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Brief Report

How a Psychopharmacology Clinical Trial Site in the Seattle Area Managed Clinical Trials and Patient Care During the COVID-19 Pandemic

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ABSTRACT

Objectives: *As the COVID-19 pandemic developed in March 2020 in greater Seattle, our clinical trial site faced several ethical and clinical dilemmas. We remained open to research patients including high-risk elderly patients and adapted to changing health recommendations.* ***Methods:*** *Beginning March 14, 2020 we developed an in-person evaluation for potential risk of COVID-19. Included are the first 3 weeks of screening by our physicians for potential exposure to COVID-19, common symptoms, temperature, blood oxygen saturation, and heart rate. Individuals with higher risk (n = 23) were identified and managed.* ***Results:*** *The 825 evaluations included 37 staff, 167 patients, and 152 visitors. No one needed isolation or transfer to acute care facility, staff attendance was 95%, all 33 geriatric patients continued in phase II trials, and others decreased by 5%.* ***Conclusion:*** *We share how we incorporated COVID-19 Center for Disease Control health recommendations to a clinical trial center and addition of pulse oximetry.* (Am J Geriatr Psychiatry 2020; 28:999–1003)

INTRODUCTION

On February 29, 2020 the first known death due to coronavirus disease of 2019 (COVID-19) in Washington State was reported. Governor Inslee declared a state of Emergency on February 29, 2020; and on March 23, 2020, a stay – at – home order was issued.[1] This first death was in a hospital less than 10 miles away from the Northwest Clinical Research

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Center, an independent multispecialty psychopharmacology clinical trial center with special focus for geriatric research in Parkinson's and Alzheimer's dementias. Initially, we had 220 clinical trial patients and 41 staff members of which 11 are physicians.

Due to the pandemic, we were confronted with research, medical and ethical dilemmas. The trials we conduct have significant mortality and morbidity especially in our geriatric population requiring on-site monitoring. The risk of closing our center was high; our research participants would not be able to get investigational medication, not have access to medical evaluation, and be at risk for medical and psychiatric decompensation, and loss of research data.

We considered iatrogenic spread which was seen in Wuhan, China[2] and closing or converting to telemedicine is difficult. Our Phase II clinical trials include investigational medications with potential side effects of cardiac arrythmias, QTc prolongation, or hepatic toxicity and a device hypothesized to change white matter circulation. Thus, clinical interviews, electrocardiograms, and bloodwork to evaluate hepatic, renal, and hematological toxicity and specific markers including antibodies are essential. Many patients have cognitive deficits and challenges with insight and judgment due to the nature of illnesses such as Alzheimer's or Parkinson's dementia or schizophrenia making it difficult to participate in telemedicine. As an example, patient X is a 79-year-old lady with Parkinson's dementia who we attempted to call mid-morning Friday, March 13, 2020 to check in. She answered the second call and said she was too frightened and fragile to come in. We told her we would call her back the following Monday with recommendations. However, she called again that night at 9pm and twice each of the next two days each time forgetting all previous calls. Patient Y is a 34-year male with paranoid schizophrenia who at baseline has delusions of contamination, yet he has not brushed his teeth for decades. He called the office to report that he coughed one time 4 days prior.

Given the complexities of clinical trials and vulnerability of the patients involved, after reviewing COVID-19 data from the Center for Disease Control[3] and guidance from Washington State, Governor Inslee,[4] and the United States Food and Drug Administration directive that clinical trials were to be carried with modifications as appropriate and not to stop them[5] we stayed open.

In forming a plan, we looked to descriptions of known cases. Wang et al.[2] described 138 COVID-19 cases with associated pneumonia, most of them showing ground glass opacities with high mortality likely related to acute respiratory distress syndrome, cardiac arrythmias and shock after prolonged ventilation suggesting to us that monitoring of temperature, oxygen saturation, and heart rates may help evaluate risk. To assess triage for oxygen, we reviewed Majumdar et al.[6]; nonchronic obstructive pulmonary disease subjects with pulse oximetry oxygen saturation (SPO2) of less than 92% indicate severe respiratory distress and for those with COPD, the threshold may be as low as 88%. In addition, Ong et al.[7] suggested that cleaning of surfaces and equipment was likely to prevent further spread of COVID-19.

We hypothesized we would be able to identify potential signs and symptoms of COVID-19 and continue to serve vulnerable populations and collect safety data as per protocols.

METHODS

Starting Saturday, March 14, 2020 all patients, staff, and other visitors were screened in person with the following principles;

1. Follow the CDC guidelines for universal sterile precautions with daily review.
2. Divide clinic into patient and staff only areas and avoid congregation
3. All patients, companions and other visitors to the Northwest Clinical Research Center will be individually evaluated upon arrival by our medical staff (SM and AM) for general well-being, COVID-19 exposure, COVID-19 symptoms (cough, difficulty breathing, sore throat), and vital signs (temperature and oxygenation). If fever or cough present and the oxygen level is below 92% (below 88% for known COPD) contact the health department and coordinate. If febrile but had oxygen level over 92%, discuss quarantine, self-monitoring of oxygen levels (using pulse oximeters) and contacting health department. After evaluation patients directly taken to 1 of 15 examination rooms with 2 additional isolation rooms in emergency.
4. Each staff member checked check temperature and oxygen saturation upon arrival to work and

discussed COVID-19 known contacts or COVID-19-related symptoms with medical director.
5. Patient contact areas to be cleaned before and after each encounter with cleaning products containing antiviral and antibacterial properties or >60% alcohol based.
6. Each staff member could use their sickness/other paid time off as needed.
7. Face masks were provided to everyone. We started with a limited supply of N95 and surgical masks and made masks for patients and visitors until additional obtained. Hand washing/sanitizing upon arrival.

We increased social distancing amongst staff necessitating four nonclinical staff to be placed on furlough and three placed on a flexible schedule. We incorporated each individual sponsoring trial company recommendations on their own staff visiting.

Table 1 includes the first 3 weeks of data collected including age, sex, temperature, oxygen saturation, heart rate, and situations encountered requiring additional clinical evaluation. We did not collect age data for visitors. Heart rate screening was added on March 24, 2020.

RESULTS

We collected data for 37 staff (Table 1) which included 424 evaluations of 28 females (72%), 27 were between ages 20−44 (72%), 6 were between ages 45−64 (16%), 3 were between ages 65 and 74 (8%) and one was above 75 years old (3%). The mean temperature was 96.6°F ± 0.4 range 94.5°F−99.0^0 F. The mean oxygen saturation was 98% ±1.2 range of 93%−100%. Of a possible total of 444 working days, 26 days (5.8%) of work were missed. Three staff called out sick. One had pharyngitis/laryngitis which responded to ampicillin and two had acute gastroenteritis of which one was tested for COVID-19 antigen with negative results.

Of our 220 patients, 167 had scheduled study visits during this time (Table 1). Their mean age was 44 years ± 20.2 and 55% were female. Some had more than one scheduled visit. The mean temperature was 96.7°F ±0.4 range of 94.6°F−98.9°F. The mean oxygen saturation was 97.2% range of 92%−100%. Heart rate was later added and 87 ± 14.6 per minute range of 51 −134. In the evaluations, 22 signs or symptoms were positive and required further discussion, but all patients were able to be seen for their visit.

We had 33 patients (15%) with Alzheimer's or Parkinson's with severe dementia. Of these, 24 were scheduled for study visits during the 3-week period; 18 (75%) of them came in with their caregiver for office visits and 6 (25%) including 2 from Canada completed telephone visits with study medications were sent via couriers. Among the remaining 187 patients, 11 (5.8%) discontinued participation, primary in migraine trials.

There were 152 visitors including those accompanying patients, service personnel and pharmaceutical study monitors all who had vital signs within defined normal limits (Table 1) and 7 signs or symptoms requiring additional interview.

Most sponsoring pharmaceutical companies provided guidance for maintaining current study patients but stopped new patient recruitment (15 of the 22 trials, 77%). New patient recruitment fell dramatically.

DISCUSSION

Our aim was to evaluate if a clinical trials research center with vulnerable patients including patients with dementia and other severe mental illness in high risk phase II clinical trials could adapt to changing CDC health recommendations to managed patients, staff, and visitors safely and obtain meaningful safety and efficacy clinical data. We have found that we have been able to implement CDC guidelines and found incorporation of a mobile pulse oximeter to be easy and useful.

The turnout of both staff and patients has been high with staff attendance at 94.2% and of the patients with dementia, 75% came in with caregivers and the rest were able to complete their visits via phone with delivery of study medication.

Of a total of 825 evaluations, no one had a fever, dyspnea or acute respiratory distress syndrome, vital signs outside defined limits, nor did anyone need isolation or transfer to acute care. Twenty-three people (3%) required further evaluation but all were able to be seen. If these screens were done over the phone, these people would not been seen.

The low number of symptoms related to COVID-19 may be due to precautions in Washington State. However, because of lack of COVID-19 testing it is unclear if any us were asymptomatic carriers or had

TABLE 1. Screening for Signs and Symptoms of COVID-19 in Person at Northwest Clinical Research Center in Bellevue, WA from March 16, 2020 to April 2, 2020

Group (N[a])	Sex (%Male)	Age Range (Years)	Temperature (°F) (N [b]) Mean ± SD [c] (R [d])	SPO2 (%) (N [b]) Mean ± SD [c] (R [d])	Heart Rate (BPM) (N [b]) Mean ± SD [c] (R [d])	Additional Screening for 23 Individuals (N[e])
Patients (167)	44.3%	<20	(22) 97.1 ± 0.7 (95.7−98.4)	(22) 98 ±2 (92.0−100.0)	(12) 96.9 ± 17 (71−134)	Contact history (1)
		20−44	(114) 96.8±0.8 (94.6−98.9)	(114) 97.6 ±_1.5 (94.4−100.0)	(68) 88.7 ± 13.9 (51−113)	Cough (6), Rhinnorhea (1), Sore throat (5), Contact history (1),
		45−64	(42) 96.5 ± 0.8 (94.9−98.8)	(42) 97±1.5 (94.0−100.0)	(17) 84 ± 12.5 (61−100)	Cough (2), Sore throat (1), Fever history (1), Shortness of Breath (1)
		65−74	(35) 96.6 ± 1 (94.5−98.9)	(35) 96.3±2 (93.0−100.0)	(18) 81.3 ± 15 (56−112)	Cough (3)
		>75	(18) 96.4 ±1 (93.5−97.6)	(18) 96.4 ±1.7(93.0−99.0)	(6) 82 ± 14.7 (62−101)	None
Others [f] (152)	53.9%	N/A	(163) 96.7± 0.8 (94.7−98.3)	(163) 97.3 ± 1.8 (91.0−100.0)	(72) 82.3±15.1 (54−120)	Cough (4) Travel History (1) Contact history (1) Sore throat (1)
Staff (37)	24.3%	20−44	(308) 96.6±0.87 (94.5−99.0)	(299) 98±1.4 (93.0−100.0)	N/A	Gastrointestinal distress (2) [g] Pharyngitis/laryngitis (1) g
		45−64	(76) 96.8 ±0.8 (95.0−98.2)	(72) 97.5 ± 1.5 (93.0−100.0)	N/A	None
		65−74	(28) 96.5 ± 0.8 (95.0−98.0)	(26) 98.1 ± 1.1 (96.0−100.0)	N/A	None
		>75	(12) 96.6 ± 1.1 (95.3−98.7)	(12) 96.8 ± 1.2 (95.0−98.0)	N/A	None
Total (356)	46.3%	All	(818) 96.7±0.8 (93.5−99.0)	(803) 97.6±1.7 (91.0−100.0)	(193) 85.5±1.7 (51−134)	

[a] Number of people.
[b] Number of evaluations.
[c] Standard deviation.
[d] Range.
[e] Number of symptoms.
[f] Caregivers/visitors/patient relatives.
[g] Called out sick from home.

already recovered. This will need further review when testing becomes more widespread.

AUTHOR CONTRIBUTIONS

Dr. Shirin Schilling prepared the manuscript and formulated ideas about review and implementation of COVID-19 heath guidelines. Dr. Sinthuja Mohanarajah and Dr. Abraham Mengstu have collected and collated data. Dr. Arif Khan has provided review and conceptualization of this project. Dr. Walter Brown has provided feedback and review of this work.

DISCLOSURE

The authors report no conflicts with any product mentioned or concept discussed in this article.

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