



Silver Nanoparticles with Bronchodilators through Nebulisation to Treat Covid 19 Patients

Dr. Subhasish Sarkar^{*,†}

Resident Medical Officer Department of General Surgery College of Medicine and Sagore Dutta Kolkata

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Dr. Songul B. Diler

Department:

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1 INTRODUCTION:

There are no effective antiviral drugs available against the pandemic causing COVID 19 virus. The complex protein - protein interaction between the virus and host is yet to be determined for designing of precise antiviral drugs against corona virus. The pandemic had claimed several thousand lives and had resulted most devastating effects on our mankind. In this scenario a potent drug is needed which will kill the viruses with minimal side effects on human body. Here I propose a novel antiviral therapy for effective killing of COVID19 with minimal side effects.

2 HYPOTHESIS:

Application of water dispersed silver nanoparticles (AgNP) size 10 nm with bronchodilators in lungs through nebulization with simple nebulizer machine or bi-level ventilation in Corona patients may result in better outcome. Silver has potent antiviral activity. There will be the following effects

1. The silver nanoparticles will directly kill the viruses over respiratory epithelium. Antiviral activity with immunomodulatory effects of silver nanoparticles (AgNP) has already been established in treating RSV [1].
2. Inhalation route for administering silver nanoparticles (AgNP) have never been tried before. Ag⁺ ions will leach out from the nanoparticles and will exert its antiviral effects through binding with phosphorus or sulfur containing bio-molecules of the virus [2].
3. The Ag⁺ ions released from the AgNP will result in alteration of pH of the respiratory epithelium to alkaline. This environment will be hostile for the viruses to survive. Experimental evidence suggests there is direct

low pH dependent fusion activation of Corona Viruses during entry into host cells [3].

4. As the viral load is reduced in the respiratory epithelium there will be less chance of spread from the infected person to healthy ones. The main source of spread is via coughing or sneezing with expulsion of virus loaded droplets [4].

5. Overall silver has no significant side effects in low concentrations. Preclinical data of avian corona viruses [3] already exists which further strengthen our proof-of-concept

We have to try in different concentrations to determine the maximum antiviral effects and also safety. Till now there is no experimental animal model of COVID 19 is present. So we have to administer silver nanoparticles directly initially in low doses and titer up.

3 LITERATURE REVIEW:

The antiviral effects of AgNP may be due to binding of AgNP to surface glycoproteins of RNA viruses preventing the fusion of the virus to host cells [5]. AgNP administration in mice has resulted in significant reduction of pro-inflammatory cytokines such as IL-6, TNF- α , CCL5 and IFNs [1]. All these features suggest that AgNP will be an effective drug against the COVID 19.

In a pre-clinical study BALB/c mice was inoculated with AgNP and respiratory syncytial virus (RSV) and significant antiviral and immunomodulatory effect was seen. AgNP up to dose of 4 mg/kg body weight was used without any significant toxicity [1]. On A549 epithelial cell line AgNP (10 – 12 nm size distribution at dose 50 microgram/ml has shown maximum anti viral property without toxicity [1].

AgNP has a very long half life and up to 35-36% of inhaled AgNP can be recovered from rat lungs 56 days after single 6 hours exposure [6].

4 DOSE CALCULATION:

Systemic use – from the first study we can calculate systemic dose of AgNP for human model [7].

Human equivalent dose (HED)

$$\text{HED (mg / kg)} = \text{Animal NOAEL (mg/kg)} \times (\text{Weight}_{\text{animal}} [\text{kg}] / \text{Weight}_{\text{human}} [\text{kg}])^{(1-0.67)}$$

Considering reference body weight of mouse = 0.02 kg, Human – 60 kg, NOAEL – 4 mg/kg

We get HED = 0.3mg/kg

We have to apply this dose of AgNP in divided doses.

REFERENCES

1. Morris D, Ansar M, Speshock J, Ivanciuc T, Qu Y, Casola A, Garofalo RP. Antiviral and Immunomodulatory Activity of Silver Nanoparticles in Experimental RSV Infection. *Viruses*. 2019 Aug;11(8):732.
2. Park S, Park HH, Kim SY, Kim SJ, Woo K, Ko G. Antiviral properties of silver nanoparticles on a magnetic hybrid colloid. *Appl. Environ. Microbiol.*. 2014 Apr 15;80(8):2343-50.
3. Chu VC, McElroy LJ, Chu V, Bauman BE, Whittaker GR. The avian coronavirus infectious bronchitis virus undergoes direct low-pH-dependent fusion activation during entry into host cells. *Journal of virology*. 2006 Apr 1;80(7):3180-8.
4. AFRICA A. Modes of transmission of virus causing COVID-19: implications for IPC precaution recommendations.
5. Speshock JL, Murdock RC, Braydich-Stolle LK, Schrand AM, Hussain SM. Interaction of silver nanoparticles with Tacaribe virus. *Journal of nanobiotechnology*. 2010 Dec;8(1):19.
6. Sung JH, Ji JH, Park JD, Yoon JU, Kim DS, Jeon KS, Song MY, Jeong J, Han BS, Han JH, Chung YH. Subchronic inhalation toxicity of silver nanoparticles. *Toxicological sciences*. 2009 Apr 1;108(2):452-61.
7. Nair AB, Jacob S. A simple practice guide for dose conversion between animals and human. *Journal of basic and clinical pharmacy*. 2016 Mar;7(2):27.