Editorial

‘Between a rock and a couple of hard places’

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DOI: 10.5830/CVJA-2023-001

The management of the pregnant patient with a mechanical prosthetic valve remains a challenging clinical problem, even with recent advances in valve technology, diagnostic and therapeutic strategies. The WHO classification for the assessment of pregnancy risk gives it a class III, which is a significant risk to mother and foetus.

The recent ROPAC registry data showed an event-free pregnancy with a resultant live birth in 58% of women with mechanical valves compared to 78% in women with cardiac disease and no valve intervention.[1] The morbidity and mortality rates for both mother and foetus relate largely to complications stemming from the use of anticoagulation and bleeding, and thromboembolic events.

Jenneker *et al*. (page 322) provides a comprehensive overview of the current literature and some of the recommendations put forward by the two major international guideline bodies, the American Heart Association/American College of Cardiology (AHA/ACC) and the European Society of Cardiology (ESC). They go on to make a recommendation/algorithm for assessment that is used in their local setting, Inkosi Albert Sisulu Central Hospital, in Durban, KwaZulu-Natal.

Rightfully, the importance of pre-conception counselling and planning is highlighted, together with the proposal of shared decision-making, consisting of a robust and honest discussion of risks and benefits of each regimen with the prospective mother.

The three most frequently used strategies are (note, all strategies, swop over to a heparin-based regimen at 36/37 weeks of gestation):

- Warfarin throughout all three trimesters: this regimen is only really to be considered if the required dose of warfarin is to remain within the therapeutic international normalised ratio (INR) range of < 5 mg per day. This is the one considered to have the lowest rate of maternal thrombotic complications, but with a higher rate of foetal miscarriage. The foetal complications are dose dependent (AHA /ACC[2] class IIa B/ ESC[3] class IIa C recommendation).
- Low-molecular-weight heparin (LMWH) or intravenous (IV) unfractionated heparin (UFH) in the first trimester with switching to warfarin in the second and third trimesters (AHA/ACC[2] class IIa B/ESC[3] class IIa C).
- LMWH or UFH throughout all three trimesters: although this regimen poses the lowest risk to the foetus, the rate of maternal thrombotic complications can be as high as 33% (AHA/ACC[2] class IIb B/ESC[3] class IIb C). Unless there is a particularly valid reason with a high risk of warfarin complications, this option is not ideal.

The data supporting these recommendations are from observational studies and meta-analyses, all of which are wrought with problems of heterogeneity, making direct comparisons between different treatment regimens extremely difficult. The recommendations are therefore frequently noted as level of evidence C (expert opinion or consensus based).[2,3]

When deciding on a particular strategy, the following considerations are to be taken into account in determining the risk–benefit ratio to both the mother and foetus. Some of these challenges are particularly amplified in the South African context and include:

- Adequate anticoagulation with vitamin K antagonists (VKA) (warfarin) and time in therapeutic range (TTR). Numerous local observational studies have noted the difficulty in maintaining TTR in South Africa. A recent retrospective, observational study conducted at two large INR clinics in the Western Cape showed that the mean TTR was 47%, with a mere 25.1% of patients achieving good INR control.[4] Given the increased thrombotic risk in pregnancy, it is imperative to have facilities available for effective testing and more frequent INR testing compared to the non-pregnant state.
- Staffing, bed availability and IV access. The strategy of IV UFH poses a number of challenges. Patient admission and IV access for a number of weeks is required. The risks of infection from drip sites and the added burden of continued intensive clinical care (doctor and nursing care) in resource-poor environments make this a less attractive option.
- The availability of factor X levels timeously and regularly is a prerequisite to LMWH use. Both the AHA/ACC[2] and the ESC[3] give the use of LMWH without regular factor Xa monitoring a class III recommendation, which means it could constitute harm. During pregnancy, the faster renal clearance may result in lower levels. There is no true consensus on the frequency of monitoring levels. The ESC recommends weekly levels whereas the ACC/AHA makes no time recommendation. A big concern remains that although the use of LMWH has gained widespread popularity in our clinical environment, with a favourable risk-factor profile, there is a distinct paucity of availability and resources for factor Xa level monitoring.
- What is a definite ‘NO’? It is important to note that there is no place for the use of aspirin on its own. The addition of aspirin to VKA, although acceptable by the AHA/ACC (class IIb), is not recommended by the ESC, who raise the concern of limited data supporting benefit but with an increased risk of bleeding complications. Given the difficulty of access to emergency care in South Africa, this is to be used with extreme caution.

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The use of a direct-acting oral anticoagulants for anticoagulation of mechanical prosthetic valves is contra-indicated. A landmark phase 2 study of dabigatran versus warfarin in 252 patients with mechanical prosthetic mitral or aortic valves was stopped early due to excess thromboembolic and bleeding complications in the dabigatran arm. For this reason, novel oral anticoagulants are not recommended as an alternative to warfarin in mechanical prosthetic valves.[5]

The clinical decision-making in the pregnant patient with a mechanical prosthetic valve remains challenging. Each case is to be considered on an individual level, with consultation and buy-in from both the patient and clinician in a suitably resourced environment.

References

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Systemic corticosteroids a potential treatment for heart failure: Spanish study

Intravenous corticosteroids did not hurt people with acute heart failure (HF), and could be a potential treatment for those with more inflammation, according to a hypothesis-generating study based on Spain's Epidemiology of Acute Heart Failure in the Emergency Departments (EAHFE) registry.

Whereas acute HF patients receiving corticosteroid therapy in the emergency department (ED) saw no improvement in all-cause mortality at 30 days, there was a trend of more favourable point estimates for survival in those with elevated C-reactive protein (CRP) levels.

Medpage Today reports that potential for an association between corticosteroid therapy and better outcomes was observed among people with the most inflammation, defined as CRP > 40 mg/l – findings that were nevertheless statistically non-significant based on the available data:

- All-cause mortality at 30 days: 11.8% with corticosteroids vs 19.4% without (HR 0.56, 95% CI 0.20–1.55)
- Post-discharge ED revisit at 30 days: 42.3 vs 43.8% (HR 0.92, 95% CI 0.52–1.62)
- In-hospital all-cause mortality: 8.8 vs 13.4% (HR 0.61, 95% CI 0.17–2.14).

'The present analysis suggests that corticosteroids might have the potential to improve outcomes in acute HF patients with inflammatory activation,' wrote study authors Dr Gad Cotter of Momentum Research in Chapel Hill, North Carolina, and colleagues in *ESC Heart Failure*.

Inflammation has been linked to HF, though anti-inflammatory therapies have failed in chronic HF, the researchers said, citing the failures of infliximab and etanercept in the older ATTACH and RENEWAL studies, respectively.

'Although corticosteroids have been classically viewed as anti-inflammatory agents, they can cause sodium and water retention, potentially leading to worsening of HF. However, it has been reported that the administration of corticosteroids to patients with severe acute HF produced a potent diuretic effect and improved fluid overload and renal function,' said the investigators.

'Added to previous studies of potentially improved diuresis, the [present] results suggest that future randomised trials on anti-inflammatory therapy are needed to assess potential benefit in patients with the highest degree of inflammation,' Cotter and co-authors said.

EAHFE was a registry that included 45 Spanish EDs from 2007 to 2018. For the present analysis, the investigators included 1 109 people (median age of 81.2 years, 45% of whom were men) with NT-proBNP > 300 pg/ml and CRP > 5 mg/l in the ED. The team excluded people taking chronic systemic corticosteroids and those who had had acute HF triggered by an infection.

Of the study cohort, 10.9% of patients received at least one IV bolus corticosteroid treatment. This group tended to have higher systolic blood pressure, lower room air oxygen saturation, and were more likely to have cerebrovascular disease, peripheral artery disease, chronic obstructive pulmonary disease and dementia. Their index acute HF episode was more commonly triggered by hypertensive crisis, compared with non-corticosteroid users.

The retrospective study was limited by the potential for confounding, a relatively small sample of corticosteroid users, and a lack of details regarding dose and duration of treatment in the database, Cotter and colleagues acknowledged.

Source: *MedicalBrief* 2022