Impact of Multi-Denominational Prayer on Morbidity and Mortality of Patients Admitted to the Intensive Care Unit with Corona Virus Infection (The COVID PRAYER Study)

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I. CLINICAL

1. Introduction

Background

COVID-19 is the disease manifestation (primarily pulmonary disease) of SARS-CoV2 - a coronavirus responsible for the 2020 pandemic. To date there are close to 2 million patients that are affected with over 115,000 deaths. The mortality ranges from 1-5% in several parts across the globe. As there are no proven treatments, much of the available therapies are supportive. There are over 1000 clinical trials that have been launched studying various treatment modalities mostly in the pharmacologic space. For a pandemic of this unprecedented nature that has affected humans of every culture, nation, religion, race and language a therapeutic answer is much sought after.

Prayer is often used as a medium to invoke divine intervention for affirmation of life, healing of the sick and protection of the vulnerable. This often remains a controversial intervention from a scientific perspective. Although used regularly in the inpatient setting of critically ill patients, the benefit of prayer on healthcare outcomes has been heavily debated. While historical studies have aimed at demonstrating improved health outcomes in patients who pray, these studies are typically difficult to reproduce and are subject to bias. Many studies have attempted to focus on improvement in quality of life or improvement in symptoms of psychiatric disease. The lack of available information regarding the impact of prayer on inpatient outcomes prompted our further investigation. Prior studies on the impact of prayer on patient outcomes are limited and have only demonstrated marginal improvement in surrogate outcome scoring systems [Byrd Score and Mid-America Heart Institute Coronary Care Unit (MAHI-CCU) Score]. The MAHI-CCU Score was originally developed in 1999 by Harris et al. as part of an assessment for intercessory prayer in CCU patients. In the study, a 10% reduction in weighted MAHI score was demonstrated with intercessory prayer in comparison to usual care but similar to Byrd et al., there was no observed correlation with inpatient outcomes. Among multiple different inpatient outcome scoring systems, Acute Physiology and Chronic Health Enquiry (APACHE) score is commonly used. APACHE II is a validated predictive outcome score ranging from 0-71 of patients admitted to the ICU setting and is typically performed within 24 hours of admission. Incremental increase in score portends higher mortality rate. Patients with an APACHE II score of > 25 have an associated >50% mortality where patients with a score of >35 have a mortality of >80%. Since its original development for evaluation of patients in sepsis, the Sequential Organ Failure Assessment (SOFA) Score has been found to have utility beyond a single sepsis evaluation and can be used as part of serial assessment as a prognostic indicator. Although most studies highlighting benefit to serial evaluation for predictive scoring systems use SOFA score, there appears to also be some limited data suggesting correlation of serial APACHE II scores to outcomes.

Unlike the prior studies that have used a single religious denomination the current study is designed to use a multi-denominational approach. Using modern assessment tools and outcome data, we sought to evaluate the impact of a universal multi-denominational prayer in a randomized controlled trial.

2. Objectives

Primary Objectives

The primary objectives of this study are the following:

1) Assess the impact of multi-denominational prayer on clinical outcomes of critically ill COVID-19 patients in the Intensive Care Unit on mortality.

2) Assess differences in patient outcomes – APACHE-II score, SOFA score, number of days in the ICU, number of days on Ventilator, number of days on vasopressor drugs.

3. Study Design

3.1 Overview

This is a multicenter; double blind randomized controlled study investigating the role of multi-denominational prayer on clinical outcomes in COVID-19 + patients in the intensive care unit. All patients and treating physicians enrolled will be blinded to use of prayer vs. no prayer in a 1:1 ratio. Each patient randomized to the prayer arm will receive a "universal" prayer offered by five (5) religious denominations, in addition to standard of care. Whereas the patients randomized to the control arm will receive standard of care outlined by their medical teams.

During ICU stay, patients will have serial assessment of multi-organ APACHE-II/SOFA scores serial evaluation performed on a daily basis until discharge from ICU. Data collected include items listed below.

Patients from all over the world can be enrolled by the participating institutions. This is a truly first of a kind global web-based study where any health care organization from around the world that is currently involved in providing critical care to COVID patients in the intensive care unit. Investigators interested in the study can quickly register and sign the study participation form and start enrolling patients de-identified through a unique patient ID created by the study. (http://www.covidprayerstudy.com). The enrolling investigator inputs a de-identified patient's age and gender into the study enrollment counter which in turn generates a unique COVID PRAYER STUDY Identification (CPS-ID). Patients are randomized to either the study arm or the control arm. The patients who are randomized to the study arm will receive daily prayer from 5 denominations. A "universal" prayer will be recited in the name of the CPS ID every day through out the patients stay in the ICU. The control arm will not receive the multidenominational prayer and standard care will be provided for both groups.

Primary Outcomes

a)Mortality rate differences

Secondary Outcomes

a) APACHE II Score change during ICU stay from baseline.
b) ICU Length of Stay
d) Hospital Length of Stay, length of ventilator support, length of vasopressor support
e) SOFA Score change during ICU stay

Baseline Demographic Data

a) Date of ICU admission
b) Age
c) Sex
d) BMI

Clinical (baseline)

a) Hypertension
b) Diabetes
c) Congestive heart failure (CHF)
d) Chronic Kidney Disease (CKD)
e) Hyperlipidemia
f) Hypertension
g) Smoking
h) Alcohol use – mild/moderate/heavy
i) Left Ventricular Ejection Fraction (LVEF)
j) Cardiac dysrhythmias – atrial fibrillation, ventricular tachycardia, AV block, Sinus node dysfunction
k) Lung disease - Chronic Obstructive Pulmonary Disease (COPD)/Asthma
l) Neurological disorders - Stroke/Transient Ischemic Attack (TIA)/Parkinson's disease
m) Thyroid Disease
n) Liver Disease
o) Cardiac device – pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy device

24 - 48 hour follow up

a) Date of data collection
b) APACHE II Score – [History of severe organ failure/immunocompromised, Age, Temperature, MAP, pH, HR, Pulse, RR, Na, K, Creatinine, Evaluation for Acute Renal Failure, Hematocrit, WBC Count, GCS, FiO2].
c) SOFA score
d) Did patient die
e) Patient discharged from ICU
f) Is patient on ventilator
g) Is patient on vasopressor medication

4. Duration

4.1 Duration of Subject Participation

Subjects will be enrolled in the study upon admission to the ICU and will be followed up on a daily basis up until - A) clinical improvement, which necessitates transfer out of the ICU or B) death.

4.2. Duration of the Study

It is estimated that it will take three (3) months to complete enrollment at all study sites. Hence, estimated site participation will be approximately three (3) months.

5. Number of Subjects/Consent Process

5.1 Number of Subjects

We plan to enroll 1,000 patients for the study (500 in Prayer arm and 500 in Control arm).

5.2 Consent Process

Due to the double-blinded nature of the study performed among critically ill patients with COVID-19, with no identifiable data no consent will be necessary or obtained.

6. Subject Eligibility

6.1 Inclusion Criteria

Patients will be enrolled in this study if they meet the following criteria:
a) Male or Female greater than 18 years of age
b) Confirmed positivity or high index of clinical suspicion for COVID-19
c) Admitted to intensive care unit

Exclusion criteria

a) Under 18 years of age
b) Admission to ICU for diagnosis other than COVID-19

Dear God
We pray you to bless our friend (CPS ID)
We pray you to give our friend the strength to pull through this sickness
We pray you to heal our friend from this disease that is consuming him
We pray you to give the health care professionals involved in our friend's care, the necessary courage, wisdom and protection
We pray you to quickly put an end to this global scourge, save the world and prevent sickness to the rest of our brothers and sisters
We pray you to bring solace, strength and resolve to fight this deadly virus with all our might
Thank you for hearing us out and bestowing your divine will on our friend and many others around us.

7. Screening Process

Patients who are evaluated for entry into the study and fail to meet the inclusion and exclusion criteria are defined as screening failures. A screening log, which documents the screening number, patient's initials, and reason for screen failure/admission, is to be maintained by the investigator for all potential patients. A copy of the screening log should be retained in the investigator's study files.

8. Data Collection and Timeline

Assessments will be performed on a daily basis on patients admitted to ICU that are enrolled. This will continue until A) the patient is transferred out of the ICU or B) death of the patient.

9. Risk/Benefits

Risk

Patient identity is not at risk as the patients name is never identified in the study data that is collected. They will be identified as CPS#. The site investigator will maintain the linking list with the patients information at the site and not share this with anyone outside the study team. This will limit the risk of identifiable patient information resulting from a breach of patient confidentiality.

Benefit

Potential benefits at listed below:
a) Potential for improvement in outcomes
b) Mortality benefit

10. Data Analysis

Standard statistical tools will be utilized. SPSS version 23.0 will be used to analyze the data. Continuous data will be described as the mean value ± SD, and categorical data will be described as frequencies/percentages. The association between a clinical event/endpoint and specific clinical variables will be evaluated. Chi square or Fishers exact test will be used to compare categorical data and student t-test or Mann-Whitney-U test will be used for comparison of continuous data. A 'p' value <0.05 will be considered statistically significant. Bivariate and multivariate analysis will be conducted to examine the study objectives. Variable significant in the bivariate analysis will be included in multivariate analysis.

II. ADMINISTRATIVE

1. Ethical Considerations

1.1. Declaration of Helsinki

This study shall be conducted in accordance with the Declaration of Helsinki.

1.2. Institutional Review Board (IRB) or Independent Ethics Committee (IEC)

Prior to starting the study, the Investigator will submit the study protocol, with supporting documentation to the IRB (or other organized and recognized IECs) of the institution where the study will be conducted and obtain IRB exemption for this study from the participating institution. This is a double-blind study with no procedural intervention and no possible harm to the patient. The patient is de-identified at all times and no HIPAA identifiable information is collected.

1.3. Informed Consent

Each eligible participant will automatically be enrolled with a waiver of consent for the study.

1.4. Permission to Review Source Records

The investigator agrees that the Sponsor, its employees, or agents, will have the right to audit and review pertinent medical records relating to this clinical trial.

2. Patient Confidentiality

All reports and communications relating to patients in the study will identify each patient only by CPS and by the patient's study number that is computer generated. The investigator at the participating site will maintain a patient identification linking list connected to the Study ID for each individual patient. This information should be treated with strict adherence to professional standards of confidentiality and be kept by the investigator under adequate security and restricted access along with any other study records. Patient ID or any other identifiable information will not be collected for the purpose of the study.

3. Monitoring and Recording of Study Data

3.1. Monitoring of the Study

As an integral part of conducting this study, periodic monitoring of the data at the central level by a duly identified study monitor team that is independent of the study team (James L. Vacek MD; Buddhadeb Dawn MD).

3.2. Recording of Study Data/Storage of Study Data

All study data must be recorded in the secure website provided by the Sponsor in accordance with the following instructions:

- All entries on the CRFs must be made on the established website with a unique patient identifier as provided on initial input.
- Only the Investigator or an assistant authorized by the Investigator may make entries on the website.

3.3. Cost/Payment to Subjects

- There is no additional cost to subjects for participating in this research study.
- There is no payment to patients for participating in the research study.

3.4. Analysis and Reporting of Study Data

Data will be collected via electronically through the study website linked to the data collection sheet and will have de-identified information. The parent sheet containing patient identification information will be kept in a password secure manner electronically by the primary investigator at the participating site and will not be accessible to the central data collection and processing site. The true ID of the patient will never be collected for the study purpose and will not be subsequently used. Individual patient level data will not be provided to the participating sites. Site investigators, central study personnel and prayers groups are totally blinded to the process and at no point patient is identified.

The Investigator's CRFs will be completed on an ongoing basis during the study. The Investigator will provide the Sponsor a written report on the conduct of the clinical study within thirty (30) days after completion of the study. This report will include the following:

1. The number of candidates screened during the study
2. The number of subjects enrolled in the study
3. The number of subjects who successfully completed the study
4. The number of protocol deviations with explanations

3.5. Amendments to the Protocol

It is specified that the appendices attached to this protocol, and referred to in the main text of this protocol, form an integral part of the protocol. No changes or amendments to this protocol may be made by the Investigator after the protocol has been agreed to and signed by all parties unless such change(s) or amendment(s) have been fully discussed and agreed upon by the Investigator, the IRB(s), and Study Group. Any change or amendment agreed upon will be recorded in writing, the written agreement will be signed by the Investigator and the Sponsor, and the signed agreement will be appended to this protocol.

3.6. Investigator Agreement to Conduct the Study

I, the Investigator named below, attest:

1. I have carefully read this protocol and agree that it contains all the necessary information required to conduct the study and I agree to conduct this study as outlined
2. All research activities will be completed following the procedures outlined in this protocol
3. I understand that this trial will not be initiated without exemption of the appropriate institutional review committee
4. I understand that my signature (or that of a sponsor-approved Co-Investigator) on each completed data points online indicates that I have carefully reviewed each page and accept full responsibility for the contents thereof.

Name of Investigator:_____

Signature:_____ Date:_____

Circle one: Primary Investigator Co-Investigator

Institutional Affiliation:_____

Address:_____

_____

PI Signature:_____ Date:_____

Copies of this form may be made for each Investigator participating in this trial and filed in your site's regulatory record.

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