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Research Letter

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Allergy therapy for patients with a cardiac channelopathy: Do not withhold lifesaving treatments

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It is a widely held belief that patients with cardiac channelopathies have contraindications to potentially lifesaving allergy therapies. For long QT syndrome (LQTS) and catecholaminergic polymorphic ventricular tachycardia (CPVT), this stems both from prior guidelines that considered beta blockers (a cornerstone of LQTS and CPVT treatment) to be a contraindication to allergen immunotherapy (AIT) and from hesitancy to use epinephrine during anaphylaxis for fear of triggering an LQTS- or CPVT-related cardiac arrest. However, current allergy practice guidelines acknowledge that beta blockers can generally be continued during AIT.[1] For Brugada syndrome (BrS), concerns arise from the use of certain antihistamines (terfenadine, fexofenadine, diphenhydramine).[2] Here, we review the historical evidence behind this controversy and provide our experiences with allergy therapy in the Windland Smith Rice Genetic Heart Rhythm Clinic.

The concerns about beta blockers and allergies stem from fundamental pharmacology. Epinephrine is an α- and β-adrenergic receptor agonist that counteracts vasodilation and bronchoconstriction in anaphylaxis. In theory, β-adrenergic receptor antagonism would counteract these lifesaving mechanisms of epinephrine. Furthermore, unopposed α-agonism could theoretically lead to hypertensive crises. These effects of beta blockers were thought to contribute to treatment-resistant anaphylaxis.[3]

Prospective studies demonstrate that these beliefs are likely to be unfounded. In a prospective study on AIT,[4] of 3178 patients who received AIT for 1 year (68 with beta blockers), systemic reactions developed in 143 (4.6%) non–beta blocker patients and 1 (1.5%) taking beta blockers. In the latter, the reaction was easily reversed with epinephrine.[4] A 2019 meta-analysis of observational studies concluded that the quality of evidence suggesting that beta blockers worsen anaphylaxis is low.[5] This is now reflected in the 2023 American practice guidelines for anaphylaxis.[1]

In the last 25 years, we have treated 2333 patients with LQTS, CPVT, or BrS. From an allergy perspective, 794 patients (34%) had an allergy listed in their medical record, 233 (10%) of which were environmental or food allergies. Of these, 54 patients sought consultation with an allergist, and 17 had AIT prescribed or considered. Of these 17 patients, 15 had LQTS, 1 had CPVT, and 1 had BrS. Of the patients with LQTS, 9 (60%) were receiving beta blockers and had QTc of 449 ± 27 ms. Reasons for not taking beta blockers included intentional nontherapy for low-risk LQTS phenotype or beta blocker intolerance requiring left cardiac sympathetic denervation or implantable cardioverter-defibrillator. The 1 patient with CPVT was not taking a beta blocker because of intolerance and was treated with flecainide and left cardiac sympathetic denervation.

From an allergy therapy standpoint, 12 of 17 (71%, 11 LQTS and 1 CPVT) received antihistamines, 6 of 17 (35%, all LQTS) were using short-acting β-agonist inhalers, 4 of 17 (24%, all LQTS) had as-needed intramuscular epinephrine prescribed, and 8 of 17 (47%, 6 LQTS, 1 CPVT, and 1 BrS) underwent AIT. The patient with BrS was not receiving antihistamines. For the 11 patients with LQTS taking antihistamines, 5 were receiving fexofenadine, 3 cetirizine, 2 levocetirizine, and 1 loratadine. None were receiving diphenhydramine. Concerningly, there was 1 patient for whom a cardiologist had raised concerns of intramuscular epinephrine use despite the presence of life-threatening allergic reactions. Of those receiving AIT, 2 of 8 (25%) were taking beta blockers, with the most

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common reason for not receiving beta blockers being intentional nontherapy in a low-risk patient. None of the patients receiving AIT experienced adverse events from therapy.

Notably, for 9 of 17 (53%) of the patients for whom AIT was considered, the treating allergist decided not to proceed with AIT, including 2 cases in which beta-blocker therapy was specifically cited as the primary reason for AIT denial (before the 2023 American practice guidelines for anaphylaxis).[1]

Limitations of this study include the small sample size. None of our patients were using long-acting β-agonist inhalers. Only 2 patients undergoing AIT were receiving beta-blocker therapy. Whereas these numbers are small, they show that more than half of our patients taking beta blockers had indicated allergy therapies denied to them. Additional patients and family members raised concerns by their allergists about beta blockers and subcutaneous epinephrine use.

Allergy practice guidelines were updated only recently; it will undoubtedly take time for practitioners to adopt them. It is incumbent not only on allergists but also on heart rhythm specialists to be up to date with present guidelines. We need to advocate for a more nuanced approach with discussions of risks and benefits. In cardiac channelopathy patients with severe allergies, the stakes are high. Neither beta blockers that are needed to reduce the risk of sudden death nor lifesaving/life-changing allergy therapies should be withheld without appropriate consideration of the risks and benefits. It is also critical to dispel any qualms about using epinephrine for anaphylaxis. Epinephrine is the first-line therapy for anaphylaxis in patients taking beta blockers, and glucagon can be considered in patients taking beta blockers with treatment-refractory anaphylaxis.[1] Even in patients with cardiac channelopathies for whom catecholamines may be arrhythmogenic, epinephrine should be used as arrhythmias are irrelevant if the patient does not survive anaphylaxis.

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