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Menopause und COVID-19

Originalpublikation

Cattrini C, Bersanelli M, Latocca MM, Conte B, Vallome G, Boccardo F (2020) Sex Hormones and Hormone Therapy during COVID-19 Pandemic: Implications for Patients with Cancer. *Cancers (Basel)* 12(8):E2325

Abstract

The novel coronavirus disease 2019 (COVID-19) shows a wide spectrum of clinical presentations, severity, and fatality rates. The reason older patients and males show increased risk of severe disease and death remains uncertain. Sex hormones, such as estradiol, progesterone, and testosterone, might be implicated in the age-dependent and sex-specific severity of COVID-19. High testosterone levels could upregulate transmembrane serine protease 2 (TMPRSS2), facilitating the entry of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) into host cells via angiotensin-converting enzyme 2 (ACE2). Data from patients with prostate cancer treated with androgen-deprivation therapy seem to confirm this hypothesis. Clinical studies on TMPRSS2 inhibitors, such as camostat, nafamostat, and bromhexine, are ongoing. Antiandrogens, such as bicalutamide and enzalutamide, are also under investigation. Conversely, other studies suggest that the immune modulating properties of androgens could protect from the unfavorable cytokine storm, and that low testosterone levels might be associated with a worse prognosis in patients with COVID-19. Some evidence also supports the notion that estrogens and progesterone might exert a protective effect on females, through direct antiviral activity or immune-mediated mechanisms, thus explaining the higher COVID-19 severity in post-menopausal women. In this perspective, we discuss the available evidence on sex hormones and

hormone therapy in patients infected with SARS-CoV-2, and we highlight the possible implications for cancer patients, who can receive hormonal therapies during their treatment plans.

Für die Praxis

Es ist allgemein bekannt, dass COVID-19-Infektionen bei älteren Menschen schwerer verlaufen. In dieser Studie wird auf diese schwereren Verlaufsformen bei postmenopausalen Frauen hingewiesen. Weiters scheinen Östrogen und Progesteron eine immunmodulierende und damit protektive Wirkung bei COVID-19-Infektion zu haben.

Originalpublikation

Ding T, Zhang J, Wang T, Cui P, Chen Z, Jiang J, Zhou S, Dai J, Wang B, Yuan S, Ma W, Ma L, Rong Y, Chang J, Miao X, Ma X, Wang S (2020) Potential Influence of Menstrual Status and Sex Hormones on female SARS-CoV-2 Infection: A Cross-sectional Study from Multicentre in Wuhan, China. *Clin Infect Dis.* <https://doi.org/10.1093/cid/ciaa1022>

Abstract¹

Background. Recent studies indicated that females have a lower morbidity, severe cases rate, mortality and better outcome than those of male. However, it remained to be addressed why this was the case.

¹ Reprinted from Ding T, Zhang J, Wang T, Cui P, Chen Z, Jiang J, Zhou S, Dai J, Wang B, Yuan S, Ma W, Ma L, Rong Y, Chang J, Miao X, Ma X, Wang S (2020) Potential Influence of Menstrual Status and Sex Hormones on female SARS-CoV-2 Infection: A Cross-sectional Study from Multicentre in Wuhan, China [published online ahead of print, 2020 Jul 22]. *Clin Infect Dis*; ciaa1022. <https://doi.org/10.1093/cid/ciaa1022>, by permission of Oxford University Press

Methods and findings. To find the factors that potentially protect females from COVID-19, we recruited all confirmed patients hospitalized at three branches of Tongji Hospital ($n=1902$) from January 28 to March 8, 2020, and analyzed the correlation between menstrual status ($n=509$, including 68 from Mobile Cabin Hospital)/female hormones ($n=78$)/cytokines related to immunity and inflammation ($n=263$), and the severity/clinical outcomes in female patients under 60 years of age. Non-menopausal female patients had milder severity and better outcome compared with age-matched men ($p<0.01/p<0.01$). Menopausal patients had longer hospitalization times than non-menopausal patients (hazard ratio [HR], 1.91; 95 % confidence interval [CI], 1.06–3.46, $p=0.033$). Both anti-müllerian hormone (AMH) and estradiol (E2) showed a negative correlation with severity of infection (AHR=0.146/0.304, 95 % CI = [0.026–0.824]/[0.092–1.001], $p=0.029/0.05$). E2 levels were negatively correlated with IL-2R, IL-6, IL-8 and TNF α in luteal phase (Pearson Correlation = -0.592, -0.558, -0.545, -0.623; $p=0.033$, 0.048, 0.054, 0.023), and with C3 in follicular phase (Pearson Correlation = -0.651; $p=0.030$).

Conclusion. Menopause is an independent risk factor for female COVID-19 patients. AMH and E2 are potential protective factors, negatively correlated with COVID-19's severity, among which E2 is attributed to its regulation of cytokines related to immunity and inflammation. Hormone supplement might be a potential therapy for COVID-19 patients.

Für die Praxis

In dieser Studie aus Wuhan mit 1902 hospitalisierten COVID-19-Patienten wurden einige wesentliche Trends dieser

Akupunktur bei rezidivierenden Harnwegsinfektionen von Frauen

Chinesische und australische Wissenschaftler führten ein Review mit Metaanalyse zu Akupunktur und verwandter Techniken bei unkomplizierten rezidivierenden Harnwegsinfektionen von Frauen durch. Sie fanden zu dieser Fragestellung in verschiedenen internationalen und chinesischen Datenbanken 5 randomisierte kontrollierte Studien mit 341 Teilnehmerinnen.

Die methodische Studienqualität und Evidenzstärke wurde als gering bis mäßiggradig beurteilt. Die Chancen auf eine Heilung stellten sich mit einer komplexen Behandlung einschließlich Akupunktur größer dar als mit Antibiotika (3 Studien mit 170 Teilnehmerinnen, RR=1,82, 95% CI 1,31 bis 2,81). Das Rezidivrisiko war mit Akupunktur geringer als ohne Behandlung (2 Studien mit 135 Teilnehmerinnen, RR 0,39, 95% CI 0,26 bis 0,58) oder unter Sham-Akupunktur (1 Studie, 53 Teilnehmerinnen, RR 0,45, 95% CI 0,22 bis 0,92).

Schlussfolgerung: Akupunktur scheint zur Behandlung und Prävention von rezidivierenden Harnwegsinfekten bei Frauen mit begrenzter Evidenz von Nutzen zu sein. Angesichts wachsender Antibiotikaresistenzen besteht ein Bedarf an qualitativ hochwertigen Studien zu nicht-medikamentösen Behandlungsverfahren wie Akupunktur.

Literatur:

Qin X, Coyle ME, Yang L, et al (2020) Acupuncture for recurrent urinary tract infection in women: a systematic review and meta-analysis. BJOG. doi: 10.1111/1471-0528.16315. Online ahead of print

Axel Wiebrecht

Erkrankung ausgewertet: Menopausale Patientinnen waren länger im Krankenhaus als prämenopausale Frauen.

Weiters zeigten sowohl AMH als auch Östradiol eine negative Korrelation mit der Schwere des Krankheitsverlaufes. Insgesamt scheint die Menopause ein unabhängiger Risikofaktor für die COVID-19-Verlaufsform zu sein und eine Hormontherapie eine potentielle Therapiemöglichkeit.

Originalpublikation

Papadopoulos V, Li L, Samplaski M (2020) Why does COVID-19 kill more elderly men than women? Is there a role for testosterone? Andrology. <https://doi.org/10.1111/andr.12868>

Abstract²

Background. Recent epidemiological data indicate that there may be a gender predisposition to COVID-19, with men predisposed to being most severely affected, and older men accounting for most deaths.

Objectives. Provide a review of the research literature, propose hypotheses, and therapies based on the potential link between testosterone (T) and COVID-19 induced mortality in elderly men.

Materials and methods. A search of publications in academic electronic databases, and government and public health organization web sites on T, aging, inflammation, severe acute respiratory syndrome (SARS) due to coronavirus (CoV) 2 (SARS-CoV-2) infection, and COVID-19 disease state and outcomes was performed.

Results. The link between T, the immune system, and male aging is well-established, as is the progressive decline in T levels with aging. In women, T levels drop before menopause and variably increase with advanced age. Elevated IL-6 is a characteristic biomarker of patients infected with COVID-19 and has been linked to the development of the acute respiratory distress syndrome (ARDS). Thus far, half of the admitted COVID-19 patients developed ARDS, half of these

patients died, and elderly male patients have been more likely to develop ARDS and die. Low T is associated with ARDS. These data suggest that low T levels may exacerbate the severity of COVID-19 infection in elderly men. It may also stand to reason that normal T levels may offer some protection against COVID-19. SARS-CoV-2 binds to the angiotensin-converting enzyme 2, present in high levels in the testis.

Conclusion. At present, it is not known whether low T levels in aging hypogonadal males create a permissive environment for severe responses to COVID-19 infection or if the virus inhibits androgen formation. Given the preponderance of COVID-19 related mortality in elderly males, additional testing for gonadal function and treatment with T may be merited.

Für die Praxis

IL-6 scheint ein wesentlicher Parameter bei der COVID-19-Infektion zu sein. Niedrige Testosteronspiegel bei Männern scheinen die Infektion zu triggern und zu einem ARDS zu führen. Die Autoren implizieren, dass bei menopausalen Frauen relativ stabile Testosteronspiegel die Frauen schützen. Umso mehr schlagen die Autoren eine Therapie mit Testosteron vor. Insgesamt scheint der Testosteronspiegel eine Rolle beim Krankheitsverlauf zu spielen.

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