

New approach to protect the hearts of patients with muscular dystrophy

A team of researchers has recently shown that the administration of sildenafil protects the heart in mice with Duchenne muscular dystrophy. This study was led by Dr. Christine Des Rosiers from the Université de Montréal and the Montreal Heart Institute, in collaboration with Dr. Basil Petrof of the Research Institute of the McGill University Health Centre (MUHC) and Dr. Christian Deschepper of the Institut de recherches cliniques de Montréal. The study findings are published today in the online edition of the *Proceedings of the National Academy of Sciences*.

“This achievement was a true team initiative and is the culmination of sustained efforts on the part of Dr. Maya Khairallah, who was a doctoral student at the time, and all of the researchers from participating centres,” says Dr. Des Rosiers.

“I’m pleased that my work has sparked interest in an eventual application for humans,” says Dr. Khairallah. The study received financial support from the Canadian Institutes of Health Research, the Fonds de la recherche en santé du Québec, the Heart and Stroke Foundation of Canada, the Muscular Dystrophy Association and the National Heart, Lung and Blood Institute in the U.S.

Improved cardiac function and reduced cell death

The researchers explain that the choice of sildenafil was based on their previous studies indicating that the hearts of dystrophic mice do not function as effectively and are more susceptible to stress-induced cell death. These studies suggested that this may be due to a decrease in the formation of a molecule named cGMP (cyclic guanosine monophosphate).

In the present study, researchers used two different approaches to increase cGMP production in the heart, with the result that the hearts were able to function more effectively and were less susceptible to cell death.

“One of these approaches involved the use of sildenafil, which increased cGMP concentration by preventing its degradation by the phosphodiesterase 5 enzyme,” explains Dr. Petrof, who works at the MUHC’s Meakins-Christie Laboratories. “Our work had shown for many years the benefits of cGMP on the heart and the present study confirms the therapeutic potential of this molecule”, adds Dr. Deschepper.

About muscular dystrophy

Muscular dystrophy is characterized by weakness and progressive degeneration of the muscles, including the heart muscle. It is caused by a genetic mutation of dystrophin, a protein that acts as the “backbone” of muscular cells. This disease, whose most common forms are those of Duchenne and Becker, has an incidence of one in 6,000 births and a prevalence of roughly one in 3,600 boys.

The first signs of muscular weakness appear at roughly age 5, leading to a progressive loss in the ability to walk by the age of 13. Cardiac problems can occur at the age of 10 and progress very quickly, affecting the majority of patients by the age of 20. They are also an important cause of death among patients with muscular dystrophy.

“Research on this disease used to focus on the degeneration of skeletal muscles,” says Dr. Des Rosiers, “but it is important to take into account all muscular problems, including cardiac problems, when treating these patients so that we can improve their quality of life.”

The researchers point to another study showing the beneficial effects of a medication similar to sildenafil on the other muscles of dystrophic mice. Thus, the benefits of this approach may not be limited to the heart. Sildenafil is already prescribed for erectile dysfunction and pulmonary hypertension. However, Dr. Petrof mentions that “further clinical studies will be required before Viagra is prescribed to dystrophic young children.”

“These experimental results give us hope that one day it will be possible to treat with this approach cardiac problems in patients with muscular dystrophy, and perhaps even treat other heart diseases,” Dr. Jean-Claude Tardif, director of the Montreal Heart Institute Research Centre and professor of medicine at the Université de Montréal. “It also demonstrates our researchers’ commitment to conducting basic research that has the potential to transform the practice of medicine.”

Source: University of Montreal

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