MEDDOCS
Open Access Publisher

International Journal of Innovative Surgery

Open Access | Editorial

Non vitamin K antagonist oral anticoagulation- The future of anticoagulation following mitral reparative surgery

Ishtiaq A Rahman*; Hunaid Vohra

Bristol Heart Institute, University Hospital Bristol NHS Foundation Trust, Bristol, England, UK

***Corresponding Author(s): Ishtiaq A Rahman,**

Specialist Registrar in Cardiac Surgery, Bristol Heart Institute, University Hospital Bristol NHS Foundation Trust, England, UK

Email: ishtiaqrahman@nhs.net

Received: Feb 27, 2018

Accepted: Apr 12, 2018

Published Online: Apr 16, 2018

Journal: International Journal of Innovative Surgery

Publisher: MedDocs Publishers LLC

Online edition: http://meddocsonline.org/

Editorial

Warfarin has established itself as the anticoagulation of choice following mitral valvular surgery in the absence of beneficial effect in randomised controlled trials. Although being cumbersome to the patient its role has been secured in part due to the lack of a suitable alternative option. In 2013, around 2000 mitral valve repairs were performed in Great Britain and Ireland [1] with an associated mortality ranging from 1.09% (isolated mitral valve repair) to 2.79% (combined mitral valve repair and coronary artery bypass grafting (CABG)) [1].

The arrival of non-vitamin K antagonist oral anticolagulants (NOACs) has renewed interest in the potential for an alternative option to provide enhanced post-operative recovery and reduce healthcare costs compared to the current standard warfarin in mitral valvular surgery.

Currently there is no definite consensus on the management of anticoagulation after mitral valve repair. The latest American College of Cardiology/American Heart Association (ACC/AHA, 2014) guidelines for the management of patients with valvular heart disease do not provide recommendations [2] and neither do the American College of Clinical Pharmacy (ACCP) guidelines [3]. There are no randomised controlled trials on this subject. The European Society of Cardiology has suggested considering oral anticoagulation for 3 months (Class IIa) after mitral valve repair based on expert consensus (Level C). It is widely acknowledged that many surgeons do not follow this guideline.

Currently, vitamin K antagonists are the only anticoagulants approved for long term treatment of cardiac valve replacement and target international normalised ratio (INR) is adapted to the characteristic of the prosthesis and the patient. Warfarin requires regular blood testing, controlled alcohol consumption,

Cite this article: Rahman IA, Vohra H. Non vitamin K antagonist oral anticoagulation-the future of anticoagulation following mitral reparative surgery. Int J Innov Surg. 2018; 1: 1001.

is associated with major bleeding complication rate of 1%/year resulting in significant lifestyle considerations. As non-vitamin K antagonist oral anticoagulation have demonstrated superior efficacy and reduced length of hospital stay [4] in non-valvular AF management, when compared to warfarin, there has been growing interest in widening their application to post-cardiac surgery patients. The thromboprophylaxis effect of Dabigatran in a swine model after mechanical mitral valve replacement was found to be promising in a recent study. Compared to warfarin, a significant mortality benefit as well as less incidence of bleeding was observed [5]. Disappointingly though, these findings were not translated into humans receiving mechanical valves in the randomised RE-ALIGN study which showed an excess of thrombo-embolic and bleeding events in the Dabigatran group [6]. Whether an alternative NOAC agent in a non-mechanical mitral valve setting (mitral valve repair or tissue bioprosthesis) would be efficacious and safe has not been investigated to date.

In a retrospective review of patients undergoing mitral valve repair or mitral valve bioprosthetic replacement at a single academic US institution a comparison revealed those receiving four to six weeks postoperative warfarin (n=315) did not alter the incidence of stroke, pleural effusion, pericardial effusion or bleeding complications compared to those receiving no warfarin (n=257). Propensity adjusted (Kaplan-Meier) data did not demonstrate any long term survival benefit [7]. These findings have been corroborated in a retrospective review of 249 mitral valve repair or bioprosthetic replacement patients. 77% of patients received warfarin postoperatively and the remainder did not. Thirty day mortality from the index hospitalisation and overall survival was similar for the two groups, with 1.2% and 84% respectively, as was bleeding complications [8]. Indeed in the setting of tissue mitral valve replacement a comparison of postoperative acetylsalicyclic acid or vitamin K antagonist or no specific antithrombotic therapy yielded no evidence to suggest any specific therapy would be superior in preventing valve thrombosis [9].

As the benefit of warfarin following mitral valve repair or tissue mitral valve replacement is questionable it is reasonable to suggest an alternative agent for thromboprophylaxis. With potential application for patients with warfarin resistance [10] and offering the lack of need for blood testing in a financially constrained health service, the use of NOACs resonates.

Apixiban, an oral direct factor Xa inhibitor, is approved for the prevention of stroke and systemic embolism in patients with nonvalvular atrial fibrillation. The Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) trial included a substantial number of patients with valvular heart disease and only excluded patients with clinically significant mitral stenosis or mechanical prosthetic heart valves. Of the 18,201 patients enrolled in ARISTOTLE, 4,808 (26.4%) had a history of moderate or severe valvular heart disease or previous valve surgery. Patients with valvular heart disease had higher rates of stroke or systemic embolism and bleeding than patients without valvular heart disease. There was no evidence of a differential effect of apixaban over warfarin in patients with and without valvular heart disease in reducing stroke and systemic embolism, causing less major bleeding, and reducing mortality [11]. Apixiban has also been shown to be of benefit in a number of settings including acute venous thromboembolism [12] and recurrent venous thromembolism [13] without increasing the rate of major bleeding. These studies raise the possibility of a potential alternative to warfarin.

NOACs have been designed to overcome warfarin limitations by administering in fixed doses and not requiring routine coagulation monitoring. However, the absence of laboratory monitoring makes adherence more difficult to assess. Conversely in those requiring urgent surgery or with life threatening bleeding the lack of an antidote, to reverse NOAC effect, has raised concerns [14]. Recently, Idarucizamab [15] has received FDA approval for the reversal of dabigatran and promisingly antidotes for oral factor Xa inhibitors are under development [16]. Cost considerations do exist, though cheaper than LMWH, the NOACs are more expensive than warfarin.

Appropriate patient selection is critical for optimal use of the NOACs. NOACs, particularly dabigatran, should be used with caution in patients with a creatinine clearance of less than 30mL/min, and NOACs should not be used in those with a creatinine clearance of below 15mL/min. In patients started on a NOAC, follow-up is needed to monitor renal function, particularly in those with impaired kidney function at baseline, and to ensure adherence [17]. Not all patients are candidates for NOACs. Contraindications include those with mechanical heart valves [6], pregnant women and nursing mothers due to the potential for NOACs, as small molecules, to pass through the placenta or to be excreted in breast milk.

A review of the current literature and international guidelines would suggest that the short term use of NOACs, for example Apixiban, following mitral valve repair would be safe to use, potentially more efficacious than warfarin in thromboprophylaxis and could reduce bleeding complications, hospital length of stay, 30 day mortality, overall costs and improve long term survival. To this end we would recommend this to be the focus of future research endeavours.

References

1. Blue Book online. SCTS GB and Ireland. 2013
2. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: executive summary. A report of the American College of Cardiology/American Heart Association task force on practice guidelines. Circulation 2014; 129: 2440-2492.
3. Salem DN, Stein PD, Al-Ahmad A, et al. Antithrombotic therapy in valvular heart disease – native and prosthetic. The seventh ACCP conference on antithrombotic and thrombolytic therapy. Chest 2004; 126: 457-482.
4. Farr AM, Jing Y, Johnston S, et al. Comparison of hospital length of stay between hospitalized non-valvular atrial fibrillation patients treated with either apixaban or warfarin. Hosp Pract. 2015; 43: 172-179.
5. Schomburg JL, Medina EM, Lahti MT, et al. Dabigatran versus warfarin after mechanical mitral valve replacement in the swine model. J Invest Surg. 2012; 25: 3.
6. Eikelboom JW, Connolly SJ, Brueckmann M, et al. RE-ALIGN Investigators. Dabigatran versus warfarin in patients with mechanical heart valves. N Engl J Med. 2013; 369: 1206-1214.
7. Thourani VH, Gunter RL, Hurst S, et al. Postoperative warfarin following mitral valve repair or bioprosthetic valve

replacement. J Heart Valve Dis. 2013; 22: 716-723.

8. Schwann TA, Engoren M, Bonnell M, et al. Mitral valve repair and bioprosthetic replacement without postoperative anticoagulation does not increase the risk of stroke or mortality. Eur J Cardiothorac Surg. 2013; 44: 24-31.

9. Colli A, D'Amico R, Mestres CA, et al. Is early antithrombotic therapy necessary after tissue mitral valve replacement? J Heart Valve Dis. 2010; 19: 405-411.

10. Yasar AS, Balbay Y, Maden O, et al. Early mechanical mitral valve thrombosis in a patient with warfarin resistance. J Heart Valve Dis. 2007; 16: 200-202.

11. Avezum A, Lopes RD, Schulte PJ, et al. Apixaban in Comparison With Warfarin in Patients With Atrial Fibrillation and Valvular Heart Disease: Findings From the Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation (ARISTOTLE) Trial. Circulation. 2015; 132: 624-632.

12. Agnelli G, Buller HR, Cohen A, et al. for the AMPLIFY Investigators. Oral apixiban for the treatment of acute venous thromboembolism. N Engl J Med 2013; 369: 799-808.

13. Agnelli G, Buller HR, Cohen A, et al. for the AMPLIFY-EXT Investigators. Apixiban for extended treatment of venous thromboembolism. N Eng J Med 2013; 368: 699-708.

14. Reiffel JA, Weitz JI, Reilly P, et al. Cardiac Safety Research Consortium presenters and participants. NOAC monitoring, reversal agents, and post-approval safety and effectiveness evaluation: A cardiac safety research consortium think tank. Am Heart J. 2016; 177: 74-86.

15. Eikelboom JW, Quinlan DJ, van Ryn J, et al. Idarucizumab: The Antidote for Reversal of Dabigatran 2015; 132: 2412-2422.

16. Lu G, Deguzman FR, Hollenbach SJ, et al. A specific antidote for reversal of anticoagulation by direct and indirect inhibitors of coagulation factor Xa. Nat Med 2013; 19:446-51.

17. Weitz JI1. Expanding use of new oral anticoagulants. F1000Prime Rep. 2014; 6:93.