Atrial Fibrillation: Beyond Rate Control

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CME Activity

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Learning Objectives: On completion of this article, you should be able to (1) understand indications for pursuing a rhythm control approach; (2) describe the advantages and disadvantages of various antiarrhythmic drugs; and (3) identify common drug-drug interactions encountered in the primary care setting.

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Abstract

Atrial fibrillation is the most common cardiac dysrhythmia encountered in the primary care setting. Although a rate control strategy is pursued by physicians for the initial treatment of atrial fibrillation, the efficacy of a rhythm control approach is often undervalued despite offering effective treatment options. There are many pharmacological therapies available to patients, with drug choice often dictated by safety concerns (toxicities and proarrhythmic adverse effects) as well as patient characteristics and comorbidities. This article presents a simplified approach to understanding the rhythm control strategy, including the advantages and disadvantages of various antiarrhythmic drugs and common drug-drug interactions encountered in the primary care setting.

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Atrial fibrillation (AF) is the most common cardiac arrhythmia, with an estimated prevalence of 33.5 million individuals globally. It has reached epidemic proportions as the number of individuals affected with AF is expected to double in the next several decades because of an increasingly older population, underscoring the need for cost-effective outpatient management of AF.[1] Aside from addressing the role of thromboembolism prophylaxis when AF is detected, the primary care physician is faced with a wealth of treatment options that often fall into 2 broad overlapping categories: rate or rhythm control.

Rate control involves the use of negatively chronotropic drugs (eg, β-blockers or calcium

channel blockers) to reduce the rapid ventricular rate frequently found in AF. Conversely, rhythm control involves the use of pharmacological, electrical, or surgical cardioversion to convert AF to normal sinus rhythm. The aim of these options is to reduce symptoms, including dizziness, shortness of breath, and palpitations, as well as prevent complications, such as heart failure. Some studies have also suggested that catheter ablation (CA) of AF is associated with a decreased risk of stroke and mortality in patients with a high CHA_2DS_2-VASc score (congestive heart failure, hypertension, age ≥75 years [doubled], diabetes, stroke/transient ischemic attack/thromboembolism [doubled], vascular disease [prior myocardial infarction, peripheral artery disease, or aortic plaque], age 65-75 years, sex category [female]).[2]

Most commonly, a rate control strategy is pursued by physicians for the initial treatment of AF. Rhythm control is typically initiated when adequate rate control is not achieved or when patients have a high degree of symptoms despite achieving rate control. However, the efficacy of a rhythm control approach is often undervalued despite offering effective treatment options. It is important to understand the rhythm control approach, who the "ideal" patient is for this approach, and how to manage these patients, especially in the primary care setting. Additionally, modifiable risk factor management has emerged as an important pillar in AF treatment. Studies have found that improved management of both established and independent risk factors, including obesity, sleep apnea, hypertension, diabetes, excessive alcohol consumption, and a sedentary lifestyle, likely reduce AF burden. Furthermore, eating heart-healthy foods and incorporating dietary modifications may also reduce the risk of development of AF.[3]

PHARMACOLOGICAL THERAPY FOR AF

There are many pharmacological therapies available to patients, and drug choice is often dictated by safety concerns (toxicities and proarrhythmic adverse effects) as well as patient characteristics and comorbidities. For example, a patient with severe left ventricular (LV) hypertrophy, heart failure, and coronary artery disease would have more restricted options in terms of antiarrhythmic drug (AAD) therapy than a younger patient without these comorbidities. Furthermore, the presence of hepatic or renal dysfunction also plays an important role in drug consideration.

UPSTREAM THERAPY

Although this article largely focuses on antiarrhythmic therapy, it is worthwhile mentioning upstream therapies. Upstream therapy refers to the use of non-AADs that modify the atrial substrate— or target-specific mechanisms to prevent the occurrence or recurrence of AF. These drugs include angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, statins, or omega-3 polyunsaturated fatty acids. Animal studies have provided reasonable data on the benefit of upstream therapy, but translation to humans has been limited and largely insufficient to suggest widespread use of these agents for AF prevention.[4-6]

AAD THERAPY

Historically, AADs have been classified according to the Vaughan-Williams classification scheme by their mechanism of action: sodium channel blockers (class I), β-blockers (class II), potassium channel blockers (class III), and calcium channel blockers (class IV). Furthermore, class I drugs are subdivided into class IA, class IB, and class IC on the basis of drug affinity for sodium channels. After deciding on a rhythm approach, it is important to realize there is no "one size fits all" choice, and the selection of the AAD will depend on several factors (Figure 1). The following AADs are available for treatment of AF.

Class IA Agents

Quinidine, procainamide, and disopyramide are class IA antiarrhythmic agents. Historically, quinidine was one of the most commonly used antiarrhythmics for AF. Although effective in maintaining sinus rhythm, it has been surpassed by other AADs given its unfavorable safety profile, in particular the increased mortality associated with its use in patients with heart failure.[7] Although it is especially useful in the treatment of Brugada syndrome, worldwide supplies are unfortunately limited.[8,9] Disopyramide can also be used for AF rhythm control, but its use is rare. Like quinidine, disopyramide should be avoided in those with heart failure because of its negative inotropic effect. However, disopyramide in combination with

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