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Efficacy of Interferential Therapy on Selected Cardiopulmonary Parameters of Asthmatic Patients with Post Covid 19 Exposure: A Sstudy Protocol of A Randomized Control Trial

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ABSTRACT

Background: Interferential Therapy (IFT) is the administration of two medium-frequency currents to the skin, stimulating varying systems in the body using specific frequencies and frequency ranges. IFT in the thoracic region aims to reduce muscle soreness in the chest and upper back, reduce muscular fatigue and induce mucus expectoration. This study is designed to test the efficacy of IFT on bronchial asthma patients exposed to the SARS-CoV-2 virus.

Methods: IFT will be administered as an intervention to 28 asthma patients with and without a history of COVID-19 exposure for 20 minutes. Six continuous outcome variables at different points will be utilized as an outcome measure; the selected Baseline Pulmonary Function Test (PFT) and Cardiopulmonary Variables (CVS) will be assessed upon entry into the study and after every intervention, while asthma quality of life and asthma control test will be measured fortnightly. In addition, participants will be required to visit the study location 3 times per week for 12 weeks.

Results: The means ± SD will be compared, while the participant's outcome variables will be evaluated for study homogeneity at baseline. Repeated measures of MANOVA will be used to evaluate the study outcome within group participants. In contrast, a one-tail independent t-test will be used to evaluate the efficacy of IFT on bronchial asthma patients with Post COVID-19 exposure across groups. The level of significance will be set at $P<0.05$.

Discussion and Conclusion: Asthma control in the SARS-CoV-2 virus is still unclear; this study aims to evaluate the effect of airway smooth muscle relaxation induced by IFT on the possible long-term manifestations of SARS-CoV-2 virus on asthma control, quality of life, and selected cardiopulmonary variables of asthma patients. This study will add to the knowledge of managing severe acute respiratory syndrome.

Keywords: COVID-19, IFT, ASTHMA, ACT, AQLQ, PFT, CVS.

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INTRODUCTION

COVID-19 is caused by the severe acute respiratory system coronavirus 2 (SARS-CoV-2); it has a case fatality rate of 2-3%, with higher rates among patients with comorbidities and the elderly population [1]. The outbreak of COVID-19 has had a dramatic impact worldwide; it has affected over 100,000 patients globally since its occurrence in December 2019 [2]. The disease can cause significant alveolar damage resulting in hypoxemic acute respiratory failure (ARF), leading to the use of mechanical ventilation in the majority of patients. [3, 4].

Asthma is a heterogeneous disease characterized by chronic airway inflammation and reversible airway obstruction [5]. Airway hyperresponsiveness (AHR) and airway inflammation are distinct features of asthma (6). The disease affects over 300 million persons worldwide, accounting for approximately 250,000 annual deaths [7].

Zhang and Liu [3], in a report on the clinical characteristics of 140 cases of community-acquired COVID-19 in Wuhan, 82 cases were classified as non-severe. In contrast, 58 were classified as severe; there was no self-reported allergic disease, including asthma, allergic rhinitis, food allergy, atopic dermatitis, and another type 2 allergic disease documented amongst the incident 140 cases. Similarly, only a single case of asthma was identified among 290 laboratories that confirmed hospitalized COVID-19 cases when PCR- positive and PCR result was compared (Zhang et al., 2020). Reported to date, the chronic respiratory disease had the third highest case fatality ratio, after cardiovascular disease and diabetes, in the largest case series [8].

Interferential Therapy (IFT) involves the application of two medium-frequency currents to the skin in such a way that they "interfere" with each other to produce a "beat" frequency (9). Interferential current (IFC) is a simple and noninvasive treatment often used to induce analgesia [10], elicit muscle contractions [11], and reduce oedema [12, 13].

Lung function tests (also called pulmonary function tests, or PFTs) asses the efficiency of the lungs. PFTs are non-invasive diagnostic tests that provide measurable feedback about the function of the lungs [14]. The tests determine the lung volume, airflow speed in and out of the lungs, and the perfusion ratio. It can be used to diagnose lung disease, measure the severity of lung problems, and check to see how well treatment for a lung disease is working [14].

Globally there has been an exponential rise in Coronavirus cases, a total number of 961,692 cases worldwide, with the United States of America accounting for 23.09% of this number as at 2nd of April 2020. In Africa, South Africa accounts for 1462 cases, approximately 22% of the total number of cases found in Africa as at 2nd of April 2020 (15). On the other hand, Nigeria, with a population of 206,139,589 people, accounts for 2.6% of cases in Africa and 0.02% of the global occurrence as at 2nd of April 2020 [15].

For many years, the effectiveness of asthma medications has been assessed by measuring their impact on conventional clinical outcomes such as expiratory flow rates, symptoms, the need for other medications, and airway responsiveness [16]. For example, Aweto, Tella [17] demonstrated the efficacy of Interferential current in the management of bronchial asthma, Jackson, Trujillo-Torralbo [18] highlighted poor asthma control as a risk factor for virus-induced exacerbation in asthma, while Johnston [8] based on existing literature, identified the relationship between SARS-CoV-2 and asthma exacerbation while emphasizing the importance of asthma control as a measure of preventing respiratory complications that may arise from the viral exposure.

This study is therefore designed to investigate the efficacy of a noninvasive electrophysical modality on the cardiopulmonary parameters and quality of life of asthmatic patients exposed to the COVID-19 virus. The outcome of this study may provide a noninvasive solution to the symptoms frequently experienced during an asthma attack and prevent respiratory complications that might have emerged post-COVID-19 exposure.

It is expected that the outcome of this study will establish the effect of IFT on asthma patients with post-SARS-CoV-2 exposure.

Ethical Considerations and consent to participate.

The Biomedical Research Ethics Committee has approved this study of the University of KwaZulu Natal (South Africa) (Ethics Number: BREC/00001883/2020) and by the Human Research Ethics Committee of Lagos State University Teaching Hospital, Ikeja, Lagos, Nigeria, West Africa (LREC/06/10/1428). The study is registered with ClinicalTrial.gov with the following registration number: PACTR202005890624077. A written and signed informed consent will be obtained from all participants recruited for this study through a third party independent of the study team. The Biomedical Research Ethics Committee of the University of KwaZulu-Natal (BREC) designed the consent form to meet the WMA Helsinki Declaration and good clinical practice (GCP).

During this trial's conduct, the PI will communicate in writing to the RECs in the event of the need to modify or amend the protocol, especially the inclusion or exclusion criteria of the study.

Operational Definition of terms

Interferential Therapy: Interferential Therapy uses two medium-frequency currents that pass through the tissues simultaneously and interfere with each other to give rise to a beat frequency with low-frequency stimulation characteristics [19].

Spirometry: Spirometry is a type of pulmonary function test that measures the amount of air taken in (volume) and exhaled as a function of time [20].

Cardiopulmonary parameters refer to the cardiovascular and pulmonary systems' variables [21].

METHOD

Study Design: The study is a parallel, 12-week randomized control trial. The study will involve two (2) intervention groups and two parallel placebo control groups.

Participants: This study will consist of male and female adult bronchial asthma patients aged 18 years and above attending Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria, West Africa.

The inclusion criteria involve patients with bronchial Asthma aged 18 years and above attending the respiratory clinic of LASUTH.

The exclusion criteria involve patients with COPD other than bronchial Asthma, hypersensitive to B2 agonist. Patients on a cardiac pacemaker, recent surgery, supplemental oxygen therapy, cardiac conditions, and patients with psychological impairments.

Participants who met the required criteria will be asked to read and sign an informed consent approval for this study by the appropriate institutional review board.

Sample size: Pulmonary function test and Cardiovascular parameters are the primary outcome of interest for the study and the expected clinically relevant difference for Interferential Therapy on asthma patients recently exposed to the SARS-CoV-2 virus using LLN and GLI reference equation proposed by Quanjer PH (22). Therefore, the sample size (N) will be determined using G-Power statistics software. The power is selected at 95% =0.95, confidence level at 5% =0.05, and effect size of 1.1 from a similar study by Aweto A Happiness (23). We intend to investigate the main effects, within and between interactions, for three factors, namely:

Factor A – Therapy with two levels (No therapy and Interferential Therapy)

Factor B – Asthma with two levels (COVID AND NON-COVID Exposure), nested within factor A (Figure 1). This translates to the possibility of recruiting between 7 and 13 patients per group. Hence, the sample size estimates suggest that recruiting more than 13 patients per group for this kind of study will be a waste of resources.

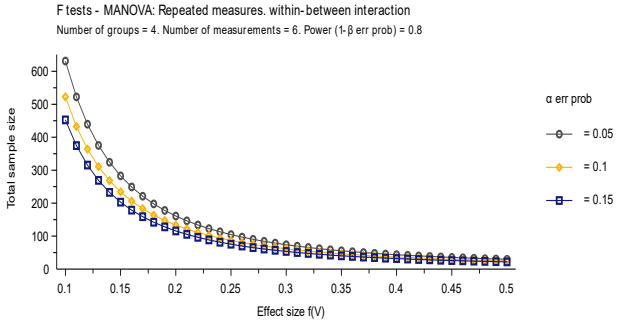


Figure 1. Ftests -Manova

Randomization and blinding: The contact numbers of participants will be randomly extracted from the respiratory patients' database attending Lagos State University Teaching Hospital Ikeja's respiratory clinic. A bulk Text message captioned "Invitation to a study on ASTHMA will be circulated using the Luxury bulk SMS platform. Respondents will be assessed for eligibility, and those that meet the inclusion and exclusion criteria will participate in the study.

Participants will be randomly selected by simple randomization using a computer software program's randomization table [24]. The software program (www.randomization.com) will allocate participants into study group A and control group B. Furthermore, the two groups will be divided into subgroups x,y, e, and f using the same simple random sampling technique. A homogenous purposive sampling technique will be used to stratify participants into subgroups x, y, e, and f based on their characteristics, with x and e connoting asthma patients with post covid-19 exposure, while y and f representing participants without covid-19 exposure. The final group will be allotted into a single treatment table of seven subjects per block, resulting in 4 groups of 7 participants per block, each labeled as x, y, e, and f, respectively. A unique identification number will be assigned to individual participants.

Procedure for Data Collection

Twenty-eight [28] subjects will be recruited for this study. The subjects will be randomly assigned into two significant groups of fourteen (14) subjects per group, and four (4) subgroups of Seven (7) subjects per subgroup.

Assessment

The subjects' medical records will be properly screened for possible contraindications to the study. Subjects' baseline respiratory parameters will be determined using Koko PFT spirometer

The Asthma Control Test questionnaire and Asthma quality of life will be administered to the control and study group at the beginning and every 2 weeks interval for a period of 12 weeks of the study. The baseline spirometry will be conducted on the 2 groups before and after the commencement of the study.

Interferential unit "Nu-Tek E-Stim Pro" will be used for the study intervention, the treatment period will be increased by two minutes, with each application up to a total application time of 20 minutes.

Intervention

Participants will be briefed about the nature of the study, effect, and benefit of the study. They will be encouraged to clarify issues regarding the study, if any. Written informed consent will be obtained from participants before the commencement of the study. Participants will be randomly assigned into two groups: Study (Group A) and Control group (Group B). Interferential Therapy will be demonstrated to the study group alone. Asthma Control Test, Asthma Quality of life questionnaire, and Spirometry score will be measured and recorded before intervention in both groups. Reassessment will be done after the 2nd, 4th,6th, 8th, 10th, and 12th week of the study intervention.

The study group (Group A) will receive interferential

Therapy; this modality selection is only acceptable in the absence of a history of cardiac disease, in which case it should not be used (25). In the absence of such a history, the subjects will be divided into two subgroups and labeled x and y. Subgroup x will consist of Asthma patients with documented evidence of post COVID-19 exposure while subgroup y will be asthma without a history of COVID-19 exposure. In both instances all patients will undergo a reverse transcription polymerase chain reaction (RT-PCR) before commencement of the study (26).

Sub group x and y will receive interferential Therapy; this modality selection would only be accepted in the absence of a history of cardiac disease, in which case the patient will be excluded from the study (27). In the absence of such a history the participants will be placed in a dorsal recumbent position, two electrodes will be positioned over the upper limits of the trapezius bilaterally on the upper back, and the other two will be placed anteriorly over the lower ribs (25). If the subject is experiencing respiratory difficulty while the intervention is on-going, the procedure will be discontinued. With a 4,000 Hz base current, the interferential current range will be set from 10 to 150 Hz and initially applied for 10 minutes, being careful to monitor the patient's condition during the treatment period. If the patient presents any sign of distress during treatment, the current will be turned off. As long as the subject experiences no distress with the IFC application, the treatment period will be increased by two minutes, with each application for up to 20 minutes.

The control group (Group B), in addition to the baseline pulmonary function test, will also receive counseling on asthma and enjoy free musculoskeletal assessment. They will be divided into two subgroups and labeled e and f as Asthma patients with post covid-19 exposure and those without Covid -19 exposure respectively. In both instances all patients will undergo a reverse transcription polymerase chain reaction (RT-PCR) before the commencement of the study (26).

Data analysis

The Statistical Package for Social Sciences (SPSS Inc, Chicago, II) version 27.0 for the Windows package program will be used to analyze data. Descriptive mean, standard deviation, frequency, and percentage statistics will summarize the results. Bar charts, pie charts, and histogram will be utilized for pictorial illustration. Multilevel analysis of variance (MANOVA) will be used to compare the outcome variables [selected cardiovascular variables (RR, HR, SBP, and DBP), pulmonary function variables (FEV1, FVC, FEV1/FVC), asthma control test (ACT), and standardized asthma quality of life questionnaire (AQLQ)] among each group; dependent t-test will be used to compare the pre and post-test results while independent t-test will be used to compare the outcome variable across the two groups. The level of significance will be set at p0.05.

Data Management

All data would be collected on a sheet of papers (form) and, kept confidential under lock & key, and transferred to an Excel sheet electronically on a password-protected computer at the Physiotherapy Department, college of health sciences, University of KwaZulu-Natal, Durban for five years, only the researchers will have access to it after this period all documentation will be destroyed.

RESULTS

Findings of this study will be presented as descriptive and inferential statistics, with illustrations using charts, graphs, and pictograms

Harms

This study carries minimal risks; the procedures are not life-threatening and should not cause harm or negative effect. This may include temporary muscle soreness, increased heart rate, blood pressure, sweating, and dizziness. Necessary care will be in place to prevent the occurrence of an adverse event. However, in case of a report of serious adverse events (e.g., comorbidities, injuries, persistent excruciating pain, dizzy spells, headache, etc.) after intervention or at any point during the trial, then we would consider unblinding the participant to the intervention for his/her safety. Additionally, the participants will be instructed to report any adverse events to the PI or the physiotherapist supervising their group. To ensure the participants' adequate supervision and safety, we will limit the number of participants per group in a day to a maximum of 3. Arrangements have been made with the hospital's Accident and Emergency units, where we will conduct the research to provide a standby medical team. However, the University of KwaZulu-Natal insurance scheme on clinical trials has fully covered the participants in this type of study.

DISCUSSION

The relationship between Asthma, SARS-CoV-2, and the recovery pattern in bronchial Asthma is still not well justified. Furthermore, the relationship between the mode of delivery of electrophysical agents is yet to be considered.

A study by Karashurov, Gudovskii (28), programmed Electrostimulation of the sinocarotid nerves implanted to 78 patients with bacterial Asthma for six years prevented the majority of asphyxia attacks, reduced their frequency by 2.7-fold, and the need for In medications by 2.7-3.4-fold.

Aweto, Tella [17], studied the efficacy of IFT on cardiopulmonary parameters of 42 BA patients for six weeks. The researcher reported a significant improvement in the systolic blood pressure (p=0.004), Forced Expiratory Volume in one second (p=0.02), Forced Vital Capacity (p=0.04), and Peak expiratory flow rate (p=0.007). At the same time, group B had significant reductions in these pulmonary parameters. In addition, there were significant improvements (increases) in the ACT score (p=0.0001) and AQLQ (p=0.001).

Mohammed and Elyazed [29], studied Thirty Egyptian children who have Asthma, and age ranged from 9-15 years, with BMI 18.5 to 24.9 kilogram/ meter2. The pre-and post-

treatment variables revealed a significant improvement in the three groups' pulmonary functions, favoring a laser puncture therapy group and interferential therapy group over diaphragmatic exercise.

Although studies by Aweto et al. (2016), Karashurov, Gudovskii [28], and Mohammed and Elyazed (29) identified the effect of an electrophysical agent in the management of Asthma, their findings did not consider asthma as a comorbidity in a severe acute respiratory syndrome. Consequently, it is expected that this study's outcome will further reveal the effect of electrophysical modality on the symptoms frequently experienced by asthma patients who have been exposed to SARS-CoV-2 exposure.

CONCLUSION

In conclusion, this study may give an evidence-based solution to managing severe acute respiratory syndrome using an electrophysical modality. Furthermore, the study outcome may create a pathway for a remission of symptoms in asthma pending the arrival of a wholistic medical care, which will be an advantage to a low-income environment with a scarcity of resources.

Access to Protocol

https://pactr.samrc.ac.za/Researcher/ManageTrials.aspx The protocol was registered on 1st of May 2020 with identifier number PACTR202005890624077 and the trial organization is Pan African Clinical Trial Registry.

Consent to publication

Not Applicable

Availability of data and materials

The corresponding author will make available the datasets for the study upon reasonable request. However, the findings from the study would be made available to participating researchers as required by law.

Competing interests

The authors declared that they have no competing interests.

Funding

Awolola Eniola Oladejo funds the study. The study design, manuscript writing, collection, and data analysis are independent of the institutions used for the study.

No funding was received from any external source for the study.

Abbreviations

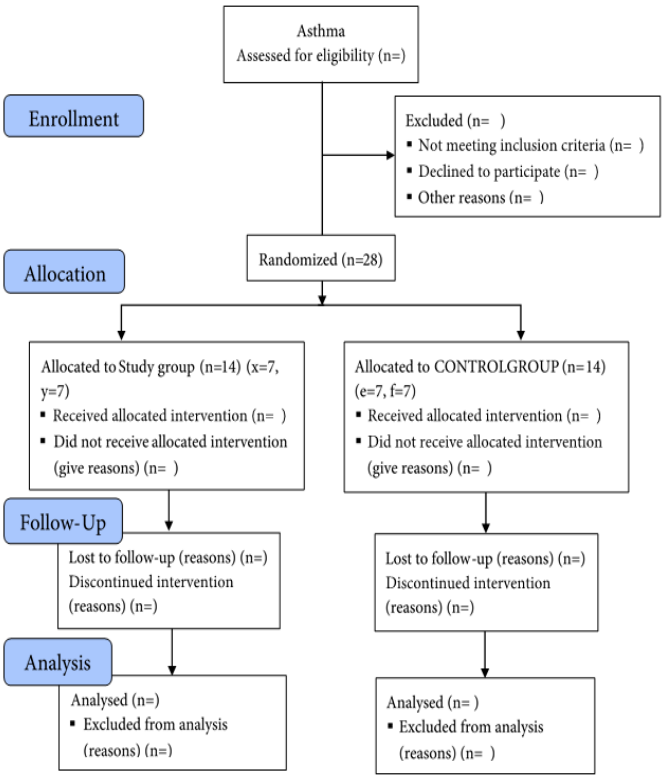
ANOVA - Analysis of Variance
COPD - Chronic Obstructive Pulmonary Disease
FEV1 - Forced expiratory volume in 1 second
FVC - Forced Vital Capacity
FRC - Functional residual Capacity
GLI - Global Lung Initiative
IFC. - Interferential Current
IFT. - Interferential Therapy
LASUTH - Lagos State University Teaching Hospital
LLN - Lower Level of Normal
MANOVA - Multiple Analyses of Variance
MS - Microsoft
PEFR - Peak expiratory flow rate
PFT - Pulmonary Function Test
RCT - Randomized Control Trial
ROM - Range of Motion
SPSS - Statistical Package for Social Sciences
UKZN -University of Kwazulu-Natal

Authors' Contributions

AOE developed the idea for the study; AOE and MSS developed the title and contributed to the study design. All authors were involved in the design of the procedure and the selection of outcome measures for the study. In addition, AOE was responsible for drafting the initial manuscript.

CONCEPTUAL FRAMEWORK

IFT FLOWCHART



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