT), INR, and activated partial thromboplastin time (aPTT); the thrombin time, ecarin clotting time, activated clotting time and endogenous thrombin potential are also available, albeit less widely. In patients with ongoing hemorrhage, the PT is preferred over the aPTT for the estimation of coagulation factor levels, because the results are quickly available, it offers a good correlation with average factor concentrations and response to plasma replacement, and there is no interference with nonspecific lupus anticoagulant inhibitors, elevated factor VIII, and heparin contamination [14]. The modified thrombin time (also commercially known as the HEMOCLOT thrombin time assay; and ecarin clotting time are the best tests for measuring the anticoagulant effect of dabigatran [16]. A normal thrombin time would exclude clinically significant dabigatran in systemic circulation. Although anti- factor IIa level testing is available at present, not enough information on its characteristics is known – such as linearity for and responsiveness in patients on dabigatran. To the contrary, the anti-factor Xa level has good correlation with rivaroxaban/apixaban activity. The recommended test to measure the anticoagulant effect of rivaroxaban is the PT (using reagent Neoplastin plus; Diagnostica Stago, Asnières-sur-Seine, France) and anti-factor Xa assay. Dabigatran and rivaroxaban drug levels can be used as surrogate markers to assess the need for anticoagulation reversal, but they are also not widely available[16]. Both warfarin and heparin have good linear correlation with the PT/INR and the aPTT respectively, but the utility of the traditional coagulation profile testing is questioned with the advent of newer anticoagulants. Viscoelastic assays that measure whole blood coagulation and provide a dynamic coagulation profile, such as thromboelastography and rotational thromboelastometry, are being increasingly used to provide rapid assessment of hemostasis [8].

These assays measure the increasing viscoelasticity of blood as it clots, which is proportional to clotting factors and platelet count/function[10]. Their advantages are a rapid turnaround time, and the detection of fibrinolysis. Clinical situations where viscoelastic assays have been used to evaluate hemostasis include trauma resuscitation[9], during cardiopulmonary bypass 11 and AICH 13. One study reported dose-dependent shortening of the clot-lysis time in the presence of dabigatran[12]. These laboratory tests might hold promise in the near future, although further studies and experience are needed.

Case Report

A 29yr old women visited general medicine department with Chief complaint of sudden loss of vision. She was previously diagnosed with chronic rheumatic heart disease along with severe mitral stenosis and atrial fibrillation. She had gone through a surgery of mitral valve replacement previously before month. She had experienced involuntary maturation and vomiting and headache before admitted into the general medicine department. Her blood pressure was 90/50, RR is 14/min, PR is 70 bpm.she had history of using Acenocoumarol 3mg previously.On neurological examination she had developed chronic subdural hemorrhage measuring 6.8mm in thickness noted in left fronto parietal temporal region. Laboratory data including CRP we're all within normal limits. Physician discontinued Acenocoumarol,

started inj mannitol along with IV fluids. After some days they gave prophylactic IV heparin 5000 IU 8th hrly. However her symptoms are gradually worsened and also had facial palsy. There was no progress at the time of discharge.

Discussion

We have experienced a female patient of age 29 yrs who had taken Acenocoumarol 3mg and developed intracranial haemorrhage and sudden loss of vision. The mechanism by which Acenocoumarol induces ICH is not clear considering that the lesion distribution does not differ between Acenocoumarol induced ICH and spontaneous ICH. Their underlying processes might be similar. The presence of Acenocoumarol could result in a tiny bleed enlarging even under normal haemostatic mechanisms. Our study shows that the outcome of ICH in patients treated with anticoagulants is only slightly worse than in those without, despite the significantly larger hematoma volumes in treated patients. The degree of anticoagulation was not treated to the occurrence of ICH.

Conclusion

Many questions pertaining to the management of AICH remain unanswered. Conducting a systematic randomized trial in this subpopulation of patients is difficult. The available literature (although mostly retrospective and case series) recommends rapid correction of coagulopathy, early surgical intervention if appropriate and holding resumption of anticoagulation during the acute phase. Newer oral anticoagulants are marketed to be safe with lower incidence of AICH and can be potentially considered when resumption of anticoagulation is warranted. However, the lack of optimal reversal agent in case of complications may deter clinicians from using them. The development of safe and novel reversal agents for newer generation anticoagulants should thus take precedence, given their booming use and the current naivety and inexperience of the healthcare provider in managing their hemorrhagic complications. Better studies are needed to guide clinicians in appropriate management and to help prognostication. Given the overall poor functional outcome of patients with ICH in general, and perhaps AICH in particular, a need exists to explore preventative avenues. Hence, emphasis should be also placed on patient education, lifestyle and risk modification and discussion of the risk–benefit ratio before anticoagulants are prescribed.

Abbreviations

ACS, acute coronary syndrome; ACT, activated clotting time; AF, atrial fibrillation; aPTT, activated partial thromboplastin time; CVST, cerebral venous sinus thrombosis; ECT, ecarin clotting time; HIT, heparin-induced thrombocytopenia; INR, International Normalized Ratio; i.v., intravenous; LMWH, low molecular weight heparin; PCC, prothrombin complex concentrate; p.o., per oral; PT, prothrombin time; rFVIIa, activated recombinant factor VII; s.c., subcutaneous; TT, thrombin time; UFH, unfractionated heparin; VTE, venous thromboembolism. FEIBA™ from Baxter (Deerfield, IL, USA). AF, atrial fibrillation; AICH, anticoagulant-related intracranial hemorrhage; ARISTOTLE, Apixaban for Reduction in Stroke and Other Thromboembolic Events; BID, twice daily; CAD, coronary artery disease; CHF, congestive heart failure; DM, diabetes mellitus; DVT, deep venous thrombosis; EINSTEIN-PE, Oral Rivaroxaban Alone for the Treatment of Symptomatic Pulmonary Embolism; h/o, history of; INR, International Normalized Ratio; LVEF, left ventricular ejection fraction; PE, pulmonary embolism; RE-LY, Randomized Evaluation of Long Term Anticoagulant Therapy; ROCKET-AF, Rivaroxaban Once-daily Oral Direct Factor Xa Inhibition Compared with Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation; SDH, subdural hematoma; TIA, transient ischemic attack; VKA, vitamin K antagonist; VTE, venous thromboembolism. aPTT, activated partial thromboplastin time; ECT, ecarin clotting time; ETP, endogenous thrombin potential (thrombin generation assay); NA, not applicable; PT, prothrombin time; TT, thrombin time.

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