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REVIEW

Managing patients with endocrine dysfunction during COVID-19: Review of literatures

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Abstract

Coronavirus disease (COVID-19), caused by the severe acute respiratory distress syndrome. Coronavirus 2 (SARS-CoV-2) is labeled as a global pandemic by the World Health Organization (WHO) on 12th March 2020, is sweeping across the world. There has been documented evidence from China that those patients who have endocrinological disorders face additional risks from COVID-19. Healthcare professionals consider people with diabetes are at higher risk of severe illness. As such people with diabetes are not more likely to get COVID-19 than the general population, but they experience severe symptoms, complications and worse outcome even death, once infected. Hence specific measures are advised for the diabetic patients. The same goes for people with autoimmune conditions that lead to adrenal insufficiency. There may be primary (Addison's disease), secondary or tertiary adrenal insufficiency in some patients. They regulate the blood pressure, the immune response and body's stress response. However, nearly 5% of the population takes long-term steroids for inflammatory conditions like bronchial asthma, inflammatory bowel diseases etc.; out of which many would have some degree of insufficient adrenal response in a crisis. As it relates to COVID-19, any such patient who has been on long term corticosteroid therapy; with a dry continuous cough, breathing difficulty and fever should immediately double their daily oral steroid dose and continue this regimen until the fever has subsided. It is recommended for people with adrenal insufficiency. Apart from that, they should seek immediate medical help to avoid complications.

Keywords: COVID-19; diabetes; endocrinological disorders; SARS-CoV-2

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Introduction

During the coronavirus disease (COVID-19) pandemic, a series of recommendations have recently been published by endocrinologists for people with diabetes, and other hormone disorders. These patients need special attention to prevent adverse events.

COVID-19, caused by the Severe acute respiratory syndrome, coronavirus 2 (SARS-CoV-2) and labeled as a global pandemic by the World Health Organization (WHO) on 12th March 2020, is sweeping across the globe, even though it started first in China in December 2019.

"There is early evidence from China that those patients who have endocrinological disorders face additional risks from COVID-19. The scientific picture indicates that these people need to self-isolate, to try and reduce the chance of infection in the same way as the background population" as stated by Senior Prof. Paul Stewart, a Professor of Medicine at the University of Leeds in the United Kingdom [1].

Different endocrine glands/ organs that can be affected by COVID-19

1. *Diabetes:* Worse outcomes in diabetic patients.
2. *Pituitary:* Possible hypothalamic-pituitary dysfunction and alterations in antidiuretic hormone metabolism.
3. *Thyroid:* Sick euthyroid syndrome.
4. *Adrenal:* Probable higher susceptibility to COVID-19 in adrenal insufficiency and Cushing's syndrome.
5. *Bone:* Low vitamin D may be linked to more severe disease. Increased risk of hypocalcemia.
6. *Testicle:* Higher susceptibility and worse outcomes have been reported in men.
7. *Obesity:* Worse prognosis in obese patients.

Hence, the main objective is to create awareness among the practioners as well as patients, so that the complications and death rates can be reduced.

Discussion

How COVID-19 spreads

COVID-19 is thought to spread mainly through close contact from person-to-person in respiratory droplets from someone who is infected. People who are infected often have symptoms of illness. Some recent studies have suggested that COVID-19, some people without symptoms may be able to spread virus, they are asymptomatic carriers.

- Between people who are in close contact with one another (within about 6 feet).
- Through respiratory droplets produced when an infected person coughs, sneezes or talks.
- These droplets can land in the mouths, eyes or noses of people who are nearby or possibly be inhaled into the lungs.

It may be possible that a person can get COVID-19 by touching a surface or object that has the virus on it and then touching their own mouth, nose, or possibly their eyes. This is not thought to be the main way the virus spreads, but we are still learning more about this virus. Duration of survival of the virus on different surfaces are variable. The virus that causes COVID-19 is spreading very easily and sustainably between people.

The COVID-19 pandemic is unlike anything that most people have ever seen. It presents unique challenges to doctors working to treat high risk groups, such as those with existing respiratory conditions and those whose immune systems are compromised.

Healthcare professionals consider people with diabetes are at higher risk of severe illness, according to the Centers for Disease Control and Prevention (CDC) and American Diabetes Association. In general, it is assumed that this risk can be reduced, though not completely eliminated, through good glycemic control.

Adrenal insufficiency and COVID-19

The increase in morbidity and mortality in adrenal insufficiency could also be accounted by an insufficient compensatory self-adjusted rise of the hydrocortisone dosage at the time of the beginning of an episode of the infection. Achieving physiological plasma concentration is not easy in adrenal insufficiency patients who are taking lifelong replacement treatment. The physiologic cortisol requirements may unbalance in many circumstances, either organic and/or psychological. COVID-19 pandemic may be one more reason to worry [2].

The same goes for people with autoimmune conditions that lead to adrenal insufficiency. Though rarer, the consequences for people with primary (otherwise known as Addison's disease), secondary, and tertiary adrenal insufficiency could be even more serious. Primary adrenal insufficiency affects around 100–140 people per million. Secondary or tertiary insufficiency affect around 150–280 people per million. The adrenal glands produce hormones that, alongside the pituitary gland and hypothalamus, regulate blood pressure, the immune response, and the body's response to stress.

However, the same caution should extend to the 5% of the population who take long-term steroids

for inflammatory conditions — half of whom would have some degree of insufficient adrenal response in a crisis.

First, for patients treated with glucocorticoids, it will be invaluable to reiterate "sick day rules" for our known patients with primary and secondary adrenal insufficiency taking glucocorticoid replacement therapy. As it relates to COVID-19, any patient with a dry continuous cough and fever should immediately double their daily oral glucocorticoid dose and continue on this regimen until the fever has subsided. Deteriorating patients and those who experience vomiting or diarrhea should seek urgent medical care and be treated with parenteral glucocorticoids [3].

More impactful will be the extension of these guidelines to the ~5% of patients in our populations taking chronic therapeutic corticosteroids by different routes for underlying inflammatory conditions. The prevalence of adrenal insufficiency in these patients is high (~50%) irrespective of mode of delivery [4]. Currently there is little evidence to guide us on when to intervene in terms of duration of prior corticosteroid exposure or on the impact of dose, either at a higher dose where supplemental steroid cover may not be necessary or a lower dose where adrenal suppression may not be as prevalent. In the interim, it seems logical, if not essential, that we identify all patients taking corticosteroids for whatever reason as high risk. We know from the published reports to date that these patients will be over represented in those at greatest risk of dying from COVID-19—the elderly and those with co-morbidities that include diabetes, hypertension, and chronic inflammatory disease [5, 6]. Moreover, those patients taking supra-physiologic doses of glucocorticoids may have increased susceptibility to COVID-19 as a result of the immunosuppressive effects of steroids, comorbidities of underlying immune disorders for which the steroids were prescribed, or immune-modulatory actions of other therapies prescribed in conjunction with glucocorticoids for the underlying disease. Reversing potential adrenal failure as a cause of mortality with parenteral glucocorticoid therapy is easy and simple to do once the issue has been recognized. The intent here is to ensure that no patient with a history of prior exposure to chronic glucocorticoid therapy (>3 months) by whatever route should die without consideration for parenteral glucocorticoid therapy. As a community, we will be key to ensuring recognition, management, and implementation of these important measures.

Cushing's syndrome

There may be higher risk of COVID-19 infection,in patients with Cushing's disease, especially those under supra-physiologic doses of steroids [7] because of the steroids and their potential immunosuppressive action. In these cases, under empiric principles, it might be recommendable to follow the same rules as patients with adrenal insufficiency.

When extensive differential diagnostic testing is not feasible, it should be deferred for diagnosis and therapy of patients with endogenous Cushing's. As the potential of viral contamination and infection of laboratory staff, salivary cortisol/cortisone tests should be avoided. Co-morbidities (such as hypertension and diabetes) treatment should be optimized and medical treatment must be initiated. In order to ease the monitoring block and replace regime (metyrapone or ketoconazole plus glucocorticoid) to be considered [8].

"Sick day rules" for adrenal insufficiency

It is recommended that people with adrenal insufficiency and those taking long-term glucocorticoids follow their "sick day rules." This is a series of procedures agreed on with a physician for when they feel unwell, including drinking plenty of fluids and doubling their daily dose in line with the doctor's recommendations. Although "glucocorticoid treatment has no role to play in the treatment of COVID-19 per se," in people who have previously taken glucocorticoids and are deteriorating due to COVID-19, it may be necessary to deliver high doses — perhaps even via an intravenous route. However, at the same time, people must take glucocorticoids very carefully, because at large doses, the treatment can actually suppress the immune system and weaken the body's ability to fight the novel coronavirus.

Diabetes and the new corona virus

COVID-19 is proving to be a more serious illness than seasonal flu in everyone, including people with diabetes. Diabetes, including type 1, type 2, or gestational, may put people at higher risk of severe illness from COVID-19.

People with diabetes are not more likely to get COVID-19 than the general population, but they experience severe symptoms, complications and worse outcome even death, once infected. Like other infections, body's ability to fight off an infection is compromised, with uncontrolled or poorly controlled diabetes, fluctuating blood sugars and associated with other co-morbid conditions like heart disease. And they become very sick. Viral infections can also increase inflammation, or internal swelling, in people with diabetes.

When sick with a viral infection, people with diabetes do face an increased risk of DKA (diabetic ketoacidosis), commonly experienced by people with type 1 diabetes. DKA can make it challenging to manage fluid and electrolyte balance, following sepsis. Sepsis and septic shock are some of the more serious complications that some people with COVID-19 have experienced. If blood sugar has registered high (greater than 240 mg/dl) more than 2 times in a row, ketones should be checked, to avoid DKA.

Whereas the risk of contracting a viral illness is no greater in diabetes, than those without diabetes mellitus; but severity of disease from viral infections is notably greater. Recent published reports from the Wuhan province in China [5, 6] reveal that those with diabetes mellitus and hypertension were over represented among the most severely ill patients with COVID-19 and those succumbing to the disease. Whether this susceptibility to illness severity is especially greater in the case of COVID-19 or simply a reflection of the greater risk posed by diabetes remains uncertain at this point. Current guidance from the Centers for Disease Control and Prevention for prevention of COVID-19 for those with diabetes is no different than the general population, but the recognition that diabetes poses a greater risk for severity of illness should prompt health-care providers to be more vigilant in the assessment of such patients, who present with concerning symptoms (i.e., dry cough, shortness of breath, fever, potential dehydration etc.,) [9].

Human dipeptidyl peptidase 4 (DPP-4) has been identified as a functional receptor for the S-protein of MERS-Co-V [10]. MERS-CoV interacts with T cells and nuclear factors, such as nuclear factor kappa b (NF-kB) important factor in the pathogenesis of inflammatory disorders, through binding to the DPP-4 receptor-binding domain. DPP-4 regulation on immune system comes by activating T cell repertoire and upregulating nuclear factor kappa b pathway [11]. With this, whether DPP-4 inhibitors used currently for treatment of type 2 diabetes play a role not just regarding metabolic control, but also contributing to modify COVID-19 attack in these patients, either inducing protection or progression of infection is the question. Inhibition of DDP-4 with the antidiabetic drugs such as sitagliptin, vildagliptin or linagliptin may impair the virus/DPP-4 interaction, thereby protecting the cell from virus entrance. But more studies required in order to clarify this question,as the binding of SARS-CoV-2 and MERS-CoV takes place at residues not located nearby the DPP-4i binding pocket of current gliptin drugs [12]. As DDP-4 inhibition modulates inflammation and has anti-fibrotic effects; depending on the potency of these properties, some protective effects may be seen with DPP-4 inhibitors in case of severe COVID-19 infection [2].

A potentially exciting endocrine-connected observation is the elucidation of the mechanism of entry of SARS-CoV-2 into cells. Here, angiotensin-converting enzyme 2 (ACE2) is now established as the SARS-CoV receptor [13] but with conflicting data as to its translational relevance. It has been suggested that angiotensin-converting enzyme inhibitors/ angiotensin receptor blockers might increase susceptibility and severity to COVID-19 through up-regulation of ACE2 and thereby possibly explain the over-representation of hypertensive patients in patients dying from COVID-19 [14]. Up-regulation of ACE2 might also explain the poor outcome in smokers versus non-smokers, but it is important to stress that these are preliminary reports and should not result in changing prescribed medications at this stage [15]. APN01 is a recombinant human ACE2 developed by APEIRON for the treatment of acute lung injury, acute respiratory distress syndrome, and pulmonary arterial hypertension; by slowing viral entry into cells and viral spread, it may be beneficial, and clinical trials are underway [16]. Conversely, angiotensin II is known to stimulate alveolar epithelial cell apoptosis, and inhibition of this with angiotensin receptor 1 blockers such as losartan might reduce mortality from acute respiratory distress syndrome in COVID-19 infection [17].

Perhaps justifying greater excitement is the downstream trans-membrane protease serine 2

required for SARS-CoV-2 viral spike protein priming and onward transmission [18]. Camostat mesylate, a transmembrane protease serine 2 inhibitor, has been approved in Japan for the treatment of pancreatic inflammation and when tested on SARS-CoV-2 isolated from a patient prevented the entry of the virus into lung cells. Endocrine-related targets are at the forefront of discovery science as we collectively tackle this pandemic.

The pituitary and COVID-19

Leow et al. first reported the evidence of altered pituitary function in SARS. After the recovery from SARS outbreak sixty-one survivors were evaluated: 40% had evidence of central mild hypocortisolism was observed in 40% of patients whereas central hypothyroidismin 5% [19]. In the hypothalamus on autopsy studies edema and neuronal degeneration along with SARS-CoV genome have been identified [19]. Both the hypothalamic and pituitary tissues express ACE2 and could also be viral targets in the case of COVID-19 [20].

Recommendations for people with pituitary disorders regarding COVID-19 infection: All patients should receive medical therapy, as the management of pituitary tumors without mass effects and without hormonal hypersecretion can be deferred for several months and if possible [21]. Surgery is the treatment of choice, with previous assessment of COVID-19 status in the case of pituitary tumors (except prolactinomas) with severe visual deterioration [22].

In severe cases of COVID-19 perturbations in plasma sodium may be more common in patients with pre-existing endocrine conditions. Since patients have limited accessibility to blood testing, the priority should be to avoid hyponatremia in the management of diabetes insipidus [23]. This can be performed by delaying desmopressin to prevent dilutional hyponatremiaas it allows regular periods of free water clearance. Daily body weight measurement is also useful. Close monitoring should be there in patients with diabetes insipidus who develop respiratory complications of COVID-19 as they are at significantly increased risk of dysnatremia [23].

The thyroid and COVID-19

Very scarce data is available on thyroid involvement by coronavirus. A study conducted during the SARS outbreak in 2003, both during the acute and convalescent phases the serum Triiodothyronine and thyroxine levels were lower in patients with SARS as compared to controls. This may imply an underlying euthyroid sick syndrome. Marked destruction of the follicular and parafollicular thyroid cells [24] and not a reduction in thyroid follicular size associated with euthyroid sick syndrome as seen with the autopsy in five patients with SARS as identified as a low triiodothyronine and thyroxine profile [25]. Thyroid function or thyroid pathology in COVID-19, data is yet not available [20].

Graves' disease, COVID-19 may be a precipitating factor for initiation or relapse of the disease (M. Marazuela, personal experience). Special care must be given to the patients with hyperthyroidism receiving antithyroid drugs as recommended by Several medical societies, because symptoms of the rare side effect of agranulocytosis can overlap with COVID-19. Hence agranulocytosis should be ruled out immediately with a full blood count if symptoms of COVID-19 appear [2].

During the COVID-19 pandemic, diagnostic work-up of thyroid nodules as well as thyroid surgery for either benign or malignant thyroid nodules for differentiated thyroid cancers have been generally postponed [26] -although based on accurate risk profile analysis choices must be individualized. Interestingly, 1 out of 12 patients showed interstitial pneumonia on single photon emission computed tomography, who received radioiodine for differentiated thyroid carcinoma [27].

Calcium & Hypoparathyroidism and COVID-19

Calcium plays a key role in viral fusion for many enveloped viruses such as SARS-CoV, MERS-CoV and Ebola virus as shown by several studies. By interacting with fusion peptides of these viruses, calcium promoted their replication directly [28]. Patients with SARS (60% of patients at hospital admission), although generally mild [29], and in patients with Ebola virus disease (62%) [30], hypocalcemia had already shown to be common. Very recent retrospective single Institution study showed a high prevalence of hypocalcemia (in about 80% of cases) on initial hospital evaluation which included 531 patients with COVID-19. With

more linear correlation between calcium levels and LDH and PCR levels, hypocalcemia was seen more frequently in elderly male patients. Finally, since hypocalcemia may have negative impact on cardiac outcomes [31], all hospitalized patients with COVID-19 infection calcium evaluation, monitoring and adequate supplementation if needed is recommended. Hypocalcemia was an independent risk factor associated with hospitalization in multivariate analyses, but only in univariate analysis it predicted ICU admission and mortality [32].Therefore, postsurgical hypoparathyroidism should be adequately treated to avoid severe acute hypocalcemia, which can be life-threatening [33]. Moreover, surveillance required formild hypoparathyroid patients not requiring chronic treatment, particularly if overweight/ obese in areas hit by outbreak of COVID-19 outbreaks [34].

Androgens and COVID-19

Susceptibility to the virus infection and worse clinical outcomes and COVID-19 deaths were higher in men compared with women, among all age groups of adult patients [35]. Compromised antiviral immune response to SARS-CoV-2 in men could be a possible explanation that might drove the clinical outcomes. With the immune suppressive effect of androgens and inflammatory disease disproportionately affected women. In animal studies with SARS-CoV infected mice, gonadectomy or treatment with an antiandrogen compound did not affect the morbidity and mortality in males; whereas, increase in both morbidity and mortality observed with estrogen depletion by ovariectomy or treatment with an estrogen receptor antagonist dramatically, suggesting a protective effect for the estrogen receptor signaling pathway [36]. In addition, upregulated estrogen receptor signaling by estrogen treatment, silenced the cytokine storm and lead to an improved survival rate in animal experiments.

The angiotensin converting enzyme-2 (ACE2) and the transmembrane protease, serine 2 (TMPRSS2) were the two host proteins required for the SARS-CoV-2 viral entry [37]. TMPRSS2 gene requires androgen receptor activity for the transcription [38] and in primary prostate cancer it is the most frequently altered gene [39]. The male predominance of COVID-19 infection has been postulated bythe modulation of TMPRSS2 expression by testosterone [40]. The usage of TMPRSS2 inhibitors, currently being used for prostate cancer, represents an appealing target for prevention or treatment for COVID-19 pneumonia as TMPRSS2 is expressed also at pulmonary level [37].

Higher prevalence of comorbidities, including hypertension, cardiovascular disease, and lung disease in men could also be the cause of adverse outcomes of COVID-19 [2].

COVID-19 and obesity

There is increased risk of morbidity and mortality in patients with obesity regarding COVID-19 infection. Obesity is associated with decreased expiratory reserve volume, functional capacity and respiratory system compliance. Severe obesity causes sleep apnea syndrome and in those with increased abdominal obesity, pulmonary function is further impaired by decreased diaphragmatic excursion.

Potential mechanisms that link obesity to worse outcomes in COVID-19

Obese patients have: (1) a impaired respiratory function; (2) associated cardiovascular, metabolic and thrombotic comorbidities which reduce the capability to cope with COVID-19. In addition, obese patients have (3) increased viral shedding and viral load and (4) an amplified immune response due to altered balance between inflammatory and regulatory cells. During COVID-19 infection there is also an altered immune response that is amplified by the dysregulated immune system of the obese patients.

Recommendations for people with obesity regarding COVID-19 infection

Obese patient needs constant surveillance, early detection, testing and proactive therapy policies for COVID-19. The assessment of metabolic phenotype is crucial, which includes body mass index, waist and hip circumferences and levels of glucose. Both, in the primary care setting and in the hospital setting to accurately assess the risk of these persons, such measurements might not be forgotten to be done.

Critical cut-off for mortality risk is that patients with body mass index greater than 40 [41], all the possible precautions to avoid infection needs to be taken. To prevent severe health consequences, and now the risk of severe COVID-19 infection losing

weight, lowering blood pressure and controlling blood sugar was important.

Persons with obesity who infected with COVID-19 and became ill, require treatment in intensive care units. They present with very important challenges in their therapeutic management such as more difficult to intubate them, difficult to obtain diagnostic imaging (as there are weight limits on imaging machines) and difficult to position and transport by nursing staff. The decision to extubate is more challenging when it comes to these patients. Healthcare systems in general are not yet well coped up enough to manage an increasing number of patients with obesity in ICUs and the current crisis could probably highlight their limitations even more.

An Italian anatomical pathologist reports that the Pergamo hospital made a total of 50 autopsies, Milan 20; the Chinese have only made 3, which seems to fully confirm the information that, patients who died from COVID-19, it is not pneumonia, because the virus does not kill pneumocytes of its type only but uses an inflammatory storm to create an endothelial vascular thrombosis, with the corresponding diffuse thrombosis the lung is the most affected because it is the most inflamed, but also, it produces a heart attack or stroke, and many other thrombotic diseases. It is a case of disseminated intravascual coagualation (DIC) (Thrombosis). So, the way to combat it is with antibiotics, anti-inflammatories and anticoagulates. If thrombo-embolism is not resolved first. Ventilating a lung where blood does not reach is useless. It is venous micro-thrombosis and not pneumonia that determines mortality. The inflammation destroyed everything and created the ground for the formation of thrombi, because the main problem is not the virus, but the immune reaction that destroys the cell where the virus enters.

Actions to take

- Continue taking your insulin and diabetes medicines as usual.
- Test your blood sugar every 4 hours and keep track of the results.
- Drink extra calorie-free liquids*, and try to eat as you normally would.
- Weigh yourself every day. Losing weight without trying is a sign of high blood glucose.
- Check your temperature every morning and evening. A fever may be a sign of infection.

Drink plenty of fluids – 4 to 6 ounces every half-hour – to prevent dehydration. You may also need to drink beverages with sugar if you cannot get 50 grams of carbohydrates every 4 hours from other food choices. Drink small portions of these sweet beverages to keep your blood sugar from getting too high or too low.

- Wash your hands often with soap and water. If soap and water are not available, use an alcohol-based hand rub. Also, routinely clean frequently touched surfaces.
- Covering coughs and sneezes with a tissue or your elbow.
- Maintaining good social distance (about 6 feet) is very important in preventing the spread of COVID-19.
- Prevent spread from contact with contaminated surfaces or objects
- Follow the sick day guidelines for people with diabetes.

Managing sick days

These tips can help people with diabetes prepare for getting sick and take care of themselves if they do become ill.

Like everyone, people with diabetes can get sick even when trying their best to prevent it. So being prepared and knowing what to do if you get sick is very important. There are several things you can do now. These tips can help you take care of yourself if you get sick. Pay attention for potential COVID-19 symptoms including fever, dry cough and shortness of breath. If you feel like you are developing symptoms, call your doctor.

When you call the Doctor: Have your glucose reading available. Have your ketone reading available. Keep track of your fluid consumption (you can use a 1-liter water bottle) and report. Be clear on your symptoms (for example: are you nauseated? Just a stuffy nose?).

Prepare now before getting sick

- Make sure that at least a two-week supply of your diabetes medicines and insulin is available. Fix foods in your home, enough to met the need for several weeks.
- Medicines and supplies like PPIs, antacids, pain killers, NSAIDS, medicines for diarrohea,

constipation and vomiting, ORS etc should be stored at home. Thermometer, pulse oxymeter, digital blood pressure measuring device, glucometer & its accessories also should be available.

If you can't eat meals, you will need to eat or drink about 50 grams of carbohydrates every 4 hours, such as 1½ cup of unsweetened apple sauce or 1½ cup of fruit juice.

If you get sick

If you do get sick, your blood sugar can be hard to manage. You may not be able to eat properly, which can affect blood sugar levels. Your doctor may ask you to test your blood sugar more often because you are sick.

Keep good written records of your blood sugar, medicines, temperature, and weight etc. You may need to test your urine for ketones if your blood sugar goes very high. Follow these additional steps even if your blood sugar is within your target range:

Emergency warning signs

If you develop emergency warning signs for COVID-19 get medical attention immediately. Keep attention of the following:

- Shortness of breath or trouble breathing,
- Persistent pain or pressure in the chest,
- Bluish lips or face,
- Vomiting and / or diarrhea for more than 6 hours,
- Temperature is over 101 degree F for 24 hours,
- Feel too sick to eat normally and are unable to keep down food more than 24 hours,
- New confusion or inability to arouse,
- Lose 5 pounds or more during the illness,
- Can't keep any liquid down for more than 4 hours,
- Moderate to high risk of high blood sugar and / or high ketone levels,
- Blood sugar is lower than 60 mg/dl,
- Feel sleepy or can't think clearly. Someone else in the family should call the Doctor, to take you to emergency room.

Conclusion

Glucocorticoids are steroid hormones that help the body fight infection. They are insufficient in the bodies of people with adrenal gland disorders. It is recommended that people taking glucocorticoids who develop symptoms of COVID-19 should immediately double their daily dose. Everyone taking corticosteroids are in the high risk category for COVID-19. People with diabetes are not more likely to get COVID-19 than the general population, but they experience severe symptoms, complications and worse outcome even death, once infected. Follow the sick day guidelines for people with diabetes and adrenal insufficiency. Adrenal, Pituitary, Thyroid, Parathyroid insufficiency, and Obesity – all have specific impact in SARS-CoV infection; should be followed stipulated protocols to deal with. Angiotensin-converting enzyme 2 (ACE2) is now established as the SARS-CoV receptor, angiotensin receptor 1 blockers such as losartan might reduce mortality. APN01 is a recombinant human ACE2 may be of benefit.

References

[1] Managing patients with endocrine dysfunction during COVID-19. Available from: https://www.medicalnewstoday.com/articles/managing-patients-with-endocrine-dysfunction-during-covid-19

[2] Marazuela M, Giustina A, Puig-Domingo M. Endocrine and metabolic aspects of the COVID-19 pandemic. Rev Endocr Metab Disord. 2020; 21(4): 495–507.

[3] Arlt W; Society for Endocrinology Clinical Committee. Society for Endocrinology Endocrine Emergency Guidance: Emergency management of acute adrenal insufficiency (adrenal crisis) in adult patients. Endocr Connect. 2016; 5(5):G1–G3.

[4] Woods CP, Argese N, Chapman M, Boot C, Webster R, et al. Adrenal suppression in patients taking inhaled glucocorticoids is highly prevalent and management can be guided by morning cortisol. Eur J Endocrinol. 2015; 173(5):633–642.

[5] Yang X, Yu Y, Xu J, Shu H, Xia J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med. 2020; 8(5):475–481.

[6] Guan W, Ni Z, Hu Y, Liang WH, Ou CQ, et al. China Medical Treatment Expert Group for Covid-19. Clinical characteristics of coronavirus disease 2019 in China .N Engl J Med. 2020; 382:1708–1720.

[7] Mazziotti G, Formenti AM, Frara S, Roca E, Mortini P, et al. Management of Endocrine Disease: Risk of overtreatment in patients with adrenal insufficiency: current and emerging aspects. Eur J Endocrinol. 2017; 177:R231–R248.

[8] Newell-Price J, Nieman L, Reincke M, Tabarin A. Endocrinology in the time of COVID-19: Management of Cushing's syndrome. Eur J Endocrinol. 2020; 183(1):G1–G7.

[9] Gupta R, Ghosh A, Singh AK, Misra A. Clinical considerations for patients with diabetes in times of COVID-19 epidemic. Diabetes MetabSyndr. 2020; 14(3):211–212.

[10] Raj VS, Mou H, Smits SL, Dekkers DHW, Müller MA, et al. Dipeptidyl peptidase 4 is a functional receptor for the emerging human coronavirus-EMC. Nature. 2013; 495 (7440):251–254.

[11] Julián MT, Alonso N, Colobran R, Sánchez A, Miñarro A, et al. CD26/DPPIV inhibition alters the expression of immune response-related genes in the thymi of NOD mice. Mol Cell Endocrinol. 2016; 426:101–112.

[12] Lu G, Hu Y, Wang Q, Qi J, Gao F, et al. Molecular basis of binding between novel human coronavirus MERS-CoV and its receptor CD26. Nature. 2013; 500 (7461):227–231.

[13] Yan R, Zhang Y, Li Y, Xia L, Guo Y, et al. Structural basis for the recognition of the SARS-CoV-2 by full-length human ACE2. Science 2020; 367(6485):1444–1448.

[14] Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respir Med. 2020; 8(4): e21–e21.

[15] European Society of Cardiology. Position Statement of the ESC Council on Hypertension on ACE-Inhibitors and Angiotensin Receptor Blockers. Available from: https://www.escardio.org/Councils/Council-on-Hypertension-(CHT)/News/position-statement-of-the-esc-council-on-hypertension-on-ace-inhibitors-and-ang

[16] APEIRON's respiratory drug product to start pilot clinical trial to treat coronavirus disease COVID-19 in China. Available from: https://pipelinereview.com/index.php/2020022673884/Proteins-and-Peptides/APEIRONs-respiratory-drug-product-to-start-pilot-clinical-trial-to-treat-coronavirus-disease-COVID-19-in-China.html

[17] Gurwitz D. Angiotensin receptor blockers as tentative SARS-CoV-2 therapeutics. Drug Dev Res. 2020; 81(5):537–540.

[18] Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020; 181(2):271–280.e8.

[19] Leow MK-S, Kwek DS-K, Ng AW-K, Ong K-C, Kaw GJ-L, et al. Hypocortisolism in survivors of severe acute respiratory syndrome (SARS). Clin Endocrinol. 2005; 63(2):197–202.

[20] Pal R, Banerjee M. COVID-19 and the endocrine system: exploring the unexplored. J Endocrinol Invest. 2020; 43(7):1027–1031.

[21] Melmed S, Bronstein MD, Chanson P, Klibanski A, Casanueva FF, et al. A consensus statement on acromegaly therapeutic outcomes. Nat Rev Endocrinol. 2018; 14(9):552–561.

[22] Fleseriu M, Karavitaki N, Dekkers OM. Endocrinology in the time of COVID-19: Management of pituitary tumours. Eur J Endocrinol. 2020; 183(1):G17–G23.

[23] Christ Crain M, Hoorn EJ, Sherlock M, Thompson CJ, Wass JAH. Endocrinology in the time of COVID-19: management of hyponatraemia and diabetes insipidus. Eur J Endocrinol. 2020;183(1):G9–G15.

[24] Wei L, Sun S, Xu C-H, Zhang J, Xu Y, et al. Pathology of the thyroid in severe acute respiratory syndrome. Hum Pathol. 2007; 38(1):95–102.

[25] De Jongh FE, Jöbsis AC, Elte JW. Thyroid morphology in lethal non-thyroidal illness: a post-mortem study. Eur J Endocrinol. 2001; 144(3):221–226.

[26] Vrachimis A, Iacovou I, Giannoula E, Giovanella L. Endocrinology in the time of COVID-19: Management of thyroid nodules and cancer. Eur J Endocrinol. 2020; 183(1):G41–G48.

[27] Albano D, Bertagna F, Bertoli M, Bosio G, Lucchini S, et al. Incidental findings suggestive of COVID-19 in asymptomatic patients undergoing nuclear medicine procedures in a high-prevalence region. J Nucl Med. 2020; 61(5):632–636.

[28] Nathan L, Lai AL, Millet JK, Straus MR, Freed JH, et al. Calcium ions directly interact with the Ebola virus fusion peptide to promote structure-function changes that enhance infection. ACS Infect Dis. 2020; 6(2):250–260.

[29] Booth CM, Matukas LM, Tomlinson GA, Rachlis AR, Rose DB, et al. Clinical features and short-term outcomes of 144 patients with SARS in the greater Toronto area. JAMA. 2003; 289(21):2801–2809.

[30] Uyeki TM, Mehta AK, Davey RT, Liddell AM, Wolf T, et al. Clinical management of ebola virus disease in the United States and Europe. N Engl J Med. 2016; 374(7):636–46.

[31] Bossoni S, thyroidectomized woman with Covid-19 infection. Endocrine. 2020; 68:253–254

[32] Di Filippo L, Formenti AM, Rovere-Querini P, Conte CM, Ciceri F, et al. Hypocalcemia is highly prevalent and predicts hospitalization in patients with COVID-19. Endocrine. 2020; 68(3):475–478.

[33] Tecilazich F, Formenti AM, Frara S, Giubbini R, Giustina A. Treatment of hypoparathyroidism. Best Pract Res Clin Endocrinol Metab. 2018; 32(6):955–964.

[34] Formenti AM, Tecilazich F, Frara S, Giubbini R, De Luca H, et al. Body mass index predicts resistance to active vitamin D in patients with hypoparathyroidism. Endocrine. 2019; 66(3):699–700.

[35] Chen N, Zhou M, Dong X, Qu J, Gong F, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020; 395(10223):507–513.

[36] Channappanavar R, Fett C, Mack M, Ten Eyck PP, Meyerholz DK, et al. Sex-based differences in susceptibility to severe acute respiratory syndrome coronavirus infection. J Immunol. 2017; 198(10):4046–4053.

[37] Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell. 2020; 181(2):271–280.e8.

[38] Lucas JM, Heinlein C, Kim T, Hernandez SA, Malik MS, et al. The androgen-regulated protease TMPRSS2 activates a proteolytic cascade involving components of the tumor microenvironment and promotes prostate cancer metastasis. Cancer Discov. 2014; 4(11):1310–1325.

[39] Tomlins SA. Recurrent fusion of TMPRSS2 and ETS transcription factor genes in prostate cancer. Science. 2005; 310(5748):644–6448.

[40] Stopsack KH, Mucci LA, Antonarakis ES, Nelson PS, Kantoff PW. TMPRSS2 and COVID-19: Serendipity or Opportunity for Intervention? Cancer Discov. 2020; 10(6):779–782.

[41] Petrilli CM, Jones SA, Yang J, Rajagopalan H, O'Donnell LF, et al. Factors associated with hospitalization and critical illness among 4,103 patients with COVID-19 disease in New York City. 2020. Available from: https://www.medrxiv.org/content/10.1101/2020.04.08.20057794v1