



FOCUS ON RESEARCH

DO PHOSPHODIESTERASE 5 INHIBITORS IMPROVE EXERCISE CAPACITY IN PATIENTS WITH COPD ASSOCIATED PULMONARY HYPERTENSION?

Researchers

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Aim

The study investigated whether pulmonary arterial vasodilating drugs such as phosphodiesterase 5 inhibitors (PDE5-Is) improve exercise capacity in patients with chronic obstructive pulmonary disease (COPD) and associated pulmonary hypertension (PH), an increased blood pressure within the lungs. The drug tested was tadalafil. The study also looked to determine the influence of PDE5-Is on quality of life measures and cardiac function.

Project Outline/Methodology

This was a randomised controlled trial. The primary endpoint was exercise capacity as measured by the six minute walking distance (6MWD). Secondary endpoints were quality of life (QOL) measures assessed through questionnaires: St. George's Respiratory (SGRQ), Short Form-36 (SF-36) and Minnesota living with heart failure questionnaires. Echocardiography was performed at the beginning and end. One hundred and twenty patients were recruited, 60 per arm. The active group received daily tadalafil for 12 weeks, the other arm receiving matched placebo. Inclusion criteria were moderate-severe COPD defined by lung function tests (spirometry) and PH as defined by echocardiography. Exclusion criteria were any significant disease of the left side of the heart (poor heart function or significant valvular disease).

Key Results

All 120 patients were recruited with 113 patients completing. Patients had well matched baseline characteristics and had severe COPD and mild PH. Tadalafil did not increase 6MWD over placebo. There were small but consistent divergence of quality of life measures particularly relating to activity levels (SGRQ) and physical function (SF-36) in favour of the active group although failing to reach statistical significance. Significant changes in a number of the echocardiography parameters, particularly the pulmonary acceleration time (PAT), suggested a reduction in the pulmonary arterial pressures although no changes in right ventricular function or cardiac output were noted. Finger probe determined

oxygen saturations did not change significantly between groups allaying concerns that PDE5-Is may detrimentally allow increased blood flow to areas of poorly ventilated lung (so called V/Q mis-match) resulting in worsening blood oxygenation.

Conclusions

Tadalafil does not increase 6MWD in patients with COPD associated pulmonary hypertension. Positive and consistent trends in QOL measures do however suggest that further research in this area is required. It remains possible that with higher doses in those with more severe PH greater benefit may occur.

What does this study add to the field?

Tadalafil should not be used to improve exercise capacity in patient with severe COPD and mild PH. Tadalafil does not appear to cause V/Q mismatch when administered chronically. PAT is an excellent echo screening tool for PH and responds to drug therapy suggesting that it could be a complementary tool to assess treatment response.

Implications for Practice or Policy

This study highlights that in COPD associated mild PH, PDE5-Is do not increase exercise capacity (6MWD). PAT aids in the diagnosis of PH and is a treatment responsive measure.

Where to next?

Further trials are required to confirm or refute the possible favourable trends seen in this study and to consider whether longer periods of therapy can attenuate the decline of activity levels and physical function. Trialists should also consider using a higher dose. Other primary endpoints other than the 6 minute walk test should be sought. Future trials should include the use of the pulmonary acceleration time as this is readily available in COPD patients and is responsive to pulmonary vasodilator drug therapy. The long-term consequences of an improvement in the PAT are unknown and warrant further study.

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