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Review Article

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Applied successful therapeutic protocol for COVID-19 in Arab Homeland

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Abstract

Therapeutic protocol for COVID-19 has been written in this manuscript and explained in-depth with detailed information. The protocols are divided into 3 main sections: generic protocol, the specific protocol for children, and a specific protocol for pregnant women and breast feeders. The basic concept is to treat viral infection symptoms, therefore medicines were selected accordingly. Garlic and onion consumption have been strongly recommended as immuno-stimulants. The advantages of this protocol include: no deaths, cure and recovery within a few days up to one week is guaranteed (cure may extend up to 10 days in very rare cases), no hospital admission, no need for Extracorporeal Membrane Oxygenation (ECMO) machines or any other type of ventilators (CPAP or BPAP). Also, this protocol can be applied without fear of interference with hypertensive or diabetic patients (although betamethasone causes slight temporary hyperglycaemia, this can be easily controlled by taking normal anti-diabetic medicines where there is no drug interaction between the medicines used in this protocol and anti-diabetic medicines) and finally no drug interference between the medicines used in this protocol and the medicines commonly used for asthma, thalassemia and goiter, allergic individuals, autoimmune diseases, heart problems etc. Disadvantages of this protocol include very rare cases of patients who have the previous hypersensitivity to some of the medicines mentioned in this protocol (estimated about less than 10 persons per million cases which is statistically nothing). This protocol has been/is being applied on thousands of COVID-19 patients (all age groups both genders, without causing any complications or deaths). This protocol is currently a national plan across the whole country (Iraq) where Iraqi physicians are using it to treat COVID-19 patients (ongoing work, unpublished data), plus it was circulated all over the Arab homeland. Amazing, promising, and astonishing data has been/is being collected and collated in files and it will be published most probably after getting acceptance of this paper in your respectful decent journal.

Keywords Therapeutic protocol, COVID-19, Children, Pregnant and breast feeders' women, No complications, No deaths.

Introduction

2019 nCov virus was an emerging virus discovered in the end of 2019 in Wuhan (China), one of the biggest Chinese cities (Zhu et al., 2019). The name of the virus was changed to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) and the disease was named COVID-19 disease (Gorbalenya et al., 2020). The disease started as a local epidemic disease (outbreak) in China, but a few weeks later,

World Health Organization (WHO) declared the disease as a pandemic on the 11th of March 2020, where the disease spread globally (WHO). Up to this day (29 April 2021), COVID-19 hits around 150 million people worldwide with more than 3 million deaths (data registered on 29 April 2021) and both morbidities and mortalities are still rising (Worldmeter 2021).

Many medicines have been used and protocols have been clinically applied to fight COVID-19, but unfortunately, none of them was completely successful or at least stopped deaths

(Yavuz and Ünal, 2020; Zhai et al., 2020). The mortality and morbidity rates are still increasing in a non-stoppable way which raised scientists' concerns and urged us as a team to find a suitable program and to select the best medicines to cure these patients who suffered a lot and it is the time to give a helping hand to those sufferers. Therefore, consultations were requested from Iraqi pharmacists with regards to the medicines involved in this protocol. Drug-drug interactions were determined and addressed; thus, the best medicines have been chosen relying on medical scientific bases. British National Formulary (BNF) plus British National Formulary for Children (BNFC) were used as solid medical references for selecting medicines.

This protocol is generic and it has been applied on a wide range of patients including hypertensive or diabetic patients (although betamethasone causes slight temporary hyperglycemia, this can be easily controlled by taking normal anti-diabetic medicines where there is no drug interaction between the medicines used in this protocol and anti-diabetic medicines) and finally no drug interference between the medicines used in this protocol and the medicines commonly used for asthma, thalassemia, goiter, allergic individuals, heart problems, immunocompromised patients who were addressed to have autoimmune diseases such as Rheumatoid Arthritis (RA), Infectious Bowel Disease (IBD), Systemic Lupus Erythematosus (SLE), neurologic diseases and disorders, organ graft (especially renal transplantation) etc.

However, some rare cases require special therapeutic protocols such as leukaemia or certain types of malignant cancer. Specialists and professional physicians may use mentioned medicines in this protocol to treat their patients, but they may adjust doses, change medicines and use any alternative drug whenever needed based on the special requirements of rare cases. This protocol may be updated according to the new situations because it is a well-known fact that SARS-CoV-2 has a high affinity to produce new strains through mutations (Pachetti et al., 2021; Pathan et al., 2020; Vilar and Isom, 2021) which may require new medicines.

1.1 Criteria of consideration COVID-19 patients

Laboratory test "Polymerase Chain Reaction (PCR)" was used as a first diagnostic method for COVID-19 patients in combination with chest CT scan (Wang et al., 2020a). Haematological picture represented by complete blood count (CBC) was requested as a further test for more confirmation (Ozbalak et al., 2021). SPO₂ level plus clinical symptoms were linked to the basic classification of the severity of the disease.

1.2 Methods for treatment of viral diseases with a focus on COVID-19

There are simply two concepts to cure viral infections. The first method is the availability of effective antiviral drug(s) which is mostly the fastest way to defeat viruses but there is a lack of these antivirals against the vast majority of viruses. The second method is represented by boosting immune

response which in turn fights viruses, but it is slower than the first method (Fukano et al., 2019). Symptomatic therapy is essential concerning both methods.

As a fact, most of the medicines used to treat COVID-19 did not show 100% efficacy, and this was seen globally where death rates continued everywhere; therefore, this protocol relies on boosting the immune system and it has shown excellent results. The main obstacle and challenging manifestation in COVID-19 patients is lymphocytopenia (decrease in the lymphocytes' count) and here is the key feature of this disease (Fathi and Rezaei, 2020; Tan et al., 2020; Tavakolpour et al., 2020).

The target of this therapeutic protocol is to stimulate the production of lymphocytes and pumping them into the site of infection to attack the virus and this is successfully achieved.

1.3 Essential notes must be considered by every individual

Healthy food consumption is strongly advised to everyone with a focus on garlic and onion which are strongly recommended as immunostimulants as well as their therapeutic role as they are known to have antimicrobial and antiviral properties (Ashfaq et al., 2021; Bhutada et al., 2020; Bisen and Emerald, 2016; Chakraborty and Majumder, 2020; Corzo-Martínez et al., 2007; Črnivec et al., 2021; Pawar and Patil, 2020). Omega 3 is one of the most important food supplements used in this protocol for every COVID-19 patient because of its important role in boosting the immune system (Arnardottir et al., 2021; Asher et al., 2021; Fu et al., 2021; Hamada, 2020; Hathaway et al., 2020; Rogero et al., 2020).

1.4 Herbal medicine (Chinese Medicine)

This includes medicinal plants and herbs used to boost the immune system to defeat viruses (including SARS-CoV-2) and this applies to all COVID-19 patients. Herbal medicine was/is being used to treat COVID-19 patients (all cases, mild, moderate, severe, and critically ill patients). Herbal medicine helped a lot to mitigate the severity of the infection and to boost the immune system. These herbs include (a long list but the most important items worked well on the respiratory system) turmeric, curcumin, cinnamon, green tea, black seed (*Nigella sativa*), which are strongly recommended to be taken mixed with honey except for diabetic people, chamomile, thyme mixed with olive oil, mint, menthol vapour, wormwood (*Artemisia absinthium*), ginger (*Zingiber officinale*) and ginseng (*Panax ginseng*) (Ang et al., 2020a and b; Dandara et al., 2020; Fan et al., 2020; He et al., 2020; Kwon et al., 2020; Li et al., 2020c and d; Luo et al., 2020; Panyod et al., 2020).

2. Generic therapeutic protocol

British National Formulary (BNF) Textbook Online (BNF, 2020) was used as a reference for selecting medicines applied in this protocol. The exceptions are listed as separate references. BNF can be accessed via this link <https://www.bnf.org/products/bnf-online/>

Therapeutic protocol can be divided into 2 major parts:

2.1 Asymptomatic, mild and moderate COVID-19 infections

These are self-cured therefore, no medicines are needed except paracetamol to control mild fever and multivitamins and minerals to cover the nutritional deficiency hence boosts the immune system.

2.2 Severe and critically ill patients

These cases require the following medicines

- a) Paracetamol 500 mg tablet orally. The dose is determined based on the severity, but generally, the recommended dose is 500mg four times a day. IM/IV injections are also available.
- b) Multivitamins and minerals (Tonics): twice per day in case of anorexia. If the appetite is not affected, a normal regular dose (once a day) is recommended.
- c) Levofloxacin 500 mg once a day because this antibacterial medicine is thought to work as anti-SARS-CoV-2 besides its activity as an antibacterial (Karampela and Dalamaga, 2020).
- d) An herbal mixture but not chemical antitussive medicine (Melrosum Syrup S 100 ml is mostly preferred for COVID-19 patients). This is strongly needed even after recovery and can be used as one spoonful every 4 hours.
- e) Anticoagulants: physicians decide which one is the best for each case. These anticoagulants must not be given when D-dimer is below 0.5 µg/ml (Favaloro and Thachil, 2020; Garcia et al., 2020; Li et al., 2020a). Below is a list of best-selected anticoagulants:

1. Clopidogrel 75 mg, once daily. It prevents venous thromboembolism (VTE), which is quite a common lethal symptom in COVID-19 disease (Llitjos et al., 2020; Middeldorp et al., 2020; Wichmann et al., 2020).
2. Enoxaparin, also known as low molecular weight heparin IV injection (dose determined by specialists ranged between 2000 up to 8000 IU). Essential for the treatment of arterial and venous thromboembolism in COVID-19 patients (Cattaneo and Morici, 2020; Cattaneo et al., 2020; Lodigiani et al., 2020)
3. Rivaroxaban, the best and strongly recommended anticoagulant in this protocol. Its functions and uses are as the same as mentioned in point 2 (Enoxaparin). Rivaroxaban has been preferred medically and clinically over Enoxaparin in the literature (see section 2.3).

- f) Ondansetron, 4mg, 8mg, or 24mg tablets or available as 4 mg IV/IM injections (antiemetic) (Medscape 2021). For COVID-19 patients, it is preferred to take tablets (8 mg orally), but if it is repelled out with the vomitus, then 4mg IM injection for those who weigh up to 80 Kg (dose should be increased according to body weight over than 80 Kg) is the alternative route of

administration. Less than 15% of COVID-19 patients recorded vomiting symptoms (Andrews et al., 2021; Wong et al., 2020).

- g) Dextrolyte sachets, Oral Rehydration Solutions (ORS). For the treatment of diarrhea because the virus attacks the digestive system and replicates in the gastrointestinal tract (GIT) which forms less than a quarter of COVID-19 patients symptoms (D'Amico et al., 2020; Li et al., 2020b).
- h) Betamethasone (2 mg/ml IM injection). Diprofos ampule is betamethasone dipropionate and betamethasone sodium phosphate 2mg+5mg per ml. single dose is given only. Betamethasone must be given only for severe or critically ill patients. Betamethasone must not be given except in two conditions (Chest pain, and dyspnoea "difficult breathing" when SPO₂ is below 80 because these indicate pathognomonic symptoms of cytokine storm). Betamethasone is strongly recommended to treat respiratory affections (Grandordy et al., 1987; Kashanian et al., 2018; Schmitz et al., 2019) with an excellent history of fighting respiratory viral infections such as Rhinovirus (Waltl et al., 2018).
- i) For those who suffer from gastric hyperacidity mzor ulcer or any similar gastric problems, it is recommended to take Famotidine tab 20 mg twice per day before the meal because Famotidine has thought to have some inhibitory effect on SARS-CoV-2 virus (Freedberg et al., 2020; Janowitz et al., 2020; Mather et al., 2020).

2.3 General notes related to the above protocol

Rivaroxaban is the same as Enoxaparin in terms of potency, functioning, and efficacy (Faqah et al., 2020). However, other references preferred the use of Rivaroxaban and considered it safer, much effective, and better than Enoxaparin when treating venous thrombo-embolism (VTE) in patients suffering from cancer (Xing et al., 2018), and also Rivaroxaban is preferred for the prevention of VTE after non-major orthopedic surgery (Buzby, 2021).

Patients who have been critically ill can be given Betamethasone single dose (must not be repeated for whatever reason) IM injection. The cure is seen within 2 days. This is only guaranteed when no multiple doses of short-acting cortisones have been given (especially dexamethasone or methyl prednisolone). If dexamethasone or methyl prednisolone was given in multiple doses, betamethasone would do nothing (failed). It is recommended to give one single dose of Dexamethasone for life-saving when a COVID-19 patient is critically ill because it has rapid action (acts faster than Betamethasone) to save the life (recommended only in this case) and followed by Betamethasone IM injection after approximately 8 hours.

If none of above medicines worked, and the case is not responding to any of above treatments (which was rarely happened, but just in case), convalescent plasma (CP) therapy from recovered patients is the last choice of treatment. However, the efficiency of CP method did not exceed 80% (the percentage of survivals) in curing COVID-19 patients, thus, it is not the best method but it worked well

(Zhai et al., 2020) and it was approved by FDA (March 2020) which may save the life (Tanne, 2020).

2.4 Additional tips about this protocol

The above medicines are not the standard prescription for every COVID-19 positive case, therefore, and it is a well-known fact, treatment of viral infections is always symptomatic (BNF, 2021), i.e. the harmful symptoms should be cleared and treated correctly and appropriately. This means if there is no cough, there is no need to use antitussive medicines. If there is no fever, there is no need to give antipyretics. If there is no vomiting, there is no need to give antiemetics and so on etc.

2.5 Pros and cons of this protocol

Advantages of this protocol are as follows: no mortalities, cure, and recovery within one week is guaranteed including severe cases (cure may extend up to 10 days in some cases), while similar cases could last for several weeks in hospitals (when other protocols are followed and patients most often died), no hospital admission, no need for Extracorporeal Membrane Oxygenation (ECMO) machines or any other type of ventilators (CPAP or BPAP).

In addition, this protocol can be applied without fear of interference with hypertensive or diabetic patients (although betamethasone causes slight temporary hyperglycaemia, this can be easily controlled by taking normal anti-diabetic medicines where there is no drug interaction between the medicines used in this protocol and anti-diabetic medicines) and finally no drug interference between the medicines used in this protocol and the medicines commonly used for asthma, thalassemia and goitre, allergic individuals, autoimmune diseases, heart problems etc. Disadvantages of this protocol include very rare cases of patients who have the previous hypersensitivity to some of the medicines mentioned in this protocol (estimated about less than 10 persons per million cases which are statistically nothing). This protocol was/is being applied on COVID-19 patients (all age groups both genders), without causing any complications or deaths.

3. Specific protocol for COVID-19 positive cases of children

British National Formulary for Children (BNFC) Textbook Online (BNFC, 2021) was used as a reference for selecting medicines applied in this protocol. BNFC can be accessed through this link <https://www.nice.org.uk/bnfc-uk-only>.

The therapeutic protocol can be divided into 2 major parts:

3.1 Asymptomatic, mild and moderate COVID-19 children infections

These represent 90% of total children, which are self-cured (Han et al., 2020; Treibel et al., 2020; Yu and Yang, 2020). Therefore, no medicines are needed except paracetamol to control mild fever (just in case of fever) and multivitamins and minerals to cover the nutritional requirements of the body which includes boosting the immune system. However, a few publications proved the presence of some exceptions

(around 1 to 2%) represented by severe pediatric hospitalised ill cases of COVID-19 have been recorded in Washington, USA (DeBiasi et al., 2020), Wuhan, China (Wang et al., 2020), UK and some European countries (Carroll et al., 2020; Mahammedi et al., 2020). These severe cases require special therapeutic protocols.

3.2 Severe COVID-19 cases in children (less than 10% of total children) require the following medicines

These cases require the following medicines

- a) Paracetamol syrup. Antipyretic is given on need. The dose varies according to age and severity.
- b) Multivitamins and minerals (Tonics): twice per day in case of anorexia. If the appetite is not affected, a normal regular dose (once a day) is recommended.
- c) Dextrolyte sachets, Oral Rehydration Solutions (ORS). For the treatment of diarrhea because the virus attacks the digestive system and replicates in the gastrointestinal tract (GIT).
- d) An herbal mixture but not chemical antitussive medicine (Melrosom Syrup S 100 ml is mostly preferred for COVID-19 patients). This is strongly needed even after recovery and can be used as one cup spoonful every 4 hours.
- e) Ondansetron 4mg / 5 ml syrup on need as an antiemetic (Medscape, 2021). If it is repelled out with the vomitus, 4mg IM ampule is recommended. It is preferable to prescribe Hyoscine butylbromide IM to relieve GIT spasm. Dose for Child 6–11 years 10 mg 3 times a day. For Child 12–17 years. 20 mg 4 times a day. Symptoms in children disappear within less than 3 days normally.
- f) Probiotic (Biolact sachets worked well), which has both *Bifidobacterium lactis* and zinc to be mixed with water, milk, or juice once daily. There was a clue for the antiviral effects of probiotic metabolites on COVID-19 (Anwar et al., 2020; Balmeh et al., 2021).
- g) Betamethasone (2 mg/ml IM injection). Half dose of Diprofos ampule is betamethasone dipropionate and betamethasone sodium phosphate 2mg+5mg per ml. single dose is given only. Betamethasone must be given only for severe or critically ill patients. Betamethasone must not be given except in two conditions (Chest pain, and dyspnoea “difficult breathing” when SPO₂ is below 80 because these indicate pathognomonic symptoms of cytokine storm).

3.3 General notes about this protocol

Above medicines are not the standard prescription for every COVID-19 positive case, therefore, and it is a well-known fact, treatment of viral infections is always symptomatic (BNF, 2021), i.e. the harmful symptoms should be cleared and treated correctly and appropriately. This means if there is no fever, there is no need to use antipyretic medicines. If there is no diarrhea, there is no need to give anti-diarrheal

medicines. If there is no vomiting, there is no need to give antiemetic and so on etc.

3.4 Important information about COVID-19 infection in children

Children are mostly immune against COVID-19 and this is explained in a detailed review article I wrote with some of Iraqi paediatricians to discuss why children are mostly resistance against COVID-19? (The paper was sent for publication last month). About 90% of COVID-19 cases of children are asymptomatic or with mild symptoms that do not need any therapy and self-cure is the main outcome (Han et al., 2020; Miri et al., 2020; Tezer and Demirdağ, 2020; Vermund and Pitzer, 2020). Therefore, there is no fear or worries about the infection of children with COVID-19 disease except a few exceptional cases of children who have underlying issues.

4. Specific protocol for COVID-19 positive cases of pregnant and breast feeders

Women are clinically affected less than men by COVID-19 disease, and it seems that their immune defence mechanism is stronger than that in men and this could be attributed to the hormonal effect where oestrogen (a dominant sexual steroid hormone in females) plays a powerful role against the virus. Therefore, COVID-19 is clinically mostly mild to moderate in adult females (Bwire, 2020; Conti and Younes, 2020; Cutolo et al., 2020; Sharma et al., 2020).

British National Formulary (BNF) Textbook Online <https://www.bnf.org/products/bnf-online/> (BNF, 2021) was used as a reference for selecting medicines applied in this protocol. The exceptions are listed as separate references.

Therapeutic protocol can be divided into 2 major parts:

4.1. Asymptomatic, mild, and moderate COVID-19 infections

These cases are self-cured therefore, no medicines are needed except paracetamol to control mild fever and multivitamins to cover the nutritional requirements of the body which includes boosting the immune system.

4.2. Severe COVID-19 cases and critically ill patients

These require the following medicines

- a) Paracetamol 500 mg tablet orally. The dose is determined based on the severity, but generally, the recommended dose is 500mg four times a day. IM/IV injections are also available.
- b) Multivitamins and minerals (Tonics specific for pregnant women e.g. Pregnacare tablets): twice per day in case of anorexia. If the appetite is not affected, a normal regular dose (once a day) is recommended.
- c) Herbal mixture but not chemical antitussive medicine (Melrosum Syrup S 100 ml is mostly preferred for COVID-19 patients). This is strongly needed even after recovery and can be used as one spoonful every 4 hours.

- d) Erythromycin 500mg every 6 hours. There is evidence of this antibacterial to have specific antiviral effect on SARS-CoV-2 (Al-Kuraishy et al., 2020; Ohe et al., 2020).

e) Anticoagulants include:

- 1) Aspirin 81 mg as anti-platelets once daily which is quite common and safe for pregnant women. Clopidogrel 75 mg is not recommended for pregnant and breast feeders (BNF, 2021).
 - 2) Enoxaparin, also known as low molecular weight heparin IV injection (dose determined by specialists ranged between 2000 up to 8000 IU). Essential for the treatment of arterial and venous thromboembolism in COVID-19 patients (Cattaneo and Morici, 2020; Cattaneo et al., 2020; Lodigiani et al., 2020).
 - 3) With regards to Rivaroxaban, FDA approved its prescription for pregnant women with cautions but not recommended for breastfeeders (Singh and Emmady, 2020).
- f) Meclozine hydrochloride/pyridoxine hydrochloride (Navidoxine) is prescribed only when there is vomiting (antiemetic).
- g) Dextrolyte sachets, Oral Rehydration Solutions (ORS). For the treatment of diarrhea because the virus attacks the digestive system and replicates in the gastrointestinal tract (GIT) which forms less than quarter of COVID-19 patients symptoms (D'Amico et al., 2020; Li et al., 2020b).
- h) Betamethasone (2 mg/ml IM injection), Diprofos ampule is betamethasone dipropionate, and betamethasone sodium phosphate 2mg+5mg per ml. single dose is given only. Betamethasone must be given only for severe or critically ill patients. Betamethasone must not be given except in two conditions (Chest pain and dyspnoea "difficult breathing" when SPO₂ is below 80 because these indicate pathognomonic symptoms of cytokine storm). Betamethasone is strongly recommended to treat respiratory affections (Grandordy et al., 1987; Kashanian et al., 2018; Schmitz et al., 2019) with an excellent history of fighting respiratory viral infections such as Rhinovirus (Walzl et al., 2018). Betamethasone injection for pregnant is controversial i.e. most recent studies recommend it to develop body organs (especially the lung) of the preterm foet uses (ABC, 2020; Cahill et al., 2019; Foissac et al., 2020). While, a few and old references did not recommend the use of Betamethasone due to some side effects (Kjer and Hess, 1983; Mastrobattista et al., 2001; Teagarden and Picardo, 2011).
- i) For those who suffer from gastric hyperacidity or ulcer or any similar gastric problems, it is recommended to take Famotidine tab 20 mg twice per day before the meal. FDA approved the use of Famotidine for pregnant

and breast feeders women only when there is a benefit (Drugs.com, 2021).

4.3. General conceptions related to above protocol

Patients who have been critically ill can be given Betamethasone single dose (must not be repeated for whatever reason) IM injection. Cure will be seen within 2 days. This is only guaranteed when no multiple doses of short acting cortisones have been given (especially dexamethasone or methyl prednisolone). If dexamethasone or methyl prednisolone was given in multiple doses, betamethasone would do nothing (failed), and the case will not respond. It is recommended to give one single dose of Dexamethasone (must be single dose only) for life saving when COVID-19 patient is critically ill because it has rapid action (acts faster than Betamethasone) to save the life (recommended only in this case) and followed by Betamethasone IM injection after approximately 8 hours.

If none of above medicines worked, and the case is not responding to any of above treatments (which was rarely happened, but just in case), convalescent plasma (CP) therapy from recovered patients is the last choice of treatment. However, the efficiency of CP method did not exceed 80% (the percentage of survivals) in curing COVID-19 patients, thus, it is not the best method but it worked well (Zhai et al., 2020) and it was approved by FDA (March 2020) which may save the life (Tanne, 2020).

Above medicines are not the standard prescription for every COVID-19 positive case either pregnant or a breast feeder woman, therefore, and it is a well-known fact, treatment of viral infections is always symptomatic (BNF, 2021), i.e. the harmful symptoms should be cleared and treated correctly and appropriately. This means if there is no cough, there is no need to use antitussive medicines. If there is no fever, there is no need to give antipyretics. If there is no vomiting, there is no need to give antiemetic and so on etc.

5. Explanations and alternative medicines

Below medicines have been selected from British National Formulary (BNF). We are not going to discuss the pharmacology of each drug, but we will focus on the clinical uses only. These include the following:

5.1 Paracetamol 500mg

Paracetamol is used as an antipyretic and analgesic. It is essential to use it to control fever and fatigue resulted from any disease including (COVID-19) disease (Jóźwiak-Bebenista and Nowak, 2014; Trivedi et al., 2015; Williams et al., 2014). No recommendations for any other alternative medicines. However, there is a warning to avoid using of the non-steroidal anti-inflammatory drug (NSAID) as an alternative medicine for Paracetamol but this is not confirmed (Capuano et al., 2020; FitzGerald, 2020; Paprocki, 2020).

5.2. Multivitamins and Minerals (Tonics)

Vitamins and minerals are required for body need every day. Multivitamins and Minerals contains vitamins and minerals

calculated precisely and in specific doses and they were proved to play an essential role in defeating many diseases and even cancer (Huang et al., 2006; Kaduk, 2019; Moyer, 2014; Neuhouser, 2009; Velloso et al., 2019).

Tonics must not be given to certain cases such those who suffer from chronic and multiple urinary tract infections or renal transplantation, pernicious or megaloblastic anaemia, Wilson's disease, hemochromatosis, hypoparathyroidism or severe penetrative gastric ulcer (tonics must not be given through oral route) according to British National Formulary (BNF) Textbook (BNF, 2021).

Tonics used for children are essential for the overall growth, improvement of kids' general health as well as to boost their immune response (BNFC) to fight viruses. These tonics work as an appetizer as well.

5.3 Levofloxacin

Levofloxacin is one of the quinolones (a group of antibiotics) which possess excellent antibacterial properties especially on respiratory system with special characteristics of treating bacterial pneumonia better than Azithromycin (Garcia et al., 2017; Noreddin and Elkhatib, 2010; Noreddin et al., 2011). The reason why it has been selected in this protocol is that the specific anti-COVID-19 activity (Karampela and Dalamaga, 2020). This means Levofloxacin would work as an antibacterial and antiviral in the same time (2 in 1).

But why antibacterial drugs are given where the causative agent is virus? The answer is simply because the mortality rates are too high due to secondary bacterial infection and that is why antibacterial medicines are "strongly recommended" (Cox et al., 2020).

Alternatives include Moxifloxacin 400mg, once daily. These antibacterial medicines have the same properties as of Levofloxacin, i.e. they have specific anti-COVID-19 activity plus their antibacterial role (2 in 1) dual activity (Karampela and Dalamaga, 2020).

There is an extra benefit for this protocol in the Middle East (especially in Iraq), how? *Salmonella typhi* causes Typhoid fever and it is epidemic in Iraq. Clinical symptoms are approximately similar to those of COVID-19 disease which confused physicians in the diagnosis and treatment. Therefore, one of the best drugs used for Typhoid fever is "Levofloxacin", which is (or its alternatives) will remove the confusion and the physicians would prescribe it with high confidence, and this is a bonus in this protocol (Jianguo et al., 2002; Nelwan et al., 2006; Usman et al., 2013).

5.5 Herbal mixture but not chemical antitussive medicine (Melrosum Syrup)

Melrosum syrup is an internationally famous antitussive drug. It stops all types of cough (dry, wet, productive and non-productive cough). It consists of a long list of herbs and plants and honey which works perfectly on any type of cough (Abu-darwish and Al-Ramamneh, 2009). The constituents of Melrosum syrup (herbs, plants and honey) have 3 benefits: First, relief all types of cough; Second, boost immune system especially in the lung because the immunological properties

of the herbs, plants and particularly honey have been reviewed and empirically studied in many publications on these constituents (Baracchi et al., 2011; DeGrandi et al., 2015; Simone et al., 2009). Third the excretion of this medicine is not harmful to the body and there no or very least side effects because it consists of biologically natural products (not chemicals, neither synthetic product) as mentioned in BNF.

Alternatives to Melrosum syrup have approximately similar functions and properties, but less effective than Melrosum syrup include Herbikof syrup (United Arab Emirates, UAE), Koflet (Himalaya, India), Zecuf either tablets or syrup (India), and Covonia Chesty Cough Mixture Mentholated (Boots, UK) for resident Arabs in the UK. These medicines showed excellent antitussive against COVID-19 annoying cough.

5.6. Famotidine

It is one of the best medicines used for the treatment of gastric ulcer. It is classified as a selective histamine type 2 receptor blockers. There are many medicines can do this job (e.g. Esomeprazole, Lansoprazole, Omeprazole, Pantoprazole, Rabeprazole, Cimetidine, Nizatidine, and Ranitidine etc) as mentioned in the BNF, and the question here why Famotidine? The answer is simply because Famotidine has a vital role in targeting and reducing SARS-CoV-2 virus activity as mentioned in the literature (Malone et al., 2020; Singh et al., 2020). This means Famotidine has two functions; antiulcer and antiviral (2 in 1).

5.7 Betamethasone (the novel key remedy for COVID-19)

Betamethasone is a glucocorticosteroid medicine used clinically for the treatment of many disease and disorders such as asthma, allergy (including anaphylaxis when some drugs administered), shock resulted from surgical or accidental trauma or devastating infection, acute adrenal crisis caused by abnormal stress in Addison's disease, Simmonds' disease, hypopituitarism following adrenalectomy, and when adrenocortical function has been suppressed by prolonged corticosteroid therapy, soft tissue lesions such as tennis elbow, tenosynovitis and bursitis, rheumatoid lung, osteoarthritis, rheumatoid arthritis, gouty arthritis, anti-inflammatory, dermatological disorders, collagen vascular disease, autoimmune disorder and Felty's syndrome (EMC-UK, 2021; Everyday-health, 2021).

It is not a new fact that Betamethasone works well against allergy especially respiratory allergy and prevent anaphylaxis (which cause death sometimes) as well as treatment of shock. If you look at above diseases (and disorders) you can easily know why the authors selected Betamethasone for the treatment of COVID-19. The main fatal symptoms of COVID-19 are the cytokines storm (devastating immune reaction against the virus), and the other cause of death in COVID-19 cases is respiratory failure, hence Betamethasone can do the job to tackle these 2 reasons that could cause death.

Betamethasone can neutralise cytokine storm better than any other steroid with less side effect compared by others, how?

It worked perfectly in the treatment of respiratory allergy (reference : consultation from a group of specialist physicians in respiratory system and clinical pharmacists) and in the literature it has been mentioned that Betamethasone worked in an excellent way against respiratory viruses such as Rhinovirus and it was used perfectly to treat smokers infected with this virus, thus Betamethasone is not the first time used for treatment of respiratory viruses (Waltl et al., 2018). Betamethasone can prevent respiratory distress in newborns and that is another supporting evidence for its efficacy in the treatment of respiratory affections (Foissac et al., 2020; Kashanian et al., 2018; Schmitz et al., 2019).

As mentioned earlier in this paper, Betamethasone is not a new medicine, it has been used for a long time in the treatment of respiratory system affections. In this context, and in the past, Betamethasone was recommended for the treatment of asthma successfully in a clinical trial (McAllen et al., 1974) and further studies focused on the brilliant effect of Betamethasone on the respiratory system affections (Grandordy, 1987) and this reputable benefit of this medicine means (based on above evidences), Betamethasone can treat respiratory failure resulted from COVID-19 severe and critical cases and save the lives of patients.

Recent studies confirmed the fantastic therapeutic role of Betamethasone on the respiratory system and added more diseases that can be treated by Betamethasone which include autoimmune diseases (for example, systemic lupus erythematosus, autoimmune hepatitis, sarcoidosis); joint and muscle diseases (for example, rheumatoid arthritis); and allergies as well as asthma (Stewart, 2021). As you can see Betamethasone was used successfully for the treatment of immunological disease (autoimmune diseases), hence why not use to treat cytokine storm (immune reaction) resulted from COVID-19 disease? We strongly recommend it, and we claim that Betamethasone injection is the key therapy for COVID-19 severe cases and critically ill patients.

Betamethasone must not be prescribed for preventive or prophylactic purposes at all against any disease including COVID-19. It is like any cortisone as mentioned in the BNF that has immunosuppressive properties. However, the level of immunosuppression in case of betamethasone is dramatically fewer and less than any other cortisones and this is seen by experience of the second author, the senior pharmacist who suffer from seasonal allergy and used to inject Betamethasone annually once or twice, which had never shown severe side effect of never complain from any immuno suppression which means that Betamethasone is mild immunosuppressive drug (in spite the fact that confirm it is potent anti-inflammatory) and this is why we thought about it to cure COVID-19 severe and critically ill cases. For this purpose, Betamethasone is the best steroid used in the treatment of COVID-19 disease. Also Betamethasone can be prescribed safely for aged people while other cortisones are contraindicated (especially dexamethasone) see this British reference (EMC-UK, 2021) and this interprets the high fatality rates of COVID-19 aged patients.

Betamethasone is strongly recommended and must be given for COVID-19 patients when 2 clinical symptoms are

noticed; chest pain and dyspnoea “difficult breathing” when SPO₂ level drops below 80. These 2 symptoms are warning signs of initiation of cytokine storm (reference: advice taken from experienced professional physicians certified in respiratory system diseases).

If COVID-19 patient general condition is poor and the patient general health is collapsed (fainted), a single dose of dexamethasone for life-saving (single dose only and must not be repeated for whatever reason), followed by a single dose only of Betamethasone injection after 8 hours of giving dexamethasone. The reason for that is that Betamethasone is slow-acting medicine and its action (onset) is delayed for about 12 hours, which requires a fast-acting steroid (dexamethasone) to rectify the situation. This will save lives quickly and this is an emergency case that is absolutely needed elective and immediate decision by physicians. Any delay in making this decision may lead to death.

For patients who are on ECMO and given multiple doses of dexamethasone (or methyl prednisolone), it is useless to prescribe Betamethasone injection because the immune system was destroyed. After all, steroids’ side effect is immunosuppression. Betamethasone would not work, and the decision is absolutely up to the physician to decide which method and which drug can be used.

5.8 Erythromycin

Most antibiotics are contraindicated for pregnant and breast feeders (BNF). Therefore, erythromycin is relatively safely prescribed for pregnant and breast feeders to prevent secondary bacterial infection (as it is mentioned in this paper the cause of 50% mortality of COVID-19 patients).

Erythromycin is not only antibacterial medicine, a recent study has found that erythromycin could inhibit interleukin-6 and prevent SARS-CoV-2 replication which means 2 in 1 (antibacterial plus antiviral medicine) at the same time (Lisanti, 2021).

Alternatives: Amoxicillin which has proven to have specific anti-COVID-19 properties in a clinical trial study <https://clinicaltrials.gov/ct2/show/NCT04363060>, thus it has the same effect as erythromycin, 2 in 1 (antibacterial and antiviral).

5.9 Clinical application of this protocol

This protocol has been applied on thousands of COVID-19 Iraqi and Arabic patients (all age groups both genders) with no deaths. This included aged people (more than 70 years old), diabetic, hypertensive, asthmatic patients and those of thyroid gland illnesses and disorders (goitre) as well as thalassemia, autoimmune diseases e.g. Rheumatoid Arthritis “RA”, Systemic Lupus Erythematosus “SLE”, neurological disorders etc. This means this protocol fits the requirements of a wide range of ill people.

Conclusion

This therapeutic protocol is designed and planned with the help, guidance, and advice of Iraqi pharmacists and physicians. There are 3 protocols; generic, one for children,

and the last one for pregnant and breast feeders’ women. In fact, there is no specific protocol for the treatment of viral infections, but the only way is when symptoms are cured (symptomatic treatment). In this paper, a list of symptoms has been mentioned plus the best remedy (and its alternatives) for each symptom. The medicines have been selected in a way that does not interfere with the immune system as much as possible. The key remedy in this protocol is Betamethasone which plays a vital role in saving the lives. This protocol has been applied on thousands of individuals and the case fatality rate was 0%. This included aged diabetic and hypertensive people as well as so many people with underlying health issues (immuno compromised). This protocol may be updated according to the new situations because SARS-CoV-2 has high affinity to produce new strains through mutations (Pachetti et al., 2020; Pathan et al., 2020; Vilar and Isom, 2021) which may require new medicines.

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Consent for publication

The author declares that the work has consent for publication.

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