Sildenafil was safe and improved erectile function and quality of life in men with moderately severe congestive heart failure

Webster LJ, Michelakis ED, Davis T, Archer SL. **Use of sildenafil for safe improvement of erectile function and quality of life in men with New York Heart Association classes II and III congestive heart failure: a prospective, placebo-controlled, double-blind crossover trial.** Arch Intern Med. 2004;164:514-20.

QUESTION

In men with moderately severe congestive heart failure (CHF), is sildenafil safe and effective for improving erectile function and quality of life, and for reducing symptoms of depression?

METHODS

Design: Randomized, placebo-controlled, crossover trial.

Allocation: {Concealed}†.*

Blinding: Blinded {patients}†.*

Follow-up period: 12 weeks.

Setting: University hospital in Edmonton, Alberta, Canada.

Patients: 35 men (mean age 60 y) with New York Heart Association Classes II and III CHF, a history of erectile dysfunction, absence of ischemia, and adequate functional capacity who were not using nitrates. Exclusion criteria were symptomatic hypotension, systolic blood pressure < 80 mm Hg at baseline, positive stress test result in the previous year, history of myocardial ischemia, psychotropic therapy, significant valvular disease, or recent history of alcohol or drug abuse.

Intervention: Sildenafil citrate, 50 mg, or placebo for the first 6 weeks with subsequent crossover to the opposite regimen for the remaining 6 weeks. Patients were instructed to ingest the medication about 1 hour before anticipated sexual activity for a maximum of once per day.

Outcomes: Erectile function, quality of life, depression, pulse, and blood pressure.

Patient follow-up: 100% (intention-to-treat analysis).

MAIN RESULTS

Erectile function (measured by the International Index of Erectile Function) improved at week 4 for those who received sildenafil first ($P < 0.001$); for those who received placebo first, erectile function improved after receiving sildenafil ($P < 0.001$ at wk 10). Quality of life (measured by the Minnesota Living with Heart Failure Questionnaire) improved during the period that sildenafil was used ($P = 0.02$). Symptoms of depression were reduced during the period when sildenafil was used, as measured by the Beck Depression Inventory ($P \leq 0.02$) and the Center for Epidemiological Studies Depression Scale ($P \leq 0.04$). No significant hemodynamic effects or other known adverse effects of sildenafil were reported.

CONCLUSION

In men with moderately severe congestive heart failure, sildenafil was effective for improving erectile function and quality of life and for reducing symptoms of depression and did not cause symptomatic hypotension.

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*See Glossary.

†Information provided by author.

COMMENTARY

The placebo-controlled, crossover trial by Webster and colleagues investigated the safety and efficacy of sildenafil in patients with class II and III CHF. Although CHF is only a relative contraindication to sildenafil, concerns about inducing hypotension or ischemia can be a deterrent to prescribing it for patients with this condition. Therefore, whether sildenafil can be used safely and effectively in patients with CHF is a clinically relevant question.

Patients were excluded if they were taking nitrates, which may interact with sildenafil to cause symptomatic hypotension. The 35 patients who were included had adequate functional capacity and no evidence of reversible ischemia on exercise stress testing or nuclear perfusion scanning. In this subgroup of patients with CHF, the investigators showed that sildenafil improved erectile function in most of the participants and improved depression scores.

Have the investigators shown that sildenafil is safe? The endpoints of pulse and blood pressure are surrogate measures for cardiovascular morbidity and mortality. It is encouraging that no patients in this study had symptomatic hypotension. However, the study's small sample size and selective cohort does not allow us to claim that sildenafil is safe in all or even most patients with CHF. No power calculation was given for safety endpoints. It is thus difficult to determine the level of confidence for excluding the possibility that some patients with CHF may have a dangerous reaction to sildenafil.

I am now more inclined to discuss sildenafil treatment for erectile dysfunction with patients with CHF. However, patients should be advised that it is easier to quantify its benefits than its risks, and that the tentative conclusions of safety in this study apply only to patients in whom recent testing has been done to exclude reversible ischemia.

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