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Provision of Medical Care to Underage Patients Suffering from Diseases of the Endocrine System in Conditions of the Spread of Coronavirus Infection

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ABSTRACT

The article examines the possibilities of providing medical care to underage patients suffering from diseases of the endocrine system in conditions of the spread of coronavirus infection. It was determined that due to the still rather high incidence of COVID-19 worldwide, it is important for pediatric endocrinologists to know about the interaction of SARS-CoV-2 with the endocrine system and the peculiarities of managing patients with concomitant diseases who have developed COVID-19 disease. Despite the fact that children and adults have common risk factors that affect the risk of complications in SARS-CoV-2 infection, it becomes clear that the responses in the pediatric population differ, and the results of studies for adults cannot be extrapolated.

Among children and adolescents, the majority of chronic patients are pediatric endocrine patients with diabetes mellitus, thyroid diseases and obesity. Providing assistance to such patients, especially if they have symptoms of coronavirus infection, both in a hospital setting and remotely, is one of the main activities of modern pediatric endocrinology.

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INTRODUCTION

The 2019 Coronavirus disease pandemic (Covid-19) has caused enormous grief, social unrest, social change and economic consequences around the world. Millions of lives were lost, many people suffered, families lost their loved ones, and the consequences for everyday life were enormous. On the one hand, it is important to remember and document these facts. On the other hand, life goes on, and the full extent of the changes caused by the pandemic can only be observed in the coming years. The pandemic and its consequences have revealed failures in health systems and management strategies, as has been the case for many centuries after numerous previous epidemics.

The main strains of Covid-19, in general, were easily tolerated by children; however, the incidence of Covid-19 in children corresponded to the incidence rates among the adult population, at least in areas with a low incidence of Covid-19. However, the rates of overweight and obesity in children and adolescents increased during the pandemic crisis and the associated closure of schools and preschools.[1]

In addition, pediatric services, in particular children's polyclinics, were used less frequently in some societies. Last but not least, children's leisure time has changed during periods of isolation and school closures. In addition, serious and very stressful psychological consequences of school closures are reported.

The researchers noted that during the pandemic crisis, the care of children with endocrine and metabolic diseases could deteriorate. The severity, for example, of diabetes manifestations, could increase during periods of self-isolation and/or due to fear of infection, which could prevent families from seeking medical help. Initially, it was thought that children and adolescents experience similar but less severe symptoms and complications of SARS-CoV-2 infection. Currently, it is obvious that children experience unique manifestations of SARS-CoV-2 infection, including multisystem inflammatory syndrome (MIS-C)

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and various endocrine reactions. For this reason, the purpose of this work is to consider the specifics of providing medical care to underage patients suffering from diseases of the endocrine system in conditions of the spread of coronavirus infection.

MATERIALS AND METHODS

The analysis of specialized medical literature in the field of assistance to children with endocrine diseases in the era of the development of coronavirus infection was carried out through the use of comparative and analytical research methods.

RESULTS

The SARS-CoV-2 virus has multiple pathophysiological relationships with the endocrine system and can cause disorders of the pituitary gland, adrenal glands and thyroid gland, glucose metabolism and mineral metabolism. The existing data are generally favorable for endocrine complications of COVID-19 in children.[2]

While most pediatric patients with endocrine disorders caused by COVID-19 have asymptomatic or mild symptoms, it is important to note that patients with type 1 or type 2 diabetes were not only more likely to suffer from COVID-19, but also had moderate symptoms, severe symptoms, especially in the presence of other concomitant diseases.

As a result, the number of diabetic patients admitted to intensive care units increased. Diabetes and obesity are risk factors for increased morbidity and mortality in adult patients with COVID-19, but it is encouraging that in patients younger than 25, the mortality rate is approaching zero even with diabetes or obesity.

Although there is some data on adult patients, little is known about the effect of COVID-19 on other endocrine diseases in children. The current experience of pediatric endocrinologists indicates that the management of diabetes requires much more efforts than the treatment of other endocrine diseases.

There is a two-way relationship between COVID-19 and diabetes mellitus. In adults, uncontrolled diabetes is associated with the severity of COVID-19. Moreover, severe metabolic complications were observed in patients with COVID-19 either at the onset of the disease or with pre-existing diabetes. Although pediatric patients with diabetes do not appear to be at a higher risk of contracting SARS-CoV-2, it is still reasonable to avoid infection and take all possible preventive measures.[3]

It has also been suggested that SARS-CoV-2 itself may be diabetogenic, as in patients with pneumonia caused by the SARS 1 coronavirus. However, this association has not yet been confirmed and requires further study in both adults and children.

The COVID-19 pandemic has led to delayed hospitalizations for diabetes and other endocrine diseases, which has led, for example, to a higher proportion of severe cases of diabetic ketoacidosis, as has been observed in other studies. A safe way without COVID-19 through pediatric emergency departments is necessary to help and reassure parents who want to get their children to the hospital in a timely manner and avoid unnecessary complications with diabetes and other endocrine diseases.

After the establishment of an endocrine disease, it is important to maintain continuous communication with medical professionals, as recommended by many endocrine societies, especially with telemedicine, in order to avoid crowded waiting rooms.

However, despite the need to minimize unnecessary hospital visits during the pandemic through contactless communication via video calls, text messages and emails, routine visits to doctors remained the most common method of consultation.

Increasing knowledge about telemedicine can help families and patients gain confidence in this method of care. To avoid complications in these patients, especially in conditions of limited resources, it is necessary to prioritize guidance on care management and accelerated innovations in the field of telehealth. Video platforms have been introduced in many institutions, especially in educational ones, although not all allow the use of telemedicine for inpatient treatment.[4]

Many parents were concerned about the safety of sending their children with endocrine disorders, especially diabetes, back to school during the COVID-19 pandemic, believing that they were more likely to get infected with the coronavirus. It is encouraging, however, that most of them were familiar with the school instructions and made sure that the patient care plan was in place.

Free access to medicines and supplies for the treatment of the endocrine system and diabetes, which was already a problem in many parts of the world before the pandemic, is vital. Due to the fact that important infrastructure, such as clinics and public transport, is severely limited due to the pandemic, access problems have worsened, although daily self-help, hospital management and survival depend on the availability of medical supplies.

COVID-19 has been associated with endocrine diseases and concomitant diseases, while obesity and hypertension were most common in all endocrine diseases. Children and adolescents who needed intensive care often had concomitant diseases. Therefore, it is important to understand which modifiable risk factors may play a role in increasing the severity of COVID-19.

Indeed, some children have suffered from a more serious variant of COVID-19, but the reasons remain unclear; comorbidities are less common in young patients than in adults, which may explain why children are less vulnerable to COVID-19, but why some of them still get critically ill. Taking into account the recent increase in the incidence of type 2 diabetes and obesity among young people, a significant number of children may be at higher risk.

The COVID-19 pandemic has exacerbated concomitant mental illnesses throughout society, not least in patients with diabetes and other endocrine disorders. Children are a particularly vulnerable group, as their nervous system, endocrine system and hypothalamic-pituitary-adrenal system are insufficiently developed.[5]

Psychological crises often lead to feelings of abandonment, despair, incapacity and exhaustion in children and even increase the risk of suicide. It should be noted that our study

revealed reports of suicide attempts during the pandemic in children with a wide range of different endocrine diseases.

Psychosocial support for children and their families, especially children with chronic illnesses, should be part of the health response to natural disasters and recovery after them. Timely and appropriate remedies are needed to prevent psychological and behavioral problems.

DISCUSSION

The issues of management of children and adolescents with concomitant endocrine disorders, including those who have developed COVID-19 disease, are very important in modern conditions.

Children with multiple pituitary hormone deficiency may be at increased risk of complications and mortality from COVID-19. The current guidelines for adults with growth hormone deficiency recommend stopping taking growth hormone during hospitalization with COVID-19; however, there is not enough data on the effects of growth hormone treatment for COVID-19 disease in children.

Recommendations for the treatment of central diabetes insipidus in patients with mild COVID-19 do not differ from the usual recommendations for the treatment of diabetes insipidus at home. However, patients of all ages with diabetes insipidus are at risk of sodium imbalance during hospitalization and should be closely monitored. Hypernatremia can be caused by the inability to give free water to patients who cannot take care of themselves, and the inability to rely on the mechanism of thirst in critically ill patients.[16]

Patients are also vulnerable to hyponatremia due to overtreatment of DI and excessive ADH on the background of pneumonia caused by COVID-19. Treatment of DI with subcutaneous or oral desmopressin, rather than intranasal desmopressin, should be considered if there are concerns about nasal congestion. Patients with severe COVID-19 desmopressin should be administered intravenously. Osmolality and urine volume should be monitored, as well as the serum sodium content should be measured at frequent intervals (every 2-4 hours) to maintain eunatremia.

Patients with COVID-19 may have severe respiratory illness, including pulmonary edema, since hypernatremia is not considered a risk factor for mortality in COVID-19, tolerance to mild hypernatremia may be required in these circumstances to prevent pulmonary edema.

Individuals with steroid addiction or suspected adrenal suppression should first of all be careful to avoid infection with SARS-CoV-2. Patients should be treated in accordance with existing recommendations for dosing under stress during symptomatic COVID-19 disease.

The RECOVERY study, a randomized open trial of oral or intravenous dexamethasone (6 mg) daily compared to conventional treatment, showed a significant reduction in mortality among patients receiving invasive mechanical ventilation and among those who received oxygen without invasive mechanical ventilation, but not among those who did not receive respiratory support during randomization.

In the guidelines published on September 2, 2020, the World Health Organization strongly recommended systemic corticosteroid therapy for patients with severe and critical COVID-19, as well as conditional recommendations not to use corticosteroids in patients with mild COVID-19.[7]

Viral diseases may be more difficult to treat in people with diabetes due to increased insulin resistance and ketone production. Since a higher level of A1C positively correlates with the frequency of diabetic ketoacidosis in children with diabetic ketoacidosis, a significant part of the child population with DM1 may be at increased risk of developing diabetic ketoacidosis against the background of COVID-19 infection. It is extremely important that clinicians take the time to review the recommendations for sick days and be available for guidance during illness to reduce the risk of developing diabetic ketoacidosis.

During COVID-19 disease, patients should be advised to monitor their blood glucose levels more often, either with continuous glucose monitors or with finger sticks. More frequent titration of the insulin dose and additional corrective boluses of fast-acting insulin may be required to avoid severe hyperglycemia and ketoacidosis.

Patients should check ketones regardless of blood sugar levels and, if ketones are present, increase the correction dose and fluid intake. Encouraging remote monitoring of blood glucose levels with CGM is a valuable tool that should be offered to all families.

For children with DM2, additional recommendations are similar to the recommendations set out in the section on obesity below. It is imperative that all children maintain regular physical activity and strive for a healthy diet during this pandemic.

The closure of schools, camps and extracurricular sports and activities due to the pandemic has already had a serious impact on the health of children and adolescents due to social isolation, lack of activity and food insecurity in socially and economically disadvantaged households. In one of our centers, we observed a significant increase in the number of children under the age of 19 with newly diagnosed diabetes, while most of the increase in new cases is due to an increase in type 2 diabetes (RM; unpublished data).[8]

It is more important than ever to strengthen healthy eating habits and give age-appropriate recommendations on nutrition and physical activity. Racial/ethnic and socio-economic differences have exacerbated health inequities, especially related to weight control during the COVID-19 pandemic. Healthcare professionals should continue to educate patients about healthy eating and regular exercise. We encourage access to telemedicine interventions as an adjunct to weight management in children.

The risk of premature atherosclerotic cardiovascular disease (ASCVD) in young people who have had MIS-C is not yet known; however, patients with a history of Kawasaki disease and residual aneurysmal dilatation are considered to be at high risk of ASCVD. In MIS-C, coronary artery aneurysms were found in 6-24% of patients, and signs of Kawasaki disease were documented in 40%.

Recent evidence suggests that pediatric patients with MIS-C who have been treated with IVIG or IL-6 antagonists such as

tocilizumab recover without complications. 79 However, given the unknown risk of complications, longer follow-up by a cardiologist is required for children who have recovered from MIS-C.

It remains to be determined whether vitamin D replacement will provide protection against COVID-19 or complications. Randomized trials are currently underway to help determine whether vitamin D supplements can prevent or reduce the severity of COVID-19.

Prolonged periods of home quarantine, designed to stop the spread of COVID-19, may limit the time spent outdoors, which increases the risk of vitamin D deficiency and related complications, including rickets, osteomalacia and symptomatic hypocalcemia. Clinicians should continue to follow current recommendations for vitamin D supplementation for patients at risk of deficiency. For patients with hypophosphatemic rickets, the FDA recently approved home injection of burosumab during the COVID-19 pandemic.[9, 10]

A joint statement by the American Society for Bone and Mineral Research, the American Association of Clinical Endocrinology, the Endocrinological Society, the European Calcified Tissue Society and the National Osteoporosis Foundation offers recommendations for the treatment of osteoporosis in adults during the COVID-19 pandemic, some of which may need to be changed for pediatric patients.[11-13]

In children with low bone density, basic interventions to maintain bone health should be encouraged, including adequate intake of calcium and vitamin D and replacement therapy with sex steroids as indicated. Weight management is an important component of optimizing bone health and should not be neglected; physiotherapy services are now widely available through telemedicine and should be used for home therapy when needed. Extended treatments should be continued whenever possible.[14]

In adult patients, due to the prolonged action of intravenous bisphosphonates, it is usually considered safe to postpone treatment for at least 6-9 months. However, in children, the continued growth of a new bone and the appearance of stress factors in conditions of intermittent administration of bisphosphonates may increase the risk of fractures if treatment is significantly delayed.

Consideration should be given to transferring patients from pamidronate to zoledronic acid, which is administered over a shorter period of time and requires less frequent infusions. Clinicians may consider conducting laboratory tests before repeated infusions if the patient has no history of hypocalcemia during previous infusions, receives sufficient amounts of calcium and vitamin D with food or supplements, has no kidney disease and overall health is stable. DXA scanning and other imaging methods may be postponed in most patients if the results of DXA scanning do not change the treatment tactics.

Author Contributions

All authors contributed in reviewing the final version of this paper.

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