CBD treatment during Covid-19 Pandemic

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Definition

At the end of 2019, a new disease —COVID-19—was identified, and a few months later, the World Health Organization announced a pandemic. It is now known that SARS-CoV-2 is highly contagious and most confirmed infections are mild to moderate. The situation is particularly difficult for dentists due to the high risk of virus transmission in the dental surgery. Complications including, but not limited to, problems with the respiratory and cardiovascular systems have been reported in patients with SARS-CoV-2. Several changes in the coagulation system, such as lower platelet numbers or increased prothrombin time, as well as increased D-dimer and fibrinogen, were observed. This review is intended to systematize the knowledge on the treatment of patients with congenital bleeding disorders (CBD) during the SARS-CoV-2 pandemic. Extensive literature research was conducted into COVID-19 and the general medical and dental treatment of patients with CBD. Case studies, research results and recommendations of international societies were used in the study. The results of this research are presented in the form of recommendations for the treatment of patients with coagulopathies. It should be remembered that the impact of COVID-19 on the health condition of patients with CBD is unknown to date.

1. Introduction

COVID-19 is an acute airway infection caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)[1]. The first outbreaks were identified at the end of 2019 in Wuhan, Hubei Province, China and, initially, the etiology of the disease was unknown [2]. On 11 March 2020, the World Health Organization (WHO) declared the SARS-CoV-2 pandemic due to the public health threat [3]. The speed at which the virus spreads proves how contagious it is. This is not the first pandemic in human history, but it is the first to cover the whole world. Globalization and the ease of travel are factors that have contributed to the virus's migration. Based on measurements and recommendations from previous pandemics, many international public health, governmental and other societies have provided guidance which is regularly updated, and several approaches have been implemented in order to control transmission, including reliable monitoring of the SARS-CoV-2 transmission rates and severity, mitigation of the impact of COVID-19 in healthcare and social care settings, detection of clusters or outbreaks in specific settings, and, once achieved, maintenance of COVID-19's elimination status. The data on previous virus epidemic/pandemic procedures, such as Ebola virus or MERS-CoV (Middle Mast respiratory syndrome coronavirus) and influenza (H1N1 influenza A pandemic or swine flu pandemic), with their severe socio-economic burdens, have been implemented into the current guidelines and recommendations, including those from the WHO and the European Centre for Disease Prevention and Control (EDCD). According to WHO data, as of 11 July 2020, there were 12,322,395 confirmed cases of COVID-19, 556,335 deaths and 216 countries and territories affected [4]. For comparison, another virus from the coronavirus family described in 2012—MERS-CoV, from September 2012—according to WHO data, covered only 27 countries and there were 2494 confirmed cases [5]. Previous pandemics have highlighted the lack of readiness of health professionals to work in a pandemic [6] and the need to provide up-to-date knowledge[7]. Moreover, they have taught medics that in order to prevent epidemics/pandemics, pathogens must be identified quickly, and their transmission should be kept to a minimum. When a new infectious agent is discovered, health authorities assess the risk of blood-borne viral/bacterial transmission, possibly due to the HIV pandemic, in which patients with hemophilia, among others, were inadvertently infected. Based on previous epidemics/pandemics—H1N1, H5N1, SARS, and MERS—we can conclude that there is a low risk of transmission of infection by transfusion [8][9] and a high risk of virus transmission in the dentist's office due to aerosol formation [10]. In addition, previous pandemics/epidemics, for example the HIV pandemic, have drawn attention to high-risk patients, including CBD patients. Due to the epidemiological situation, healthcare systems around the world are under constant pressure, and the diagnosis and treatment of patients with SARS-CoV-2 has become a priority. As a result, healthcare systems around the world are under constant pressure, and the diagnosis and treatment of patients with SARS-CoV-2 has become a priority. Healthcare facilities are adapting to the current epidemiological situation and it has become a goal and challenge to avoid becoming a source of COVID-19 transmission, which has an impact on the pattern and interdisciplinarity of the treatment

of patients with congenital bleeding disorders (CBD), including patients with hemophilia or von Willebrand disease. In truth, the clinical symptoms of infection mimic those of seasonal flu, but the course of the disease can vary greatly, from asymptomatic infections to fatal cases. Those most at risk of increased mortality due to COVID-9 are people with comorbidities and those over the age of 65 [11][12][13][14][15][16]. For this reason, treatment of the underlying disease has become extremely important. In patients with a confirmed SARS-CoV-2 infection, several changes in the coagulation system were observed, which may be related to vascular endothelial damage, inflammatory response with cytokine, activation of complement pathways and neutrophil extracellular traps due to infection [17][18]. The impact of COVID-19 on the health of patients with congenital bleeding disorders (CBD) is still under discussion. The literature suggests the possibility of thromboembolic disorders, also in patients with CBD [19]. There are known cases of bleeding related to COVID-19 infection [20] and also the influence of VWF factor level on the risk of complications is discussed[21][22]. The aim of this article is to give recommendations to doctors and dentists for the optimal management of patients with CBD during the SARS-CoV-2 pandemic.

2. Normal Hemostasis

Hemostasis, the process of blood clot formation at the site of vessel injury, consists of primary and secondary hemostasis. In primary hemostasis, after endothelia injury and the contraction of the vessel wall, platelets adhere to the collagen through platelet aggregation, secretion and further procoagulant activities leading to a platelet plug which is pivotal for the initial hemostatic response to stop bleeding. Secondary hemostasis causes permanent mechanical closure of the wound with local generation of fibrin and the subsequent formation of a fibrin-based clot based on coagulation factors, which is then followed by repair and scar formation. Initiation of the clotting of secondary hemostasis begins with the generation or exposure of tissue factor at the wound site with activated factor VII, generating a small amount of thrombin which activates factor XI, leading to amplification of thrombin generation in the propagation phase by enzyme complexes (intrinsic tenase and prothrombinase). All these processes reinforce the initial platelet plug and form a clot with a stable fibrin network with activated factor XIII that stabilizes and crosslinks the overlapping fibrin stands [23][24].

3. Bleeding Diathesis–Pathomechanism and Symptoms

Hemorrhagic disorders can be congenital or acquired and may result from vascular changes, deficiency of clotting factors, or dysfunction or reduction of thrombocytes. The most common inherited bleeding disorder is von Willebrand disease (VWD) [25]. VWD is caused by a quantitative or qualitative disorder of the von Willebrand factor[26]. This factor is essential for the adhesion of thrombocytes to the endothelium at the site of a damaged vessel. This abnormality is mainly related to primary hemostasis. Abnormalities of secondary hemostasis occur, among others, in hemophilia. Hemophilia is a hemorrhagic diathesis in which there is a decrease in factor VIII (hemophilia A), factor IX (hemophilia B) or factor XI (hemophilia C) [27]. In contrast to VWF, hemophilia A and B are an X-linked disease, therefore the diathesis affects only males or homozygous females [28]. Due to the factor deficiency, thrombin generation and clot formation is disturbed with impaired hemostasis and subsequent bleeding complications. The activity of the deficient or residual clotting factor level in the blood correlates with the severity of hemophilia and the severity of the symptoms. Severe (defined as <1 percent factor activity which corresponds to <0.01IU/ml), moderate (factor activity level ³1 percent of normal and £5 percent of normal) and mild levels of hemophilia (5–40% of the norm) have been distinguished [29]. In patients with hereditary bleeding diathesis, there is mainly excessive or prolonged bleeding, which may even be life threatening (Table 1) [30]. Bleeds that appear include gingival bleeding [31], intra-articular bleeding [31], excessive bleeding after injuries and surgery, for example, after tooth extraction [32][33], nasal and oral bleeding [31], gastrointestinal bleeding [31], hematomas and bleeding from small wounds [26]. Prolonged bleeding after tooth extraction may also occur in women who are carriers of hemophilia [34]. The cause of bleeding in the oral cavity, in addition to the deficiency of the coagulation factor, may be poor hygiene associated with the fear of possible mechanical injury, thus leading to gingivitis [35]. There are discrepancies in dental health and oral hygiene in individuals with CBD [35]. The literature reports a frequent occurrence of osteoporosis in patients with hemophilia [36][37], as well as the possibility of complications related to hemorrhages into muscles and joints [38]. Complications include arthropathy, synovitis, contractures, or the formation of pseudo-tumors within the loco-motor system in the course of hemophilia. In some cases, hemarthrosis may appear, and in rare cases, it may also affect the temporomandibular joint . Pseudo-tumors may occur both in the bones and muscles [39]. In exceptional cases, they are located within the craniofacial bones [40][41][42]. In addition, treatment with plasma-derived concentrates without the

appropriate virus inactivation may result in blood-borne infections, including human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), human T-cell leukemia virus (HTLV-1), or parvovirus B19 [43].

Table 1. Symptoms of congenital hemorrhagic diathesis.

Congenital Hemorrhagic Diathesis
1. Bleeding gums
2. Hemarthrosis
3. Excessive or prolonged bleeding after injuries
4. Excessive or prolonged bleeding after surgery
5. Bleeding from the nose
6. Bleeding from the mouth
7. Gastrointestinal bleeding
8. Hematomas
9. Bleeding from minor wounds

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Keywords

COVID-19;severe acute respiratory syndrome coronavirus 2;dentists;blood coagulation disorders;pandemics;cardiovascular system