Statins for aortic valve stenosis

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ABSTRACT

BACKGROUND: Aortic valve stenosis is the most common type of valvular heart disease in the USA and Europe. Aortic valve stenosis is considered similar to atherosclerotic disease. Some studies have evaluated statins for aortic valve stenosis.

OBJECTIVES: To evaluate the effectiveness and safety of statins in aortic valve stenosis.

METHODS:

Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, Embase, LILACS - IBECS, Web of Science and CINAHL Plus. These databases were searched from their inception to 24 November 2015. We also searched trials in registers for ongoing trials. We used no language restrictions.

Selection criteria: Randomized controlled clinical trials (RCTs) comparing statins alone or in association with other systemic drugs to reduce cholesterol levels versus placebo or usual care.

Data collection and analysis: Primary outcomes were severity of aortic valve stenosis (evaluated by echocardiographic criteria: mean pressure gradient, valve area and aortic jet velocity), freedom from valve replacement and death from cardiovascular cause. Secondary outcomes were hospitalization for any reason, overall mortality, adverse events and patient quality of life.

Two review authors independently selected trials for inclusion, extracted data and assessed the risk of bias. The GRADE methodology was employed to assess the quality of result findings and the GRADE profiler (GRADEPRO) was used to import data from Review Manager 5.3 to create a 'Summary of findings' table.

MAIN RESULTS: We included four RCTs with 2360 participants comparing statins (1185 participants) with placebo (1175 participants). We found low-quality evidence for our primary outcome of severity of aortic valve stenosis, evaluated by mean pressure gradient (mean difference (MD) -0.54, 95% confidence interval (CI) -1.88 to 0.80; participants = 1935; studies = 2), valve area (MD -0.07, 95% CI -0.28 to 0.14; participants = 127; studies = 2), and aortic jet velocity (MD -0.06, 95% CI -0.26 to 0.14; participants = 155; study = 1). Moderate-quality evidence showed no effect on freedom from valve replacement with statins (risk ratio (RR) 0.93, 95% CI 0.81 to 1.06; participants = 2360; studies = 4), and no effect on muscle pain as an adverse event (RR 0.91, 95% CI 0.75 to 1.09; participants = 2204; studies = 3; moderate-quality evidence). Low- and very low-quality evidence showed uncertainty around the effect of statins on death from cardiovascular cause (RR 0.80, 95% CI 0.56 to 1.15; participants = 2297; studies = 3; low-quality evidence) and hospitalization for any reason (RR 0.84, 95% CI 0.39 to 1.84; participants = 155; study = 1; very low-quality evidence). None of the four included studies reported on overall mortality and patient quality of life.

AUTHORS CONCLUSIONS: Result findings showed uncertainty surrounding the effect of statins for aortic valve stenosis. The quality of evidence from the reported outcomes ranged from moderate to very low. These results give support to European and USA guidelines (2012 and 2014, respectively) that so far there is no clinical treatment option for aortic valve stenosis.

The full text of this review (English), the abstract (English and Polish) and the plain language summary (English and Polish) are available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009571.pub2/full

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COMMENTS

Life expectancy of the populations of Brazil and other countries around the world has increased over recent decades. Aging of the population increases the prevalence of aortic stenosis due to fibrotic calcification of valves. The risk factors for development of this etiology of aortic stenosis are the same factors that contribute towards accelerating atherosclerotic disease: dyslipidemia, systemic arterial hypertension, diabetes mellitus and smoking.[1] The classic model showing a strong association between hypercholesterolemia and aortic stenosis is homozygous familial hypercholesterolemia.[2] In this disease, in which patients present very high levels of LDL-cholesterol, aortic stenosis or supravalvular stenosis progresses very fast and is an important cause of morbidity and mortality among these patients. Treatment of dyslipidemia possibly also has the benefit of attenuating or slowing down the progression of aortic stenosis due to fibrotic calcification, given the similarity of the lesion to atherosclerotic disease.

This systematic review of randomized controlled clinical trials evaluated the efficacy and safety of statins on patients with aortic stenosis.[3] Only four clinical trials met the selection criteria and could be included. Overall, the quality of evidence was low to moderate and did not show any beneficial effect from statins on the development of aortic stenosis. This review demonstrates that, given the limitations of these studies regarding sample size and length of follow-up, the role of statins on the evolution of aortic stenosis may still be a field for research. It is in fact possible that statins will not modify the evolution of severe aortic stenosis because the mechanical and hemodynamic changes have already become established. On the other hand, they may play a role in preventing progression in patients with mild to moderate aortic stenosis caused by fibrotic calcification. A study on this profile of aortic stenosis, with adequate sample size and long follow-up may demonstrate some benefit from statins among patients with aortic stenosis. Thus, there are still some questions to be answered regarding this topic. However, it should be noted that many of the patients with aortic stenosis who would be candidates for inclusion in this type of study might already be candidates for statin treatment for prevention of coronary artery disease, given the similarity of the risk factors between these two entities.

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3. Thiago L, Tsuji SR, Nyong J, et al. Statins for aortic valve stenosis. Cochrane Database Syst Rev. 2016;9:CD009571. [Epub ahead of print]