Korean Circ J. 2024 Apr;54(4):187-188
https://doi.org/10.4070/kcj.2024.0067
pISSN 1738-5520·eISSN 1738-5555

kcj
Korean Circulation Journal

Editorial

Check for updates

Pleiotropic Effect of Dronedarone Beyond Antiarrhythmic Agent: Reduction of Hypertrophy

Jung-Joon Cha, MD, PhD

Department of Cardiology, Cardiovascular Center, Korea University Anam Hospital, Korea University College of Medicine, Seoul, Korea

▸ See the article "Dronedarone Attenuates Ang II-Induced Myocardial Hypertrophy Through Regulating SIRT1/FOXO3/PKIA Axis" in volume 54 on page 172.

OPEN ACCESS

Received: Feb 14, 2024
Accepted: Feb 26, 2024
Published online: Mar 20, 2024

Correspondence to
Jung-Joon Cha, MD, PhD
Department of Cardiology, Cardiovascular Center, Korea University Anam Hospital, Korea University College of Medicine, 73, Goryeodae-ro, Seongbuk-gu, Seoul 02841, Korea.
Email: joonletter@hanmail.net

Copyright © 2024. The Korean Society of Cardiology
This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (https://creativecommons.org/licenses/by-nc/4.0) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ORCID iDs
Jung-Joon Cha
https://orcid.org/0000-0002-8299-1877

Funding
The author received no financial support for the research, authorship, and/or publication of this article.

Conflict of Interest
The author has no financial conflicts of interest.

Data Sharing Statement
The data required to reproduce these findings cannot be shared as this is an editorial.

Dronedarone represents a significant advancement in managing atrial fibrillation and atrial flutter.[1)2)] Highlighted by the ATHENA (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter) trial, dronedarone has shown to enhance the combined outcome of mortality and cardiovascular hospitalizations in atrial fibrillation patients with comorbid risk factors.[3)] In addition, it effectively reduces the recurrence of atrial fibrillation and associated hospitalizations compared to placebo in nonpermanent atrial fibrillation cases.[1)4)] While not as effective as amiodarone in preventing recurrent atrial fibrillation, dronedarone serves as a viable option for managing nonpermanent atrial fibrillation through rhythm-control or rate-control strategies, without a clear superiority of one approach over the other.[1)4)] However, its use is discouraged in patients with permanent atrial fibrillation and those at high risk of cardiovascular complications or severe heart failure due to an increased mortality risk.[1)2)4)]

Dronedarone is classified as a class III antiarrhythmic medication, designed to treat and prevent atrial fibrillation and flutter by modulating the heart's electrical activity.[4)5)] Its primary mechanism involves the inhibition of potassium channels, leading to an extended action potential duration and refractory period in the atria, effectively preventing arrhythmias.[4)5)] Additionally, dronedarone decelerates the transmission of electrical impulses by blocking sodium channels and targets calcium channels to lessen heart muscle contractions. This dual action aids in heart rate regulation and deters rapid atrial rates.[5)] Beyond ion channel inhibition, dronedarone acts as a beta-adrenergic receptor blocker and a non-competitive antagonist at adrenergic receptors, reducing heart rate and neutralizing the sympathetic nervous system's arrhythmogenic effects.[5)6)] Furthermore, its potential anti-fibrotic effects could minimize heart tissue scarring, maintaining normal electrical pathways and reducing the risk of arrhythmias.[7)]

Chen et al.[8)] present a detailed study on the interaction between dronedarone and Angiotensin II within the context of myocardial hypertrophy leading to heart failure and cardiovascular diseases. The research aims to explore dronedarone's efficacy in counteracting myocardial hypertrophy induced by Angiotensin II, highlighting its ability to reduce cell size, suppress hypertrophy-associated genes including ANP, BNP, β-MHC in both H9C2 cells, and potentially enhance cell survival. Similar results were observed in and alleviated TAC surgery-induce myocardial hypertrophy of rats. A novel finding of the present study was its regulatory

Generated by ⁄miinkpress

The contents of the report are the author's own views and do not necessarily reflect the views of the *Korean Circulation Journal*.

impact on the SIRT1/FOXO3/PKIA axis, a crucial pathway in diminishing myocardial hypertrophy through its influence on cellular growth and apoptosis.[8] This suggests SIRT1 as a target gene for myocardial hypertrophy suppression by dronedarone, shedding light on its cardioprotective attributes. However, the relationship between PKIA and myocardial hypertrophy necessitates further evaluation due to contradicting results in prior studies.[9] Additionally, another research indicates that dronedarone's NFATc4/ERK/AKT pathway blockade, implicated in cardiac hypertrophy and remodeling, could correlate with reduced blood pressure.[10] In context, further research is necessary to explore how dronedarone's influence on certain pathways could improve clinical outcomes to understanding this relationship could lead to more effective treatments for cardiovascular conditions.

The authors also compared between dronedarone and amiodarone, particularly in terms of structural similarities and their ability to suppress hypertrophy-associated genes, underscores the significance of benzofuran derivatives in managing myocardial hypertrophy.[8] This analysis enhances our comprehension of dronedarone's utility in addressing cardiovascular conditions beyond atrial fibrillation, specifically its action against Angiotensin II -induced myocardial hypertrophy. Dronedarone is preferred over amiodarone for atrial fibrillation treatment, offering fewer thyroid side effects and cardiovascular benefits such as myocardial remodeling. Despite its safety advantages, careful monitoring for liver and lung damage is crucial.[1][2] In conclusion, Chen et al.'s research[8] highlights dronedarone's pleiotropic effect in reducing myocardial hypertrophy by influencing the SIRT1/FOXO3/PKIA axis, underscoring its significance in managing cardiovascular diseases and providing a strategic approach for treating both atrial fibrillation and myocardial hypertrophy.

REFERENCES

1. Kim D, Yang PS, Joung B. Optimal rhythm control strategy in patients with atrial fibrillation. *Korean Circ J* 2022;52:496-512. PUBMED | CROSSREF
2. Joglar JA, Chung MK, Armbruster AL, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2024;149:e1-156. PUBMED | CROSSREF
3. Hohnloser SH, Crijns HJ, van Eickels M, et al.; ATHENA Investigators. Effect of dronedarone on cardiovascular events in atrial fibrillation. *N Engl J Med* 2009;360:668-78. PUBMED | CROSSREF
4. Rosa GM, Bianco D, Parodi A, et al. Pharmacokinetic and pharmacodynamic profile of dronedarone, a new antiarrhythmic agent for the treatment of atrial fibrillation. *Expert Opin Drug Metab Toxicol* 2014;10:1751-64. PUBMED | CROSSREF
5. Iram F, Ali S, Ahmad A, Khan SA, Husain A. A review on dronedarone: Pharmacological, pharmacodynamic and pharmacokinetic profile. *J Acute Dis* 2016;5:102-8. CROSSREF
6. Heusch G, Schulz R. Pleiotropic effects of dronedarone on ischemia/reperfusion injury in heart and brain. *Cardiovasc Drugs Ther* 2012;26:257-63. PUBMED | CROSSREF
7. Quintana-Villamandos B, Gomez de Diego JJ, Delgado-Martos MJ, et al. Dronedarone produces early regression of myocardial remodelling in structural heart disease. *PLoS One* 2017;12:e0188442. PUBMED | CROSSREF
8. Chen C, Hu S, Hu HJ, et al. Dronedarone attenuates Ang II-induced myocardial hypertrophy through regulating SIRT1/FOXO3/PKIA axis. *Korean Circ J* 2024;54:172-86. CROSSREF
9. Sotomayor-Flores C, Rivera-Mejías P, Vásquez-Trincado C, et al. Angiotensin-(1-9) prevents cardiomyocyte hypertrophy by controlling mitochondrial dynamics via miR-129-3p/PKIA pathway. *Cell Death Differ* 2020;27:2586-604. PUBMED | CROSSREF
10. Pazó-Sayós L, González MC, Quintana-Villamandos B. Inhibition of the NFATc4/ERK/AKT pathway and improvement of thiol-specific oxidative stress by dronedarone possibly secondary to the reduction of blood pressure in an animal model of ventricular hypertrophy. *Front Physiol* 2020;11:967. PUBMED | CROSSREF

https://doi.org/10.4070/kcj.2024.0067