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**Antiarrhythmic Therapy for Atrial Septal Defect in Adults: A Mini-Review**

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**Abstract**

This review describes the current problem of treatment of atrial arrhythmias in adult patients with atrial septal defect (ASD), which is one of the most common adult congenital heart diseases (ACHD). Due to the development of surgical techniques and pharmacotherapy, the number of adult patients with ASD is steadily increasing, but the medical management of arrhythmias in this group remains poorly understood.

The authors analyzed the current literature from the PubMed database for the last 5 years using specific key queries. The limited number of publications directly addressing antiarrhythmic therapy in ASD should be noted, which is explained by the individualized approach to the treatment of this category of patients and the low level of evidence of existing studies.

The review considers different groups of antiarrhythmic drugs. Particular attention is paid to amiodarone, the drug with the best results in rhythm control strategy, whose use is limited by toxic effects in long-term use. Dronedarone and sotalol are considered as less toxic alternatives, although their efficacy requires further study. Beta-blockers show beneficial effects but are inadequate as monotherapy.

Class IC drugs (flecainide, propafenone) have limitations in use due to contraindications in structural heart disease, although they may be useful in the presence of an implantable cardioverter-defibrillator. Calcium channel antagonists may be used after evaluation of systemic ventricular function.

The importance of correcting heart failure is separately emphasized, as its presence and arrhythmogenic changes are interrelated. Therefore, a comprehensive approach to the treatment of arrhythmias in ASD is necessary and further studies are needed to improve the efficacy of therapeutic strategies.

**Introduction**

Adult congenital heart disease (ACHD) is becoming more and more common every year due to the steadily increasing life expectancy of such patients. The reasons for this phenomenon are obvious: the expansion of surgical options for the correction of malformations, including during infancy, as well as the use of pharmacotherapy [1]. One of the most common ACHD population outside the fact of surgical correction are septal defects, namely, atrial septal defect (ASD), which can be asymptomatic for a long time without significantly disturbing hemodynamics [2, 3]. While the expected results after surgical correction of such a malformation are predictable, the issues of pharmacotherapy of CHD complications, in particular arrhythmias, remain not fully resolved. It is noteworthy that surgical correction of CHD in childhood does not guarantee the absence of arrhythmias in the future [4, 5, 6, 7]. The existence of uncompensated arrhythmias against the background of CHD leads to the progression of other complications, such as heart failure, and increases the risk of thrombosis, consequently increasing disability and mortality in this group of patients [8, 9].

**Purpose of the review:** To summarize the most relevant information available in

databases on the use and efficacy of antiarrhythmic therapy for atrial septal defect.

## Materials and Methods

To compile this mini-review, literature was analyzed from the PubMed publications database for the last 5 years using the queries: “antiarrhythmic atrial septal defect in adults”, ‘beta blockers atrial septal defect in adults’, ‘rhythm control atrial septal defect in adults’, ‘amiodarone atrial septal defect in adults’ ‘propranolol atrial septal defect in adults’, ‘dronedaron atrial septal defect in adults’, ‘flecainide atrial septal defect in adults’. Also, to improve the accuracy of the query and increase the amount of information covered, “atrial septal defect in adults” was replaced by “adult congenital heart disease” in all of the above queries.

## Results and Discussion

The small number of published articles concerning antiarrhythmic therapy against the background of ASD is noteworthy: in total, only 22 articles were published during the studied period of time. If we consider the number of publications on antiarrhythmic therapy for CHD in general, their number increases to 283, but still remains small.

At the same time, the overwhelming majority of papers were not included in this analysis due to the inconsistency of the request and purpose of the study on the fundamentally important points: publications often referred to pediatric patients or patients with other cardiovascular pathology. Also, a significant part of the authors note the low level of evidence of these works, because the approach to pharmacotherapy of arrhythmias in patients with CHD is highly individualized and rarely fits into the generally accepted algorithms of arrhythmia treatment [10].

It is known that the very fact of surgical correction of the malformation acts as a substrate for future arrhythmias and increases the risk of their occurrence, since scar tissue is formed in the area of surgical intervention, the conductivity of which differs from that of intact cardiomyocytes [11, 12, 13].

The choice of drugs for the treatment of arrhythmias on the background of ASD in adult patients is extremely limited and, alas, is often not characterized by high efficacy [14].

Amiodarone is one of the most studied drugs for the treatment of arrhythmias in CHD, in particular, ASD. It shows some of the best results within the rhythm control strategy, but its toxicity during long-term administration is a significant limitation in its use [10, 11, 14, 15]. Dronedaron may be a less toxic alternative to amiodarone, but its efficacy in associated CHD requires further study [16]. Another class III antiarrhythmic drug, dofetilide, has similar but even scarcer data [14].

The role of beta-blockers in the treatment of arrhythmias against CHD background is defined as positive, but as monotherapy the efficacy is insufficient [14, 17]. So, sotalol shows relatively good results comparable to amiodarone within the rhythm control strategy, but studies show shorter-term retention of sinus rhythm. [11, 14, 18]. Relating the difference in the number of side effects from long-term use of these drugs, the advantage of sotalol is undeniable [10, 18].

The efficacy of IC class antiarrhythmic drugs is currently insufficiently studied, which shows the importance of continuing studies of this group of drugs in the treatment of arrhythmias in the background of ASD and other ACHD. Flecainide and propafenone are contraindicated in structural heart disease, which limits their use in a large number of patients with ACHD. Nevertheless, there are data on the potential benefit of these drugs against the background of an implantable cardioverter-defibrillator [11, 14].

Non-dihydropyridine calcium channel antagonists in general can be recommended for the control of arrhythmias against the background of ASD, but it is necessary to evaluate the systemic ventricular function beforehand. If its dysfunction is detected, this group of drugs is inapplicable due to decreased myocardial contractility [14]. No works devoted separately to calcium channel blockers for arrhythmias management against the background of ASD have been published for the last 5 years.

But not only antiarrhythmic therapy itself can positively affect the course of arrhythmia. A team of authors from Canada and France published a paper in 2021, where the relationship between rhythm disturbances and heart failure on the background of CHD was established: in addition to the fact that arrhythmias themselves can lead to heart failure, as well as uncorrected heart failure leads to the development of arrhythmias due to structural (fibrosis, dilatation of chambers, myocardial hypertrophy, for example) and electrical remodeling effects. This fact shows the indirect influence of successful heart failure therapy on the course and drug control of arrhythmias, and, consequently, its greater effectiveness [14, 19].

## Conclusion

ASD in adults is a common congenital heart defect often accompanied by atrial arrhythmias. Antiarrhythmic therapy for ASD is difficult due to lack of studies and low evidence. Amiodarone is the most studied, but its long-term use is limited by toxicity. The alternatives, dronedaron and sotalol, are promising but require further study and have a more short-term effect. Beta-blockers are effective but inadequate as monotherapy. Class IC drugs (flecainide, propafenone) and class IV drugs (nondihydropyridine calcium antagonists) are limited because of contraindications in structural heart

disease. Drug correction of heart failure is also important, as its course is interrelated with the occurrence of arrhythmias. To improve the efficacy of conservative antiarrhythmic therapy and to improve the prognosis of patients with ASD, a comprehensive approach and further studies are needed.

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