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Short Communication

Where do we Stand in the Treatment of HCM in Children? The Role of Disopyramide and New Medications on the Horizon

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ABSTRACT

Pediatric Hypertrophic Cardiomyopathy (HCM) has a wide range of clinical manifestations. Left Ventricular Outflow Tract Obstruction (LVOTO) at rest is present in up to one-third of children with HCM, with a further 50%-60% of symptomatic children developing a gradient under exertion. Treatment options are limited and there is a relative lack of data on the pediatric population. Disopyramide is a sodium channel blocker with negative inotropic properties. This therapy effectively reduces LVOTO in adults with HCM and delays surgical interventions, but it is not licensed for use in children. This study aimed to review and analyze the influence of disopyramide over the pathophysiological, clinical, electrocardiographic and echocardiographic characteristics of patients with HCM in infancy, childhood, adolescence and adult age. While disopyramide remains a basis in the management of pediatric HCM, the advent of mavacamten and aficamten heralds a new era of potential advancements. These emerging therapies could significantly improve the quality of life and prognosis for young patients with HCM.

Keywords: HCM (Hypertrophic Cardiomyopathy); Children; Disopyramide; Mavacamten; Aficamten

DESCRIPTION

This study provides a comprehensive overview about the role of disopyramide in treating paediatric Hypertrophic Cardiomyopathy (HCM) [1].

HCM is the second most common cardiomyopathy in children and it represents the leading cause of sudden cardiac death in young adults [2].

In pediatric patients, up to one-third present with resting LVOT obstruction, while approximately 50%-60% develop a significant gradient during exertion. This variability underscores the need for personalized treatment approaches [3-5].

Although disopyramide is not officially approved for use in children, its application has shown promising results in managing symptoms, particularly in reducing the Left Ventricular Outflow Tract (LVOT) obstruction gradient.

Disopyramide was introduced in the 2014 ESC and 2011 AHA guidelines as a recommendation for treating HCM, primarily to reduce the risk of arrhythmias and to lower the LVOT gradient [6,7]. Its mechanism of action is based on its negative inotropic effect, reducing the velocity of blood flow during early systole and thus reducing Systolic Anterior Motion (SAM) of the mitral valve, which contributes to the obstruction.

Multicenter studies by Sherrid et al., demonstrated that disopyramide can reduce the LVOT gradient by 50%-60%, with concurrent symptom improvement. Similar results have been observed in pediatric patients, confirming the drug's effectiveness in improving quality of life and potentially reducing the need for surgical interventions [8].

One of the most common side effects of disopyramide is QT (Q wave, T wave) interval prolongation, which may increase the risk of ventricular arrhythmias. However, studies such as those by Coppini have debunked the severity of this risk, demonstrating that QT prolongation is generally proportional to the baseline value and does not induce significant arrhythmias [8]. Nonetheless, continuous monitoring of the QT interval is essential, particularly during the first months of treatment, to ensure patient safety. Another common side effect is the drug's anticholinergic effect, manifesting as dry mouth, constipation

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and ocular redness, which tend to subside over time [9]. In some pediatric patients, disopyramide was discontinued due to side effects, but the discontinuation rate was lower than in adults [10].

CONCLUSION

The benefits of using disopyramide are well known and in this article we aimed to analyze the efficacy of this drug in the pediatric population as well. Despite the effectiveness of disopyramide, new drugs like mavacamten and aficamten are emerging as potential therapeutic options for HCM. Mavacamten, a novel myosin inhibitor recently approved by the Food and Drug Administration (FDA), has shown significant efficacy in reducing the LVOT gradient and improving functional capacity in adult patients. Its efficacy appears to be dose-dependent and echocardiographic monitoring is critical to avoid adverse effects, such as a reduction in ejection fraction.

Aficamten, another myosin inhibitor, has demonstrated promising results with a faster therapeutic onset and fewer drug-drug interactions compared to mavacamten. However, both drugs require further clinical trials in pediatric populations to evaluate their safety and optimal dosing. The article provides a detailed view of disopyramide's role in managing pediatric HCM. While the drug has proven effective in symptoms management and reducing the LVOT gradient, emerging therapies such as mavacamten and aficamten offer potential advancements in the treatment landscape.

However, it remains essential to continue research and conduct pediatric-specific clinical trials to ensure the highest efficacy and safety of these treatments.

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