Sildenafil reduces Raynaud's frequency in patients with systemic sclerosis

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Researchers in Europe reported that treatment with modified-release sildenafil significantly reduced the frequency of attacks of Raynaud's phenomenon in patients with limited cutaneous systemic sclerosis (lcSSc), also known as scleroderma. The double-blind, placebo-controlled trial found that sildenafil was well tolerated with only some subjects experiencing minor or moderate side effects. Full findings are available in the March issue of *Arthritis & Rheumatism*, a journal published by Wiley-Blackwell on behalf of the American College of Rheumatology (ACR).

Raynaud's phenomenon (RP) is a major feature of systemic sclerosis and causes the blood vessels supplying the skin surface to spasm in response to cold temperatures or stress. These vasospasms can affect the fingers, toes, ears and other skin surfaces and can lead to serious complications in patients with systemic sclerosis such as digital ulceration, soft tissue or bone infection, or gangrene. According to the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) this phenomenon occurs in 90% of all scleroderma cases.

The multicenter trial of sildenafil was conducted in 57 men and women (ages18-75) with Raynaud's secondary to lcSSc between January and June 2003. For one to two weeks prior to the start of treatment, patients recorded the number of RP attacks. To be eligible for the study, subjects had to report at least 7 RP attacks per week. RP was defined as an episode where fingers or toes turned white (pallor) followed by blue (cyanosis) and/or red (erythema) in response to cold or emotion. At the

onset of the treatment phase, participants were randomized in a one-to-one ratio, receiving either 100 mg of modified-release sildenafil for three days followed by a 200-mg modified-release dose daily for 25 days, or placebo for 28 days. Researchers used a two-step dosing to enhance tolerability, and a modified-release formulation to permit once daily dosing.

"Our findings indicate that modified-release sildenafil reduced the frequency of Raynaud's attacks in patients with systemic sclerosis," confirmed lead author, Ariane Herrick, M.D., from the University of Manchester in the U.K. Results showed a 44% reduction in attacks per week (from baseline to day 28) for subjects receiving sildenafil treatment compared with 18% in the placebo group. Researchers also reported that the mean number of attacks per week improved from 30.5 at baseline to 18.7 after sildenafil treatment, compared with 25.0 at baseline to 19.3 after placebo treatment.

Secondary endpoints, including Raynaud's Condition Score, duration of attacks, and RP pain score, were not significantly different between the two groups. The most frequent adverse events reported were headache and indigestion with the majority of these events being mild or moderate. Researchers did not observe any serious adverse events. Dr. Herrick concluded, "Modified-release sildenafil was well tolerated and reduced the attack frequency in patients with Raynaud's secondary to lcSSc. Our results, coupled with existing medical evidence of the favorable safety profile of sildenafil in non-SSc patient populations, may offer a beneficial treatment option in lcSSc patients with secondary Raynaud's."

More information: "Modified-Release Sildenafil Reduces Raynaud's Phenomenon Attack Frequency in Limited Cutaneous Systemic Sclerosis." Ariane L. Herrick, Frank van den Hoogen, Armando Gabrielli, Nihad Tamimi, Carol Reid, Damian O'Connell, Maria-Dolores

Va´zquez-Abad, and Christopher P. Denton. Arthritis & Rheumatism; Published Online: February 25, 2011 (DOI:10.1002/art.30195); Print Issue Date: March 2011.