RAPID COMMUNICATION

Cardiac side effects of RNA-based SARS-CoV-2 vaccines: Hidden cardiotoxic effects of mRNA-1273 and BNT162b2 on ventricular myocyte function and structure

Rolf Schreckenberg, Nadine Woitasky, Nadja Itani, Laureen Czech, Péter Ferdinandy, Rainer Schulz

First published: 12 October 2023
https://doi.org/10.1111/bph.16262

Abstract

Background and Purpose

To protect against SARS-CoV-2 infection, the first mRNA-based vaccines, Spikevax (mRNA-1273, Moderna) and Comirnaty (BNT162b2, Pfizer/Biontech), were approved in 2020. The structure and assembly of the immunogen – in both cases, the SARS-CoV-2 spike (S) glycoprotein – are determined by a messenger RNA sequence that is translated by endogenous ribosomes. Cardiac side effects, which for the most part can be classified by their clinical symptoms as myo- and/or pericarditis, can be caused by both mRNA-1273 and BNT162b2.

Experimental Approach

As persuasive theories for the underlying pathomechanisms have yet to be developed, this study investigated the effect of mRNA-1273 and BNT162b2 on the function, structure, and viability of isolated adult rat cardiomyocytes over a 72 h period.

Key Results

In the first 24 h after application, both mRNA-1273 and BNT162b2 caused neither functional disturbances nor morphological abnormalities. After 48 h, expression of the encoded spike protein was detected in ventricular cardiomyocytes for both mRNAs. At this point in time, mRNA-1273 induced arrhythmic as well as completely irregular contractions associated with irregular as well as localized calcium transients, which provide indications of significant dysfunction of the cardiac ryanodine receptor (RyR2). In

Conclusions and Implications

Here we demonstrated for the first time, that in isolated cardiomyocytes, both mRNA-1273 and BNT162b2 induce specific dysfunctions that correlate pathophysiologically to cardiomyopathy. Both RyR2 impairment and sustained PKA activation may significantly increase the risk of acute cardiac events.

Supporting Information

Filename	Description
bph16262-sup-0001-Video_S1.mp4 MPEG-4 video, 14.8 MB	**Video S1.** Representative video sequences: A) untreated cardiac muscle cell – regular contraction; B) after BNT162b2 application – increased contraction; C-F) after mRNA-1273 application – arrhythmic, irregular as well as partly “peristaltic” contraction (C – top: non-beating but morphologically intact myocyte).
bph16262-sup-0002-Video_S2.mp4 MPEG-4 video, 17.1 MB	**Video S2.** Visualization of calcium transients using Fluo-4, AM. Representative video sequences: A,B) untreated cardiac muscle cell – regular transients; C,D) after BNT162b2 application – regular transients with increased intensity; E-G) after mRNA-1273 application – focal or irregular as well as arrhythmic transients (E – top, F – left: hypercontracted cardiac muscle cell with calcium overload).

Please note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries (other than missing content) should be directed to the corresponding author for the article.