UWHealth

Intravenous Ascorbic Acid for the Treatment of COVID-19 (Abbreviated Monograph)

DRUG NAME: Ascorbic acid

CLINICAL PHARMACOLOGY

Ascorbic acid (AA) is a vitamin (i.e. an organic compound required in the diet because it cannot be synthesized by the body) with pleiotropic effects in disease states. AA protects pulmonary endothelial barrier integrity and function, scavenges free-radicals, prevents activation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB), enhances macrophage activity, T cell function and proliferation, prevents neutrophil apoptosis, increases phagocytosis, and is a critical co-factor for catecholamine production.[1] High concentrations may be found in macrophages, neutrophils, lymphocytes, which support AA's role in innate and adaptive immune function. Supraphysiologic dosing may potentiate immunologic effects.[1]

SUMMARY OF CLINICAL STUDIES

Animal Studies: H3N1 flu was shown to be more lethal in *gulo*−/− mice mice deficient in the enzyme necessary for AA synthesis compared to wildtype mice.[2] *Gulo*−knockout mice had worse lung injury in H1N1.[3] Strong dose dependent reduction of mortality and lung injury with IV AA in mice with H1N1 induced pneumonia.[4] Nearly all animal models of bacterial sepsis report protective effects of IV AA in reducing either organ damage, inflammatory markers, or mortality.[1]

Clinical Studies in ARDS/Severe Pneumonia: A multi-center, double-blind RCT in ARDS patients (CITRIS ALI) found lower mortality (29% vs 46%, p<.05) in patients treated with AA as a secondary outcome.[5] A recently published post-hoc analysis of this same study that accounted for early deaths in placebo group, which had not contributed to the severity score in the original analysis, found the primary outcome of SOFA score was significantly reduced in AA-treated patients.[6] In a single-center, propensity matched trial of severe pneumonia in the ICU, the IV AA-treated cohort had lower mortality (17% vs. 39%, p<.04)[7] A prospective RCT conducted in 1989 found that an anti-oxidant regimen which included IV AA led to an ICU mortality of 30% compared to 70% in the control regimen (p<.01).[8]

There is very little data to support a benefit of AA in mild respiratory or viral illness. Long clinical use, however, suggest that AA is not harmful (see Safety and Monitoring, below).

PHARMACOKINETICS

- Bioavailability: For doses up to 200 mg, nearly 100%; absorption declines with increasing doses with ~33% absorbed with a single 1250mg dose
- Metabolism: Oxidized to active metabolite, dehydroascorbic acid (DHA)
- Excretion: Eliminated in the urine when high serum concentrations are above the renal threshold
- Half-life: 10 hours

DOSING AND ADMINISTRATION

- Mild respiratory illness: if 02 requirement is ≤4L, initiate AA 500-1000mg PO BID
- Lung Injury: 02> 4L or CXR abnormal, start 3 grams IV q6h until either <4L 02 requirement, CXR resolved, or extubated (earliest parameter achieved)

SAFETY AND MONITORING

Mylan pharmaceutical insert: no evidence of toxicity in normal adults at doses up to 6 grams a day; case reports of hemolytic anemia in G6PD patients at "very high doses" (40-70 grams); case reports of renal oxalate stones with long-term supplementation (none yet described in short-term use in critical illness); possible pro-oxidative effect in case of iron overload; falsely elevated serum glucose readings in certain glucometers (thus, leading to missed hypoglycemia); decreased cyclosporine levels; blunting of bortezomib efficacy.

Abbreviations: RCT, randomized clinical trial. ARDS, Acute Respiratory Distress Syndrome.

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Full guideline: Coronavirus Disease (COVID-19): Treatment – Adult – Inpatient/Emergency Department

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