Timely Appropriate Dynamic Doses of Corticosteroid: Life Changer in COVID-19 Management as Home based Care of COVID Patient through Proper Monitoring by Teleconsultation

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1. Introduction

After 1st wave of COVID-19 second wave for COVID-19 pandemic, in India, has devastated hospitals (Government and Private) by having long queue of ambulances to enter the premises due to non availability of beds or ICU or oxygen supply specifically in big metro cities like Delhi and Mumbai, Ahmedabad etc. This has not been restricted to hospital line-ups but also run out for cremation space with a waiting list for people to be cremated with full honor. However, report from village, town and small cities is still to be anticipated [1].

In-order to decrease the hospital admission load for mild to moderate cases and severe case early to prevent mortality of serious sick patients due to delayed or non availability of hospital admission can be overcome by having telemedicine consultation and counseling of mild to moderate patient and severe also.

Deployment of telemedicine as a substitute for in-person care throughout the country and worldwide was aimed at achieving the triple objectives of (1) caring for the patients requiring isolation and intensive care, (2) continuing to care for customary patients, and (3) protecting providers and patients from infection. [2]

Figure 1: (Different phases of COVID-19 infection and Treatment)
Looking at the present upsurge of the second pandemic wave we, with our 18 years of clinical experience in respective specialty started giving telemedicine consultation and counseling to diagnosed COVID family members and friends were we not only prescribed them the appropriate medication as per the guidelines for OPD basis but also identified early hospitalization required for the respective patient depending on the Clinical criteria, biochemical and SpO2 trends, Pulse Rate and temperature monitoring at home by the by patient with proper monitoring charts that sample chart attached with this presentation also to help others with their clinical symptoms which they could explain telephonically. Monitoring the CBC, CRP Serum ferritin is of great help in treatment protocol to detect severity early.

Most important is proper monitoring of all positive or false negative symptomatic patient of family with proper monitoring sample charts and by clinical and biochemical and SpO2 trends because 80 to 85 of patients are mild not required specific treatment but rest 10 to 15 % may be moderate to severe and detection of these patients early and treatment with proper doses of medicine and proper tapering is primarily important. Minimal dose of steroids 80 mg prednisolone or methylprednisolone but we used Tab prednisolone for orally in our OPD patients and intravenous methyl prednisolone in admitted as glucocorticoid activity, one set of action and t1/2 (half life) of both is nearly same.

Most important is proper tapering of drug in next 2 to 3 wk to deal with ongoing inflammation and prevention of interstitial lung fibrosis and effect of corticosteroid on profile of dysregulated immune markers is clearly illustrated. [17, 18]

Steroids should be avoided in symptomatic phase (less than 5 days of initiation of symptoms) since it can increase the viral replication and proportional Inflammation also and thus can lead to further damage in terms of inflammatory reaction [20]), it should be noted that when corticosteroid used after replication phase means even in early pulmonary phase do not increase viral shedding or decrease the production of type of specific antibodies for protection of re-infection [9, 73]. Only indication of early steroid is in high risk cases with presentation of hypoxia in early phase itself.

Our Practice and experience
According to our observation and the inputs from the research, the most important part in COVID management is proper monitoring and detection of moderate or severe patients and timely treatment with proper dosage.

Our aim is to prevent the hospital load by providing telemedicine management to COVID patients using a proper course of prednisoloneoral tablets to those detected moderate to severe patient by our monitoring.

Dosage of steroids is extremely dynamic; this cannot remain identical for every patient, like researchers have identified in WHO Study [21] in which same low dose is recommended. Some might require lower dose of 80 mg day, while few might require higher pulse therapy of 1 gm/day. [4- 16]

Our experience, with approximately 2500 patients, in which majority of patients detected mild in each family but 257 detected moderate according to our clinical, biochemical and spo2trends criteria and treated properly will proper does of steroids but some patients presented late as moderate to Severe hypoxia are admitted and treated like with high flow 02 or BIPAP due to massive cytokine storm and given bolus

Figure 2: (Dynamic doses of Anti-inflammatory agent according to severity of hypoxia)
of 1 gm pulse therapy of methyl prednisolone and then infusion of 1 gm in 24 hour and then decrease progressively.

Out of total 2500 patients and 257 moderate to Severe 2 death reported. One patient consult very late with severe hypoxia and second was a stable patient but had sudden cerebrovascular ischemic stroke even after Ecosprin150 and Rivaroxaban oral anticoagulant is going on.

Atorvastatin 80 mg per day in very high risk and 40 mg per day [22-26] in all moderate case till 4 to 6 weeks and ecospirin 150 [27, 28, 29, 30, 31] in very high risk and 75 in all moderate case for 8 weeks are important to prevent microvascular coagulation and Acute coronary events because of even minimal Inflammation in their coronaries.

Control of blood sugar is very important. Hb1AC value (5.7 to 6.5) indicates pre-diabetic state while value more than 6.5 should be diabetic. The estimation of Hb1AC is important to identify undiagnosed diabetic patients so that it will be easy for physician can monitor and control patients sugar level.

Clinical case strategies
Our instructions to patients was to prepare a chart showing values for SpO2, HR, temperature and other associate symptoms and message it at least thrice a day. Indication for increased inflammatory reaction was identifies by these criteria’s:

- Persistent fever for more than 5days.
- Reappearance of fever after 5th day.
- Feeling of weakness, fatigue or malaise after 5 th day.
- Tachycardia (HR more than 100b/min) after 5 th day.
- Decrease SpO2 trends Ok (e. g., from 98 to 95).

Lab Investigation markers: 3 rd day, 6 th day 9 th day.
- Decreased trends of TLC, platelet count, Absolute lymphocytes or increased N/L ratio.
- Raising trends in CPR, S. ferritin, LDH.

Case-1
A 68 year old male with various co-morbidities; Diabetic since past 20 years on insulin 52 unit per day and with oral hypoglycemics, hypertensive since past 28 years and on multiple anti hypertensive drugs, suffering from pepticulcer, with fatty liver, dyslipidemia, and was chewing tobacco since past 40 years although a regular morning walker for 45 minutes.

The episode began with complain of throat pain with mild fever. RTPCR report showed positive on 4th day by then patient had mild throat irritation and no fever. Patient was already on Ecosprin150 and atorvastatin10 from day 5 and Atorvastatin40 was added

5th day: Lab reports; Total Leucocyte count (TLC) 4200, Lymphocyte percentage (L) 63%, Platelet count (pc) 2.8, C-Reactive protein (CRP) 1.2, S. Ferritin7.4 with SpO2 value 97 to 99

8th Day: Lab reports; TLC 4000, L 34%, pc 3.1, CRP 1.4, S ferritin10.2, with SpO2 value 97 to 99 no fever, but mild throat irritation

12th day: Reappearance of fever 99 to 100°C, SpO2 value dropped to 94 to 95.

Lab reports-TLC 4340, L 33%, pc 2.9, CRP 13.4, S ferritin38.

2 tablets of Omnicortil 40 stat followed by Omnicortil 60 mg for 5 days with proper monitoring of sugar levels at two intervals (fasting pre-lunch and pre-dinner) and modify by insulin and oral hypoglycemic drug doses. Fever stopped immediately after intake of first dose of Omnicortil with less throat irritation. SpO2 value rose to 95 to 96.

Markers were repeated on 15th day to decide 60 mg Omnicortil for 2 more days or taper subsequently.

15th day: Lab reports; TLC 5360, L 43%, PC 2.93, CRP 4.3, S ferritin 26, SpO2 97 to 98, Omnicortil tapering was done starting from 40 mg for 5 days, then 30 mg for 5 days, 20 mg for 4 day, 10 mg for 4 day and finally 5 mg for 4 days then stoppage so as to deal ongoing inflammation.

Now patient is fit and fine continuing with drugs for DM and breathing exercise

Case-2
A 58 year old female patient, wt106 kg, patient was depressed with less physical mobility having hypothyroidism and diagnosed with Diabetes Mellitus during COVID state with Hb1AC value 6.9.

Day-1: First symptom of cough and cold

3rd day: SpO2 was 86, and was admitted to a hospital LMH. Remdisivir, an antibiotic and Ecosprin was started.

5th Day: SpO2 89 in-spite of 15L Oxygen. Physician had not started steroid since CT was normal and stated that the acute phase reactant are not favoring. Our experience in the field convinced the physician 80 mg methyl Prednisolone BD with 4 cc Dexona; keeping in mind that we are supposed to treat the patient based on clinical sign and symptoms rather than investigation because investigation can confuse you but not hypoxia in COVID-19.

6th Day: At morning SpO2 rose to 96 with 6Lites of Oxygen

Pt. was on remdisivir, ivermectin, Doxy, LMH from the day of hospital admission without steroids. However addition of steroid drastically improved the condition of the patient in ICU.

After 4 days of hospital treatment patient discharged with tapering doses for Prednisolone (80 mg for 4 days, then 60 mg for 4 days, then 40 mg for 4 days, followed by 20 mg for 4 days last 10 mg and 5 mg for subsequent 4 days). Atorvastatin 40 and Ecosprin 75 were continued for next 1 month along with and tab Rivaroxaban (oral anticoagulant) for next 2 wk. Patient was instructed to continue vitamins and breathing exercises.

Patient is perfectly doing good today.
Case-3
A 72 year old male undergone angioplasty, hypertensive since past 20 years, overweight and was recently diagnosed for diabetes mellitus with HbAC 6. 6 although had been doing regular walking.

Patient presented viral like symptoms but with good general condition on 29 Nov.

He was advised to go for COVID test but refused. On our request, he went for blood investigations like CRP and TLC.

Day-2 morning: Lab reports; CRP 147, SpO2 varied from 96 to 98, refused hospital admission.

Day-2 evening: SpO2 dropped to 91, by the time patient was admitted to hospital SpO2 dropped to 79. However, patient was kept. On BIPAP, pressure support 20, PEEP 8 (PIP28), FiO2 100and SpO2 91

Hospital treatment was initiated with an antibiotics, Ecosprin150, Cloxan0.4 cc bid, Atorvastatin40 mg bid and we convinced the in-charge physician to started inj methyl Prednisolone 1 gm stat in 100 ml Normal Saline. Followed by 1 gm iv Infusion for next 24 hour.

Day-3: SpO2 95 with P support 16 PEEP 6 (PIP 24) Fio2 60%CRP, 145, S ferritin more than 1500.

Day-4: P support 14PEEP 5 (PIP 19), Fio2 50% and SpO2 94

Day-5: Lab reports CRP 131, S ferritin more than 1500 but P support 12 PEEP 5 (PIP 17), Fio2 40%, SpO2 value ranged 94 to 95.

Methyl Prednisolone Infusion was decrease to 500 mg per 24 hour and subsequently progressively reduced.

Day-6: Lab report CRP 72 and S ferritin decreased to 720. This showed that massive cytokine storm could be curbed by timely addition of steroids i. e., adding more water till whole of the fire stops, thus no further propagation of even a spark of fire this implies that the timely doses of steroid depending on severity of hypoxia and Inflammation is the most important part in treatment of this reaction.

Day-7: Patient seemed depressed and developed psychotic signs, so Placcida 0.5 bd was initiated. Within 12 hours of medications patient was stable. During that time Troponin1 was done which was within normal range.

Day-8: Patient was discharged on patient’s persistent request. Troponin1 and Procalcitonin were done before discharges which too were normal. At the time of discharge SpO2 value was 93 on 4 Lit Oxygen which was arranged at home. Lab report; CRP 5.8, S ferritin 570, D Dimer4500.

In-spite of high d dimer value patient was given DAMA. D-dimer reflects the production of cross-linked fibrin and can be a misleading marker, since its value is raised in patients having hepatic or heart disease.9

Discharge Treatment: Oral tab Prednisolone160 mg 4 days, 120 or next 4 days, 80 for 4 days, 60 for 4 days, 40 for 4 days, subsequently 20, and 10 for 4days, then 5 and lastly 2.5 for 3 weeks.

Tapering of steroid for last 5 mg and 2.5 mg should be slow so as to prevent lung fibrosis especially in such type of who were on BIPAP or High flow 02.

Tab Rivoraxaban 10 mg for 3weeks. Ecosprin and Atorvastatin 40 for lifelong due to post angioplasty.

Advised pranayam and breathing exercises with respirator for at least next 6 month. Regular breathing exercises like pranayam increases vital capacity.

Rich protein diet (24gms/day) with potassium supplement with music as well as message therapy has good home based outcome.

Day-16: SpO2 value 94 without supplement Oxygen

Patient is fit and fine even after 4 months of the disease.

This is steroid responsive disease and doses are extremely dynamic depends on severity of disease.

Case 4
A 35 year old male, known case of sickle cell disease diagnosed with positive for COVID-19 with SpO2 value 87 He was on Hydroxyurea 1.5 gm daily, folic acid and other medicine

Day-1 presented to OPD: Lab reports- CRP 5.4, S ferritin more than 2000, Hb 7.7, TLC 3400, pc 1.85

Relatives were hesitant for hospital admission but were convinced looking at the parameters and clinical signs of the patient. They could arrange a trained nurse and O2 support at home. Thus injection Methyl Prednisolone 1 gm in 100 ml NS in over 1 hour was started followed by 250 mg iv 8 hourly for next 3 days

Day-2 post OPD: SpO2 value 91 without O2 support, however we started 2 lit Oxygen so as to maintain SpO2 of 95.

Inj (Low molecular heparin) 0. 6 cc sc was started with inj basal insulin of 15 units, so as take care of sugar level. The sliding scale of insulin requirements would be less because bolus doses of steroids to patient was given thus expected raised sugar level would be the result and if required use insulin according to sliding scale.

The Fluconazole 200 mg OD and 1 broad spectrum antibiotic was give, to prevent secondary bacterial and fungal infection. Ecosprin 75 1 OD and Atorvastatin 20 OD along with and Multivitamin, Zink 50 mg 1 OD, Vit D sachet weakly.

Day-3 post OPD: Lab reports- CRP 5, S. ferritin more then 2000, TLC 4500, pc 2.3, Hb 7. 6.
Patient still was on 2 l Oxygen with methyl Prednisolone 250 Tds.

Being a sickle cell patient he started developing severe pain Cross striated, thus high doses of Tramadol 100 mg 1 tab every 6 hourly Brufen 400 mg every 6 hourly started simultaneously.

**Day-6 post OPD:** He was quite comfortable with intermittent episodes of severe pain.

Spo2 94 without O2 support.

Lab reports -- Hb 7.4, TLC 34000, pc 2.8, S ferritin 1650, CRP 4.2, Procalcitonin normal

Thus, we decided to taper the steroid doses; Methyl Prednisolone150 mg TdS for next 2 days. Rest treatment same continue

**Day-8 post OPD:** Patient did not require any oxygen support although had intermittent pain episode but comfortable.

Lab report-- Hb 7.7, TLC 54000, pc 2.7, CRP 5.3, S ferritin 789

In spite high counts Procalcitonin still was normal, as expected that inflammatory steroid causes high WBC, it is not because of secondary bacterial Infection.

Methyl Prednisolone120 mg tds for 3 day, then 80 Tds for 3 days finally start on oral tablets of Prednisolone 40 mg (4 Tab for 4 days, 3 for 4 days, 2 for 4 days then 1 for 4 Days)

**Day-10 post OPD:** Lab report-- Hb 7.3, TLC 22000, CRP 4.4, S ferritin 138

Now the patient is doing good with intermittent pain

2. Discussion

COVID-19 is a viral infection, as it is mild in 80 to 85 % of patients but rest 10 to 15 % may have moderate to severe disease, if we see basic pathogenesis of these moderate to severe patients it is Infection associated disproportionate Inflammation, we can give different name like cytokine storm or Macrophage activation syndrome or infection associated HLH (hemophagocytic lymphohistiocytosis) [32–44] so host immune disproportionate response to virus rather than virus itself which is killing the host [45 46, 47, 4839-441], damage our vital organ like lungs is most commonly affected organ. Patients presented as hypoxia but it is systemic inflammatory disease it can damage heart and other organ also and because of inflammatory damage of our vascular endothelium [45, 49, 50, 51] causing release of large aggregate of vvf and ACE 2 receptor on platelets causes massive platelet Aggregation [52, 31, 53] and then microvascular coagulation and it impair blood flow [54-67], creates VQ mismatch (ventilation perfusion mismatch) and it should be noted that the thrombotic microangiopathy appear to target predominantly pulmonary and cerebral circulation [38]. It is important other mechanism of hypoxia with parenchymal inflammatory lung damage [38, 52] and many patient may have cerebrovascular ischemic stroke also so there is role of Anti-inflammatory agent Corticosteroid, Anti platelet drug like Aspirin [28, 29, 30, 31], Anticoagulation like low molecular heparin (clexan) [66-72] to manage both inflammatory parenchymal da mg and microvascular coagulation. Most important is doses of steroids because disease is so dynamic 85 % required nothing only vitamins and paracetamol few required 1 gm bolus of methyl Prednisolone. If patient is presented in early pulmonary phase with mild hypoxia 80 mg is sufficient but if presented in late pulmonary phase with moderate to severe hypoxia like and on high flow 02 or on BIPAP may require 500 to 1 gm bolus and then 150 mg to 250 mg tds for next 3 days. it is because grades of Inflammation and proportional damage of organ is severe in these patients that is reflected in biochemical markers like CRP and ferritin also. Dynamic doses of steroids depend on severity of hypoxia and early aggressive Anti-inflammatory therapy is primarily important to improve oxygenation and decreases requirement of O2 to patient. It drastically decrease patients stay in ICU and 02 dependency and chances of secondary bacterial infection or fungal infection also decreases because of prolonged stay in ICU.

3. Conclusion

By proper Monitoring of COVID patients per family, we can detect those 10 to 15 %moderate to severe patient early by our clinical, biochemical and Spo2 Trends and can treat at home without doing CT chest in majority we can prevent lung damage with dynamic doses of steroids and if patient is presented late as moderate to severe hypoxia may required pulse doses of methyl-prednisolone.

In flames (Fire)
No fire – No water (steroid)
Minimal fire – Minimum water (80 mg) Methyl Prednisolone
Maximum fire – Maximum water (1 gm) Methyl Prednisolone

Sample Monitoring Chart 1
References


[3] In this U-tube video, Professor Britt Glaunsinger, PhD provides an outstanding review on the molecular virology of SARS-CoV-2: https://www.youtube.com/watch?v=DQVpHyvz4no


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