

Case Report

Resolution of Post-COVID-19 Pulmonary Interstitial Pneumonitis with Methylene Blue Nebulization Therapy — A Case Report

Deepak Golwalkar¹, Jwalant Pandya²

SARS-CoV-2 infection leads to multi-system involvement with brunt of the damage primarily borne by the lungs. SARS-CoV-2 viral pneumonitis manifests itself in the form of diffused lung infiltration and interstitial pneumonitis. Resultant alveolar oxygenation impairment leads to drop in SpO₂ and breathlessness. Radiologically it manifests in the form of ground glass opacities in both lung fields. These radiological findings & residual lung infiltrations usually take months to clear. However, administration of Methylene Blue (MB) in Nebulised form given to the convalescent patient dramatically hastens the clinical outcome with demonstrable clearance of radiological lesion. This paper present a a case report of Post SARS-Cov-2 convalescent, Type II DM patient with extensive bilateral residual lung involvement in the form of broncho pneumonic changes in both mid and lower zones treated with MB nebulization along with steroids and antibiotics, improved dramatically within 6 weeks of institution of MB nebulization with sequential clearance of lung infiltration documented by radiographs.

[J Indian Med Assoc 2024; 122(9): 71-2]

Key words : Fibrosis, COVID-19, Methylene Blue.

SARS-CoV-2 infection leads to multi-system involvement with brunt of the damage primarily borne by the lungs. SARS-CoV-2 viral pneumonitis manifests itself in the form of diffused lung infiltration and interstitial pneumonitis. Resultant alveolar oxygenation impairment leads to drop in SpO₂ and breathlessness. Radiologically it manifests in the form of ground glass opacities in both lung fields. These radiological findings & residual lung infiltrations usually take months to clear.

However, administration of Methylene Blue (MB) in Nebulised form given to the convalescent patient dramatically hastens the clinical outcome with demonstrable clearance of radiological lesion. MB in nebulised form is being used by us, now for a considerable period of time as an adjunct to conventional chemotherapeutic agents in treatment of SARS-CoV-2 patients with considerable success. Here is a case report of Post SARS-Cov-2 convalescent, Type II DM patient with extensive bilateral residual lung involvement in the form of broncho pneumonic changes in both mid and lower zones treated with MB nebulization along with steroids and antibiotics, improved dramatically within 6 weeks of institution of MB nebulization with sequential clearance of lung infiltration documented by radiographs.

CASE REPORT

A 54-year-old male patient with Type-2 DM, got admitted at Sir T Hospital, Bhavnagar with complaints of fever, fatigue, dry cough and breathlessness on 1st September, 2020 and was found COVID-19 positive the next day. He was admitted in government Covid facility & treated for COVID-19 positive bilateral lower respiratory tract pneumonitis & infiltration in both lung fields at

Department of Pulmonary, Dr Deepak Golwalkar Clinic, Bhavnagar, Gujarat 364002

¹MBBS, DTC, FCCP, Consultant Pulmonologist and Corresponding Author

²MD, Pathology, Senior Consultant

Received on : 21/07/2021

Accepted on : 09/02/2022

Editor's Comment :

- Methylene blue nebulization therapy in Post COVID-19 pneumonitis promotes early resolution of interstitial inflammation and prevents ensuing pulmonary interstitial fibrosis with near complete clearance of lesion on radiography.
- Our endeavor here, through this case report is to highlight & emphasize the role of Methylene Blue (MB) as an adjunct to conventional treatment in COVID-19 lung injury mitigation and speedy resolution of lung pathology.

government run Covid hospital. He was treated with full-fledged anti-Covid therapy including Remdesivir, LMWH, Steroids and antibiotics and vitamin supplements and discharged on 15th September, 2020.

Patient was brought in our OPD on 28th September, 2020 with complaints of weakness, fatigue, coughing and breathlessness on exertion. His chest radiograph on the same day revealed bilateral lung infiltration with broncho-pneumonic changes in mid & lower zones (Fig 1). His blood pressure & diabetes was under good control with medication. Patient's basal SpO₂ was 95 which dropped to 85 after 20 meters walk on first consultation. Patient's informed consent was obtained before proceeding with further line of treatment.

Patient was put on following regimen :

Tablet Ivermectin 12mg, ODx4d ; Tablet Prednisolone 5mg TD Sx 10days + Tablet Deryphylline Retard 150mg BD x 10days + Azithromycin 500 mg x 5days + days + Acetyl Cystein OD x 7days, Sublingual Methylene Blue (MB) solution, 0.1% 2.5 ml daily till completion of treatment and daily nebulization inhalation therapy. Nebulization fluid consisted of Dexamethasone 8mg + Levasalbutamol 1.25mg + Ipratropium 500 mcg + Methylene Blue (MB) 5ml 0.1% daily for 10 days.

After 10 days of above therapy Patient was reviewed on 8th October, 2020. There was marked symptomatic, clinical & radiological improvement. There was general feeling of well-being. Fig 2 showing radiological

improvement in the form of decreased pneumonitis. After 20 meters walk patient's SpO₂ dropped to 92 as compared to 85 on first visit.

Subsequently, patient was put on: Tablet Cephadroxyl 500 mg BD X 5 days + Tablet Prednisolone 5mg OD x 15days + Tablet Deriphylline 150mg BD x 15 days + Sublingual MB (0.1%) 2.5 ml OD & Nebulized inhalation therapy with Dexamethasone & MB(0.1%) 5ml & Levasabutamol Ipratropium

After 15 days on above treatment regimen, there was marked subjective, symptomatic & clinical improvement. SpO₂ remained at 95 even after 20 meter walk. Chest X-ray on 5th November, 2020 revealed appreciable improvement with markedly reduced infiltration pneumonitis.

Chest radiographs taken sequentially show regression & clearance of pulmonary infiltration and interstitial pneumonitis with complete resolution in chest radiograph taken on 3rd December, 2020. Patient's chest scan obtained on 04/12/2020, also revealed considerable reduction of lesion with 10% residual infiltration. Patient was able to complete 6-minute walk test with no drop in Spo₂, reflecting near complete resolution of underlying pathology (Figs 3&4).

DISCUSSION

Methylene Blue, an inert dye used in medical practice since time immemorial, has various applications such dermatological, IV administration in methemoglobinemia, sinus tract demarcation during surgical procedures and as in various diagnostic procedures eg, diagnosis of Broncho Pleural Fistula, Vesicovaginal fistula, etc.

Methylene Blue (MB) was the first synthetic antiseptic dye to be used therapeutically. In fact, its use was widespread before the advent of sulfonamides and penicillin. As early as 1933, NEJM cited the use of methylene blue in treatment of urinary tuberculosis. Its safety and inertness in human species has been proved by its extensive use in surgical procedures, IV administration in refractory septic shock⁶ where MB had an acute vasopressor effect in patient with hypotension not responding to other medications.

There are Several Mechanisms of Actions Postulated for the Effectiveness of Methylene Blue (MB) :

- MB prevents platelet activation, adhesion and aggregation through inhibiting the arachidonic acid metabolism in platelets. This helps in reducing interstitial pneumonitis in post COVID-19 patients
- It has been documented that MB has a direct inhibitory effect on Nitric Oxide Synthetase (NOS)³. MB being a potent NO synthetase inhibitor, neutralizes the bradykinin mediated pro-inflammatory cascades and prevents cytokine storm. Bradykinin mediates most of its pro-inflammatory effects through NO generation. MB blocks/hinders NO generation and decreases tissue injury and inflammation³.
- Antibacterial properties of MB⁴.

CONCLUSION

Our endeavor here, through this case report is to highlight & emphasize the role of Methylene Blue (MB) as an adjunct to conventional treatment in COVID-19 lung injury mitigation and speedy resolution of lung pathology. MB, when given by sublingual and inhalation (Nebulization) routes:

- MB also prevents platelet activation and adhesion/aggregation promoting fibrinolysis⁵ and clearance of



Fig 1 — Bilateral Lung Infiltration & Pneumonitis (dated 28-09-2020)



Fig 2 — Partial Resolution (dated 8-10-2020)



Fig 3 — Appreciable Resolution (dated 5-11-2020)

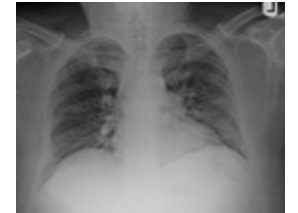


Fig 4 — Complete Resolution (dated 3-12-2020)

inflammatory infiltration. This was reflected here in this case study by subjective and clinical improvement as well objective clearance of radiological lesion.

- Reduces tissue injury by blocking pro-inflammatory mediators¹ and
- Improves O₂ availability at cellular level by facilitating oxygen release²

We have observed gratifying results by instituting Methylene Blue inhalation & sublingual application in these COVID-19 patients with advanced lung injury who recovered rapidly and satisfactorily.

More research is needed in understanding the mechanism of action of Methylene Blue in curing interstitial pulmonary pneumonitis.

Remark : Informed written consent of the Patient was obtained in advance for this case study.

Conflict of Interest : The Authors declare that research was conducted in absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

REFERENCES

- 1 Damir Bojadzic, Oscar Alcazar & Peter Buchwald.: Methylene Blue Inhibits In vitro SARS-CoV-2-ACE2 protein-protein Interaction-A mechanism that can contribute to its Antiviral action.
- 2 Seyyed Mommad Ghahestani et al. : MB may have a role in treatment of COVID-19; Medical Hypotheses : 2020
- 3 Alamdari DH, Moghaddam AB — Application of Methylene blue-Vitamin C- N-acetyl cysteine for treatment of critically ill COVID-19 patients, report of a phase-I clinical trial. European Journal of Pharmacology; 885(2020)
- 4 Ansari MA, Fatima Z — Anti-Fungal Action of MB involves Mitochondrial dysfunction and Disruption of Redox & Homeostasis. *The Open Microbiology Journal* 2016; **10**: 12-22.
- 5 Bozoy, Dimitri, Axelband — Utilization of Methylene blue in the setting of hypotension associated with concurrent renal & hepatic failure: a concise review. *OPUS 12 Scientist* 2008; 21-9.
- 6 Preiser, Jean-Charles, Lejeune — Methylene blue administration in septic shock; A clinical trial, *Critical Care Medicine* 1995; **23**: 259-64
- 7 Schenk P, Madl C, Rezaie-Majd S, Lehr S, Muller C — Methylene blue improves the hepatopulmonary syndrome. *Ann Intern Med* 2000; **133**: 701-6
- 8 Zirlik S, Hildner KM, Neurath MF — Methylene Blue-Aided In Vitro Staining of Central Airways during Flexible Bronchoscopy. *Scientific World Journal* 2012; 2012: 625867.