International Journal of Cardiovascular Sciences. 2019;32(5):435-437

EDITORIAL

Rheumatic Heart Disease - How are We in 2019, Have We Evolved?

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Acute rheumatic fever (ARF) is the result of an autoimmune response to pharyngitis caused by infection with the sole member of the group A *Streptococcus* (GAS), *Streptococcus pyogenes*. ARF leads to a condition characterized by various combinations of joint pain and swelling, cardiac-valve regurgitation with the potential for secondary heart failure, chorea, skin and subcutaneous manifestations, and fever.

Rheumatic heart disease (RHD) is a disease of poverty that affects children and working-age adults. The global economic impact of early death from RHD is still very high. In Brazil, the average cost of RHD-related damage is around 89 million Brazilian reals (close to US$ 28 million) a year. Information from the Brazilian Unified National Health System database (DATASUS) indicates a cardiac mortality rate of about 7.9% from chronic rheumatic fever (RF).[1]

RHD control programs were successfully implemented in some low- and middle-income countries during the latter part of the 20th century, prompting the World Health Organization (WHO) and others to downscale their RF (rheumatic fever)/RHD activities by the early 2000s.[2]

Cardiac valves have been studied extensively, especially the mitral valve. There is an evident inflammatory process from the VCAM-1 expression on the valve surface endothelium. Further, CD4+ and CD8+ T lymphocytes localize over the valve endothelium as well as in the immediate subendothelial layer. The T lymphocytes (both CD4+ and CD8+) adhere to and extravasate through the valve endothelium, and neovascularization of the diseased valves is associated with the same phenomenon of T lymphocytes adhering to and extravasating through the endothelium of the newly formed blood vessels.[3]

Studies have suggested that virulent clones of GAS organisms present in the community have emerged, causing RF. Proteomic/genomic studies on organisms (such as M1, M3, or M18) obtained from RF epidemics or RF patients, compared with the same M types not causing RF are necessary. These studies would help to identify proteomic/genomic differences (in particular, the antigenic proteins/glycoproteins) between the virulent clone and the non-virulent organism (not causing RF).[4,5]

Long-term morbidity and mortality from ARF are mainly caused by RHD, which, in turn, is mostly a function of the extent of the acute cardiac involvement of ARF and the incidence of subsequent episodes of recurrent ARF.[5]

In the study "Evolutive Study of Rheumatic Carditis Cases Treated with Corticosteroids in a Public Hospital", 93 cases of rheumatic carditis in patients under 18 years old treated with corticosteroids were evaluated in the period of 2000-2015.[6] In the study, 93.5% developed moderate or severe carditis, and mitral regurgitation was detected in 100% of the sample. The progress of the cases was favorable in 71%. Comparisons of the initial with posterior valve lesions regarding the use of corticoids showed statistically significant results ($p < 0.001$). A difference between the ejection fraction medians was observed ($p = 0.048$). Surgery was performed in 23.7% of patients – mitral, aortic and/or tricuspid valve repair or replacement. Mortality rate was 5.4%.

Keywords

Rheumatic heart disease; chronic valvular heart disease; control programs; corticosteroids; echocardiography.

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DOI: 10.5935/2359-4802.20190041

The real benefit of using corticosteroid therapy for ARF remains controversial. Corticosteroids reduce the inflammatory markers of ARF, especially fever and acute phase reactants, and have been widely used in severe acute carditis with heart failure, even though there is little evidence showing that their superiority over usual strategies such as bed rest, fluid restriction and cardiac medications.[5] Most articles do not show evidence for improvements in the severity of chronic valvular heart disease with corticosteroids one year after ARF.

There is a strong argument for the need of a multicenter randomized clinical trial of corticosteroids versus placebo in ARF, using echocardiographic endpoints for acute carditis (6 weeks) and chronic valvular disease (6 months to 1 year). Such a study would need to be powered to account for the natural improvement of carditis after the acute phase but would provide an evidence-based approach to corticosteroid therapy for active rheumatic carditis. Corticosteroids have been frequently used to treat severe carditis around the world. Similar multicenter studies of other immunomodulators, informed by an expanded understanding of ARF immunopathogenesis, could eventually be considered, but there is no role for small, underpowered studies.[7]

Cardiac surgery is usually deferred until the acute inflammation is subsided so that the repair is technically easier, and a more durable repair can be achieved. The philosophy of cardiac surgery in the young is to repair rather than to replace the mitral valve.[8] A retrospective report of 81 patients aged 3–19 years comparing mitral valve repair versus replacement showed not only a lower morbidity (less endocarditis and no thromboembolism), but also that the need for reoperation was not increased in the repair compared with the replacement group.[9]

Large-scale screening programs aimed at disease control and not only at defining RHD epidemiology are required. Economic and cost-effectiveness evaluation could then be calculated. In the meantime, mathematical models using existing data could allow the prediction of the effectiveness of these programs. Realistic estimates of disease burden should add impetus to producing an effective GAS vaccine. Moreover, echocardiography would have an important role in trials assessing[10] the safety and the efficacy of GAS vaccines, and in the RHD epidemiology for targeting vaccine delivery.[11]

Despite the disappearance of RHD in developed countries, the disease is still unstoppable in poor and developing countries. The recent REMEDY study documented high rates of disability and premature death in African and Asian countries.[12] In 2015, a civil society movement, the RHD Action, was launched to raise awareness and support countries. Broader societal engagement in advocacy efforts, with the involvement of citizens' groups and nongovernmental organizations, is needed for the success of the ARF and RHD control.[2] In May of 2018, the World Health Assembly adopted a resolution to reinvigorate global and national RF/RHD prevention and control efforts.

An arduous and constant work in the prevention of RHD must continue and gain strength. We take advantage of this editorial to thank the commitment and dedication of Professor Bongani Mayosi in RF eradication, Rachel Snitkowisk, who developed RF prevention projects that have spread all over Brazil and Cleonice C Mota for all her dedication in this area, along with several others in our country.[13]

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