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COVID Issue Paper

Cerebrovascular Disorders During COVID-19 Pandemic: What Should We Know

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Abstract

A New detected a virus called COVID-19 reported by World Health Organization (WHO) as pandemic at March 2020 COVID-19 is affected mainly by respiratory illness, but it can also affect the brain. Cerebrovascular disorders are recorded COVID-19 pandemics but are not effectively addressed how to deal and treat them. In this review, I try to discuss the postulated neuronal mechanisms of the coronavirus infection sequelae. After made midlines about this topic and collected more international papers. I discuss prevalence, pathogenesis, and then put a proposal on how to deal with Cerebrovascular disorders with COVID-19. Also, I discuss the protocol algorithm for anticoagulants in the COVID-19 era.

The aim of this review is to educate and update the neurologists and health team who working with suspected cases of COVID-19 with Cerebrovascular disorders.

Introduction

At the end of 2019, at Wuhan, China new strain virus of CORONA group spread all over the world called

COVID-19 [1,2].This virus mainly affected respiratory system. However, about 36.4% (78/214) of patients with COVID-19 developed many neurological symptoms, including **Cerebrovascular disorders** [3]. The affection of CNS occurred in severe cases rather than mild or moderate [4-9].

Central Nervous System involved during COVID-19 include, acute cerebrovascular disease [5,6,8,10,11].

My aim in this review is to update according to my knowledge, the neurologists working with suspected cases of COVID-19 or with patents without respiratory symptoms and developed **Cerebrovascular disorders.** Also, I try to put a proposal to how to deal and treat **Cerebrovascular disorders** patients with neurological disorders and COVID-19.

Search Strategy and Selection Criteria

I searched Medline, Egyptian Knowledge Bank, Scopus, Elsevier, PubMed, and Google Scholar. I collected data published between Jan 1, 2019, and June 15, 2020, using keywords " COVID-19", "Coronavirus", "pandemic", "SARS COV-2", management's strategy of neurological "neurology", "neurological", "stroke", **Cerebrovascular disorders**; anticoagulant. My Search limited only to the English language.

How COVID-19 Invade CNS

As previously known, Coronaviruses are not invading neurons primary. They invade respiratory epithelium first [3]. Then they invade CNS by a different mechanism. The coronaviruses invaded the nervous system either by direct or indirect pathways. In addition, it has a chronic phase in the affection of CNS.

Direct mechanisms are through the olfactory nerve, through the blood circulation system and through direct invade neuronal pathways, attached to ACE2 receptors which present in glial cells in the brain and spinal neurons then, multiply and damage the neuronal cells [10]. In addition, the difficulty of breathing is common even in moderate to severe cases of COVID-19. So, there is a possibility that a primary infection could take place in the brain stem [12].

Meanwhile, the coronaviruses have **Indirect mechanisms** include hypoxic brain injury and immune-mediated damage to the CNS. hypoxic brain injury resulted from severe respiratory distress led to hypoxia, hypercarbia, hypoxia and anaerobic metabolism, accumulation of toxic compounds. These factors leaded to neuronal swelling and brain edema hence brain damage [10]. Immune mediated pathway resulted from cytokines storm which led to activations of T lymphocytes, macrophages, and endothelial cells. This then led to an accumulation of inflammatory substances including interleukin-6 (IL-6), alpha tumor necrosis factor (TNF-α), IL-10, IL-15, IL-1β, soluble TNF receptor, and interferon- gamma (IFN-γ). In addition to lymphocytes, in particular, natural killer cells (NK) CD56 that lead to brain injury by altering BBB by trypsin and matrix [4]. These inflammatory substances leaded to vascular leakage, activation of complement and coagulation cascade, disseminated intravascular coagulation, and end hence neuronal damage [13-15].

Chronic Phase: As lack of permeability of CNS cerebral blood vessels made a barrier to viruses to invade the brain, but also a barrier to viruses 'elimination in case of brain invasion. The elimination of viruses is limited

and depends on the role of cytotoxic T-cells and apoptosis of infected neurons which led to a lack of major histocompatibility complex antigen in nerve cells. So, it led to chronic existence of viruses and may facilitate exacerbation of neurologic damage and degeneration [16-18].

Prevalence of Neurological Disorders With COVID-19

One large study involved 214 confirmed COVID-19 cases. It revealed (36.4%) had neurological manifestations, including (24.8%) with the central nervous system (CNS) [19]. Other study reported acute cerebrovascular disease in about 2.8% [20].

How to Deal With Some Neurological Disorders During Pandemic

Patients with neurological disorders ether developed from the virus as complications or preceded the infection should take more attention during the pandemic. In this review, we try to discuss each illness.

Cerebrovascular Stroke

COVID-19 lead to increase the prevalence of stroke, about 5% of COVID-19 patients with over 80% of them being ischemic stroke [21]. Hyperinflammatory state resulted from COVID-19 infection lead to hypercoagulable state that considered a direct cause for ischemic stroke [22]. We studied multiple protocols for patients with stroke to put that proposal for stroke during pandemic [2,21,23-27]. This proposal consists of:

1. Improving stroke awareness education, public health education activities to minimize stroke burden.

2. Fast-track system applied in emergencies for COVID-19 screening. Establishing telemedicine, phone, WhatsApp, connection with the stroke patients to treat in home mild symptoms

3. Healthcare providers engaged in acute stroke care are at risk of acquiring COVID-19 infection from stroke patients with COVID-19 infection. So, all protective measures should be taken as a designated area or pathway for suspected patients, surgical mask, surgical gown, gloves, face shield, cap, covers of shoe.

4. Early identification and separation of confirmed and suspected COVID-19 infected patients and identify other organ/systems dysfunction particularly: coagulation profile (PT, INR, APTT); platelet count; renal and hepatic function, CT Scan or CT angiography and/or CT perfusion and concurrent CT chest to identify COVID-19

5. Patients who at time window (3-4:30 h) and candied for intravenous rt-PA is recommended for selected patients with consider a reduction in expected benefit due to COVID-19 and coagulation abnormalities. Also, additional tests for assessing coagulation profile such as thromboelastography and serum concentration of D-dimers should be done in sepsis and hepatic dysfunction to determine risk-benefit ratio prior to intravenous rt-PA administration

6. Mechanical thrombectomy in selected patients balance between expected benefit and transmission risk.

7. As usual, antiplatelet medication may be avoided if possible, for the first 24 h after receiving intravenous rt-PA and mechanical thrombectomy or before maneuver.

8. However, single or dual antiplatelet medication may be considered for acute ischemic stroke who do not receive intravenous rt-PA and / or mechanical thrombectomy in patients with suspected or confirmed COVID-19.

9. Additionally, there is no clear data indicating the superiority of an antiplatelet agent to another in secondary prevention of stroke in these patients [20,25,28].

10. All admitted patients with moderate or severe COVID with high risk as increase D- dimer, creatinine, and CRP, should admitted to ICU and receive heparin drip or Enoxaparin 1mg/kg BID. if not admitted Enoxaparin SC 1mg/kg BID or Apixaban 5mg PO BID. Hold anticoagulation if: - Platelet count < 50,000; INR>1.5 or evidence of current or recent bleeding If patients take AC at home: - May switch to therapeutic enoxaparin or heparin (as per algorithm) for the duration of hospitalization unless contraindicated Rivaroxaban may be used in place of Apixaban at any indication [29-33].

11. Patients with COVID-19 often suffer from pro-longed prothrombin time and coagulopathy-increasing the risk of secondary cerebral hemorrhage, as clinical challenges implicit in treating the thrombotic consequences of COVID-19 cases recorded had ICH were on the treatment dose anticoagulation prior to their ICH, and the remaining were on a prophylactic dose of LMWH [34-37].

Conclusion

There is a clear emerging group of neurological manifestations during and after SARS-CoV-2 infection. The COVID-19 pandemic is still affecting many people all over the world. The medical fraternity is posed with a huge challenge. **Cerebrovascular disorders** related to COVID-19 are common due to direct, indirect, or as chronic. The relationship between COVID-19 and **Cerebrovascular disorders** with a consistent chronological sequence is widely accepted. Available treatment options might potentially lead to a wave of neurological sequelae. Now we are facing unknown possible neurological complications of COVID-19. So, many types of researches should be developed to postulate this pointing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Conflict of Interest

I declare that I have not conflict of interest.

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