Prophylaxis of Infective Endocarditis in Dentistry: Analysis of the Situation After Almost a Decade of Clinical Practice Guidelines. Response

Análisis de la situación de la profilaxis de la endocarditis infecciosa en odontología tras casi una década de guías de práctica clínica. Respuesta

To the Editor,

We appreciate the interest and comments of Silva Conde et al. regarding our article.[1] In fact, they published an article in 2012 in *Revista Española de Cardiología* on how closely dentists followed the recommendations on infectious endocarditis (IE) prophylaxis.[2] Their results were similar to those of our study, carried out 6 years later.[1] Indeed, we cited their study in a previous article in which we compared IE prophylaxis approaches in different healthcare professionals (dentists, primary care physicians, and cardiologists) in Cordoba.[3]

Prophylaxis should be avoided in patients with no indication (those with atrial fibrillation, stents, or coronary artery bypass grafting). However, in other situations such as native valve disease or mitral prolapse, we believe that caution should be exercised, as several very recent studies[4,5] indicate a high risk of IE in these conditions. In one Spanish study,[5] the incidence of *Streptococcus viridans* IE was higher in patients with a bicuspid aortic valve and mitral prolapse than in those with conditions considered moderate or high risk. Another study also reported a high incidence of IE after invasive procedures (transfusions, coronary surgery, bronchoscopy, dialysis),[4] which contradicts current recommendations.

In conclusion, we should avoid misuse of antibiotics in situations that are clearly no-risk, but exercise caution in light of the new evidence that the risk of IE in moderate-risk cardiac disease (essentially valve disease and congenital heart disease) may be higher than previously thought.

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Use of Oral Anticoagulation for Patients With Atrial Fibrillation and End-stage Renal Disease: What Is Needed Nowadays?

Anticoagulación oral en pacientes con fibrilación auricular e insuficiencia renal terminal: ¿qué es lo más apropiado?

To the Editor,

Patients with atrial fibrillation (AF) and end-stage renal disease (ESRD) are at greater risk for stroke. However, it remains controversial whether anticoagulation is of benefit in these patients due to the high bleeding risk. In *Revista Española de Cardiología*, Mahmood and Lip published an article on anticoagulation therapy in AF patients with ESRD.[1] Some points should be further discussed.

The CHA_2DS_2-VAS_C score is broadly used for predicting the risk of ischemic stroke in patients with AF. However, it has not been validated in patients with ESRD and AF. Other proposed risk score algorithms that include chronic kidney disease in the model, such as the R_2CHADS_2 score, have shown no added value.[2] Recently, Chao et al.[3] reported that the CHA_2DS_2-VAS_C score was useful in predicting ischemic stroke in AF patients with ESRD. However, the authors suggested that anticoagulant therapy may be suitable for these patients when CHA_2DS_2-VAS_C score ≥ 6, due to the greater risk of bleeding. Based on these studies, there is a need to develop a specific scoring system for anticoagulation in AF patients with ESRD. If the CHA_2DS_2-VAS_C score is used, the cutpoint for recommendation of anticoagulation in ESRD should be further evaluated.

The article by Mahmood and Lip states that there is more evidence supporting warfarin for its use in AF patients with ESRD. However, observational studies have shown that the use of warfarin was not associated with a reduction in stroke risk or mortality in AF patients with ESRD, but with greater bleeding risk.[4] The lack of data on quality of warfarin anticoagulation (eg, time in therapeutic range) may be a potential confounder in such observational studies. However, in real-world clinical practice, the target of time in therapeutic range is hard to achieve in patients with ESRD. Currently, given the lack of clear evidence, the European Heart Rhythm Association does not provide any recommendations,[5] whereas the Kidney Disease: Improving Global Outcomes (KDIGO) consensus[6] caution against the routine use of any oral anticoagulation therapy in AF patients with ESRD. Given the lack of randomized control trials, anticoagulation therapy (using warfarin or any nonvitamin K antagonist oral anticoagulants) for AF patients with ESRD is still a matter of debate.

Nowadays, apixaban is approved for use in AF patients with ESRD by the Food and Drug Administration, but not in other contexts. A retrospective cohort study showed that there was no difference in the risks of stroke between apixaban and warfarin, but apixaban was associated with a lower risk of major bleeding.[7] As mentioned in the article by Mahmood and Lip, 2 ongoing randomized control trials,[4] the RENAL-AF and AXADIA study, are evaluating the safety and efficacy of apixaban vs warfarin or phenprocoumon, respectively.

However, none of these trials included a control group with no oral anticoagulation, which is needed to access whether anticoagulation therapy is of benefit in these patients. It is important to wait for the results of the Oral Anticoagulation in Haemodialysis Patients (AVKDIAL) study, which will compare the hemorrhagic and thrombotic risks of vitamin K antagonists with no anticoagulation in hemodialysis patients with AF.

In conclusion, considering the strong uncertainty and conflicting results about anticoagulation in AF patients with ESRD, we advocate the following: *a)* the development of specific scoring systems for the prediction of stroke and bleeding; and *b)* the need for randomized control trials evaluating the risk-to-benefit ratio of anticoagulation compared with placebo instead of comparing various oral anticoagulants in this population.

CONFLICTS OF INTEREST

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Use of Oral Anticoagulation in Patients With Atrial Fibrillation and End-stage Renal Disease: What Is Needed Nowadays? Response

Anticoagulación oral en pacientes con fibrilación auricular e insuficiencia renal terminal: ¿qué es lo más apropiado? Respuesta

To the Editor,

We thank Huang et al. for their interest in our review.[1] Dialysis patients in all CHA_2DS_2-VASc risk strata have a higher risk of stroke,[2] but this validated score still appears to be the most accurate in predicting ischemic stroke and warfarin may be considered especially in high risk patients.[3] This must be balanced with bleeding risk factors, but the net benefit is generally positive, especially with well managed warfarin.

Atrial fibrillation patients with end-stage renal disease (ESRD) have been excluded from trials of nonvitamin K antagonist oral anticoagulants and thus any recommendations from regulatory authorities are not supported by trial evidence. Warfarin may reduce the risk of ischemic stroke, although this is controversial,[4] since major bleeding is frequent in ESRD. A major caveat is that previous studies variably consider the quality of anticoagulation control, as reflected by time in therapeutic range, and a high therapeutic range is associated with good outcomes in ESRD.

Hence, an individualized patient approach is required, although the benefits of stroke and mortality reduction usually outweigh the risks of serious bleeds.[5] For instance, if a stable ESRD patient can maintain a therapeutic range $\geq$ 70%–which is hard to achieve but not impossible–and has significant risk factors for stroke (CHA_2DS_2-VASc $\geq$ 2) and a low bleeding risk (HAS-BLED score $<$ 3), warfarin may be considered after an in-depth risk/benefit discussion.[6] Patients on peritoneal dialysis and hemodialysis should be analyzed separately because of the potential differences in drug removal in these renal replacement modalities.

CONFLICTS OF INTEREST

G.Y.H. Lip is a consultant for Bayer/Janssen, BMS/Pfizer, Medtronic, Boehringer Ingelheim, Novartis, Verseon and Daiichi-Sankyo and a speaker for Bayer, BMS/Pfizer, Medtronic, Boehringer Ingelheim, and Daiichi-Sankyo; he declares not directly receiving any personal fees derived from these activities.

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