**Use of ACE Inhibitors in Chronic Mitral Regurgitation in Pediatric Population**

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Mitral regurgitation (MR) is the most common form of valvular heart disease and can result from acquired heart diseases or congenital heart defects in the pediatric population. Primary MR involves abnormalities in the valve itself or its structures including the leaflets, chordae tendinae, papillary muscles or the annulus. Primary MR can result from AV canal defects, Rheumatic fever, mitral valve prolapse or other etiologies. Secondary MR, which is less common, involves abnormalities in the structures holding the valve together including left ventricular dilatation or stretching of the annulus which can happen as a result of hypertrophic cardiomyopathy, heart failure, or consequences of myocardial ischemia. Although primary MR is common in the pediatric population, there is no general consensus on its management including whether or not ACE inhibitors are therapeutic in the treatment of MR. In the literature, there is currently limited evidence of ACE inhibitors’ effect on mitral regurgitation in the pediatric population, however, it is common for off-label use of ACE inhibitors based on adult studies. The 2014 ACC/AHA Valvular Heart Disease Guidelines recommend against using ACEI/vasodilator medications in asymptomatic patients with chronic primary mitral regurgitation and only recommend its use in patients with symptomatic heart failure. Furthermore, mitral regurgitation is not without its side effects, as it can contribute to hypotension as well as renal failure. Due to the inconsistencies between the existing guidelines and clinical practice, a review of recent literature was performed to assess the role of ACE inhibitors in chronic mitral regurgitation in pediatric patients.

The PubMed MeSH database and SCOPUS were utilized for search terms “Enalapril”, “ACE inhibitor”, “Angiotensin-converting enzyme inhibitors” and “mitral regurgitation”. There was paucity of relevant studies and three studies were included in this analysis. The studies included were all randomized controlled trials, two of which were blinded and the third which was not blinded. Endpoint measurements which were compared between studies were LVDD (left ventricular end diastolic dimension), LVDS (left ventricular end systolic dimension), LV mass and RF (regurgitation fraction), which are echocardiographic measurements used to assess the degree of MR. Li et al. (2011) was a blinded, randomized controlled trial which evaluated pediatric patients with chronic, moderate to severe MR after AVSD repair. Unfortunately, due to poor design and small number of samples, the study was terminated. Although there were no definitive results, it was an important article to review as it involved multiple centers throughout the country and it provided many key lessons on how to improve future study designs. Rivera et al. (2003) was a blinded, randomized controlled trial looking at chronic MR caused by rheumatic disease. MR was measured by LVSD, LVDD and RF though LV mass was not evaluated. There was statistically significant improvement in LVSD though no significant change was seen in LVDD or RF. The study was found to be generalizable, applicable, but its limitations included the short length of time the patients were on the intervention (30 days). This study showed that at least one parameter (LVSD) as measure of MR could improve with 30days of ACE inhibitor therapy. Lastly, Mori et al. (2000) was a non-blinded, randomized controlled trial which studied patients with MR post AVSD and VSD repair. Though this study measured long-term outcomes (with average of 3.4years of treatment of ACE inhibitors) and reported that there was statistically significant improvements in LVDD, LVSD and LV mass, there were also major flaws in the study. The control patients were on other medications which could have affected the results. Additionally, patients in the control and case groups had different types of regurgitation, either MR or Aortic Regurgitation, but were still compared to each other which diminishes the integrity of the positive study results.

Based on the three studies, overall conclusion was that in pediatric patients with chronic MR, there is not yet enough evidence to support the use of ACEI in decreasing the severity of mitral regurgitation (RF) or improve LV size (LVDD, LVSD, LV mass), regardless of the etiology of MR (consequence of AVSD repair or rheumatic disease). It was clear that the pediatric population is still under-represented in cardiovascular clinical trials. In the future, it will be important to conduct prospective double-blind, randomized controlled trials with use of ACEI for long term outcomes at multiple centers. Future studies should address ECHO parameters which correlate with clinical outcomes, include larger study samples, different types of MR, side-effects of ACE inhibitors and have consistency of endpoint measurements.

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