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Anti-androgens: possible new treatment against COVID-19 infection?

Antiandrógenos: ¿posible nuevo tratamiento contra la infección por COVID-19?

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ABSTRACT

Recent studies suggest men are more affected by coronavirus disease than women. Coronavirus infectivity depends on the entry via; it binds its viral spike (S) protein to the angiotensin-converting enzyme 2 (ACE2) receptor, and on S protein priming by transmembrane serine protease type II (TMPRSS2). The androgen receptor activity is required for the TMPRSS2 transcription. ACE2 is also affected by androgenic hormones. This androgen-dependent regulation in the lungs may explain the increased susceptibility of men to COVID-19 infection. Androgen deprivation therapies may represent a promising treatment against SARS-CoV-2 infection.

KEYWORDS: *androgenetic alopecia, COVID-19, anti-androgens, finasteride, dutasteride, spironolactone.*

RESUMEN

Estudios recientes sugieren que los hombres son afectados más frecuentemente por COVID-19 que las mujeres. La infecciosidad del coronavirus depende de su vía de entrada; une la proteína (S) de pico viral al receptor de la enzima convertidora de angiotensina 2 (ECA2) y en la proteína S por la proteasa transmembrana de serina tipo II (TMPRSS2). Se requiere la actividad del receptor androgénico para la transcripción de la TMPRSS2. La ECA2 también es afectada por los andrógenos. Esta regulación andrógeno-dependiente en los pulmones podría explicar la susceptibilidad de los hombres a la infección por COVID-19. La terapia de deprivación androgénica puede representar un tratamiento prometedor contra el SARS-CoV-2.

PALABRAS CLAVE: *alopecia androgénica, COVID-19, antiandrógenos, finasterida, dutasterida, espironolactona.*

Dear editor

The current pandemic of coronavirus disease (COVID-19) has rapidly spread affecting most countries.[1] Recent studies suggest that men are more affected than women. Also, a higher morbidity, mortality, and intensive care (ICU) admission has been found among men.[2] Different authors have proposed that androgen deprivation therapies (ADT) may protect patients or be used as management for SARS-CoV-2 infection.[1]

Five main factors have been correlated with a worse prognosis after COVID-19 infection, including age, diabetes, hypertension, obesity, and in-tissue androgen exposure.[3] Its unique characteristics and mechanism of action challenge the description of its pathogenicity. Coronavirus infectivity depends on the entry via; it binds its viral spike (S) protein to the angiotensin-converting enzyme 2 (ACE2) receptor, and on S protein priming by transmembrane serine protease type II (TMPRSS2) [2]. TMPRSS2 is expressed in human lung tissue on the surface of type II pneumocytes, but also in the prostate, colon, small intestine, pancreas, kidney, lungs, and liver. The androgen receptor activity is required for the TMPRSS2 transcription. ACE2 is also affected by androgenic hormones, showing a higher activity in males.[4] This androgen-dependent regulation in the lungs may explain the increased susceptibility of men to COVID-19 infection.

A high incidence of androgenetic alopecia (AGA) in men hospitalized due to severe COVID-19 has been found,

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greater than would be expected in the general population.[5] A study that included 58 patients with prostate cancer and COVID-19, 36 receiving ADT and 22 non-ADT, found lower rates of hospitalization (p<0.02) and supplement oxygen requirements (p = 0.036) in the ADT group. ADT use was also associated with a protective effect on need for intubation and mortality.[6] Men with prostate cancer under treatment with ADT were less likely to suffer severe COVID-19.[1]

A retrospective analysis on male patients with COVID-19 infection and AGA compared frequency of clinical symptoms in patients using 5-alfa-reductase inhibitors (5ARis) to those not using 5ARis.[7] A total of 65 not using 5ARis and 48 using 5ARis for ≥6 months were included. A statistically significant reduction in frequency of 20/29 included symptoms was noted in patients using 5ARis. Goren *et al.* performed a prospective cohort study including 77 men hospitalized for COVID-19. ICU admission in the group of patients taking anti-androgens (finasteride, dutasteride, spironolactone) was significantly lower than (1/12 patients; 8%) compared to the group not using anti-androgens (38/65 patients; 58%).[8] Moreover, a randomized, double-blind, placebo controlled trial in males and females with mild-to-moderate COVID-19 infection treated with proxalutamide, an androgen receptor antagonist, showed increased SARS-CoV-2 viral clearance at day seven (82.5% in the treated group *vs.* 24.4% in placebo group) and reduced the average number of days to clinical remission.[9] The results of these studies suggest that anti-androgens either alone or in combination with TMPRSS2 inhibitors may represent a promising treatment for patients with COVID-19 infection.

Repurposing old drugs for COVID-19 management could be beneficial since the safety profile of these drugs are known, as well as contraindications and management. Physicians are encouraged to advise their patients taking anti-androgens for AGA, prostatic hyperplasia, or cancer to continue treatment. Larger studies with anti-androgens for treatment of SARS-CoV-2 should be made to support this hypothesis.

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