I-PREVENT℠

COVID PROTECTION PROTOCOL

# A GUIDE TO THE PREVENTION OF COVID-19

September 6, 2022

(Changes include: Note on added sugar in kefir/probiotics)

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# Disclaimer

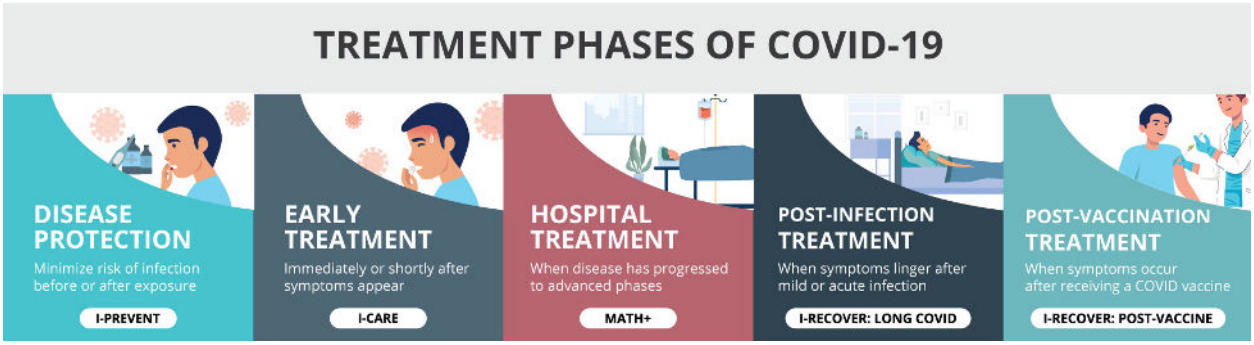
The information in this document is our recommended approach to COVID-19 based on the best (and most recent) literature. It is provided as guidance to healthcare providers worldwide on the prevention and early treatment of COVID-19. Our guidance should only be used by medical professionals in formulating their approach to COVID-19. Patients should always consult with their provider before starting any medical treatment. As this is a highly dynamic topic, we will update these guidelines as new information emerges. Please ensure you are using the latest version of this protocol.

# Overview of I-PREVENT

At the beginning of the pandemic, FLCCC developed the MATH+ protocol to provide guidance for treating the pulmonary phase of COVID-19, with the goal of reducing hospital mortality. However, it soon became obvious that our emphasis needed to shift to prevention and early treatment to protect patients from requiring hospitalization and dying from this largely preventable disease.

It is critical to recognize that infection with SARS-CoV-2, the virus that causes the disease, progresses through several stages. Treatment is therefore highly stage-specific (see Figure 1).

Figure 1. Treatment Phases of COVID-19



Source: FLCCC

Recent data suggest that ivermectin, melatonin, naso-oropharyngeal hygiene, as well as the combination of quercetin (or mixed flavonoids) and Vitamin C, may play an important role in both pre-exposure and post-exposure protection. [1-5] The evidence supporting the use of ivermectin for the prophylaxis of COVID-19 is provided by the comprehensive review by Kory et al. [6]

The following protocol can be used for both chronic and post-exposure prevention. It is important to emphasize that all the medications included in our prevention regimen are inexpensive, safe, and widely available. The I-PREVENT protocol must be part of an overall strategy that includes common sense public health actions such as good hand hygiene, avoiding crowded public gatherings, adequate ventilation, and other measures.

Chronic prevention is especially recommended for healthcare workers, and for high-risk individuals such as those over 60 years old with comorbidities, people who are morbidly obese, and residents of long-term care facilities. Follow the post-exposure prevention instructions if a household member is COVID-

positive or if you have had prolonged exposure to COVID or a COVID-positive patient but you have not developed symptoms. At the onset of any flu-like symptoms, please refer to the I-CARE early treatment protocol.

# Chronic Prevention

(in order of priority, not all required)

**Ivermectin** 0.2 mg/kg per dose; start treatment with one dose, take second dose 48 hours later, then 1 dose every 7 days (weekly). [7-12] Those at high risk of contracting COVID-19 can consider dosing twice a week.

Ivermectin is best taken with a meal or just following a meal for greater absorption. [13]

Ivermectin is a remarkably safe drug with minimal adverse reactions (almost all minor). [14] Please check Table 1 below for potential drug interactions. The most important drug-drug interactions occur with cyclosporin, tacrolimus, antiretroviral drugs, and certain antifungal drugs.

Due to the possible drug interaction between quercetin and ivermectin these drugs should not be taken simultaneously (i.e., should be staggered morning and night).

While ivermectin has a remarkable safety record, fixed drug eruptions (diffuse rash) and Stevens Johnson Syndrome have rarely been reported. [15;16] While hepatitis is commonly quoted as a side effect, we are aware of only one published case report of reversible hepatitis. [17]

The safety of ivermectin in pregnancy has not been determined. [18] Its use, particularly in the first trimester, should be discussed with a trusted healthcare provider, as it may increase the risk of congenital malformations. [18] Additionally, women should be counselled that low concentrations of ivermectin are present in breast milk; the implications of this finding are unclear. [19]

**Disclaimer: The safety of ivermectin in pregnancy has not been established.**
**Use in the first trimester should be avoided. Please discuss with your physician.**

**To read more about the safety of the vitamins and nutraceuticals listed on the FLCCC protocols during pregnancy, please review this document.**

**Table 1. Drug Interactions with Ivermectin**
Patients taking any of these medications should discuss with their treating physicians.

| SERIOUS (5)<br>Use Alternative | MONITOR CLOSELY (50) | |
|---|---|---|
| erdafitinib | amiodarone | lonafarnib |
| lasmiditan | atorvastatin | loratadine |
| quinidine | berotralstat | lovastatin |
| sotorasib | bosutinib | nefazodone |
| tepotinib | clarithromycin | nicardipine |
| | clotrimazole | nifedipine |
| | dronedarone | nilotinib |
| | elagolix | phenobarbital |
| | eliglustat | phenytoin |
| | erythromycin base | ponatinib |
| | erythromycin ethylsuccinate | quercetin |
| | erythromycin lactobionate | ranolazine |
| | erythromycin stearate | rifampin |
| | felodipine | ritonavir |
| | fosphenytoin | sarecycline |
| | fostamatinib | simvastatin |
| | glecaprevir/pibrentasvir | sirolimus |
| | indinavir | St John's Wort |
| | istradefylline | stiripentol |
| | itraconazole | tacrolimus |
| | ivacaftor | tolvaptan |
| | ketoconazole | trazodone |
| | lapatinib | tucatinib |
| | levoketoconazole | verapamil |
| | lomitapide | warfarin |

Source: Medscape

**Zinc** 30–40 mg/day. [20-27] Zinc is essential for innate and adaptive immunity. [23] In addition, zinc inhibits RNA-dependent RNA polymerase in vitro against SARS-CoV-2 virus. [22] Due to competitive binding with the same gut transporter, prolonged high dose zinc (> 50mg day) should be avoided, as this is associated with copper deficiency. [28]

Zinc supplements come in various forms, including zinc sulfate, zinc citrate, zinc gluconate and zinc oxide.

**Melatonin** (slow- or extended-release): Begin with 1 mg and increase as tolerated to 6 mg at night. Causes drowsiness. [2;29-36]. Some patients are intolerant to melatonin, having very disturbing and vivid dreams; in these patients it may be best to start with a 0.3 mg slow-release tablet and increase slowly, as tolerated. Melatonin undergoes significant first pass metabolism in the liver with marked individual variation; this explains the wide dosing requirement.

Melatonin has anti-inflammatory, antioxidant, immunomodulating and metabolic effects that are likely important in the mitigation of COVID-19 disease. [37-39] Multiple studies have demonstrated the benefit of melatonin at various stages of the disease.

**Oropharyngeal hygiene** with twice daily antiviral mouthwash/gargle (see Figures 3 and 4 below). Inhaled steam supplemented with antimicrobial essential oils (e.g., VapoRub™ inhalations) once a day have been demonstrated to have virucidal activity. [40] Antimicrobial essential oils include lavender oil, thyme oil, peppermint oil, cinnamon oil, eucalyptus oil and sage oil. [40-44] Antiseptic-antimicrobial mouthwashes (chlorhexidine, povidone-iodine, cetylpyridinium chloride and the combination of eucalyptus, menthol, and thymol [Listerine™]) have been shown to inhibit SARS-CoV-2 replication and to reduce viral load in research studies. [45-52] A mouthwash containing cetylpyridinium chloride (CPC) has broad antimicrobial properties and has been shown to be effective in controlling gingivitis and gingival plaque. [52-54] An in-vitro study demonstrated that CPC was highly virucidal against a human coronavirus. [55] In a primary prophylaxis study, a povidone-iodine throat spray administered three times daily proved to be highly effective in reducing the risk of laboratory confirmed SARS-CoV-2 infection.

Oropharyngeal hygiene will likely reduce the viral load in the upper airways, thereby reducing the risk of symptomatic disease and likely reducing disease severity. This may be particularly important with the Omicron variant, which replicates to achieve viral high loads in the nasopharynx/oropharynx.

**Table 2. Ivermectin Dosing for Chronic Prevention**

Note that ivermectin is available in different strengths (e.g., 3, 6, or 12 mg) and forms (e.g., tablets, capsules, drops). Tablets can be halved for more accurate dosing, if needed. Doses below are calculated for the upper end of the weight ranges listed.

| How much do I weigh? | | How much should I take? |
|---|---|---|
| 70–90 lb | 32–40 kg | 8 mg |
| 91–110 lb | 41–50 kg | 10 mg |
| 111–130 lb | 51–59 kg | 12 mg |
| 131–150 lb | 60–68 kg | 13.5 mg |
| 151–170 lb | 69–77 kg | 15 mg |
| 171–190 lb | 78–86 kg | 16 mg |
| 191–210 lb | 87–95 kg | 18 mg |
| 211–230 lb | 96–104 kg | 20 mg |
| 231–250 lb | 105–113 kg | 22 mg |
| 251–270 lb | 114–122 kg | 24 mg |
| 271–290 lb | 123–131 kg | 26 mg |
| 291–310 lb | 132–140 kg | 28 mg |

**Vitamin D.** Vitamin D deficiency is common in the Middle East and some countries in Asia, Europe, and North America. [56;57] Less sun exposure, sunscreen use, increased body mass index (BMI), less physical activity, and poor socioeconomic status predict lower serum 25(OH)D concentrations.

Vitamin D receptors are present on immune cells, with this vitamin playing a critical role in both innate and adaptive host immunity. [58;59] Vitamin D has numerous immunological properties that play a vital role in protecting against and limiting the severity of COVID-19. [60] Vitamin D insufficiency has been associated with an increased risk of COVID-19 infection and dying from the disease. [61-65]

Vitamin D supplementation is likely a highly effective and cheap intervention to lessen the impact of this disease, particularly in vulnerable populations (i.e., the elderly, obese, people of color, and those living

in northern latitudes). [66-82] In addition, Vitamin D supplementation may be important in pregnant patients. [62]

The greatest COVID protection benefit from Vitamin D supplementation will occur in those individuals deficient in Vitamin D. Those individuals should take Vitamin D prophylactically on a longer-term basis. When a person with Vitamin D deficiency develops COVID-19, risks increase for developing complications, and Vitamin D supplementation subsequent to infection will have less of a response. [83] This concept is supported by a recent study that demonstrated that residents of a long-term care facility who took Vitamin D supplementation had a much lower risk of dying from COVID-19. [84] Therefore the goal is to bring serum 25(OH)D concentration higher than 50 ng/ml and maintain that level throughout the pandemic.

The dosing recommendations for Vitamin D supplementation vary widely. The optimal target is > 50 ng/ml; at this level the risk of dying from COVID-19 is extremely low. [64] It may take many months/years to achieve optimal levels in patients with a Vitamin D level of < 12 ng/ml taking the standard recommended dose of 5,000 IU/day. It is therefore EXTREMELY IMPORTANT that the optimal regimen for Vitamin D supplementation for the prophylaxis of COVID-19 is provided promptly, based on the baseline Vitamin D level (see Table 3). If the level is unknown, the needed dose can be calculated from body weight or BMI, as illustrated in Table 4.

Since the highest dose of commercially available Vitamin D3 is 50,000 IU capsules, and due to its affordability (low cost) and better gastrointestinal absorption, we recommend using 50,000 IU D3 capsules for non-urgent outpatients and community setups. Together, a number of these capsules can be taken as a bolus dose [i.e., single upfront doses such as 100,000 to 400,000 IU. However, the liver has a limited 25-hydroxylate capacity to convert Vitamin D to 25(OH)D: thus, taking 50,000 IU capsules over a few days provides better bioavailability.

Table 3 presents a safe and practical treatment schedule for raising blood 25(OH)D concentrations and tissue storage without adverse effects in non-urgent situations (modified from SJ Wimalawansa with permission). [85] The dosing schedule illustrated in Table 4 should be used when recent serum 25(OH)D concentration is unavailable (from SJ Wimalawansa with permission). [85]

If necessary (optional), measure blood concentrations four weeks after a course of Vitamin D to assess whether the desired serum 25(OH)D concentrations are achieved. It is best to include both Vitamin K2 (Menaquinone [MK7] 100 mcg/day, or 800 mcg/week] and magnesium (250-500 mg/day) when doses of Vitamin D > 8000 IU/day are taken. [86;87]

**Curcumin (turmeric)** 500 mg twice a day. Curcumin has antiviral activity against a number of viruses including SARS-CoV-2. In addition, this spice has anti-inflammatory, antioxidant, and immune-modulating properties. [88-92] Emerging data suggests that curcumin improves the clinical outcome of patients with COVID-19. [93;94] As the body's absorption of turmeric is poor, it is traditionally taken with milk and black pepper to enhance absorption. Nano-curcumin preparations or formulations designed to enhance absorption are preferred for better absorption. [94-97]

***Nigella sativa* (black cumin)** 80 mg/kg daily and honey 1 g/kg daily. Both honey and *Nigella sativa* have antiviral, antimicrobial, anti-inflammatory, and immune-modulatory effects with proven safety profiles. [98-105] It should be noted that thymoquinone (the active ingredient of *Nigella sativa*) decreases the absorption of cyclosporine and phenytoin. [106] Patients taking these drugs should therefore avoid

taking *Nigella sativa*. Furthermore, two cases of serotonin syndrome have been reported in patients taking *Nigella sativa* who underwent general anesthesia (probable interaction with opiate). [107]

**Vitamin C** 500–1000 mg twice a day. Vitamin C has important anti-inflammatory, antioxidant, and immune-enhancing properties, including increased synthesis of type I interferons. [4;5;108-110] The non-absorbed fraction of Vitamin C enhances the proliferation of *Bifidobacterium*.

**Quercetin** 250–500 mg daily. Quercetin is a plant phytochemical (flavonoid) with broad spectrum anti-inflammatory, antioxidant, antiviral, anticoagulant, and immunomodulatory properties. [111-118] Quercetin inhibits SARS-COV-2 replication by a number of mechanisms. [115;118-120] In addition, quercetin inhibits mast cells, [121] and has been demonstrated to reduce neuroinflammation. [122] The major limitation of supplemental quercetin is its poor solubility and low oral absorption. [123] A lecithin-based formulation (Quercetin Phytosome®, Life Extension Bio-Quercetin) and a nanoparticle formulation have shown markedly improved bioavailability. [124;125] Quercetin Phytosome (250-500 mg BID) has shown promising results in both the prevention and treatment of symptomatic COVID-19. [3;126]

Due to the possible drug interaction between quercetin and ivermectin these drugs should not be taken simultaneously (i.e., should be staggered morning and night). The use of quercetin has rarely been associated with hypothyroidism. [127] Quercetin and other flavonoids interfere with thyroid hormone synthesis at multiple steps in the synthetic pathway. [128-131] The clinical impact of this association may be limited to those individuals with pre-existent thyroid disease or those with subclinical thyroidism. Quercetin should be used with caution in patients with hypothyroidism and TSH levels should be monitored. It should also be noted quercetin may have important drug-drug interactions; the most important drug-drug interaction is with cyclosporin and tacrolimus. [132] In patients taking these drugs it is best to avoid quercetin; if quercetin is taken cyclosporin and tacrolimus levels must be closely monitored. The safety of quercetin and flavonoids in pregnancy has not been established and they should probably be avoided.

A mixed flavonoid supplement containing quercetin, green tea catechins, resveratrol, curcumin, rutin and anthocyanins (from berries) may be preferable to a quercetin supplement alone; [133-137] this may further minimize the risk of quercetin-related side effects.

**Probiotics**. There appears to be a bi-directional relationship between the microbiome (especially Bifidobacterium) and COVID-19. Low levels of Bifidobacterium may predispose a person to COVID-19 and increase disease severity. [138-141] COVID-19 depletes the microbiome of Bifidobacterium, which may then increase the severity and duration of COVID-19 symptoms. Kefir (a fermented milk drink) is high in Bifidobacterium and other probiotics that have demonstrated health benefits. [142;143] Suggested probiotics include Megasporebiotic (Microbiome labs), TrueBifidoPro (US Enzymes) and yourgutplus+. [144] NOTE: Depending on the brand, these products can be very high in sugar, which promotes inflammation. Look for brands without added sugar or fruit jellies and choose products with more than one strain of lactobacillus and bifidobacteria. Try to choose probiotics that are also gluten free, casein free, and soy free.

**B complex vitamins** [145-149].

**Table 3. Guidance on Upfront Loading Dose Regimens to Replenish Vitamin D Stores in the Body**

When serum vitamin D levels are available, the doses provided in this table can be used for the longer-term maintenance of serum 25(OH)D concentration above 50 ng/mL (125 nmol/L). The table provides the initial bolus dose, weekly dose, frequency, and the duration of administration of oral vitamin D in non-emergency situations, in a non-obese, 70 kg adult.

| Serum Vitamin D (ng/mL) ** | Vitamin D Dose: Using 50,000 IU Capsules: Initial and Weekly $ | | Duration (Number of Weeks) | Total Amount Needed to Correct Vit. D, Deficiency (IU, in Millions) # |
|---|---|---|---|---|
| | Initial Bolus Dose (IU) | Follow-Up: $$ The Number of 50,000 IU Caps/Week | | |
| <10 | 300,000 | ×3 | 8 to 10 | 1.5 to 1.8 |
| 11–15 | 200,000 | ×2 | 8 to 10 | 1.0 to 1.2 |
| 16–20 | 200,000 | ×2 | 6 to 8 | 0.8 to 1.0 |
| 21–30 | 100,000 | × 2 | 4 to 6 | 0.5 to 0.7 |
| 31–40 | 100,000 | ×2 | 2 to 4 | 0.3 to 0.5 |
| 41–50 | 100,000 | ×1 | 2 to 4 | 0.2 to 0.3 |

Source: Nutrients'—Special Issue: "Vitamin D—Calcifediol and COVID" [150]

* A suitable daily or weekly maintenance dose to be started after completing the loading-dose schedule. The dose should be adjusted for those who are overweight (higher) or underweight (lower). ** To convert ng/mL to nmol/L, multiply the amount in ng by 2.5; One µg = 40 IU. $ Mentioned replacement doses can be taken as single, cumulative doses, two to three times a week spread out over a few weeks. $$ From the day one of week two onwards. # Estimated total vitamin D dose needed to replenish the body stores (i.e., the deficit) is provided in the last column.

**Table 4. Vitamin D Dosing in the Absence of a Baseline Vitamin D Level**

Longer-term maintenance schedules of oral vitamin D based on body weight to maintain the levels above 50 ng/mL (125 nmol/L) when the serum 25(OH)D concentrations are unknown.

| Bodyweight Category | | Dose kg/Day (IU) | Dose (IU) (Daily or Weekly) * | |
|---|---|---|---|---|
| (Age) or Using BMI (for age > 18) (kg/Ht. $M^2$) | Average Body Weight (kg) | | Daily Dose (IU) | Once a Week (IU) |
| (Age 1–5) | 5–13 | 70 | 350–900 | 3000–5000 |
| (Age 6–12) | 14–40 | 70 | 1000–2800 | 7000–28,000 |
| (Age 13–18) | 40–50 | 70 | 2800–3500 | 20,000–25,000 |
| BMI ≤ 19 | 50–60 (under-weight adult) | 60 to 80 | 3500–5000 | 25,000–35,000 |
| BMI < 29 | 70–90 (normal: non-obese) | 70 to 90 | 5000–8000 | 35,000–50,000 |
| BMI 30–39 | 90–120 (obese persons) # | 90 to 130 | 8000–15,000 | 50,000–100,000 |
| BMI ≥ 40 $ | 130–170 (morbidly obese) $ | 140 to 180 | 18,000–30,000 | 125,000–200,000 |

Source: Nutrients'—Special Issue: "Vitamin D—Calcifediol and COVID" [150]

* Example of a daily or once-a-week dose range for adults with specific body types (based on BMI for white Caucasians and body weight for other ethnic groups). Appropriate dose reductions are necessary for children. # For those with chronic comorbid conditions, such as hypertension, diabetes, asthma, COPD, CKD, depression, and osteoporosis, and to reduce all-cause mortality, higher doses of vitamin D are needed. For them, one can use the doses that are recommended for persons with obesity (BMI, 30–39: the third row). $ Those with multiple sclerosis, cancer, migraine headaches, and psoriasis, and those routinely taking medications such as anti-epileptic and anti-retroviral agents that significantly increase the catabolism of vitamin D should consider taking age-appropriate doses recommended for those with morbid obesity (BMI ≥ 40; the higher end of the daily doses in the fourth row).

**Figure 2. Naso-Oropharyngeal Hygiene**

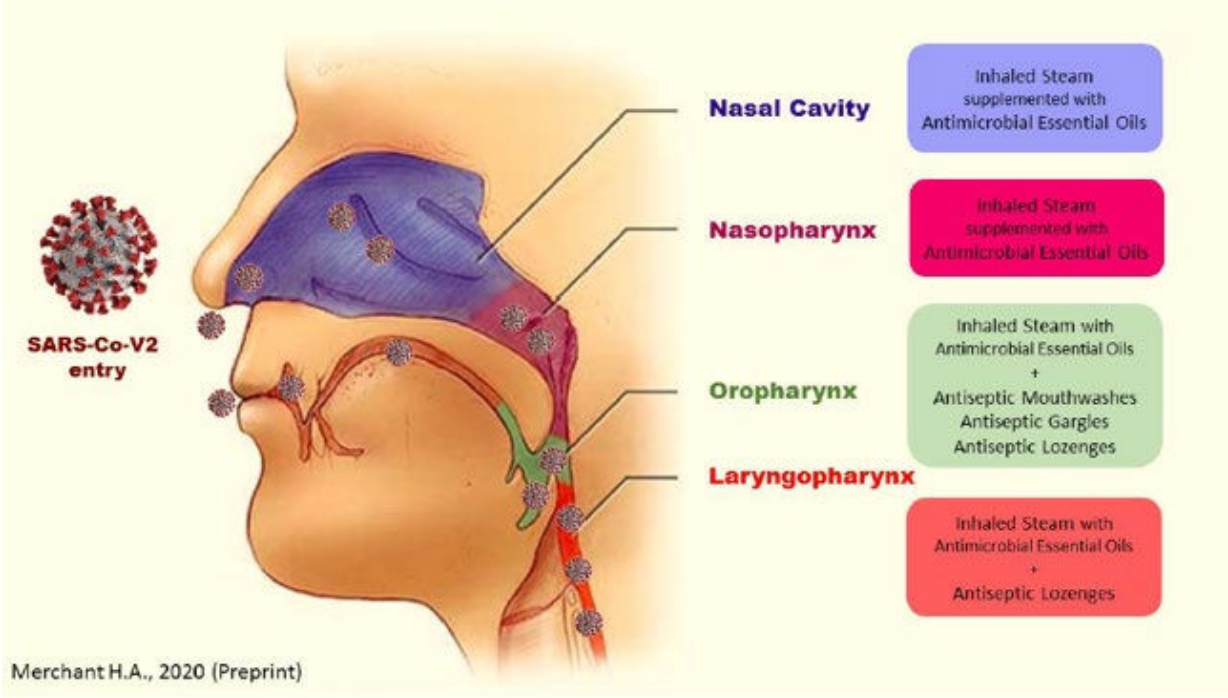


**Figure 3. Commercial Products Available for Naso-Oropharyngeal Sanitization**


Source: FLCCC

# Post-Exposure Prevention

Should COVID-19 symptoms develop, treat with I-CARE early treatment protocol as soon as possible. If symptoms do not develop, resume chronic prevention after one week.

**Ivermectin** 0.4 mg/kg immediately, then repeat second dose in 48 hours.

**Hydroxychloroquine (HCQ)** 200 mg twice a day for 5 days.

**Zinc** 75-100 mg daily. Zinc supplements come in various forms, including zinc sulfate, zinc citrate, zinc gluconate and zinc oxide.

**Melatonin** 6 mg daily, at bedtime.

**Naso-Oropharyngeal hygiene** with twice daily antiviral mouthwash/gargle (see Figures 3 and 4 below). In patients with symptomatic disease treated at home with a 1% povidone iodine mouthwash/gargle, together with nasal drops, resulted in a dramatic reduction in morbidity, hospitalization and death. [151] A nasal spray with 1% povidone-iodine (for example Immune Mist™, CoFix™ or IoNovo™ ) administered 2-3 times per day is recommended in postexposure prophylaxis and in symptomatic patients (early phase of COVID-19 infection). [47]

Due to low level systemic absorption, povidone-iodine nasal spray should not be used for longer than 5-7 days in pregnant women. While the use of an iodine-containing mouthwash over a six-month period was demonstrated to increase serum iodine levels, thyroid function tests remained unchanged. [152] It should however be noted that the IoNovo™ spray contains iodine in an amount equivalent to the daily dietary requirement and hence IoNovo Iodine is safe to ingest. In addition, IoNovo Oral Iodine is a "100% natural molecular iodine".

**Curcumin** 500 mg twice a day for 1 week.

***Nigella sativa*** 80 mg/kg daily for 1 week.

**Vitamin C** 1000 mg twice daily for 1 week.

**Quercetin** 500 mg twice daily for 1 week.

**Probiotics**.

**B complex vitamins**.

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