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EDUCATIONAL ARTICLE

Intravenous Ascorbic Acid for Supportive Treatment in Hospitalized COVID-19 Patients

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ABSTRACT

Intravenous ascorbic acid (IVAA) is a well-known intervention in medicine, which currently is rarely used in US hospitals. Due to the unusual and extreme clinical demands of hospitalized COVID-19 patients, IVAA has been implemented in Chinese hospitals, and data published by the "Expert Group on Clinical Treatment of New Corona Virus Disease in Shanghai" (Shanghai, 2019) details the use of IVAA as safe and effective adjunctive care of hospitalized COVID-19 patients. In the IVAA treated group, there was no mortality, no reported side effects, and shorter hospital stays universally. In addition, the Shanghai Expert Group recommends IVAA use in extremely critical settings within COVID-19 patients. IVAA, as an intervention, is relatively inexpensive and simple for both pharmacy and nursing staff use. The primary author has also used IVAA in the US under a NIH funded human trial (NCT01366248) and has extensive subject matter knowledge and expertise.

SALIENT CLINICAL DATA

IVAA is an FDA approved drug that is used in many settings, but until recently, has been poorly studied in US hospital systems. It is, however, commonly used in many other countries as an adjunctive therapy for multiple conditions. The crisis in China, and the presence of an expert in the use of IVAA in the Shanghai Expert Group, facilitated the addition of IVAA to their therapeutic interventions in the hospital treatment of patients with COVID-19. Background data and details are in the references, resources, and information below, but the points critical to use in this current crisis are:

- Chinese facility patient load: 358 total COVID-19 patients as of March 17th, 2020.
- Facility treated approximately 50 cases (of the 358) of moderate to severe COVID-19 infection with IVAA.
- The IVAA dosing was moderate and affordable (detail below) and dose determined by clinical status.
- All patients who received IVAA improved.
- There was no mortality in the IVAA group.
- There were no side effects reported from any patients in the IVAA group.
- Average COVID-19 patients had a 30-day hospital stay, but COVID-19 patients that received IVAA had a hospital stay that was 3 to 5 days shorter than the non IVAA treated patients.

HOSPITAL APPLICATION

The use of IVAA was in conjunction with all typical hospital / ICU therapies. For detailed data, the author has attached a two documents to this summary, which is the Consensus Document on COVID-19 from the China Journal of Infectious Diseases, 2020. The attachment is a direct English translation the author produced as the source document is in Mandarin Chinese, which is also attached. Regarding dosing there are three similar reported dosing strategies. The author has edited these to the most efficacious and simple to implement dose strategy based on his clinical and research experience. The doses used above for IVAA as adjunctive care were 100 mg / kg per day (continuous infusion) for hospitalized COVID-19 patients and

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200 mg / kg per day (continuous infusion) for the control of "cytokine storm" presentations. Pharmacy and nursing detail regarding these doses are noted below.

USE AND SAFETY OF IVAA IN THE US

IVAA has been used in trials in the United States, and some of those will be reflected in the references below (Mikirova et al., 2012; Mikirova et al. 2013; Hoffer et al., 2015; Duconge et al., 2008; Reid et al., 2016) . The author's personal use spans over two decades in clinical practice as well as specific use in a NIH funded human trial. In this trial, IVAA was used at various doses in the adjunctive care of patients with advanced cancers. As with the reports from the Shanghai Expert Panel, the author also experienced IVAA as safe, cost effective, and well tolerated intervention in even the most critical patients.

CONCLUSION

The inclusion of IVAA in the adjunctive care of hospitalized COVID-19 patients in the US is reasonable and supported by direct experience with COVID-19. IVAA is safe (Padayatty et al. 2010; Reid et al. 2016), cost effective, and easy to implement for hospital pharmacy and nursing staff. In the Chinese Expert Panel's experience, it also shortened hospital stays by 3 to 5 days over those not receiving IVAA, which would not only be a cost saving, but also free up needed hospital resources during this pandemic.

SUPPLEMENTARY RESOURCES

Pharmacy and Nursing Detail:

- Dose: 100 mg/kg given over 24 hours in a continuous infusion for general use. A dose of 200 mg/kg for use in "cytokine storm" response.
- Admixture: 50% of the total body weight dose admixed in 500 mL of 0.9% saline. For a 70 kg patient this is an addition of 14 mL (of the standard 500 mg/mL Ascorbic Acid for infusion) to the 500 mL saline bag.
- Administration: The 50% dose in 500 mL 0.9% saline is infused every 12 hours. On a continuous basis.

Approximate Drug Cost:

For a 70 kg patient the 100 mg/kg dose would cost approximately $ 12.00 per 24 hours (exclusive of the saline carrier and other consumables cost). The 200 mg/kg dose would be approximately $ 24.00 per 24 hours.

The author of this summary is available as a subject matter expert if needed and can also facilitate connection with other subject matter experts on IVAA as needed.

AUTHOR'S NOTES

The most common questions and comments about this hospital protocol revolve around the potential efficacy of the dosing, as well as why a hospital protocol would be formatted in this manner and not the "shorter and higher dose" format most often used by integrative clinicians.

There are two protocol concepts which are mostly dependent on outpatient versus inpatient status:

1. In Hospital Protocols

The Chinese "Shanghai Expert Panel" which among many other things was using IVAA in the COVID-19 positive patient population had multiple dosing strategies. All were essentially low doses given 24/7 on continuous infusions via pump or open metered infusion. These were labelled as "high dose" in relation to RDA/RDI and the amount of vitamin C that may be obtained through dietary sources.

The low doses used would not be considered oxidative therapy; do not require G6PD screening; and are not contraindicated in patients with compromised renal function. The continuous drip allows the antioxidant milieu in the lungs and RBC (of greatest concern in COVID-19 patients) to constantly be balanced, so the appropriate amount of inflammation required to trigger an immune response occurs. It also provides antioxidant substrates to prevent the 'cytokine storm' in the lungs and other tissues.

Of the 50 patients getting IVAA in hospital on a continuous infusion basis, none died and the average hospital stay was 3-5 days shorter. The larger group (initial Shanghai Expert Panel patient base from which the 50 came) was approximately 350+ COVID-19 patients.This link has the executive summary I prepared for US / Canadian hospitals to mimic the Shanghai protocol, and also contains PDF's of the Shanghai Expert Panel publication in both English and Mandarin. https://www.consultdranderson.com/iv-vitamin-c-for-hospital-use-for-covid-19/

2. Outpatient Protocols

If a patient's lab results permit the use of "higher dose" intravenous ascorbic acid, 50-75 gram infusions (as derived from our interventional human trial and presented at SIO in 2011) given with an added 50 mg of zinc are highly effective in the first 1-2 days following the onset of fever.

This approach seems to truncate the viremia. Ascorbic acid mixed with other nutrients can be beneficial if the patient requires a muti-nutrient formulation.

I have consulted with an unstable COVID-19 positive patient receiving 25 grams of IVAA per day, dripped over 4 hours, and is also receiving normobaric O2. This is done to mimic the hospital strategy and MOA above. Clinicians must treat what they see, and understand that in most cases they will be unable to mimic the hospital protocols. If the individual is an outpatient, and not requiring hospital care, than the above treatment has worked – based on my clinical experience.

CONTRIBUTIONS

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