# ACUTE COVID-19: THERAPEUTIC PLAN IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE.

## PART II. FARMACOLOGICAL MEASURES. Aguirre Chang, Gustavo and Trujillo F., Aurora. ResearchGate. November 24, 2020. (1/4)

The Initial Stage covers up to 4 days from the onset of symptoms, in this Stage usually the location is limited to the Nose and Pharynx, usually there is still no pulmonary involvement.

### INITIAL TREATMENT: EARLY START OF TREATMENT AGAINST THE VIRAL LOAD

In addition to Non-Pharmacological Measures (gargles, nasal washes, etc.), the first day the patient is instructed to focus on starting to take Ivermectin. We recommend avoiding giving a long prescription for medication the first day, since the patient could get everything, except for the Ivermectin, which is the important thing. Table 1 shows the initial treatment to indicate the first day.

Table 1. INITIAL TREATMENT FOR COVID-19 IN THE NASAL AND PHARYNGEAL STAGE

| | |
|---|---|
| IVERMECTIN* | 0.2 mg per kg of weight after lunch and dinner. If you have a fever greater than 38.5°C or semi-liquid stool or diarrhea, 1 more dose should be added after breakfast. |
| ASPIRIN 500 mg (and/ or METAMIZOL 500 mg) | 1 TB conditional on fever greater than 38.5°C (101.3°F) or severe headache. If the fever over 38.5°C persists, it can be taken every 6-8 hours. |
| VITAMINS AND SUPPLEMENTS | Continue with the vitamins and supplements that you have already been taking before, or take those that you already have available at home |

* IVERMECTIN: the equivalences according to the presentations are the following:
  - For 6 mg tablets: give 1 tablet for every 30 kg weight, per dose.
  - For 3 mg tablets: give 1 tablet for every 15 kg weight, per dose.
  - For 1% Bottles: 0.1 ml contains 1 mg, give 0.1 ml per 5 kg weight, per dose.
  - For 0.6% bottles: 1 drop contains 0.2 mg, give 1 drop per kg weight, per dose.

  You should seek to start treatment as early as possible, if the patient has already had lunch or dinner, but no more than 2 hours have elapsed, you can take the first dose of Ivermectin.

- TEMPERATURE CONTROL AT 8 AM, 4 PM, 8 PM, 11 PM: the first 2 days of treatment, and while the fever persists, a temperature control must be carried out. Without treatment, the fever rises from 5 to 6 pm, and remains at its highest levels of the day until the wee hours of the morning.
- DO NOT USE ANTIPYRETICS IF THE FEVER IS NOT GREATER THAN 38.5°C (101.3°F): fever has an antiviral effect and is useful to evaluate the response to specific treatment. Only if the fever is greater than 38.5°C give antipyretics. The problem with the use of antipyretics is that it reduces the fever even though the infection and viral load are increasing. So, it gives a false perception of improvement.

DO NOT USE ACETAMINOPHEN (PARACETAMOL): reduces Glutathione, which is a very important antioxidant with beneficial effects on COVID-19, and whose depletion increases oxidative stress. In addition, at high doses Acetaminophen can cause liver disease.

DO NOT USE ASPIRIN (ASA), IBUPROFEN OR OTHER NSAIDS IN THE FOLLOWING CASES

1) Diagnosis of duodenal or gastric ulcer, or history of Digestive Hemorrhage;
2) Clotting disorder or use of anticoagulants already established;
3) Hypermenorrhea or other gynecological pathology that presents uterine bleeding;
4) History of stroke caused by cerebral hemorrhage;
5) Uncontrolled or difficult to control arterial hypertension (presenting episodes of high pressure, which can lead to a hemorrhagic stroke);
6) Gum bleeding or presence of any hemorrhagic disease;
7) Asthma that is worsened or caused by use of Aspirin; 8)Aspirin or NSAIDS Allergy;
9) In children under 15 years of age, the risk / benefit assessment will be carried out. If you have moderate or severe symptoms, it is suggested to indicate Aspirin (ASA). In Kawasaki disease, Aspirin doses of 30 to 80 mg are indicated. per kilo of weight.

IDENTIFY COVID-19 CONTACTS AND SUSPECT: ask about the other people who live in the place of residence of the patient, in case they present symptoms that make us suspect COVID-19. If they do not present symptoms, it would be a Contact, and if they present symptoms it is a Suspect Case of COVID-19, and it will become a Confirmed Case when a test for diagnosis of COVID-19 is performed and it is positive.

POST-EXPOSURE PROPHYLAXIS (PEP) SCHEME IN CONTACTS:

All Contacts are given a dose of Ivermectin of 0.4 mg per kilo of weight.
Contacts who are men between 45 and 70 years old and women older than 70 years are indicated a second dose equal to 0.4 mg per kilo of weight on the second day.
In men> 70 years of age, and in the Caregiver, one dose per day for 3-4 days is indicated.
In addition, in men over 55 years of age and in the "People at Higher Risk" of becoming seriously ill (people with Diabetes, Coronary Artery Disease or other heart disease, Arterial Hypertension, Obesity, Cancer, Immunosuppression, HIV, Chronic Renal Insufficiency, Smoking), Aspirin 100 mg is indicated. 1 TB after lunch for 6 to 10 days.

TREATMENT OF SUSPECT COVID-19 CASES: all people in the place of residence who have symptoms that suggest COVID-19, should start treatment with Ivermectin in a similar way to the already identified COVID-19 case.

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### DAY TWO: ASSESSMENT OF RESPONSE TO TREATMENT

- The severity of the disease is expressed through symptoms and signs, and the severity of symptoms is directly related to the level of viral load.
- At 27 to 30 hours after the first dose of Ivermectin, which is equivalent to 3 to 6 hours after the dose that the patient takes at 24 hours, the response to treatment should be evaluated. We do this by evaluating improvement in symptoms.
- According to the study by L. Caly et. al., Ivermectin reduces viral load by 93% after 24 hours and by 99.9% in 48 hours, this is equivalent to approximately a 5,000-fold reduction in coronavirus RNA in 48 hours.
- Fever is the main symptom to assess, followed by sweating at night, headache with pain behind the eyes, sore throat, myalgia, hyporexia, cough, nasal congestion and conjunctival hyperemia. Not always all the mentioned symptoms are present. Fever should be included in the evaluation whenever it is. In addition, other symptoms that present in a more severe way should be included, such as headache, sweating and sore throat.
- The presence of gastrointestinal symptoms (semi-liquid stools, anorexia, nausea and abdominal pain), in the first 5 days, is indicative of a higher viral load and persistence.
- In the elderly, fever may not occur, in them hyporexia or anorexia should be considered, in addition to weakness, longer sleep or bed rest time, decreased communication, increased heart and / or respiratory rate.
- In men over 50 years old and women over 75 years old, the control of symptoms and signs must be more meticulous, since these can manifest themselves to a lesser degree, and the disease can progress stealthily or silently. These should include monitoring of oxygen saturation and heart rate with a pulse-oximeter.
- Loss of smell (anosmia) and taste (ageusia) should not be considered to assess the response in the first days to specific treatment, since it has been observed that they can persist for days after the other symptoms have resolved. What yes, anosmia and ageusia are very useful for the differential diagnosis with other pathologies.

EVALUATION AT 27 TO 30 HOURS OF THE RESPONSE TO THE TREATMENT: the details of this evaluation are shown in Table 2. The probable results are as follows:

- (A) VERY QUICK TOTAL RESPONSE (100%): as shown in Table 2, if within 3 to 12 hours of the first dose of Ivermectin, the fever, malaise and all other symptoms show a complete improvement, are fully resolved, the viral load level is estimated to have been low and would be treated of a case of Mild COVID-19 found in the Initial Stage or Nasal and Pharyngeal location, with a Very Rapid Response to Treatment. For these cases, it is only indicated to complete 3 days of treatment with Ivermectin. Also take Aspirin (ASA) 100 mg 1 TB after lunch or dinner for 6 days. If there is any contraindication for the use of Aspirin, do not take it, as it is a mild and initial case, it can be avoided. Table 3 shows the treatment to be followed in these cases.

Table 2. EVALUATION AT 27 TO 30 HOURS OF THE RESPONSE TO THE TREATMENT FOR COVID-19 AND ESTIMATION OF THE LEVEL OF VIRAL LOAD AND PERSISTENCE

| HOURS ELAPSED from First Take | RESOLUTION OF FEVER, DISEASE, RESPIRATORY AND GASTROINTESTINAL SYMPTOMS (Anosmia and Ageusia not included) | ESTIMATED VIRAL LOAD AND PERSISTENCE |
|---|---|---|
| From 3 to 12 | Very Fast Total Response: 100% improvement of all symptoms | Viral Load Low |
| From 12 to 30 | Rapid Total or Near Total Response: 97 to 100% improvement of all symptoms | Viral Load Medium |
| From 27 to 30 | Partial Response: 76 to 96% improvement on average of all symptoms | Viral Load Medium to High |
| From 27 to 30 | Partial Response: 25 to 75% improvement on average of all symptoms | Viral Load HIGH and Persistent |
| From 27 to 30 | No response or very little response: 0 to 24% improvement on average of all symptoms | Viral L. Very HIGH and Persistent |

Table 3. TREATMENT FOR CASES IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE WITH A VERY RAPID TOTAL RESPONSE TO THE TREATMENT (IN 3 TO 12 HOURS)

| | |
|---|---|
| IVERMECTIN | 0.2 mg per kg of weight after lunch and dinner for 3 days. |
| ASPIRIN 100 mg. | 1 TB after lunch or dinner for 6 days. |
| VITAM. AND SUP. | You can continue with the ones you have been taking for 6 to 12 days. |

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- (B) QUICK RESPONSE TOTAL OR ALMOST TOTAL (97 TO 100%): If fever and other symptoms resolve within 12 to 36 hours from the first dose of Ivermectin, the viral load is estimated to have been medium. In these cases, it is recommended to complete 4 days of Ivermectin and take 9 days with Aspirin, 100-200 mg/day. If present or have a history of heartburn or reflux, sodium bicarbonate will be included, half a teaspoon (3 to 4 grams) in half a glass of water at 11 am and shortly before going to bed, for 4 days. Table 4 shows the treatment in these cases.

Table 4. TREATMENT FOR CASES IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE WITH RAPID TOTAL OR ALMOST TOTAL RESPONSE TO TREATMENT (IN 12 TO 30 HOURS)

| | |
|---|---|
| IVERMECTIN | 0.2 mg per kg of weight after breakfast, lunch and dinner for 4 days. |
| ASPIRIN (ASA) 100 mg. | 1 TB after lunch or dinner for 9 days. If you weigh more than 75 kg 1 TB is indicated after breakfast and dinner (200 mg per day) x 9 days. |
| VITAM. AND SUPPL. | Continue with the ones you have been taking for 10 to 15 days. |

- (C) PARTIAL RESPONSE OF 76 TO 96% AT 27 TO 30 HOURS: If this occurs, the viral load is estimated to be medium to high. In these cases, 4 days of Ivermectin and 8 to 12 days with Aspirin, 200-300 mg per day are indicated. If there is any contraindication to the use of Aspirin, we indicate that you take L-Lysine 500 mg 3 times a day. Table 5 shows the treatment to be followed.

Table 5. TREATMENT FOR CASES IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE WITH A PARTIAL RESPONSE TO THE TREATMENT OF 76 TO 96% AT 27 TO 30 HOURS

| | |
|---|---|
| IVERMECTIN | 0.2 mg por Kg de peso después del almuerzo y de la cena x 4 días. |
| ASPIRIN (ASA) 100 mg. or L-LYSINE 500 mg. | ASA: 1 TB after breakfast and dinner x 8-12 d. If you weigh more than 75 kg 1 TB is indicated after breakf, lunch and dinner (300mg/day) x 8-12 d. L-Lysine: 1 TB at 11 am, 4 pm and before bed for 12 days. |
| SODIUM BICARBONATE | half a teaspoon (3 to 4 grams) in half a glass with water, at 11 am and 10.30 pm for 3 days, then only at 10.30 pm for 5 more days. |
| VITAM. AND SUPPL. | Continue with the ones you have been taking or, the ones you have. |

- (D) PARTIAL RESPONSE OF 25 TO 75% AT 27 TO 30 HOURS FROM THE START OF TREATMENT: in these cases it is estimated that the viral load level is high and that it is a more resistant strain with a tendency to make a persistent infection. It is recommended to add Nitazoxanide as a second drug to reduce viral load. In addition, it is indicated to increase the dose of Ivermectin to 3 a day and for at least 4 days, and that day the treatment to continue will be reevaluated. The Aspirin dose is also increased to 500 to 700 mg up to date. If there is any contraindication for the use of Aspirin, we indicate that you take Dipyridamole 300mg up to date. Besides, it includes Zinc, Vitamins D, C and A, Sodium Bicarbonate and L-Lysine. Table 6 shows the details of the treatment to be followed.

Table 6. TREATMENT FOR CASES IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE WITH A PARTIAL RESPONSE TO THE TREATMENT OF 25 TO 75% AT 27 TO 30 HOURS

| | |
|---|---|
| IVERMECTIN | 0.4 mg per kg of weight after breakfast and dinner x 4 days. That day will be reevaluated if it continues for more days. |
| NITAZOXANIDE, TB 500 mg. | 1 TB every 12 hours for 7 to 10 days. If you weigh more than 75 kg 1 TB is indicated every 8 hours (the first day may cause diarrhea). |
| ASPIRIN (ASA) 100 mg. or DIPYRIDAMOLE, TB 75 mg. | ASA: 2 TB after breakfast and dinner, 1 TB after lunch (500 mg/day) for 8 to 12 days. If you weigh more than 75 kg 2 TB is indicated after breakfast and dinner, 3 TB at lunch (700 mg per day), for 8 to 12 days. Dipyridamole: 1 TB 4 times a day: 1 hour before breakfast, 1 hour before and lunch, 5 pm and before bed, for 10 to 15 days. |
| ZINC | 100 to 200 mg a day for 15 days. Take it away from food (11 am and/or 4 pm) and avoid dairy products nearby as they reduce its absorption. |
| VITAMIN D | Between 20,000 to 50,000 IU a day for 7 to 10 days. |
| VITAMIN C | 2 gr. every 8 h. for 2 days, then 1 to 2 gr a day x 7 more days. |
| SODIUM BICARBONATE | half a teaspoon (3 to 4 grams) in half a glass with water, at 11 am and 10.30 pm for 4 days, then only at 10.30 pm for 3 more days. |
| L-LYSINE 500 mg. | 1 TB at 11 am, 4 pm and before bed for 15 days. |

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- (E) NO RESPONSE OR VERY LITTLE (0 TO 24%) AT 27 TO 30 HOURS: due to the null or little response, it is estimated that the viral load is very high and that it is a resistant and persistent strain. It is recommended to add Bromhexine, increase the dose of Nitazoxanide to 3 a day. It is also indicated to increase the doses of Ivermectin to 5 a day, of Aspirin to between 700 to 900 mg. up to date. And N-Acetylcysteine (NAC) is added, apart from Zinc, L-Lysine, Sodium Bicarbonate and Vitamins D, C and A. Table 7 shows the treatment to follow in these cases.

Table 7. TREATMENT FOR CASES IN THE INITIAL OR NASAL AND PHARYNGEAL STAGE WITHOUT ANY OR VERY LITTLE RESPONSE TO THE TREATMENT (0-24%) AT 27 TO 30 HOURS

| | |
|---|---|
| IVERMECTIN | 0.4 mg per kg weight after breakfast, lunch and dinner (1.2 mg / kg / day) for 4 days. That day the treatment will be re-evaluated. |
| NITAZOXANIDE, TB 500 mg. | 1 TB every 8 hours for 6 to 10 days. If you weigh more than 90 kg 1 TB is indicated every 6 hours (the first day may cause diarrhea). |
| BROMHEXIN | 8 mg. (5 ml.) every 8 hours for 6 days. |
| ASPIRIN (ASA) 100 mg., or DIPYRIDAMOLE, TB 75 mg. | Aspirin: 2 TB after breakfast and dinner, 3 TB at lunch (700 mg/d). If you weigh more than 75 kg: 3 TB after breakfast, lunch and dinner, x 8 to 12 d. Dipyridamole: 1 TB 4 times a day: 1 hour before breakfast, 1 hour before and lunch, 5 pm. and before bed, for 15 days. Or Clopidogrel 75 mg/day. |
| ZINC | 150 to 250 mg a day for 12 days. Take it away from food (11 am and /or 4 pm) and avoid dairy products nearby as they reduce its absorption. |
| VITAMIN D | Between 30,000 to 60,000 IU a day for 6 to 10 days. |
| VITAMIN C | 2 gr every 8 hours for 2 days, then 1 to 2 gr a day for 9 more days. |
| VITAMIN A | 75,000 to 100,000 IU per day x 3 days. Repeat on day 7 and 14, equal x 3 d |
| SODIUM BICARBONATE | half a teaspoon (3 to 4 grams) in half a glass with water, at 11 am and 10.30 pm for 4 days, then only at 10.30 pm for 4 more days. |
| L-LYSINE 500 mg. | 1 TB when getting up (fasting), 11am., 4pm and before going to bed x 15d. |
| N-ACETYL CYSTEINE | Sachet or TB of 600 mg in half a glass of water, every 6 hours x 4 to 6 d. |

### FOURTH DAY: RE-EVALUATION OF THE TREATMENT

- On the 4th day, a new evaluation of the response to treatment should be carried out, through the improvement of symptoms and signs, the viral load and the tendency to persistence are estimated.
- With 4 days of treatment, most patients with COVID-19 should no longer have symptoms or they should be in a clear decline. But it should be taken into account that just as there is a pre-symptomatic period that lasts 3 to 5 days, in a similar way there is a post-symptomatic period in which there is still a low viral load that does not produce symptoms, but that is It is important to be eliminated, even more so because the viruses that survive are the most resistant and persistent, so they can generate a reactivation of the disease. Then, after the day they stop showing symptoms, you should continue 2 to 4 more days of treatment with Ivermectin, at a dose of 0.2 mg x kg weight 2 times a day.

BEFORE PERSISTENCE OF FEVER AND /OR NO IMPROVEMENT IN O2 SATURATION, THE PRESENCE OF ANOTHER INFECTION AND /OR ADDED DISEASE MUST BE CONSIDERED:

- If fever persists, an added infection should be considered, so one of the following antibiotics is included: Doxycycline 100 mg 2 times/day, Levofloxacin 750 mg 1 time/day, Ceftriaxone 2 gr EV /day, Azithromycin 500 mg/day. Overhydration, sodium bicarbonate and Aspirin are suspended to start with Enoxaparin SC, 40 to 60 mg every 12 hours. Pulmonary CT or MRI, Procalcitonin, Platelet CBC, CRP, D-Dimer, Ferritin, Creatinine should be requested.
- A family history of diabetes should also be investigated, and the presence of hyperglycemia should be ruled out, as this causes treatment to last for a longer time. If hyperglycemia is found, it is indicated that the patient has a glucometer to be able to carry out frequent control of the glucose level, in order to receive treatment with insulin and /or hypoglycemic agents to keep their glucose controlled.
- In persistent cases there is also usually Lymphopenia, which is present in more than 80% of acute cases and basically affects T lymphocytes. It is recommended not to resort to corticosteroids as they reduce lymphocytes and generate immunosuppression. Vitamins A and C, Zinc and Selenium help increase lymphocytes. The use of human immunoglobulin (IVIG) can be used, at a dose of 400 mg/ kg./ day in slow infusion (start with 60 ml/ hour), for 3 to 5 days.
- The thymic peptide Thymosin alpha 1 (Thymalfasin, Zadaxin, Vial 1.6 mg) increases lymphocyte levels, being useful in cases of COVID-19, especially in those with significant lymphopenia.
- In addition, it should be evaluated if Melatonin, Quercetin, inhaled corticosteroids (Ciclesonide, Fluticasone or Budenoside), B Complex Vitamins, Omega 3 with a high amount of EPA, Colchicine, Probiotics, Turmeric, Chinese skullcap or Niclosamide are added to the treatment.