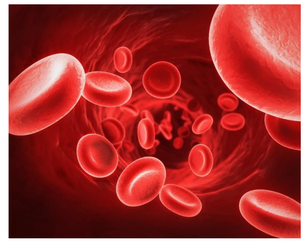
A RARE CASE OF DABIGATRAN INDUCED HEMOPERICARDIUM WITH CARDIAC TAMPONADE

Dr Sahithi Sharma [1], Dr Anupam Bhambhani [2]

[1]- House surgeon, VIMS&RC, [2]-Associate Professor, Department of Cardiology, VIMS&RC



INTRODUCTION

- **Dabigatran etexilate** is a novel oral anticoagulant used in the prevention and treatment of thromboembolism.
- It is a **direct thrombin inhibitor** which reversibly blocks the catalytic site of thrombin and produces rapid anticoagulation within 2 hours.[1]
- It has a **pharmacokinetic profile** that produces predictable anticoagulation responses and does not require frequent laboratory monitoring of clotting parameters.[2]
- Dabigatran has the added advantage of an available reversal agent-**Idarucizumab**.
- The **commonly encountered adverse effects** include bruising, minor bleeding acid-peptic disease and hepatobiliary disorders.
- **Spontaneous hemopericardium** and tamponade, is a rare and potentially fatal adverse effect of Dabigatran which entails immediate intervention.

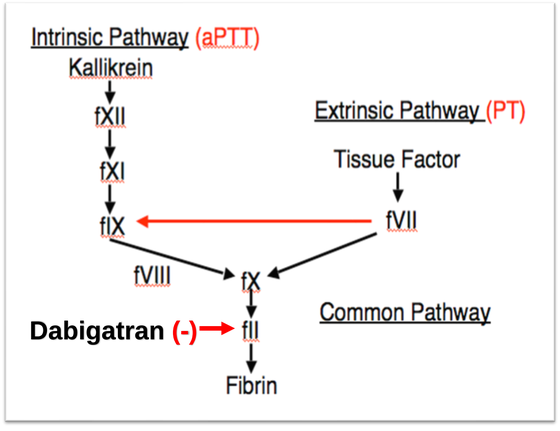


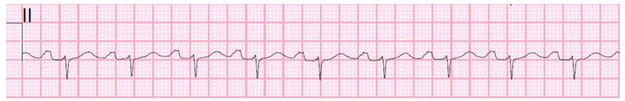
Fig 1: Mechanism of action of Dabigatran etexilate

CASE DESCRIPTION AND INTERVENTION

In the early hours of 11/07/18, a 65-year-old woman presented to the ER with sudden exacerbation of dyspnea (NYHA grade II→IV). There was no chest pain, palpitations or syncopal episodes. She was a known case of right lower limb DVT on Tab Dabigatran 150mg twice daily since 9 days with no other known co-morbidities and not concomitantly on any other medications. On examination, her systolic BP was 70 mm of Hg, JVP was elevated with multiple engorged neck veins and heart sounds were muffled. A clinical diagnosis of pericardial tamponade was made. There were no other bleeding manifestations.

O/E- PR: 110 bpm- feeble
BP: 70/50 mm of Hg
sPO2: 98% on 15 litres of O2
Pallor- present
Bilateral pitting pedal edema present
Multiple dilated and engorged neck veins present

S/E- CVS: S1, S2 present, muffled heart sounds
RS: Bilateral air entry present
CNS: conscious and restless
P/A: soft, non-tender



ECG- Fast ventricular rate with low voltage complexes

Transthoracic ECHO- Cardiac tamponade with RA/RV collapse

Lab parameters:-

WBC- 21.9	PCV- 24.4	PT- 22.1	Urea- 27	K- 4.32	Total Bilirubin- 0.3
RBC- 2.98	Platelets- 1145	aPTT- 60.9	Creatinine- 0.94	Cl- 98	Direct Bilirubin- 0.14
Hb- 7.8	D-Dimer- 2680	INR- 1.92	Na- 123	Ca- 7.9	Albumin- 1.65

Emergency pericardiocentesis yielded 460 ml of haemorrhagic pericardial fluid. Samples were sent for gram staining, cytological evaluation and culture which were all negative. The drug was discontinued following the same and substituted with Unfractionated Heparin. One pint of packed RBCs was transfused. Idarucizumab was not administered as it was unavailable in our hospital at the time. Patient recovered and serial echocardiograms done thereafter showed no re-accumulation of pericardial fluid. Further detailed evaluation following stabilisation revealed colonic carcinoma to be the cause of right lower limb DVT.

DISCUSSION

- The adverse drug reaction is classified as **Type A (augmented)** according to Wills and Brown.[3] Dabigatran can cause bleeding into the pericardial space which causes obstruction to ventricular filling and consequent hemodynamic compromise.
- **Naranjo causality scale** [4] revealed a score of 7 suggestive of a possible causation however the clinical course and investigations led us to believe that Dabigatran was the cause for hemopericardium in this case.
- Cardiac tamponade necessitated the patient to receive intensive medical care hence the reaction is classified as Level 5 (severe) by **Modified Hartwig and Siegel criteria for severity**. [5] Emergency pericardiocentesis was the life saving procedure performed to revive the patient. Transfusion of FFP is not expected to help control bleeding due to Dabigatran.[6]
- **Modified Schumock and Thornton's criteria of preventability** [7] indicated that the reaction was probably preventable. DTT(dilute thrombin test) is a viable method of monitoring coagulation status over and above PT, INR, aPTT in patients receiving dabigatran etexilate therapy.[8]

CONCLUSION

Dabigatran has a better safety profile than warfarin however spontaneous hemopericardium can occur even with appropriate use and dosing. The risk of anticoagulant induced hemopericardium is increased in patients aged >75 years and with concomitant risk factors such as pericarditis, trauma, renal failure. The use of anticoagulants warrants caution in such patients and the dose of Dabigatran must be reduced to 110mg twice daily for a better safety profile. This case study highlights the need for clinicians to be cognizant of the potential for life-threatening bleeding with use of this agent and be prepared for the same.

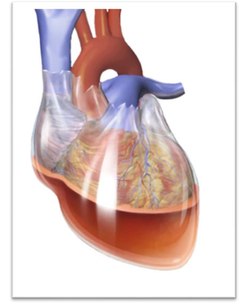


Fig 2: Illustration of pericardial effusion

REFERENCES

1. Tripathi KD. Essentials of medical pharmacology. 7th ed. New Delhi, India: Jaypee Brothers Medical Publishers; 2013. p. 82.
2. Michael Ganetsky, Kavita M. Babu, Steven D. Salhanick, Robert S. Brown, and Edward W. Boyer. Dabigatran: Review of Pharmacology and Management of Bleeding Complications of This Novel Oral Anticoagulant. J Med Toxicol. 2011 Dec; 7(4): 281–287.
3. Wills S, Brown D. A proposed new means of classifying adverse drug reactions to medicines. Pharm J. 1999;262:163–5.
4. Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. Clin Pharmacol Ther. 1981;30:239–45.
5. Hartwig SC, Siegel J, Schneider PJ. Preventability and severity assessment in reporting adverse drug reactions. Am J Hosp Pharm. 1992;49:2229–32.
6. Crowther MA, Warkentin TE. Managing bleeding in anticoagulated patients with a focus on novel therapeutic agents. J Thromb Haemost. 2009;7(Suppl 1):107–110. doi: 10.1111/j.1538-7836.2009.03429.x.
7. Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. Hosp Pharm. 1992;27:538.
8. Barton CA, McMillian WD, Raza SS, Keller RE. Hemopericardium in a patient treated with dabigatran etexilate. Pharmacotherapy, 2012

Presented at "Pharmacovigilance: Clinical Implications" CME on 19/07/2019 at VIMS&RC