www.medscape.com

Progesterone Eases Severe COVID-19 in Hospitalized Men

Mitchel L. Zoler, PhD

March 20, 2021

Editor's note: Find the latest COVID-19 news and guidance in Medscape's Coronavirus Resource Center.

Women hospitalized with severe COVID-19 generally do better than men, which led to the notion that perhaps men hospitalized for COVID-19 could be treated with female hormones.

This concept has shown "very encouraging" results in a single-center, US pilot study that randomized 42 men hospitalized for severe COVID-19. Those who received up to 5 days of treatment with injected progesterone had significantly better outcomes than those who received standard of care, researchers report in *Chest*.

The new findings "suggest that administration of progesterone at a dose of 100 mg twice daily by subcutaneous injection may represent a safe and effective approach to treatment of COVID-19 by improving clinical status of men with moderate to severe illness," write Sara Ghandehari, MD, and coauthors, most of whom work at Cedars-Sinai Medical Center in Los Angeles, California.

"The potential utility of progesterone in treatment of early COVID-19 in men is compelling," they say.

They caution, however, that further study is needed with greater numbers and a more diverse range of participants, including postmenopausal women, as well as involvement of other treatment locations.

Progesterone, a steroid hormone produced by the ovaries during reproductive cycles, naturally occurs in only premenopausal women. The hormone's potential role in treating men (or postmenopausal women) with more severe COVID-19 stems from the observation that premenopausal women with COVID-19 have fewer hospitalizations, shorter duration of hospitalizations, and less need for ventilatory support than postmenopausal women.

Higher levels of progesterone may have an immunomodulatory role that dampens the exaggerated inflammatory immune cascade associated with more severe COVID-19, the authors suggest.

Progesterone Doubles Rate of Improvement

The primary study endpoint was change in patients' clinical status, assessed using a 7-point ordinal scale, from baseline to day 7. Secondary endpoints were hospital length of stay, days of supplemental oxygen use, and need for mechanical ventilation.

Results showed that men who received progesterone had a significant median improvement in clinical score status of 1.5 points at 7 days from baseline compared with controls.

Fourteen men in the progesterone group (70%) improved during the first 7 days, compared with seven (32%) in the control group.

Additionally, during the first 7 days of the study, the cumulative probability of clinical improvement was 0.76 among the 20 men who received progesterone compared with 0.55 among the 22 controls who received placebo, a significant difference.

The progesterone group also had a 3-day decrease in median time on supplemental oxygen and a 2.5-day drop in median length of hospital stay. The need for mechanical ventilation was also lower in the progesterone vs control group (0 vs 4 patients).

No patient had a serious adverse event attributable to progesterone, no adverse events occurred that required progesterone discontinuation, and the treatment seemed well tolerated.

Two thromboembolic events occurred in one patient in the progesterone group, and one thromboembolic event occurred in each of two patients in the control group. Patients in each of the two subgroups reported comparable numbers of serious adverse events, and one patient in each group died.

The study enrolled hospitalized adult men in April to August 2020 who tested positive for SARS-CoV-2, had evidence of lower respiratory tract involvement, had an oxygen saturation of 94% or less on room air, and who were on supplemental oxygen. The study excluded men on mechanical ventilation. Patients received chemoprophylaxis for thromboembolism, a precaution recommended for all patients hospitalized for COVID-19. There is currently no evidence that exogenous progesterone at the dosage used promotes thromboembolism, the authors note.

The treatment regimen called for twice-daily injections of 100-mg progesterone for up to 5 days, but patients could stop treatment early if they improved enough for hospital discharge. The protocol also allowed for use of other treatments with presumed benefit for COVID-19. Patients in the control group who had significant deterioration after 7 days could crossover to receive progesterone. Patients were followed for up to 15 days or until hospital discharge.

Enrolled patients were an average of 55 years old, 78% were White, and most were of Hispanic ethnicity. Overall, 85% were on supplemental oxygen at entry. Average body mass index was 31.6 kg/m^2, 48% had hypertension, 45% were obese, and 25% had diabetes.

A 7-point assessment scale was used and scored based on the following criteria: 1. Death; 2. Hospitalized, on invasive mechanical ventilation or extracorporeal membrane oxygenation; 3. Hospitalized, on high-flow oxygen devices; 4. Hospitalized, requiring supplemental oxygen; 5. Hospitalized, not requiring supplemental oxygen; 6. Not hospitalized, limitation on activities; 7. Not hospitalized, no limitations on activities.

The study was investigator initiated and had no commercial support. Ghandehari and another coauthor have filed for a patent for using a progesterone agonist to treat COVID-19.

Chest. Published online February 20, 2021. Full text

For more diabetes and endocrinology news, follow us on Twitter and Facebook.

Follow Medscape on Facebook, Twitter, Instagram, and YouTube.

Send comments and news tips to news@medscape.net.

Cite this: Progesterone Eases Severe COVID-19 in Hospitalized Men - *Medscape* - Mar 20, 2021.