Non-vitamin K antagonist oral anticoagulants in adult congenital heart disease: a single-center study

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Introduction: Adults with congenital heart disease (ACHD) are at an increased risk for thromboembolic events and atrial arrhythmias are common in this population. Non-vitamin K anatagonist oral anticoagulants (NOACs) prescription is increasing, however data on efficacy and safety in ACHD is unclear, particularly in patients (P) with complex CHD. The aim of the study was to review the use of NOACs in various types of ACHD and assess its safety and efficacy.

Methods: Evaluation of consecutive ACHD P started on NOAC therapy from 2014 to 2020. P were followed-up for bleeding or thromboembolic events and mortality. CHA2DS2-VASc and HASBLED scores were calculated and risk factors for bleeding were identified.

Results: 93 ACHD P were included, mean age 52±15 years, 58% female, 44% with complex CHD (3.2% with Fontan circulation), with diagnosis of: 22.2% atrial septal defect, 20% tetralogy of Fallot, 11.1% transposition of the great arteries, 10% Ebstein's anomaly, 8.9% ventricular septal defect, 7.8% pulmonary stenosis, 5.6% ductus arteriosus, 4.4% AV septal defect, 3.4% univentricular heart, 3.4% coarctation of aorta, 2.2% supra-aortic stenosis and 1% with Uhl disease.

Most P were anticoagulated with rivaroxaban (43%), followed by edoxaban (24%), apixaban (20%), and dabigatran (13%). The indications for anticoagulation were: atrial arrhythmias (81%), pulmonary embolism (PE) (6.3%), atrial thrombi (4.3%), thromboprophylaxis in Fontan circulation (3.2%), deep vein thrombosis (3.2%) and stroke (2%). 66% of P had a CHA2DS2-VASc score $\geq$2 and 82% HASBLED score $\leq$2.

In a mean follow-up of 41±21 months (400.4 patient-years), there were embolic events in 2P (1 splenic infarction and 1 PE) albeit both were in the context of oral anticoagulation interruption. The cardiovascular mortality was 2% and allcause mortality 5%, however with no relation to thrombosis or bleeding events.

6 P (6.5%) suffered a minor and 3 P (3.2%) suffered a major bleeding, a median time of 12 (IQR 15) months after starting NOAC therapy. The annual risk for bleeding was 2.2%/patient/year. P with bleeding events showed no significant difference regarding age (55±16 vs 52±15 years, p=0.587), gender (13% female vs 5.1% male, p=0.295) or CHD type (p=0.582). 8.6% of P required dose reduction, mostly for bleeding (3.2%) or renal impairment (2.2%).

Renal disease was a strong risk factor for major bleeding (HR 14.6 [95% CI 1.23–73.6], p=0.033 and multivariate analysis showed that an increased HASBLED score was an independent predictor of minor (adjusted HR 3.44 [95% CI 1.13–10.52], p=0.030) and major (adjusted HR 5.29 [95% CI 1.14–24.45], p=0.033) bleeding complications.

Conclusion: Anticoagulation with NOACs is a safe and effective option for selected ACHD P, although bleeding complications were not negligible, particularly in P with renal disease. Larger scale research studies are required, especially regarding complex CHD such as P with Fontan circulation.