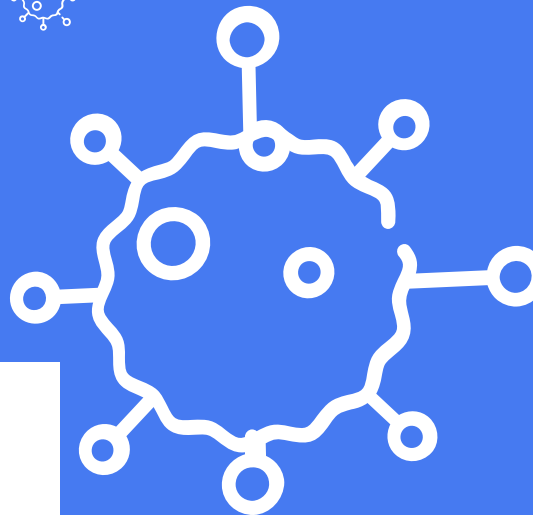


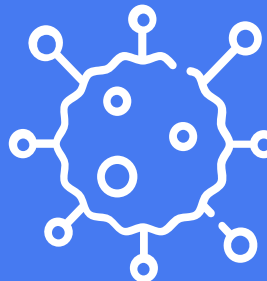
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# نقش هیدروکسی کلروکین در درمان بیماران مبتلا به کووید ۱۹

دکتر محمدحسین زمانیان

متخصص بیماری های عفونی



# Management of mild COVID-19: symptomatic treatment

- **We recommend that patients with suspected or confirmed mild COVID-19 be isolated to contain virus transmission according to the established COVID-19 care pathway.**
- **This can be done at a designated COVID-19 health facility, community facility or at home (self-isolation).**

- **We recommend patients with mild COVID-19 be given symptomatic treatment such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration.**
- **Counsel patients with mild COVID-19 about signs and symptoms of complications that should prompt urgent care.**
- **We recommend against antibiotic therapy or prophylaxis for patients with mild COVID-19.**

# Management of moderate COVID-19: pneumonia treatment

**We recommend that patients with suspected or confirmed moderate COVID-19 (pneumonia) be isolated to contain virus transmission. Patients with moderate illness may not require emergency interventions or hospitalization; however, isolation is necessary for all suspect or confirmed cases.**

- The location of isolation will depend on the established COVID-19 care pathway and can be done at a health facility, community facility or at home.**
- The decision of location should be made on a case-by-case basis and will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.**
- For patients at high risk for deterioration, isolation in hospital is preferred.**

- **We recommend for patients with suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection.**
- **We recommend close monitoring of patients with moderate COVID-19 for signs or symptoms of disease progression. Provision of mechanisms for close follow up in case of need of escalation of medical care should be available.**

- **Management of severe COVID-19: severe pneumonia treatment**
- **All areas where severe patients may be cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, Venturi mask, and mask with reservoir bag).**

- **We recommend immediate administration of supplemental oxygen therapy to any patient with emergency signs and to any patient without emergency signs and  $SpO_2 < 90\%$ .**
- **Closely monitor patients for signs of clinical deterioration, such as rapidly progressive respiratory failure and shock and respond immediately with supportive care interventions.**
- **Use cautious fluid management in patients with COVID-19 without tissue hypoperfusion and fluid responsiveness.**



## Management of critical COVID-19: septic shock

- **Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP)  $\geq$  65 mmHg AND lactate is  $\geq$  2 mmol/L, in the absence of hypovolaemia.**

- **Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] < 5th centile or > 2 SD below normal for age) or two or more of the following: altered mental status; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulses; tachypnoea; mottled or cold skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia.**

- **The following recommendations pertain to resuscitation strategies for adult and paediatric patients with septic shock.**
- **In resuscitation for septic shock in adults, give 250–500 mL crystalloid fluid as rapid bolus in first 15–30 minutes.**
- **In resuscitation for septic shock in children, give 10–20 mL/kg crystalloid fluid as a bolus in the first 30–60 minutes.**

- **Fluid resuscitation may lead to volume overload, including respiratory failure, particularly with ARDS. If there is no response to fluid loading or signs of volume overload appear (e.g. jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, or hepatomegaly), then reduce or discontinue fluid administration. This step is particularly important in patients with hypoxaemic respiratory failure.**

- **In adults, administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP  $\geq$  65 mmHg in adults and improvement of markers of perfusion.**

**In children, administer vasopressors if signs of fluid overload are apparent or the following persist after two fluid bolus:**

- **signs of shock such as altered mental state;**
- **bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children);**
- **prolonged capillary refill (> 2 seconds) or feeble pulses;**
- **tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria persists after two repeat boluses;**
- **or age-appropriate blood pressure targets are not achieved.**

**If central venous catheters are not available, vasopressors can be given through a peripheral IV, but use a large vein and closely monitor for signs of extravasation and local tissue necrosis. If extravasation occurs, stop infusion. Vasopressors can also be administered through intraosseous needles.**

**If signs of poor perfusion and cardiac dysfunction persist despite achieving MAP target with fluids and vasopressors, consider an inotrope such as dobutamine.**



# Prevention of complications in hospitalized and critically ill patients with COVID-19

**In patients (adults and adolescents) hospitalized with COVID-19, use pharmacological prophylaxis, such as low molecular weight heparin (such as enoxaparin), according to local and international standards, to prevent venous thromboembolism, when not contraindicated.**

**For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).**

**Monitor patients with COVID-19, for signs or symptoms suggestive of thromboembolism, such as stroke, deep venous thrombosis, pulmonary embolism or acute coronary syndrome. If these are clinically suspected, proceed immediately with appropriate diagnostic and management pathways.**

# Adverse effects of medications

Careful consideration should be given to the numerous, clinically significant side-effects of medications that may be used in the context of COVID-19, as well as drug-drug interactions between medications, both of which may affect COVID-19 symptomatology (including effects on respiratory, cardiac, immune and mental and neurological function).

Both pharmacokinetic and pharmacodynamic effects should be considered.

# Prevention of complications

## Anticipated outcome

## Interventions

Reduce days of invasive mechanical ventilation

- Use weaning protocols that include daily assessment for readiness to breathe spontaneously
- Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions
- Early mobilization
- Implementation of the above as a bundle of care (may also reduce delirium); such as the **A**wakening and **B**reathing **C**oordination, **D**elirium assessment/management, and **E**arly mobility (ABCDE)

Reduce incidence of ventilator-associated pneumonia

- Oral intubation is preferable to nasal intubation in adolescents and adults
- Keep patient in semi-recumbent position (head of bed elevation 30–45°)
- Use a closed suctioning system; periodically drain and discard condensate in tubing
- Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged, but not routinely
- Change heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days

Reduce incidence of catheter-related bloodstream infection

- Use a checklist with completion verified by a real-time observer as a reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed

# Prevention of complications

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Reduce incidence of pressure ulcers

- Turn patient every 2 hours

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Reduce incidence of stress ulcers and GI bleeding

- Give early enteral nutrition (within 24–48 hours of admission)
- Administer histamine-2 receptor blockers or proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for GI bleeding include mechanical ventilation for  $\geq 48$  hours, coagulopathy, renal replacement therapy, liver disease, multiple comorbidities, and higher organ failure score

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Reduce the development of antimicrobial resistance

- Utilize de-escalation protocols as soon as patient is clinically stable and there is no evidence of bacterial infection

Reduce the development of adverse drug effects

- Expose patient to empiric antimicrobial therapy for the shortest time possible, to prevent nephrotoxicity, cardiac and other side-effects from unnecessary antimicrobial use

Promote appropriate antimicrobial prescribing and use during the COVID-19 pandemic (121)

- Do not prescribe antibiotics to suspected or confirmed COVID-19 patients with low suspicion of a bacterial infection, to avoid more short-term side-effects of antibiotics in patients and negative long-term consequences of increased antimicrobial resistance
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## **Antivirals, immunomodulators and other adjunctive therapies for COVID-19**

**We recommend that the following drugs not be administered as treatment or prophylaxis for COVID-19, outside of the context of clinical trials:**

- **Chloroquine and hydroxychloroquine (+/- azithromycin), including but not limited to:**

- **Antivirals, including but not limited to:**

- Lopinavir/ritonavir**

- Remdesivir**

- Umifenovir**

- Favipiravir**

- **Immunomodulators, including but not limited to:**

- Tocilizumab**

- Interferon- $\beta$ -1a**

- **Plasma therapy.**

## Chloroquine and hydroxychloroquine +/- azithromycin:

each can cause QT prolongation and taken together can increase the risk of cardiotoxicity.

- **Lopinavir/ritonavir:** the most common adverse effects are gastrointestinal.
- **Remdesivir:** elevation of hepatic enzymes, GI complications, rash, renal impairment and hypotension.
- **Umifenovir:** diarrhoea, nausea.
- **Favipiravir:** QT interval prolongation.
- **Interferon- $\beta$ -1a:** pyrexia, rhabdomyolysis.
- **Tocilizumab:** URT infections, nasopharyngitis, headache, hypertension, increased alanine aminotransferase (ALT), injection site reactions.



# Corticosteroid therapy and COVID-19

**We recommend against the routine use of systemic corticosteroids for treatment of viral pneumonia.**

# **Treatment of other acute and chronic infections in patients with COVID-19**

## Acute co-infections

**We recommend for patients with:**  
**suspected or confirmed mild COVID-19, against the use of antibiotic therapy or prophylaxis;**  
**suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection;**

**suspected or confirmed severe COVID-19, the use of empiric antimicrobials to treat all likely pathogens, based on clinical judgment, patient host factors and local epidemiology, and this should be done as soon as possible (within 1 hour of initial assessment if possible), ideally with blood cultures obtained first. Antimicrobial therapy should be assessed daily for de-escalation.**

# Summary of pharmacology for select proposed Covid-19 Treatments

Agent	Target	Adult dose/administration	Contraindications	Toxicities	Major drug-drug interactions	Special populations
<b>Repurposed agents</b>						
Chloroquine phosphate (Aralen/generic) <sup>9-14</sup>	Blockade of viral entry by inhibiting glycosylation of host receptors, proteolytic processing, and endosomal acidification. Additional immunomodulatory effects through inhibition of cytokine production, autophagy, and lysosomal activity in host cells	500 mg by mouth every 12-24 h × 5-10 d. Available as: 250-mg tablets (salt); 500-mg tablets (salt); 500-mg tablets of chloroquine phosphate (salt) = 300-mg chloroquine base. Dose adjustments: Kidney: creatinine clearance <10 mL/min administer 50% of dose. Hepatic: No dose adjustments in hepatic impairment recommended; use with caution. Administration: Preferable to avoid crushing. If needed, may be crushed and mixed with jam, pasteurized yogurt or similar foods	Hypersensitivity to chloroquine, 4-aminoquinoline compounds, or any component of formulation. Presence of retinal or visual field changes of any etiology (unless benefit outweighs risk)	Common: Abdominal cramps, anorexia, diarrhea, nausea, vomiting. Major: Cardiovascular effects (including QTc prolongation), hematologic effects (including hemolysis with G6PD deficiency, use if benefit outweighs risks), hypoglycemia, retinal toxicity, neuropsychiatric and central nervous system effects, idiosyncratic adverse drug reactions	CYP2D6 and CYP3A4 substrate	May be used in pregnancy if benefit outweighs risks
Hydroxychloroquine sulfate (Plaquenil/generic) <sup>9,11,15-20</sup>	Hydroxychloroquine shares the same mechanism of action as chloroquine	400 mg by mouth every 12 h × 1 d, then 200 mg by mouth every 12 h × 4 d; alternative dosing: 400 mg by mouth daily × 5 d or 200 mg by mouth 3 times/d for 10 d. Available as: 200-mg tablets of hydroxychloroquine sulfate (salt) = 155 mg hydroxychloroquine base. Dose adjustments: No kidney or hepatic dose adjustments recommended; use with caution. Administration: Manufacturer does not recommend crushing tablets; however, some sources suggest that tablets can be crushed and dispersed with water OR compounded into an oral solution	Known hypersensitivity to hydroxychloroquine, 4-aminoquinoline derivative, or any component of the formulation	Adverse drug reactions similar to chloroquine but less common	CYP2D6, CYP3A4, CYP3A5, and CYP2C8 substrate	May be used in pregnancy if benefit outweighs risks
Lopinavir/ritonavir (Kaletra) <sup>21-26</sup>	3CL protease	400 mg/100 mg by mouth every 12 h for up to 14 d. Available as: lopinavir/ritonavir, 200-mg/50-mg tablets; lopinavir/ritonavir, 100-/50-mg tablets; lopinavir/ritonavir 400-mg/100-mg per 5-mL oral solution (can be given via feeding tubes compatible with ethanol and propylene glycol, contains 42% alcohol). Dose adjustments: No kidney or hepatic dose adjustments recommended; use with caution in hepatic impairment. Administration: Food restrictions: Tablets, take without regard to meals; oral solution, take with food. Do not crush tablets; oral solution not recommended with polyurethane feeding tubes	Hypersensitivity to lopinavir/ritonavir or any of its ingredients, including ritonavir. Co-administration with drugs highly dependent on CYP450 3A. Co-administration with potent CYP450 3A inducers	Common: gastrointestinal intolerance, nausea, vomiting, diarrhea. Major: Pancreatitis, hepatotoxicity, cardiac conduction abnormalities	CYP3A4 inhibitor and substrate; CYP2D6 substrate; CYP1A2, CYP2B6, CYP2C8, CYP2C9, CYP2C19 inducer. P-gp substrate; UGT1A1 inducer	May be used in pregnancy; avoid oral solution if possible due to ethanol content
Umifenovir (Arbidol) <sup>27-29</sup>	S protein/ACE2, membrane fusion inhibitor	200 mg every 8 h by mouth 7-14 d. Available as (not in the US): 50-mg and 100-mg tablets, capsules and granules. Dose adjustments: Kidney: no dose adjustment necessary. Hepatic: No specific recommendations available, caution in those with hepatic impairment. Administration: Bioavailability 40%	Known hypersensitivity to umifenovir	Allergic reaction, gastrointestinal upset, elevated transaminases	Metabolized by CYP3A4, monitor with strong inducers/inhibitors	Contraindicated in children <2 y of age (increased sensitivity)
<b>Investigational agents</b>						
Remdesivir <sup>30-32</sup>	RNA polymerase inhibitor	200 mg × 1, 100 mg every 24 h IV infusion. Available as: 5-mg/mL vial (reconstituted). Dose adjustments: Kidney: Not recommended for GFR <30. No kidney/hepatic dose adjustment currently recommended but holding doses may be considered if significant toxicities occur. Administration: 30-min IV infusion	Exclusion criteria based on specific protocols	Elevated transaminases (reversible), kidney injury	Not a significant inducer/inhibitor of CYP enzymes, monitor with strong inducers/inhibitors	Safety in pregnancy unknown, currently recommended to avoid

# Summary of pharmacology for select proposed Covid-19 Treatments

Agent	Target	Adult dose/administration	Contraindications	Toxicities	Major drug-drug interactions	Special populations
Favipiravir <sup>33,34</sup>	RNA polymerase inhibitor	Doses vary based on indication, limited data available. Available as (not in the US): 200-mg tablet. Dose adjustments: Kidney: no dose adjustment recommended, limited data available, Hepatic: Dose adjustment considered in Child-Pugh C, increased exposures observed in Child-Pugh class A to C. Administration: Tablet can be crushed or mixed with liquid, bioavailability >95%	Exclusion criteria based on specific protocols	Hyperuricemia, diarrhea, elevated transaminases, reduction in neutrophil count	CYP2C8 and aldehyde oxidase inhibitor, metabolized by aldehyde oxidase and xanthine oxidase	Contra indicated during pregnancy, metabolite found in breast milk
<b>Adjunctive therapies</b>						
Tocilizumab (Actemra) <sup>35,36</sup>	IL-6 inhibition- reduction in cytokine storm	400 mg IV or 8 mg/kg × 1-2 doses. Second dose 8-12 h after first dose if inadequate response. Available as: IV infusion injection: 80 mg/4 mL (20 mg/mL); 200 mg/10 mL (20 mg/mL); 400 mg/20 mL (20 mg/mL) in single-dose vials for further dilution prior to IV infusion. Dose adjustments: Kidney: No dose adjustments recommended in mild or moderate kidney impairment. Not studied in patients with severe impairment. Hepatic: No dose adjustments recommended (not studied); initiate based on benefit. Administration: Infuse over 60 min, should not be infused concomitantly in the same IV line with other drugs	Known hypersensitivity to tocilizumab or any components of the formulation. Caution in patients with neutropenia (<500 cells/ $\mu$ L) or thrombocytopenia (<50 000/ $\mu$ L)	Common: Increase in upper respiratory tract infections (including tuberculosis), nasopharyngitis, headache, hypertension, increased AST, infusion related reactions. Major: Hematologic effects, infections, hepatotoxicity, gastrointestinal perforations, hypersensitivity reactions	In vitro data suggested that IL-6 reduces mRNA expression for several CYP450 isoenzymes, including CYP1A2, CYP2B6, CYP2C9, CYP2C19, CYP2D6, and CYP3A4. May decrease levels of substrates	Safety in pregnancy unknown; may cause harm to the fetus

# Covid-19 Clinical Management: Frequently Asked Questions

## **1. Have any medical therapies been definitively shown to improve outcomes in a patient with COVID-19?**

At this time there are no medical therapies that have been definitively shown to improve outcomes in patients with COVID-19. A number of drugs have demonstrated in vitro activity against the SARS-CoV-2 virus or potential clinical benefits in observational or small, nonrandomized studies. Adequately powered randomized clinical trials are currently enrolling and needed to establish the efficacy of these proposed therapies.

## **2. Should hydroxychloroquine and/or azithromycin be prescribed for patients with severe symptoms from COVID-19?**

The reported clinical benefits of the combination of hydroxychloroquine and azithromycin for patients with COVID-19 come either from media reports or nonrandomized trials with small numbers of participants (<100 patients). The documented benefit of hydroxychloroquine with or without azithromycin is very limited, especially in severe disease. While these medications, individually or in combination, may prove efficacious, these benefits need to be established with randomized clinical trials prior to widespread adoption of these treatments.

## **3. Should I stop ARBs/ACE inhibitors in my older patients and those at high risk for severe illness from COVID-19?**

Major institutions and societies, including the Centers for Disease Control and Prevention, the American Heart Association, the Heart Failure Society of America, and the American College of Cardiology recommend continuation of ACE inhibitors or ARB medications for all patients already prescribed those medications for another indication. There is currently no human evidence establishing a link between the use of these medications with an increased risk of COVID-19 acquisition or illness severity.

# Covid-19 Clinical Management: Frequently Asked Questions

## **4. What is the role of immunomodulatory drugs such as IL-6 receptor antagonists or corticosteroids in the management of patients with COVID-19?**

Given the important role the immune response plays in the complications of COVID-19, active clinical trials are evaluating immunomodulatory drugs (such as IL-6 receptor antagonists) in this disease. In patients with "cytokine storm," characterized by marked elevation in inflammatory markers, use of IL-6 receptor antagonists can be considered, preferably in the context of a clinical trial, although these medications can increase risk of secondary infections. The role of corticosteroids remains controversial, and current guidelines from the World Health Organization do not recommend their use unless another concomitant indication exists such as chronic obstructive pulmonary disease exacerbation or pressor-refractory shock. However, their utility in patients with severe COVID-19 with acute respiratory distress syndrome should be further investigated in clinical trials.

## **5. Which medications have been repurposed to treat COVID-19?**

Numerous agents demonstrate in vitro activity against novel coronaviruses, including SARS-CoV-2. Small molecule database

screens identified thousands of potential agents. Of these, several repurposed agents used to treat a variety of other disease states (eg, HIV and autoimmune diseases) have been proposed as possible treatment options for COVID-19. Lopinavir/ritonavir and chloroquine or hydroxychloroquine are the medications with the most clinical evidence, either positive or negative, in the treatment of COVID-19. To date, available clinical trials have not demonstrated that any of these drugs are clearly effective.

## **6. Are there investigational drugs available to treat COVID-19?**

Remdesivir is available to COVID-19-infected patients through enrollment in a clinical trial or application for emergency access. In the United States, there are 3 ongoing clinical trials differentiated by severity of disease (eg, moderate vs severe infection) and study design (eg, placebo-controlled). Emergency access is available through an expanded access program. Sites without access to a clinical trial may obtain the drug this way. Also, individual compassionate use for pregnant women and children younger than 18 years of age with confirmed COVID-19 and severe manifestations of the disease may obtain the drug in this manner. Favipiravir is not currently available in the United States.



# Covid-19 Clinical Management: Frequently Asked Questions

## **7. How do I decide if a patient with COVID-19 needs a specific treatment or should receive only supportive care?**

The priority should be to enroll a patient in a clinical trial if they qualify. If this is not possible, patients who are stable as an outpatient or have no evidence of oxygen requirement or pneumonia by imaging can generally be managed with supportive care alone. Patients who have evidence of hypoxia or pneumonia, especially those with risk factors for disease progression such as age older than 65 years, cardiac or pulmonary comorbidities, and immunosuppression, can be considered for specific COVID-19 therapy after discussing the risks and benefits with the patient and in accordance with local hospital treatment guidance.

## **8. What are the limitations of repurposing medications to treat COVID-19?**

The use of repurposed medications relies on the assumption that the benefits (in vitro/clinical evidence) outweigh associated risks (adverse drug reactions). One limitation to using repurposed agents is the propensity of these agents to cause acute toxicity. This acute toxicity may outweigh the undefined benefit of a specific antiviral agent. Augmented toxicity with combination therapy, such as heart or liver toxicity, creates potential additional risk and need for close risk vs benefit analysis. Overall, the paucity of evidence demonstrating a clear benefit may not justify the risk of the repurposed agent(s). This is of utmost concern in patients at high risk for toxicity and in situations where adverse events may preclude entry into investigational trials.

ACE indicates angiotensin-converting enzyme; ARB, angiotensin receptor blocker; COVID-19, coronavirus disease 2019; and SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

## هیدروکسی کلروکین / کلروکین فسفات

قرص هیدروکسی کلروکین سولفات ۲۰۰ میلی گرم یا قرص کلرکین فسفات ۲۵۰ میلی گرم روز اول هر ۱۲ ساعت دو عدد و در ادامه هر ۱۲ ساعت یک عدد به مدت ۷ الی ۱۴ روز

در صورت دریافت کلترا، بیمار تک دوز ۴۰۰ میلی گرم هیدروکسی کلروکین یا ۵۰۰ میلی گرم کلروکین دریافت نماید.

کلروکین احتمالاً با مهار اسیدی شدن اندوزم باعث مهار ورود ویروس، گلیکوزیله شدن گیرنده و نهایتاً کاهش تکثیر ویروس خواهد شد. همچنین باعث کاهش آزادسازی سیتوکین ها می شود.

- قبل از شروع دارو ECG گرفته شود.
- سطح پتاسیم، منیزیم، کراتینین، قند خون و CBC Diff قبل از شروع درمان چک شود.

- با توجه به بلوک کانال های سدیم و پتاسیم باعث طولانی شدن فاصله QTc و QRS خواهد شد.

- بنابراین در تجویز همزمان با داروهایی که QTc را طولانی می کنند، با احتیاط مصرف شود.

- احتمال بروز طولانی شدن فاصله QTc در مصرف همزمان آزیترومایسین، کلترامتادون، اندانسترون (مخصوصاً در تزریق سریع)، هالوپریدول با هیدروکسی کلروکین افزایش پیدا می کند.

- ترکیب آزیترومایسین و هیدروکسی کلروکین توصیه نمی شود و در صورت نیاز از داکسی سیکلین استفاده شود.

- از ترکیب همزمان آزیترومايسين در بیماران با سابقهٔ آریتمی بطنی، برادیکاردی ( $HR < 50/min$ ) و هیپوکالمی و هیپومنیزیمی اصلاح نشده خودداری شود.

- سطح پتاسیم و منیزیم بیمار به ترتیب بالاتر از ۴ و ۲ میلی اکیوالان حفظ شود.

- به صورت استاندارد شش ساعت پس از شروع هیدروکسی کلروکین ECG گرفته شود، چهل و هشت و ۹۶ ساعت پس از شروع دارو فاصله QTc چک شود.



- تعدیل دوز در نارسایی کلیوی و کبدی توصیه نشده است.
- مصرف هیدروکسی کلروکین در دوز های بالا (۴-۵ گرم) بالقوه کشنده می باشد.

- تظاهرات مسمومیت هیدروکسی کلروکین شامل افت برون ده قلبی، شوک، تشنج می باشد.

- در صورت بروز اقدامات حمایتی شامل درمان تشنج با بنزودیازپین ها (ترجیحاً دیازپام)، استفاده مناسب از سدیم بی کربنات (در صورت وجود هیپوکالمی می توان از سالین ۵ درصد استفاده نمود) و وازوپروسور اینوتروپها توصیه شده است.

- هیدروکسی کلروکین در دوران بارداری Safe گزارش شده است.

**با تشکر از توجه شما**

