シルデナフィルは拡張期心不全患者に無効であった（Abstract # 13-LB-15755）

RELAX: 勃起不全治療薬は拡張期心不全患者を改善させなかった

RELAX: Erectile dysfunction drug shows no improvement in patients with diastolic heart failure

一般的に使用されている勃起不全治療薬の拡張期心不全治療効果に対する期待は大きかったが、有益性は認められなかったとのスタディ結果が第62回American College of Cardiology学会で発表された。RELAXスタディは拡張期心不全に対するシルデナフィルを用いた長期治療の効果を観察した初めての多施設トライアルである。スタディには拡張期心不全（LVEF≧50%、NYHAクラス2-3）の患者113人が組み入れられ、シルデナフィル20mgを1日3回3か月間内服しその後にさらに3か月間60mgを1日3回内服した。彼らはプラセボコントロール群（103人、年齢中央値68歳）と比較された。スタディの結果、一次エンドポイントである24週間後のピーク酸素摂取量の変化には有意差が認められなかった。6分間歩行検査、患者の健康状態に基づく臨床スコアおよびQOL、そして心臓超音波検査、MRIおよび血液検査によるバイオマーカーデータを含む心血管構造および機能検査などの他のアウトカムについてもまた、差はなかった。このスタディ結果は*Journal of the American Medical Association (JAMA)*オンライン版に掲載されており、3月27日号の印刷版に掲載予定である。

Full Text

Despite high expectations for a commonly used erectile dysfunction drug to treat patients with diastolic heart failure, no beneficial effects were found in a study presented at the American College of Cardiology's 62nd Annual Scientific Session.

The RELAX Study is the first multicenter trial to look at the effect of chronic therapy with sildenafil in diastolic heart failure. Sildenafil is a phosphodiesterase-5 (PDE-5) inhibitor, a class of drugs used to treat erectile dysfunction and certain types of pulmonary arterial hypertension. Positive results with sildenafil in smaller studies and animal models provided the impetus for the study. But, compared to the placebo, researchers found no beneficial effect of the drug on the primary endpoint of participants' maximum exercise capacity assessed by peak oxygen consumption nor on secondary endpoints of submaximal exercise capacity (as tested by six minute walk distance), clinical status, or cardiovascular structure and function.

"The results of our study were surprising and disappointing," said Margaret Redfield, M.D., professor of medicine at the Mayo Clinic in Rochester, Minn., and the study's lead author. "There was a lot of anticipation around this study based on other research, and we were hoping to find something that would help these patients, as there are currently few options for treatment."

While current treatment for diastolic heart failure includes recommendations for weight loss, smoking cessation and controlling blood pressure, there are no medications available specifically for its treatment. Because sildenafil can increase blood supply to the lungs, and in animal studies it improved heart and vascular structure and function, researchers believed the drug would improve heart and lung function for diastolic heart failure patients.

According to Dr. Redfield, while it is possible that factors such as insufficient drug dosage or duration contributed to their results, she thinks this is unlikely based on the outcomes of other studies finding benefits from sildenafil.

It is more likely that, compared to other types of heart failure, the disease process seen in diastolic heart failure is different and does not respond well to this category of drug, she said.

In the RELAX study, patients with diastolic heart failure were enrolled in nine primary centers that make up the Heart Failure Clinical Research Network as well as 16 associated centers. To meet inclusion criteria, participants had to do a cardiopulmonary exercise test and have heart and blood tests showing that they had severe limitations in exercise capacity and abnormalities in the structure and function of their hearts.

The study enrolled 113 patients with diastolic heart failure (LVEF ≥50%, NYHA class 2-3) who received 20mg sildenafil three times daily for three months, followed by 60 mg three times daily for another three months. They were compared to a placebo control group (n=103). The trial participant's medium age was 69 years.

The primary endpoint of the study was peak exercise capacity after 24 weeks of therapy with the drug sildenafil. Other outcomes of the study included how far participants could walk in a six-minute exercise test, a clinical score based on patients' health outcomes and quality of life, and cardiovascular structure and function tests including echocardiographs, MRIs and biomarker data from blood tests.

The study was a double-blind, placebo-controlled, randomized clinical trial. For all outcomes, study results were neutral, showing no beneficial effect of sildenafil on heart failure patients. Although sildenafil and other PDE-5 inhibitors are not labeled for heart failure, it is possible that some clinicians may be prescribing these drugs for their heart failure patients based on the results of preliminary studies, which suggest a benefit.

"RELAX study results should discourage this practice, particularly considering the high cost of the drug," Dr. Redfield said.

While Dr. Redfield does not believe a larger trial of PDE-5 inhibitors is warranted in the general population of patients with diastolic heart failure, she said further research is needed to ascertain their potential benefits with certain subgroups of patients. Other small studies have demonstrated benefits from the drug for patients with diastolic heart failure who also had high blood pressure, right ventricular dysfunction and pulmonary arterial hypertension.

"Given these results, future studies should be done with this subset of patients," Dr. Redfield said, noting that ongoing trials in the U.S. and in Europe are assessing the effect of PDE-5 inhibitors in heart failure with reduced ejection fraction.

The RELAX Study was funded by the National Heart, Lung, and Blood Institute of the National Institutes of Health, which funds the Heart Failure Clinical Research Network, now in its seventh year.

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