

## **ESPE Patient Information on COVID-19 and Pediatric Endocrine Disease**

### **Disease specific information and advice – Vitamin D deficiency**

This flyer aims to provide guidance on prevention and treatment of COVID-19 in patients with a pediatric endocrine disease. It summarizes facts about COVID-19, and what children with endocrine diseases and their parents need to know regarding their health and well-being. These recommendations are based on the latest knowledge and expert opinion. If, after reading, you still have concerns or questions, please contact your physician or healthcare provider.

#### **What is COVID-19?**

Infection by coronavirus can lead to disease COVID-19, a flu-like illness. On March 11, 2020, the World Health Organization publicly characterized COVID-19 as a pandemic. People who are confirmed to have COVID-19 have exhibited mild to severe respiratory illness with fever, coughing and shortness of breath. Additional symptoms include chills, muscle pain, sore throat, loss of taste or smell and possibly gastrointestinal symptoms like nausea, vomiting or diarrhea, skin rash, or discoloration of fingers or toes. Symptoms may appear 2–14 days after exposure to the virus. Risk on severe course of COVID-19 is associated with increasing age, being overweight or obese, male gender, high blood pressure and diabetes with health conditions.

#### **Children and COVID-19**

In children, disease course of COVID-19 is generally mild. Usually no special treatment is required, other than simple supportive measures (drink enough water, use paracetamol). Few children have complaints that are so serious that hospitalization is necessary and deaths from COVID-19 in children are extremely rare. Children who have COVID-19 and have symptoms such as fever, cough etc. are thought to be able to spread the virus in a similar way to adults. Many children with COVID-19 have no symptoms and it is not known if they can spread the virus.

#### **Introduction. Definition, phenotype and treatment of vitamin D deficiency**

More than 80% of vitamin D (VitD) in humans comes from skin synthesis. Unfortunately, environmental and individual factors such as living at higher latitudes, cloud cover and air pollution, darker skin pigmentation, aging and use of sun protection cosmetics could be responsible for insufficient vitD production. Balanced diet could cover the remaining 20% of daily demand for vitD intake. However, in the case of limited skin synthesis, even healthy and varied diet is not going to make up for deficiencies and using appropriate supplements is recommended.

VitD status is assessed by measuring blood levels of total 25OHD and its concentrations above 20 ng/ml (50 nmol/l) or above 30 ng/ml (according to other recommendations) are considered sufficient. Despite the availability of vitamin D supplementation and published recommendations for prevention, vit D insufficiency or deficiency is common worldwide. This could have a major impact on children's development and growth as well as their general health. Similarly to different cut-offs for deficiency definitions there are different recommended therapeutic protocols. The groups in risk of VitD deficiency that need individualized prevention-treatment approach (e.g. obese individuals require double dose of VitD supplementation recommended for healthy age-matched peers) have been

identified and a part of them presents with evident endocrine symptomatology. VitD deficiency has been described as a pandemic. Regardless of age and ethnicity, recent data showed that 40% of Europeans are vitamin D deficient and 13 % are severely deficient.

Based on studies the prevalence of VitD concentration below 20 ng/ml in acute and critically ill children was high and associated with increased mortality. Additionally a recently published meta-analysis confirmed that deficiency of VitD in children may have an independent relationship with up to 2.2 fold risk increase of sepsis.

### **Are patients with vitamin D deficiency at increased risk of corona infection and severe course of COVID-19?**

For several weeks there has been an increasing interest in the influence of vitD deficiency on the risk, severity and fatality of COVID-19. The number of publications related to COVID-19 risk or severity in the context of VitD deficiency increases rapidly. However, in children and young patients disease course of COVID-19 is generally mild or even asymptomatic, thus almost all observations and statistics refer directly to adult population.

Low vitamin D concentration has been associated with a significantly increased risk of pneumonia and viral upper respiratory tract infections. Previous observation, not related to COVID-19, showed that vitamin D supports production of antimicrobial peptides in the respiratory system, therefore making infection with the virus and development of COVID-19 symptoms less likely. Thus, vitamin D might help to reduce the inflammatory response to infection with COVID-19.

Only part studies on adults confirmed that vitD deficiency, without sufficient treatment, is associated with higher COVID-19 risk. The data regarding higher prevalence of hospitalization as well as higher risk of more severe COVID-19 course is inconclusive as well.

In the context of the prevalence of vitamin D deficiency in countries commonly affected by COVID-19 there is a debate regarding to the connection between geographic latitudes, vitD deficiency and severity of COVID-19. However, typically 'sunny' countries with lower latitude such as Italy (Northern Italy) and Spain, had low mean concentrations of vitD, high frequency of vitamin D deficiency and the highest infection rates in Europe. The northern latitude countries (e.g. Norway, Finland) which receive less UVB sunlight, actually had better vitD supplementation, much higher mean vitD concentrations, low levels of deficiency and lower infection and sever courses rates.

### **Do the corona virus prevention measures differ for children with vitamin D deficiency compared to the general population?**

The corona measures are no different for children with vitamin D deficiency than for healthy children. No extra precautions are needed other than the usual advice. They should go to school when permitted by the general corona virus prevention measures. The corona virus will be around for a long time; therefore, it is important for children to attend school regularly to allow for their education, as well as normal development and general well-being.

### **What should children with vitamin D deficiency do to protect themselves?**

There is no vaccine for COVID-19 yet. To prevent corona virus from spreading, there are several general recommendations. Wash your hands often with soap and water for at least 20 seconds; do not touch your eyes, nose and mouth with unwashed hands; avoid close contact with people who are sick; stay at home when you are sick; and disinfect frequently touched objects and surfaces. Strict adherence to COVID-19 prevention measures, like social distancing, is necessary. Just in case be prepared, have your doctor's phone numbers at hand, including how to reach them at night and on weekends or holidays. Remember about healthy diet and rest.

## **What is the advice on the regular monitoring and therapeutic procedures of patients with vitamin D deficiency?**

Little is known about the protective factors of COVID-19 infection. Therefore, preventive health measures that can reduce the risk of infection, progression and severity are desperately needed. Despite the lack of direct evidence on the effect of vitamin D levels on COVID-19 infection, regardless of the age-group, one could assume that vitamin D deficiency is an easily modifiable risk factor and should be actively corrected through safe, inexpensive and easily-available vitamin D supplements. Even a small decrease in COVID-19 infections would easily justify this intervention.

The general rules for vitamin D status monitoring during COVID-19 are in line with recommendations for non-COVID-19 patients. Previous studies showed that vitamin D supplementation is safe and that it protects against acute respiratory tract infection overall.

**Summary: There is not enough evidence on the association between vitamin D levels and COVID-19 risk and severity in pediatric population. Our knowledge is based on individual studies performed on adults. From previous studies, published before the COVID-19 era, we know that rate of vitamin D deficiency in acute and critically ill children was high and associated with increased risk of sepsis and mortality. Therefore, well-planned high-quality trials are required. Prophylactic vitamin D supplementation is highly recommended according to guidelines and in case of vitD deficiency therapeutic dose should be proposed.**

**Disclaimer:** Due to the emerging nature of the COVID-19 crisis this document is not based on extensive systematic review or meta-analysis, but on literature review and expert opinion. The document should be considered as guidance only; it is not intended to determine an absolute standard of medical care. Healthcare staff need to consider individual circumstances in their management for patients.

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