Dual-histamine receptor blockade with cetirizine - famotidine reduces pulmonary symptoms in COVID-۱۹ patients

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Introduction

- COVID-١٩ (SARS-CoV-٢) emerged in late ٢٠١٩ in China, and nucleic acid sequence results indicate that it was very likely from a bat vector. The disease can manifest as a hyper-immune response with pulmonary cytokine release resembling that of other respiratory infections, such as Severe Acute Respiratory Syndrome (SARS), Middle East Respiratory Syndrome (MERS), and influenza.

Introduction

- Histamine and mast cells play a fundamental role in modulating inflammation through increased capillary blood flow and vascular permeability, as well as cytokine release. Histamine-١ (H_1) receptor antagonists (e.g., cetirizine) are administered for allergies. Histamine-٢ (H_2) receptor antagonists (e.g., famotidine) are used to control acid in the stomach and heart burn. Prescription branded, generic, and over-the-counter (OTC) drugs of both classes are safe and commercially available worldwide.

Introduction

- Based upon prior efficacious dual-histamine receptor blocker studies in humans and animal models in a variety of diseases, we believe it is reasonable to bridge into humans infected by COVID-١٩ using dual-histamine receptor blockade, in order to prevent or diminish the cytokine storm.

Methods

- This physician-sponsored and -initiated cohort study was led by a team of board certified pulmonologists from a single practice group in Jackson, MS. All patients were treated in a single hospital
- The first dual drug-treated patient date was April ٣, ٢٠٢٠ and the study period for this cohort concluded on June ١٣, ٢٠٢٠.

Methods

- The inclusion criteria were: (a) Males or females of minimum age of ١٧; (b) Admission to the hospital with suspected or confirmed pulmonary symptoms of COVID-١٩. All patients were confirmed COVID-١٩ positive by RT-PCR within several days of admission. The exclusion criteria were: (a) The patient is negative for COVID-١٩ by RT-PCR diagnostic test; (b) Sensitivity or allergy to cetirizine or famotidine, if known; (c) Duration of stay of less than ٤٨ h; and (d) Treatment with the drug combination for less than ٤٨ h. The investigators anticipated that any patient who was subject to a Do Not Resuscitate (DNR) directive may be a confounding factor (e.g., with regard to old age or the extent of aggressive life-sustaining care provided). Therefore, the DNR patients' results were parsed in the analyses for comparison to all patients.

Results

- The patient demographics for the cetirizine - famotidine treatment cohort consisted of ١١٠ patients age ١٧ to ٩٧; Female ٥٩% and male ٤١%
- This group of patients manifested an average of ٢,٧ comorbidities. The most common comorbidities were hypertension (٧٨,٢%), obesity plus morbid obesity (٥٨,٢%), diabetes (٤٢,٧%), and cardiac disease (٢٦,٤%).

Results

Clinical outcomes in 110 hospitalized COVID-19 patients treated with famotidine and cetirizine for a minimum of 48 h.

Key Metric:	Including DNR	Excluding DNR
Total Patients Admitted	110	97
Total Patients Discharged	93	89
Discharge Rate	**84.5%**	**91.8%**
Total Patients Intubated	18	16
Intubation Rate	**16.4%**	**16.5%**
Total Patients Intubated After a Minimum of 48 h of Treatment	8	6
Intubation Rate After a Minimum of 48 h of Treatment	**7.3%**	**6.2%**
Total Deaths	17	8
Death Rate %	**15.5%**	**8.2%**
Average Days to Discharge	**11.0**	**10.9**

Discussion

- Here we describe an initial study of dual-histamine receptor blockade to retard the histamine-cytokine network and with the intention of blunting the cytokine storm.
- The results of this initial physician-sponsored study provide a proof-of-principle that it can reduce disease severity and the need for ventilators, and save lives.

Discussion

- The ١٥,٥% inpatient fatality rate or ٨,٢% excluding DNR patients compares favorably to published inpatient fatality rates from other regions -- ٣٠,٩% in Atlanta, ٢٣,٦% in Louisiana, ٢١% in New York City, and ٢٨,٣% in Whuan, China
- In essence, we observed an approximately one third reduction in inpatient deaths in the cetirizine - famotidine cohort relative to well documented clinical studies of hospitalized SOC patients.
- The reports of inpatient mortality rate can be dependent on multiple variables

Conclusions

- Given the recent emergence of COVID-١٩, the rapid need for safe and effective treatments deployable immediately, and the rapid evolution in the SOC treatments for inpatients, recent innovations might not permit sufficient time for the statistically robust clinical trials that are customary for an FDA regulatory approval process.
- We have demonstrated reductions in ventilator dependence and inpatient fatality rates relative to other published studies using two safe OTC medications. This dual drug approach is consistent with the historic axiom in medicine – “first do no harm”, by utilizing historically well tolerated OTC medications.