

COVID-19: INTRANASAL PROINSULIN C-PEPTIDE CASE STUDY

Date of publishing: 01. 31. 2021.

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Summary

In December 2019 a new type of coronavirus the SARS-CoV-2 appeared in China, which caused a disease named Covid-19. Since the outbreak of the Covid-19 pandemic, international studies proved consistently that the pathogenic effect is achieved primarily through attacking and damaging the immune system. The virus gets into the cells predominantly bound to the ACE2 enzyme receptor located in the epithelial cells covering the alveoli of the lung. This receptor appears not only in the cells of the lung, but also in the epithelial cells of the myocardium, the kidney, the esophagus, the stomach and the intestines, the cells lining the blood vessels as well as on the surface of certain leukocytes. As a consequence general inflammations evolve and these cause the so called „cytokine storm“, the increased production of inflammatory proteins. The disturbance of the cytokine network plays an important role in the development of the clinical symptoms and the prognosis of the disease.

After becoming infected a number of patients remain symptom free or only mild symptoms appear. Meanwhile in a higher percentage of the infected persons, mainly in the elderly and patients suffering from comorbidities severe condition is developed frequently, which may have fatal outcome due to respiratory failure on one hand and septic shock on the other hand as a consequence of the bacterial superinfection.

According to the clinical significance the temporal course of Covid-19 can be divided into 3 phases:

I. phase (early phase of the infection):

- respiratory
- gastro-enteric symptoms
- high fever

II. phase (phase of lungs complications)

- pneumonia is developed

III. phase

- development of systemic inflammation, cytokine storm with diverse clinical symptoms, appearance of MAS (macrophage activation syndrome) and HLH (hemophagocytic lymphohistiocytosis).

The adult HLH virus infections can raise the number of autoimmune, malignant, hematopoietic, neurological, hormonal and psychic diseases or worsen the state of the existing ones.

Due to the abnormal immune functioning the lungs, heart, kidney, brain, digestive system get sick, also causing endothel damage to the blood vessels of the target organs, which cause a number of irreversible symptoms specific to the affected organ. This process destroys the quality of life, makes life expectancy shorter, regardless of age, even in young ages.

Increase of blood pressure, decrease of pulse and HRV values by approximately 30% can predict the development of the disease in several cases, or it can refer to the presence of the virus.

HRV value: the responsiveness of the heart, means the whole person's emotional, hormonal, neural balance and the reactivity to situations of life. The higher value of heart rate variability (HRV) is a complex measure of health. It describes how can the heart constantly change the period between one to another heartbeat, reacting to the varying loads of the internal and external environment. The adaptability of the heart is based on the optimal interplay of the sympathetic and parasympathetic nervous system. Appropriate heart rate variability can be achieved in the body if there is balance between the two systems. If the sympathetic system is predominated, the HRV value will decrease. This than increases the risk of developing cardiovascular diseases.

The most appropriate phrase for the prime attack to the immune system is the cytokine storm, and these mean the worst consequences, causing acute mortality.

Our testing concerning the effectiveness of C-peptide proved its favourable effect on the immune system and its functioning in our studies. Therefore in our present investigation we tested the use of intranasal C-peptide in 30 cases being positive in Covid-19 testing or showing the symptoms of Covid-19.

In our present investigation we were focusing on the answers to the following questions:

- What was the percentage of the different symptoms in the patients with a positive Covid-19 test?
- What was the percentage of comorbidities?
- What was the distribution of sexes among the 30 participants?
- What kind of treatments were needed during the process of recovery?
- Apart from general therapy what kind of supplementary treatment was applied?
- Did they need hospitalization?
- What was the length of recovery while applying the spray?

Since we are aware of the possible complications, we find it necessary plan to follow up the patients in 2 and in 6 months time, since it is known from our previous studies that C-peptide is highly effective in inhibiting the later consequences due to the abnormal functioning of the immune system, which has an estimated risk of 60 percent according to the literature. The question is whether the percentage of the risk to develop complications will change favorably due to the C-peptide treatment. Unfortunately the known consequences lead to very severe harm to health, irreversible disability or even fatal outcome.

The verbal feed-back of the investigated patients expressed a concordant opinion , that the above described symptoms rapidly relieved after introducing the c-peptide treatment, therefore their well-being significantly improved, also their hope for recovery. None of those who were treated with C-peptide were observed to have the most severe complications.

Introduction / Gábor Varga

The importance of central proinsulin C peptide in the treatment of COVID-19

The increase of the inflammatory markers CRP and Il-6 predict the unfavorable course of the covid-19 infection.^{i ii} The decrease of HRV by more than 40% precedes a 50% increase in CRP during the next 72 hours according to a small study.ⁱⁱⁱ The sudden decrease of HRV may signal the weakening or collapse of the cholinergic anti-inflammatory pathway. It is supposed that by strengthening this pathway the cytokine storm could be prevented or at least mitigated.^{iv v vi} In an animal study it was shown that increased vagus nerve activity, measured by (RMSSD), the parasympathetic part of the HRV, the brain inflammatory processes, and the resulting brain damages can be mitigated.^{vii} This is highly significant, because – besides the cytokines - the spike protein of covid-19 can cross the blood-brain barrier and induce inflammatory processes in the brain leading to neuroinflammation and neurological disorders.^{viii ix x} Elderly patients with chronic diseases have impaired vagus nerve activity that may exacerbate the covid-19 disease course.^{xi} For this reason, methods increasing the vagal tone may be beneficial for the treatment or prevention of the severe consequences of covid-19 infection. One of the most promising methods is the intranasal administration of proinsulin c peptide. Systemic administration of C can increase the vagus nerve activity according to clinical trials on insulin-dependent diabetes mellitus patients that are among the most affected people regarding the mortality of covid-19 caused disease.^{xii xiii} Proinsulin c peptide administered directly into the brain seems to have even a more pronounced effect on the parasympathetic nervous system.^{xiv} Intranasal application of proinsulin c peptide is effectively transferring the peptide into the brain.^{xv}

The resident immune cells in the CNS, the microglia, are often activated in patients severely affected by the disease according to autopsic investigations.^{xvi} The hyperactivity of the molecular scissor, cofilin that regulates the shape and dynamical change of the actin cytoskeleton is responsible for the overactivation of microglia. The reduction of the hyperactivity of the cofilin is leading to the cessation of the overactivity of microglia.^{xvii xviii} Interestingly, proinsulin c peptide, besides increasing HRV, is also able to inactivate cofilin in lymphocytes that may serve as a model for microglia and neurons also.^{xix}

Description of the proinsulin C peptide spray

The participants of our study were using the Vargapeptide skin-spray off label, as an intranasal spray, on their own responsibility. The spray is produced and distributed by the Max-Immun Ltd.

This was applied in the same way as the intranasal insulin was and is administered in the population of children with Phelan-McDermid syndrome.

A 20 ml bottle contains a solution of 18 ml C-peptide. One puff off the spray contains 0,108 mg proinsulin C-peptid. In Vargapeptide 0,5 this amount is half of it, 0,05 g, in Vargapeptide 2 the amount is 0,216 mg.

The spray contains 0,8 % NaCl. The other ingredients fulfill the requirements of pharmaceutical grade purity. The purity of proinsulin C-peptid is 98-99%.

Description of the study

The effectiveness of C-peptide was investigated involving 30 patients with positive coronavirus test from the beginning of September to the end of December 2020.

- The investigated participants applied the C-peptide types 0.5, 1 and 2, each person the same type, mainly 1-1 puff every 4 hours, in case of severe symptoms 1-1 puff every 2 hours.
- The age of the patients ranged from 17 to 76 years.
- The distribution of sexes was slightly more females (20) than males (10).

The investigated symptoms were divided into 3 categories:

Frequent symptoms: occurred in more than 9 cases

Moderately frequent symptoms: prevalence of 4-8 cases

Rare symptoms: reported in 1-3 cases

Other aspects of investigation:

- oxygen therapy
- mechanical ventilation
- anesthesia

Each patient started using the C-peptide spray within 3 days after being diagnosed.

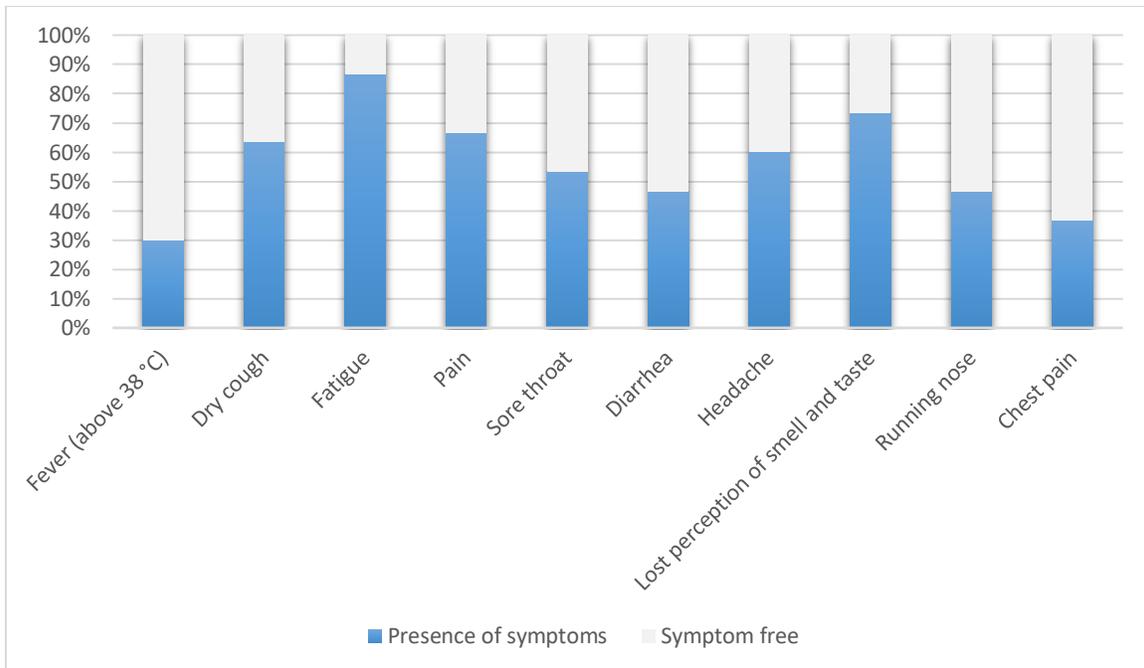
THE NUMBER, SEX, AGE AND COMORBIDITY OF THE INVESTIGATED PARTICIPANTS

Number of cases	Sex	Age (years)	Comorbidity
1.	male	17	Hepatitis caused by Epstein-Barr virus o
2.	male	49	Not known
3.	male	74	Conn syndrome, hypertonia, arrhythmia
4.	male	31	Not known
5.	male	61	Not known
6.	male	67	Morbus Chron
7.	male	34	Not known
8.	male	68	Not known
9.	male	30	Not known
10.	male	55	Not known
11.	female	53	Hypertonia, diabetes type II.
12.	female	38	Hypertonia
13.	female	44	Thyroid disease
14.	female	50	not known
15.	female	46	Hashimoto thyroiditis, Insulin resistance, Joint pain
16.	female	39	Autoimmune hyperthyroidism
17.	female	44	Not known
18.	female	47	Not known
19.	female	45	Not known
20.	female	52	Not known
21.	female	42	Psoriasis
22.	female	54	Hypertonia
23.	female	27	Deep vein thrombosis
24.	female	49	Asthma
25.	female	72	Heart disease
26.	female	42	Intestinal permeability syndrome Histamine intolerance, Adrenal fatigue
27.	female	40	Not known

Number of cases	Sex	Age (years)	Comorbidity
28.	female	58	Not known
29.	female	55	Hypertonia
30.	female	57	Not known

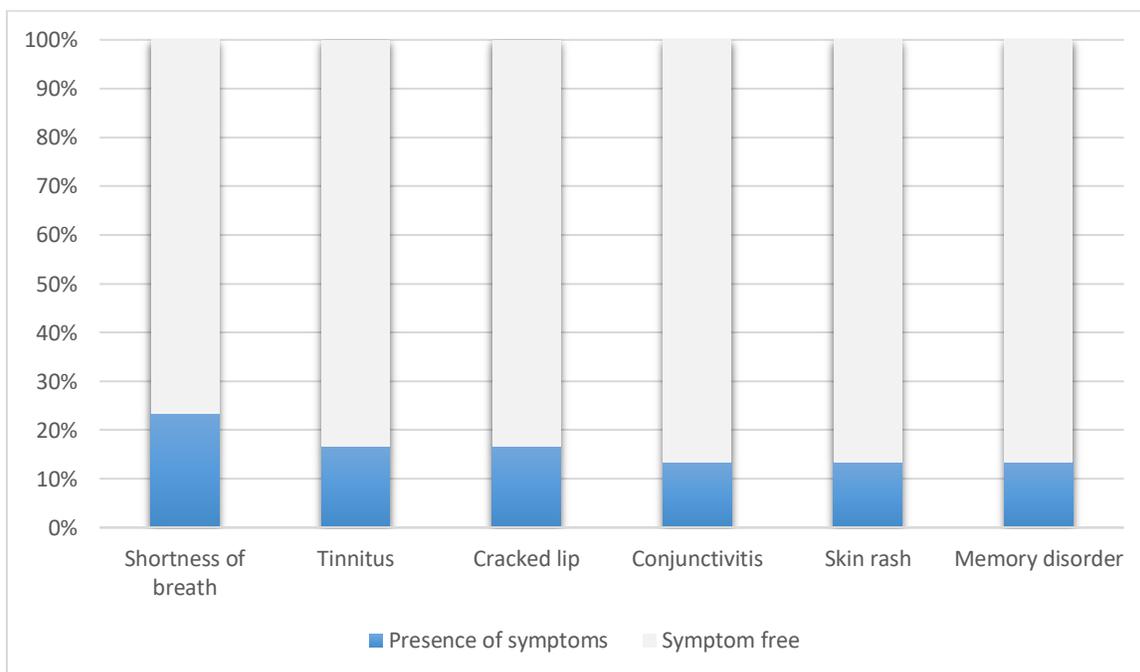
THE GROUP OF PATIENTS WITH FREQUENT SYMPTOMS

Symptoms	Frequency	Percentage	Number of participants
Fever (above 38 °C)	9	30%	30
Dry cough	19	63%	30
Fatigue	26	87%	30
Pain	20	67%	30
Sore throat	16	53%	30
Diarrhea	14	47%	30
Headache	18	60%	30
Lost perception of smell and taste	22	73%	30
Running nose	14	47%	30
Chest pain	11	37%	30



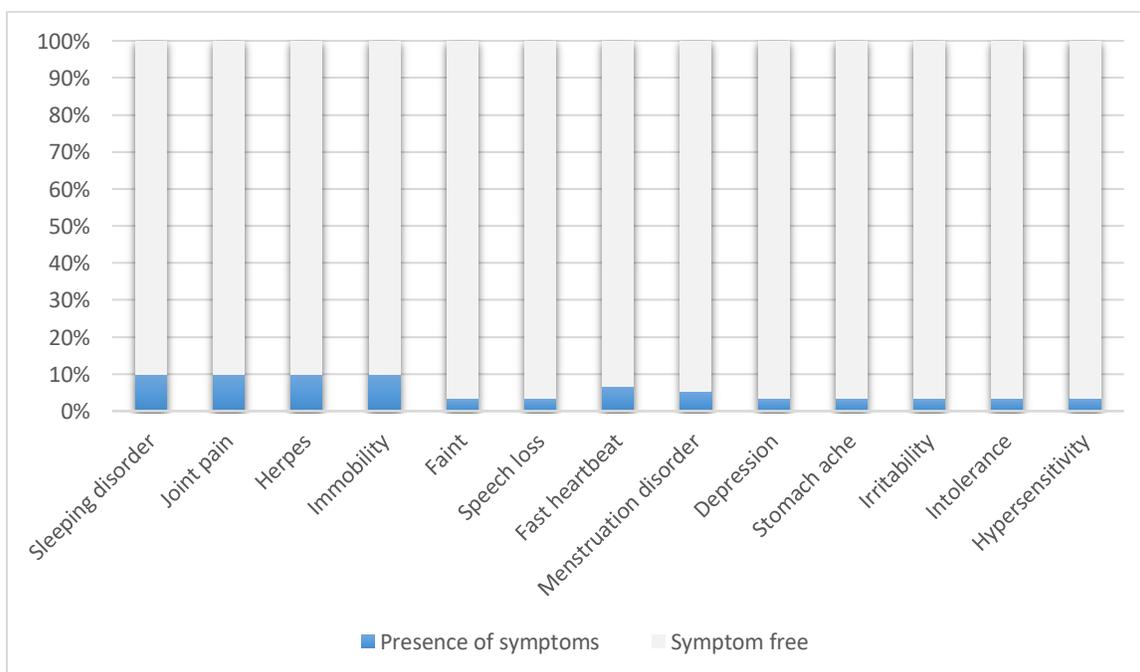
GROUP OF PATIENTS WITH MODERATELY FREQUENT SYMPTOMS

Symptoms	Frequency	Percentage	Number of participants
Shortness of breath	7	23%	30
Tinnitus	5	17%	30
Cracked lip	5	17%	30
Conjunctivitis	4	13%	30
Skin rash	4	13%	30
Memory disorder	4	13%	30



GROUP OF PATIENTS WITH RARE SYMPTOMS

Symptoms	Frequency	Percentage	Number of participants
Sleeping disorder	3	10%	30
Joint pain	3	10%	30
Herpes	3	10%	30
Immobility	3	10%	30
Faint	1	3%	30
Speech loss	1	3%	30
Fast heartbeat	2	7%	30
Menstruation disorder	1	5%	19
Depression	1	3%	30
Stomach ache	1	3%	30
Irritability	1	3%	30
Intolerance	1	3%	30
Hypersensitivity	1	3%	30



INVESTIGATION OF COMORBIDITY AND RETURNING TO WORK

Returning to work

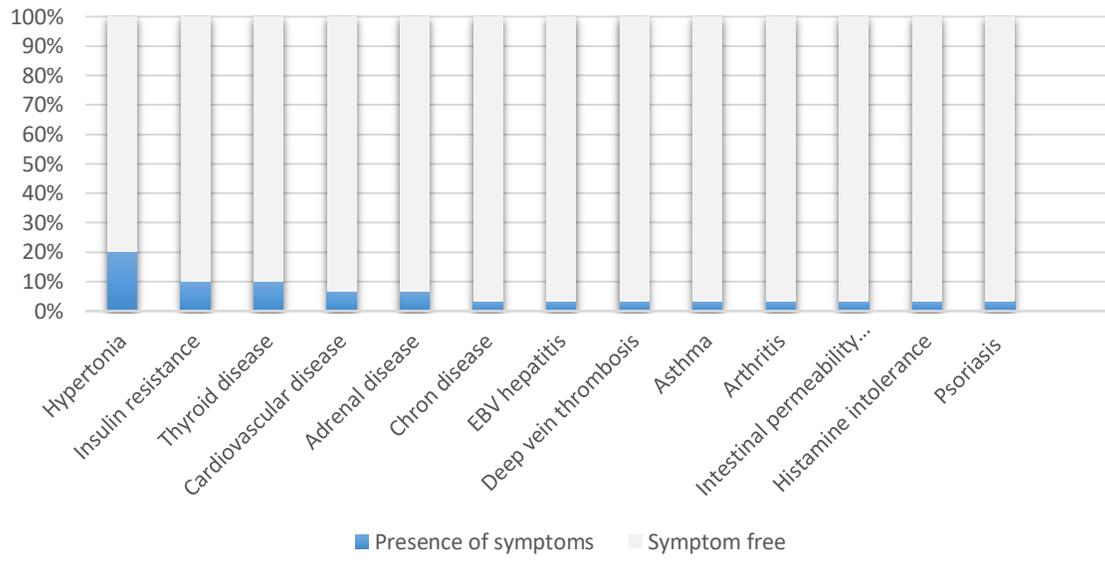
- Varied between 3-30 days, the average was cca15 days.

The proportion of persons with and without comorbidity was 1:1, among the 30 participants in the investigated group

There was comorbidity in 15 cases

Symptoms	Frequency	Percentage	Number of participants
Hypertonia	6	20%	30
Insulin resistance	3	10%	30
Thyroid disease	3	10%	30
Cardiovascular disease	2	7%	30
Adrenal disease	2	7%	30
Chron disease	1	3%	30
EBV hepatitis	1	3%	30
Deep vein thrombosis	1	3%	30
Asthma	1	3%	30
Arthritis	1	3%	30
Intestinal permeability syndrome	1	3%	30
Histamine intolerance	1	3%	30
Psoriasis	1	3%	30

Comorbidity



MOST FREQUENTLY USED ANTIBIOTIC AND ANTIVIRAL DRUGS, SUPPLEMENTARY TREATMENTS

In the group of investigated patients:

- hospital treatment became necessary in 1 case, this person was in deep anesthesia for 4 days (severe chronic disease: Conn syndrome)
- pneumonia in the early phase in 2 cases
- temporary vision loss in 1 case
- fluctuating blood pressure in 1 case
- overturning of the menstrual cycle in 1 case was observed.

Most frequently used antibiotic and antiviral therapy:

- Azithromycin therapy 6 patients
- Favipiravir: 1 patients
- Isoprinosine: 1 patients

Blood thinner therapy: 2 patients(Clexane, Marfarin)

Symptomatic treatment: Algopyrin, Advil, Coldrex, ACC

Most frequently used vitamin, minerals and medicinal fungi (supplementary treatments):

Vitamin D:	24 patients
Vitamin C:	24 patients
Zinc:	13 patients
Magnesium:	6 patients
Tawny rose extracts:	3 patients

Propolis, L-Lysin, Silver-colloid, Quercetin, A-K2 vitamin, E-vitamin, Canabidiol, Ganoderma medicinal fungi extracts, Varga medicinal fungi extracts

The verbal feed-back of the investigated patients expressed a concordant opinion , that the above described symptoms rapidly relieved after introducing the c-peptide treatment, therefore their well-being significantly improved, also their hope for recovery. None of those who were treated with C-peptide were observed to have the most severe complications.

LITERATURE RELATED TO THE PRESENT INVESTIGATION

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