Estrogen possible risk factor in disturbed heart rhythm

March 15 2023

Sara Liin, associate professor at Linköping University. Credit: Emma Busk Winquist/Linköping University

The sex hormone estrogen has a negative impact on heartbeat regulation, according to an experimental study from Linköping University, Sweden,

published in *Science Advances*. Estrogen impact seems to interact with hereditary changes causing a heart disease disturbing the heart's rhythm, while other endogenous substances may have a protecting effect.

In a lifetime, the heart beats around 2.5 billion times. Each heartbeat is triggered by an electrical impulse that causes the heart muscle to contract in a very well-coordinated movement. The heart's electrical activity is regulated by small pores, ion channels, that go through the cell's membranes and regulate the flow of electrically charged ions in and out of the cell. Some ion channels act as an accelerator and others as a brake. Together, they regulate every heartbeat throughout life.

Diseases causing an abnormal heart rhythm may, in some cases, be deadly. Long QT syndrome, LQTS, is one such disease. In LQTS patients, the heart takes longer than normal to finish every heartbeat. This syndrome is most often due to a congenital hereditary change, or mutation, affecting one of the heart's ion channels.

"We're trying to understand which substances in the body impact the function of the ion channels. If we could figure out how this regulation works, maybe we can understand why some individuals are more protected and others are hit harder," says Sara Liin, associate professor in the Department of Biomedical and Clinical Sciences at Linköping University, LiU.

In this study, the researchers have taken an interest in possible effects of the sex hormone estrogen. They came up with this idea when asked by heart specialists why women are not only more often affected than men, but also more severely affected, by certain hereditary diseases causing an abnormal heart rhythm, also known as arrhythmia. This in light of the fact that women are generally seen as having better protection against cardiovascular diseases. Could it have anything to do with women having more estrogen than men?

In their study, the researchers studied the type of ion channel most often mutated in LQTS, which is called Kv7.1/KCNE1. Reduced function of this ion channel is a risk factor increasing the risk of arrhythmia. To be able to understand estrogen impact on this specific ion channel, the researchers conducted experiments where they inserted the human variant of the ion channel into frogs' eggs, which do not have this ion channel. The researchers added the most active form of the sex hormone estrogen, estradiol, and measured the ion channel function. It turned out that ion channel function was hampered by estrogen, which the researchers interpret as an indication that estrogen may increase the risk of certain types of arrhythmia. Other sex hormones had no effect.

The researchers also found out exactly which parts of the channel were impacted by estrogen. They further examined ion channel mutations found in families with hereditary arrhythmia syndromes. Some mutations led to high estrogen sensitivity, while others led to the ion channel completely losing estrogen sensitivity.

"We show that some hereditary mutations that reduce ion channel function seem to contribute to high estrogen sensitivity, so there could be two risk factors that interact especially in women carriers of these mutations. We believe that our study gives good reason to look closer at this in patients," says Sara Liin.

The researchers point out that it is important to remember the many positive effects of estrogen, and that in women with a hereditary increased risk of LQTS, estrogen could possibly be a risk factor. LQTS is relatively rare, affecting around 1 in 2,500 people.

The LiU researchers recently published a study in *eBioMedicine* where they conducted a similar study into a group of endogenous substances known as endocannabinoids. This study showed that endocannabinoids instead seemed to function as protective factors in LQTS. According to

the researchers, the findings indicate that these factors may be important to study in humans, as this may lead to ways of increasing endocannabinoid levels to counteract arrhythmia.

More information: Lisa-Marie Erlandsdotter et al, Long-QT mutations in KCNE1 modulate the 17β-estradiol response of Kv7.1/KCNE1, *Science Advances* (2023). DOI: 10.1126/sciadv.ade7109. www.science.org/doi/10.1126/sciadv.ade7109

Irene Hiniesto-Iñigo et al, Endocannabinoids enhance hKV7.1/KCNE1 channel function and shorten the cardiac action potential and QT interval, *eBioMedicine* (2023). DOI: 10.1016/j.ebiom.2023.104459

Provided by Linköping University

Citation: Estrogen possible risk factor in disturbed heart rhythm (2023, March 15) retrieved 1 May 2023 from https://medicalxpress.com/news/2023-03-estrogen-factor-disturbed-heart-rhythm.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.