Disorders of Electrolyte Imbalance In COVID-19

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Key Points
➢ Incidence of corona virus disease ➢ Symptoms of COVID-19 ➢ Body systems affected by COVID-19 ➢ Introduction to COVID-19 ➢ Definition of hyponatremia, hypocalcemia, hypokalemia ➢ Complications of electrolyte imbalance in COVID-19 ➢ Importance of trace elements and electrolytes

The Coronavirus disease 2019 (COVID-19) is the result of an acute respiratory illness that has spread around the world. Coronavirus belongs to a group of positive-sense RNA viruses which are pathogenic to humans. Severe acute respiratory syndrome coronavirus 2 (SARS-Co-V-S) takes over the human cells by binding to the angiotensin I converting enzyme 2 (ACE2) present in the cell membrane of human tissues of vital organs including heart, liver, kidney and lungs. ACE2 acts as an important counter-regulatory mechanism of renin-angiotensin system (RAS) which pays a pivotal role in controlling electrolyte balance. SARS-CoV-S increases the degradation of ACE2 receptors resulting in reduced counter act of ACE2 on RAS thus leading to electrolyte imbalance.[1]

Fluid Electrolyte imbalance due to COVID-19 leads to disorders like hyponatremia, hypokalemia, hypocalcemia that are observed most commonly in hospitalized and intensive care patients which if left untreated may lead to increased mortality.[2]

Malnutrition and electrolyte imbalance weakens the immune system thus increasing the potential risk of being infected with covid-19. This is because vitamins i.e. A, B, C, D, E, trace elements including zinc, magnesium, copper selenium play important roles in strengthening the immune system.[3]

Hyponatremia

Hyponatremia is the most common disorder resulting due to electrolyte imbalance in COVID-19 patients. It has been reported that about 12% of COVID-19 effected patients have below normal sodium levels. A case study reported a 77-year-old male patient testing positive for SARS-CoV-2 having sodium levels as low as 123mmol/l and during investigation no other cause for hyponatremia were identified.[4] RNA sequencing studies showed that the expression of ACE2 proteins in the kidneys were 100 times greater than that expressed in lungs, hence kidneys are more potential targets of COVID-19.[4]

The pathological effects of COVID-19 on podocyte and proximal convoluted tubule cells causes AKI [acute kidney injury] hence reabsorption of essential components in glomerular filtrate i.e., Na+ ions are diminished resulting in excess loss of sodium ions in urine thus causing hyponatremia.[2]

Studies in rats have shown that high sodium diet intake causes decreased expression of ACE2 proteins while low sodium diet results in the upregulation of synthesis of ACE2 protein in kidney cells. Similar patterns were observed in humans hence it is hypothesized that low sodium levels may be a cause for the upregulation of ACE2 receptors in kidney cells. This indicates that increase in sodium diet intake by COVID patients may reduce expression of ACE2 receptors hence reducing the entry of virus into cells. In addition, deficiency of

sodium may increase the severity of COVID-19 infection.[4]

Hypokalemia

Hypokalemia occurs when the plasma potassium levels are below then normal conditions. Hypokalemia in COVID-19 patients is reported to be about 62% patients. The normal range of serum potassium is about 4-4.5 and 4.5-5.5 mmol/l. In a study of total 175 COVID- patients, 39 patients had severe hypokalemia with potassium levels less than 3mmol/l such low potassium levels can cause ventricular arrhythmia and respiratory muscle dysfunction which are life threatening disorders. 69 patients had potassium levels in the range 3-3.5mmol/l, while 67 patients had normokalaemia, potassium levels are greater than 3.5mmol/l and only 10 patients had plasma potassium levels greater than 4mmol/l.[1]

In Covid- patients two probable causes of loss potassium are high gastrointestinal losses and increases urinary loss. However, hypokalemia due to gastrointestinal loss only accounts for about 31% patients with severe hypokalemia having diarrhea while potassium loss in urine causing hypokalemia accounts for a higher percentage of covid patients.[1] The entry of virus into kidney cells decreases the ACE2 receptors and reduces angiotensin II degradation hence the secretion of aldosterone increases causing loss of potassium in urine.[3]

Hypokalemia in COVID- patients can aggravate acute respiratory distress syndrome [ARDS] and escalate the possibility of heart diseases in patients.[2]

Hypocalcemia

Hypocalcemia occurs when the blood calcium concentration is below 2.20mmol/l. in covid – cases it has been observed as one of the symptoms of SARS-CoV-2. A study conducted revealed that among COVID-19 patients, 59.3% had hypocalcemia at the time of admission in the hospital while 32.5% of patients in the control group had low calcium level (OR=3.02, 95% CI: 1.79-5.13, P<0.001). The rates of death and ICU admission were remarkably higher among the patients having hypocalcemia than those of EU calcemic group (85.7% vs 14.3% and 33.3% Vs 9.1%, respectively). In terms of the severity of the infection, 74.1% of patients in hypocalcemic group had a severe infection while 24.3% of the patients in EU calcemic group were diagnosed with severe infection (OR=8.89, 95% CI: 3.38-23.37, P<0.001).[5]

The binding or entry of COVID-19 virus into the cells is facilitated by Ca2+ ions. When the intracellular calcium ion concentration decreases the entry of virus into cells also decreases [2]. However, it is still unclear as to how a highly calcium dependent SARS-Co-2 method of action decrease the Calcium levels causing hypocalcemia. Though, it can be hypothesized that disruption in calcium homeostasis in patients with acute infection and high viral load may cause calcium reduction from blood circulation.[6]

Moreover, some common complications of hypocalcemic covid patients reported are multiple organ dysfunction syndrome (MODS), septic shock, acute kidney injury [AKI], high oxygen support, needs for MV and continuous renal replacement therapy, ARDS.[6]

Importance of trace elements and electrolytes in alleviating the severity of infection

Zinc: zinc plays an important role in both innate and adaptive immunity and in antiviral activities. In relation to COVID- zinc inhibits the activity of RNA dependent RNA polymerase [RdRp] hence decreasing the replication rate of the virus.

Selenium: selenium acts as a free radical scavenger and helps in cellular immunity. Having a daily dose of 50-100ug can help cause better and more immune responses.

Copper: it protects the DNA from oxidative stress. Studies show that human immune responses are weak when CU is deficient

Magnesium: it plays an important role in immune system comprising immunoglobulin synthesis and

immunoglobulin M [IgM] lymphocyte binding. However, its role in COVID- is not yet identified

The above examples indicate that serum electrolytes and trace elements help to strengthen the immune system and helps decrease the severity of the infection.[3]

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