## **Old Drug In New Shape With Tmp-Smx For Cure Covid 19**

Dr. M. K. Bhattacharya

Emeritus Scientist ICMR-NICED, Kolkata

Dr. Raja Bhattacharya

Associate Professor, Calcutta Medical College, Kolkata

Dr. Sadajit Banerjee

Consultant Physician, AMRI & IRIS Multidisciplinary Hospital

Abstract: Recently whole world is facing big health problem due to Covid-19. It's rapid spreading due to aerosol character. Misused long time with HQC and other antiretroviral drugs which have found ineffective. Presently Remsidevir is using in IV route along with supportive drugs. While Remsidevir is very hepato renal toxic, costly and need skilled person to use it. Moreover, we have again prove "old is gold' adjusting dose and combination of therapy. Surprisingly we have found combination of Ribavirin and TMP-SMX can cure Covid-19 effectively. The study report has been documented in details.

Keywords: COVID-19, TMP-SMX, Ribavirin

The ongoing spread of COVID 19 pandemic has put the globe in a panic stricken state by affecting a large proportion of inhabitants. Exponential surge in fresh cases is due to air bone transmission of aerosols produced by asymptomatic individuals during breathing and speaking having CT value <18 suggestive of severe transmission capability i.e. 8-9 manifold greater than moderate/ mild rate of transmission. Aerosol accumulates and persists in indoor air for hours and can be easily inhaled deep into the lungs. Couple of in vitro, poorly controlled or uncontrolled clinical studies of inadequate sample size found HCQ of great importance in inhibiting SARS COV 2 in accordance with the immunomodulatory effect that controlled the late phase cytokine storm in critically ill SARS COV 2 patients<sup>14</sup>. In India, guideline recommends use of HCQ and anti-HIV medications in SARS-COV 2 infections without any substantial evidence. Recently, WHO has declared cessation on use of hydroxychloroquine in SARS COV 2 infection due to its proven complications than hypothetical efficacy. Lopinavir and Ritonavir, can be used to treat Covid-19 patients in extreme case. Oseltamivir was ruled out due to its unproven efficacy against CoVs. However, contrary to any established evidence for treatment against COVID-19, fixed dose drug combination (Lopinavir/Ritonavir 200 mg/50 mg) to be given two

tablets every 12 hours for 14 days or for seven days after becoming symptomatic, whichever is earlier is an assigned protocol. Nonetheless, both drugs are proclaimed to be very toxic. Moreover, WHO experts claimed that Remdesivir, ineffectively developed against Ebola, found to be most promising for treating Covid-19. However it has to be use in IV route for which skill person is required. Times immemorial, the sulphonamide group of antibiotics, dapsone 4-diaminodiphenolsulphone) and cotrimoxazole (a (4. combination of trimethoprim- sulphamethoxazole) have effects upon immune system. Studies on dapsone demonstrated that the sulphonamide ring is accountable for dose-dependent reduction in generation of tissue damaging 'oxygen free radicals' from neutrophils.<sup>7-8</sup> These cytokines causes dilation of endothelial cells leading to increased capillary permeability fostering accumulation of fluid around alveoli compressing it by blocking FPR receptor. Both dapsone & trimethoprim share same sulphonamide ring which is responsible for anti inflammatory effects<sup>9,10</sup>. Though Ribavirin, an antiviral drug rejected due to reported toxicity<sup>5-6</sup>, our clinical outcomes were significant & contradictory. During outbreaks in 2010-13, about 1500 dengue and 200 chikungunya cases were admitted in Beliaghata ID Hospital, recovered completely (except one DHS and one DSS) without

any residual complication when treated with ribavirin.<sup>5</sup> On basis of this experience, we treated covid 19 positive (RT PCR) four mild to moderate patients with ribavirin 200mg TDS + Azythromycin 500 mg daily for 5 days and two moderate to severe patients with ribavirin 400mg TDS +TMP-SMX one tab BD for 5 days. The four mild to moderate and 2 borderlines moderate to severe symptomatic patients received above regimes of therapy along with other supportive care who had saturation above 95% and 93-94% respectively. Among 4 mild category patients, 3 were male and 1 female. In moderate to severe category 1 was male and 1 female. Average age group was 40 with a range from 18 to 56 years. We noticed significant symptomatic improvement in terms of frequency and intensity of fever, malaise, sore throat, cough and shortness of breath. The oxygen saturation increased subsequently. Our study postulated that hepatic obligation remains unscathed under Ribavirin therapy. Accordingly in all patients, entire liver function related blood parameters were within normal limits. We are yet to detect a case with any follow up complications. Much to agony of clinical medical scientist, an environmental catastrophe to perceive that multinational drug companies play pivotal role on judicious use of drugs. We may conclude that it is worthy to conduct proper well designed studies to get a decisive result using this Ribavirin +TMP-SMX regime using 15-20 mg of body weight Ribavirin TDS and TMP-SMX BD combination for 5 days both treatment and prophylaxis in covid care. Ribavirin syrup is also available for children and main advantages are for capsule /syrup form, less costly and easy available.

## REFERENCES

[1] Xueting Y, et al. In Vitro Antiviral Activity and Projection of Optimized Dosing Design of Hydroxychloroquine for the Treatment of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2).Clin Infect Dis; 2020.

- [2] Liu J, Cao R, Xu M, et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARS-CoV-2 infection in vitro. Cell Discov. 2020;6:16.
- [3] Yao X, Ye F, Zhang M, et al. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Clin Infect Dis. 2020.
- [4] Gautret P, Lagier JC, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents. 2020:105949.
- [5] Ghosh M. Answer to dengue and chikungunya: specific antiviral therapy. Int J Adv Med 2017;4;603-4.
- [6] Thomas E. The application and mechanism of action of ribavirin in therapy of hepatitis C. Antivir Chem Chemother. 2012 Sep 25; 23(1): 1–12
- [7] Cascella M, Rajnik M, Cuomo A et al. Features, Evaluation and Treatment Coronavirus (COVID-19). Statpearls: March 20,2020. 8. Suda T, Sukuki Y, Matsui T, Inoue O, Niide T, Yoshima H, Ochiai T. Dapsone suppresses human neutrophil superoxide production and elastase release in a calcium-dependent manner. Br J Dermatol 2005;152 (5) 887-895.
- [8] Booth SA, Moody CE, Dahl MV, Herron MJ, Nelson RD. Dapsone suppresses integrin-mediated neutrophil adherence function. J Invest Dermatol 1992;98(2):135-140.
- [9] Anderson R, Grabow G, Oosthuizen R, Theron A, Van Rensburg AJ. Effects of sulfamethoxazole and trimethoprim on human neutrophil and lymphocyte functions in vitro: In vivo effects of co-trimoxazole. Antimicrob Agents and Chemother. 1980;17(3):322-326.
- [10] Varney VA, Smith B, Quirke G, Parnell H, Rathneepan S, Bansal AS, Nicolas A. P49 The effects of oral cotrimoxazole upon neutrophil and monocyte activation in patients with pulmonary fibrosis and healthy controls; does this relate to its action in idiopathic pulmonary fibrosis? Thorax 2017:73(3):A109.