

Treatment of CFS patients with low levels of vasoactive intestinal polypeptide (VIP) and shortness of breath with tadalafil improves dysfunctional pulmonary artery responses to exercise and exercise tolerance.

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Objectives: Recent literature has supported the concept that elevated pulmonary artery pressure (PAP) is lowered by use of tadalafil, a phosphodiesterase-4 inhibitor. PAP should fall with exercise, improving pulmonary venous return to the left atrium. Stress echocardiography provides an indirect measure of PAP by measuring changes in the tricuspid jet. CFS patients were shown to commonly not show a reduction in PAP with exercise. We hypothesized that (1) the increased incidence of dyspnea with exercise seen in CFS patients could be improved by lowering PAP using tadalafil and (2) a rise in VIP levels would be associated with reduction of PAP and symptoms of exercise intolerance.

Methods: 30 male patients with CFS provided informed consent for an off-label study of tadalafil given 20 mg each every three days for 5 doses. Symptoms of shortness of breath, dyspnea and fatigue; levels of VIP; and echocardiographic measures of PAP were compared before and after treatment with 5 doses of tadalafil given by the study physician over 3 weeks. Symptoms were recorded at each visit, as was a review of possible adverse effects. PAP and VIP were measured after the last dose of tadalafil.

Results: No adverse events occurred aside from headache in 16% that did not prevent finishing the tadalafil protocol. Change in erectile behavior was noticed in 93%. Symptom reduction occurred in 90%; PAP showed improvement in 83%. VIP levels rose in 66%.

Conclusions: Use of tadalafil in male CFS patients in a short clinical trial safely lowered dyspnea and improved exercise tolerance concomitant with an improvement in pulmonary artery response to exercise. Tadalafil, a phosphodiesterase inhibitor, causes an increased intracellular level of cGMP, which in turn can lower PAP and improve erectile function in males. The increase in levels of VIP suggests a central effect of tadalafil, which in turn would result in increased intracellular levels of cAMP. The role of cAMP in CFS is not known, but this study provides Symptom improvement could be confounded by sexual side effects of tadalafil but improvement in PAP and VIP suggests the symptom reduction is not coincidental. A double blinded, placebo controlled trial in males is planned.