Comparative efficacy of interferential therapy, bronchodilators, and body positioning on asthma control and quality of life of patients with bronchial asthma: A study protocol

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Abstract

Interferential Therapy (IFT) is the application of two medium frequency currents to the skin to stimulate and activate different systems in the body using specific frequencies and frequency ranges. The aim in applying IFT is to reduce myalgia in the chest and upper back, reduce muscular fatigue, and induce mucus expectoration. This study is designed to test the efficacy of IFT in reducing the symptoms frequently experienced by patients with bronchial asthma. Forty-eight (48) patients aged 18 and above with bronchial asthma attending the respiratory clinic at the Lagos State University Teaching Hospital, Ikeja (LASUTH) will be assessed for eligibility. The study design will be a double-blinded, randomized control trial with four intervention groups and four parallel placebo control groups. IFT will be administered as an intervention to patients on short and long-acting bronchodilators in an assigned fundamental body position for 20 minutes. Six continuous outcome variables at different points will be utilized as outcome measures. A baseline Pulmonary Function Test (PFT) will be conducted on entry into the study while quality of life and asthma control will be evaluated every two (2) weeks during the study. Data obtained will be analyzed using descriptive and inferential statistics of repeated ANOVA; $P<0.05$. The study outcome will compare the efficacy of IFT on bronchial asthma, identify its effect in different body positions, and compare the relationship between its application and the bronchodilator medication frequently used by the patients.

Introduction

Worldwide, approximately 300 million people are affected with bronchial asthma.[1] It is more prevalent in developed countries, with the highest rates seen in Australia, UK, and New Zealand.[1] In the Nigerian population, the prevalence of asthma ranges from 7% to 18%.[1-4]

A study by Oni *et al.*,[5] on the prevalence, management, and burden of asthma revealed that asthma affects all age groups, races, and sex. A population-based study showed that more boys are usually affected than girls in the early decades of life, however, the prevalence becomes equal by the third decade of life, and afterward. More women were reported to be affected after the third decade.

Symptom relief, reduction in the use of on-demand inhalers, improvement in activities and lung function are the day-to-day asthma control achievements.[6] The absence of asthma exacerbations ensures the minimization of future risks by preventing accelerated decline in lung function and side-effects from medications over time.[6]

Progress is being made in the understanding and management of asthma, the inflammatory nature of the disease, use of steroids, and add-on of inhaled bronchodilator combined with steroids, devices to deliver the medications appropriately, and appreciation of the value of self-management education.[1,7]

In the treatment of airway disorders, bronchodilators are central in managing most chronic obstructive pulmonary diseases and are critical in managing asthma.[8] The recent update by GINA[9] indicates the consideration of low dose ICS-formoterol as controller medication for the management of bronchial asthma or ICS-SABA as an alternative in countries where ICS-formoterol is unavailable, low-dose.

According to Boros and Martusewicz-Boros[10] airway reversibility is a test commonly used in diagnosing obstructive lung disease; its result can be used as a differential diagnosis between asthma and chronic obstructive pulmonary disease. Chung *et al.*[11] identified FEV1/FVC<LLN or 0.70 or <LLN as a tool for diagnosing airway obstruction. Significant improvement (positive bronchodilatation test) is defined as an increase in FEV1 or FVC of more than 200 mL, or 12% of the predicted value of FEV1.[11] A bronchial provocative test can be used to determine the strength of the controller medication when FEV1 is >70% predicted value.[9]

Several studies have been conducted to understand the effect of body position on pulmonary function. The most recent, a systematic review by Katz et al.,[12] reported higher FEV1, FVC, FRC, Imax, and PEF values in most studies involving healthy subjects or patients with lung, heart, neuromuscular disease, or obesity in a more erect

position. For subjects with tetraplegia, spinal cord injury, FVC and FEV1 were higher in supine vs. sitting.[12]

Interferential therapy (IFT) involves the application of two medium frequency currents to the skin in such a way that the currents "interfere" with each other to produce a "beat" frequency.[13] The difference between the medium frequency currents is termed the beat frequency, and the body recognizes it as the required low-frequency current. Interferential therapy induces expectoration by making sputum on the bronchi surface mobile and reduces shoulder stiffness, muscular fatigue, and myalgia in the chest and upper back regions.[14]

Interferential current (IFC), a non-invasive treatment modality, is often used to induce analgesia, elicit muscle contractions, and reduce oedema.[15-17] For many years, the effectiveness of asthma medications has been assessed by measuring their impact on expected clinical outcomes such as expiratory flow rates, symptoms, the need for other medications, and airway responsiveness.[18] Although of great importance, none of the measurements indicates whether the patients can function better in their day-to-day lives.[18]

Aim of the study

The overall aim of this study is to determine the effect of IFT applied in 45° or 90° long sitting with a bronchodilator (short or long acting) on asthma control, quality of life, and selected pulmonary variables of asthmatic patients attending the respiratory clinic of Lagos State University Teaching Hospital, Ikeja, Lagos.

This study is designed to investigate the efficacy of a non-invasive therapeutic modality on airway reversibility, asthma control, quality of life of bronchial asthma (BA) patients in 2 different body positions using the GLI (LLN) 2012 reference equation for asthma classification and the 2019 Pan African Thoracic Society (PATS) and European Respiratory Society guidelines for the validation of spirometry test results. The outcome from this study may provide a non-invasive solution to the bronchospasm frequently experienced during an asthma attack.

Hypothesis

H_0

Interferential therapy (IFT) applied in 45° or 90° long sitting will have no significant effect on airway reversibility, asthma control, and bronchial asthma patients' quality of life.

Delimitation

This study will be delimited to 48 bronchial asthma patients attending the Lagos State University Teaching Hospital, Ikeja, Lagos respiratory clinic.

Significance of the study

It is expected that the outcome of this study will establish the relationship among interferential therapy, bronchodilators, and body position in asthma control, asthma quality of life, and selected pulmonary variables of patients living with bronchial asthma. It is expected that this study will provide substantial evidence on airway reversibility in bronchial asthma using IFT.

Materials and Methods

Study design

The study is a parallel, 12-week randomized control trial and will involve four (4) intervention groups and four parallel placebo control groups.

Participants

The participants for this study will consist of male and female adult bronchial asthma patients aged 18 and above attending Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria in West Africa.

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

The exclusion criteria involve patients with other types of COPD other than bronchial asthma, hypersensitive to B2 agonist, patients with a cardiac pacemaker, who have had recent surgery, supplemental oxygen therapy, or with cardiac conditions, and patients with psychological impairments.

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

Setting

Patients with bronchial asthma attending the respiratory clinic of Lagos State University Teaching Hospital, Ikeja, Lagos State, Nigeria, will be recruited for the study. The hospital is a tertiary health facility within the state and receives referrals from within and outside the state.
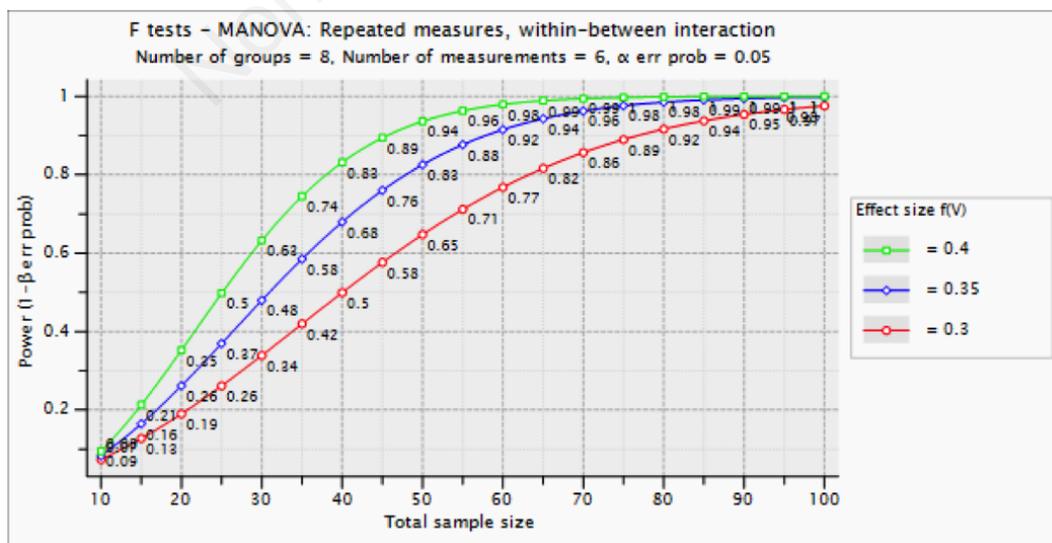

Figure 1. F tests -MANOVA: Repeated measures, within-between interaction.

Sample size

The pulmonary function test is the primary outcome of interest for the study and the expected clinically-relevant difference for pulmonary rehabilitation in various body positions using LLN and GLI reference equation proposed by Quanjer et al.[19] Therefore, the sample size (N) will be determined using the G-Power statistics software. The power is selected at 95% =0.95, confidence level at 5% =0.05 and effect size of 0.35 (Figure 1).

Randomization and blinding

The contact numbers of participants will be randomly extracted from the database on respiratory patients attending the Lagos State University Teaching Hospital Ikeja respiratory clinic (Figure 2). 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 criteria will participate in the study while those who have any of the exclusion criteria will be excluded.

Participants will be randomly selected by simple randomization using a computer software program randomization table.[20] The software program (www.randomization.com) will be used to allocate participants into study group A and control group B. Group A was further assigned to subgroup x, and y, while group B was assigned to subgroup e, and f. Subgroup x and e represents participants on SABA, while Subgroup y and f represents participants on LABA. Participants were randomly assigned to a final group of xa, xb, ya, yb, ea, eb, fa, and fb, with 'a' and 'b' connoting 45° and 90° long sitting respectively.

Procedure for data collection

Forty-eight (48) subjects will be recruited for this study. The subjects will be randomly assigned into two major groups of twenty-four (24) subjects per group, two (2) subgroups of twelve (12) subjects per subgroup, and eight (8) final groups of six (6) subjects per group.

Assessment

The subjects' medical records will be adequately screened for possible contraindications to the study. Baseline respiratory parameters will be assessed using the Koko PFT spirometer.

The Asthma Control Test Questionnaire and Asthma Quality of Life questionnaire will be administered to the control and study groups at the beginning of the study and at two-week intervals for the 12 weeks of the study. Baseline spirometry will be
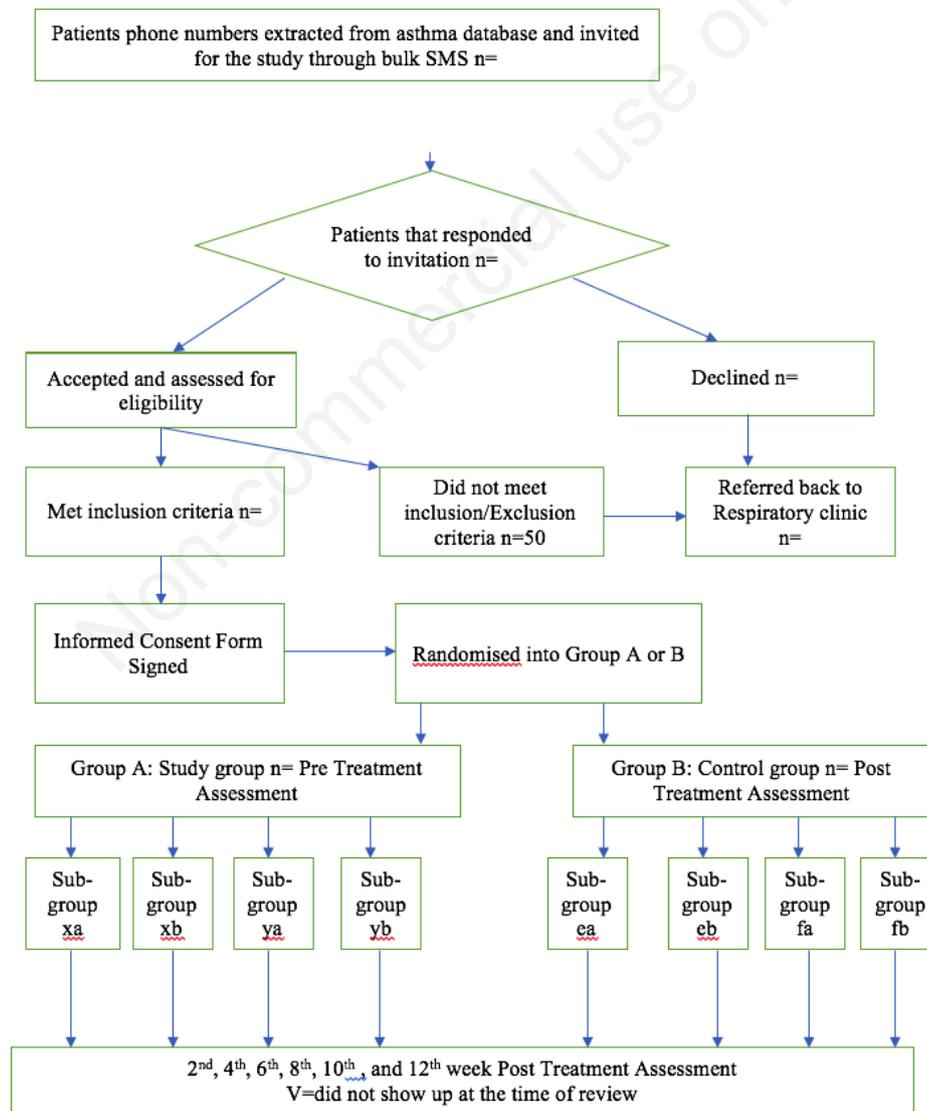

Figure 2. Recruitment and randomization of participants.

conducted on the two groups before and after the commencement of the study.

The interferential unit "Nu-Tek E-Stim Pro MT1022970" 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.

Assessment tools

Spirometry assessment

The assessment will be conducted by a spirometrist certified by the Pan African Thoracic Society. A portable spirometer (Koko SX 1000 Standalone Version 7 Pneumotach) will be used to carry out this assessment. Daily calibration of the device will be done using a 3.0-litre syringe. A brief description of the assessment procedure, including technical steps to obtain pulmonary function data and variables, will be explained to each subject. After 2-3 tidal breaths, the subject will be asked to inhale deeply to total lung capacity and then exhale rapidly (without any pause) through a disposable mouthpiece until as much air as possible has been expelled from the lungs. The test will be performed in a sitting or standing position. The assessments will be repeated three times after adequate rest. The maximum number of attempts permitted will be 8. After fulfilling the acceptability and repeatability criteria, the two best curves will be selected. The average values of the forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) will be recorded.[21]

Intervention

Participants will be briefed about the nature, effect, and benefit of the study. They will be encouraged to clarify issues regarding the study. All participants will be required to give a written informed consent before participating in the study. Participants will be randomly assigned into two groups: study group (Group A) and control group (Group B). Interferential therapy will be demonstrated to the study group alone. The Asthma Control Test, Asthma Quality of Life Questionnaire, and spirometry score will be measured and recorded before intervention in both groups. Reassessments will conducted at the end of the 2nd, 4th, 6th, 8th, 10th, and 12th weeks of the study intervention.

The study group (Group A) will receive interferential therapy; this modality selection is only acceptable in the absence of cardiac disease history.[22] In the absence of such a history, the subjects will be divided into two subgroups and labeled x and y. Subgroup 'x' will be allowed to use 400ug

of SABA delivered in metered doses via a spacer4-6 hours before the study, while subgroup 'y' will be allowed to use 24ug of LABA delivered in metered doses via a dry-powder inhaler within 24 hours of the study.[23] In both cases, the inhaler technique, as described by Basheti *et al.*[24] will be used to demonstrate the procedure to the participants. The intervention will be conducted with participants in a long sitting position, at an angle of 45° and 90° representing labels 'a' and 'b' respectively. In both intervention positions, an electrode will be placed bilaterally over the upper limit of the trapezius on the upper back and the other two anteriorly over the lower ribs.[22] The final group of participants to undergo the intervention will consist of 'xa,' 'xb,' 'ya' and 'yb.' If the subject experiences respiratory difficulty during the intervention, the procedure will be discontinued. With a 4,000 Hz base current, the interferential current range will be set between10 to 150 Hz and initially applied for 10 minutes, while carefully monitoring the patient's condition during the treatment period. If the patient shows any sign of distress during the treatment, the current will be turned off. As long as the subject does not experience any distress with the IFC application, the treatment period will be increased by two minutes with each application, for up to 20 minutes.

Participants in the control group (Group B), in addition to the baseline pulmonary function test, will also receive free musculoskeletal assessment and counselling on asthma. They will be divided into two subgroups and labelled 'e' and 'f.' Participants in subgroup 'e' will be allowed to use 400ug of SABA delivered in metered doses via a spacer 4-6 hours before the study, while subgroup 'f' will be allowed to use 24ug of LABA delivered in metered doses via a dry-powder inhaler within 24 hours of the study.[23] The intervention will be conducted with participants in a long sitting position, at an angle of 45° and 90° representing labels 'a' and 'b' respectively. The final group of participants to undergo the intervention will consist of 'ea,' 'eb,' 'fa' and 'fb.' In both cases, the inhaler technique, as described by Basheti et al,[24] will be used to demonstrate the procedure to the participants. They will be asked to maintain their respective positions for 20 minutes. If the subject experiences respiratory difficulty, the procedure will be discontinued.

Outcome measures/instruments

i) Asthma Control Test (ACT); ii) Asthma Quality of Life Questionnaire (AQLQ); iii) Spirometer (Koko SX 1000 Standalone Version 7 Pneumotach); iv) Interferential Therapy Machine (Nu-Tek E-Stim Pro MT1022970).

Description of outcome measures/instruments

Asthma Control Test (ACT)

The asthma control test is a self-administered 5-item questionnaire developed for assessing asthma control level. It evaluates the most recent four-week period. Each item is scored between 1 and 5, with a total score ranging from 5 to 25. An ACT score of 25 indicates that asthma is "controlled" whereas a score between 20 and 24 shows partially controlled asthma and a score of <20 indicates "uncontrolled" asthma.[25]

Asthma Quality of Life Questionnaire Standardised (AQLQS)

The standardized version of the Asthma Quality of Life Questionnaire (AQLQ) is a 32-item questionnaire (self-administered or clinician administered) with five domains, developed to measure the functional, physical, emotional, occupational, and social problems that are most troublesome to adults with asthma.[18] The maximum score obtainable is 7.0, which translates to no impairment. The minimum score is 1.0, indicating severe impairment, 4.0 is the mid-range score, and indicates moderate impairment.[18] The Asthma Quality of Life Questionnaire standardized version will be used to monitor the difficulty the subjects encounter in activities of daily living as a result of asthma.

Spirometer

Koko SX 1000 Standalone Version 7 Pneumotach, a portable lightweight and comprehensive diagnostic tool, will be utilized to conduct the pulmonary function test. The Koko Legend II spirometer has a built-in thermal printer and a touch screen display. It can perform FVC, Pre vs. Post, and SVC tests. Test data and patient information are stored directly on an internal SD card that can be replaced and re-used. All the stored information can be downloaded via a USB cable onto a PC for backup or storage. This device supports daily calibration checks, complies with ATS-ERS 2005, has several predicted authors, and includes GLI-2012. Daily calibration of the device will be conducted using a 3L syringe.[26]

The participant's condition can be shown by the ratio of the measured value to the predicted value. Flow rate-volume chart, volume-time chart display, data memory, delete, upload and review, trend chart display, scaling (calibration), information prompts when volume or flow goes beyond the limits are features available on the device.

Bronchodilators

The administration of bronchodilators will be primarily through inhalation devices

to deliver the drug to the lung bronchioles in metered doses. Inhalation devices come in all shapes and sizes, but critical is maximizing the amount of drug reaching the bronchioles. The best way to achieve maximum bioavailability is by fully exhaling, placing the inhaler in the mouth, and taking a full inhalation. After the patient has inhaled completely, it will be followed by 10 seconds of no breathing to wait for the medicine to dissipate into the lung space. A slow exhalation back to normal breathing will be advised.[27,28] The eight-point inhaler technique as described by Basheti, Natsheh[24] will be used to deliver bronchodilators and pre-BD reversibility testing in metered doses.

Interferential unit

The Nu-Tek Electrotherapy Machine E-Stim Pro MT1022 provides low and medium frequency outputs from a single unit. The currents available on the Nu-Tek Electrotherapy Machine E-Stim Pro MT1022 include Interferential (2 and 4-pole), Russian, Diadynamic, TENS, Sinusoidal, Faradic, Galvanic, Interrupted Galvanic, Trabert, and Medi-Wave.[29] The Nu-Tek E-Stim Pro MT1022 will be used to deliver interferential current by generating a beat frequency range of 10-150hz from two medium frequency currents undulating at a base frequency of 4000Hz to 4100Hz.[14] An interferential current will be activated with two electrodes, one placed posteriorly at the upper border of the trapezius and the other anteriorly below the ribs. A beat frequency will be generated at the point of intersection, resulting in relaxation of the smooth muscles, resolution of pain, and mobilization of secretions.[14]

Data analysis

The Statistical Package for Social Sciences (SPSS Inc, Chicago, II) version 26.0 for the Windows package program will be used to analyse data. The results will be summarized using descriptive statistics of mean, standard deviation, frequency, and percentages. Bar charts, pie charts, and histograms will be utilized for pictorial illustration. A multilevel analysis of variance (ANOVA) will be used to compare the outcome variables [body position (45 degrees long sitting and 90 degrees long sitting), pulmonary function variables (FEV1, FVC, FEV1/FVC), asthma control test (ACT), and the standardized Asthma Quality of Life Questionnaire (AQLQ)] among each group, and the dependent t-test will be used to compare the pre and post-test results while the independent t-test will be used to compare the outcome variables across the two groups. The level of significance will be set at p0.05.

Harms

This study carries minimal risks. The procedures are not life-threatening and should not cause any harm or negative effect. The effects may include temporary muscle soreness, increased heart rate, blood pressure, sweating, and dizziness. Necessary care will be taken 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, 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 adequate supervision and safety, the number of participants per group in a day will be limited to a maximum of 3. Arrangements have been made with the Accident and Emergency unit of the hospital where the research will be conducted to provide a standby medical team. However, the University of KwaZulu-Natal insurance scheme on clinical trials fully covers participants in this type of study.

Discussion

The relationship between medication-induced airway reversibility and reversibility obtained through electrophysical modalities is still not well justified. Furthermore, the relationship between the mode of delivery of electrophysical agents and the recovery pattern in bronchial asthma is yet to be fully understood.

A study by Karashurov et al.[30] on programmed electrostimulation of the sinocarotid nerves implanted to 78 patients with bacterial asthma for six years was reported to have prevented the majority of asphyxia attacks, reduced their frequency 2.7-fold, and the need for medications 2.7-3.4-fold.

Aweto et al.[31] in a study of the effect of IFT on the cardiopulmonary parameters of 42 BA patients for six weeks reported a significant improvement in 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), while the control group had significant reductions in pulmonary parameters. There were significant improvements (increases) in the ACT score (p=0.0001) and AQLQ (p=0.001).

Mohammed and Elyazed[32] studied thirty Egyptian children aged 9-15 with BMI 18.5 to 24.9 kg/m², who had asthma. The pre- and post-treatment variables revealed a

significant improvement in pulmonary functions in favor of laser puncture therapy and interferential therapy over diaphragmatic exercise.

Although studies by Aweto et al.,[31] Karashurov et al.,[30] and Mohammed and Elyazed[32] identified the effect of an electrophysical agent in the management of asthma, their findings did not ascertain the possible effect of the medication used by the patients during the procedure. Consequently, it is expected that this study's outcome will further reveal the effect of the electrophysical modality on the symptoms frequently experienced by asthma patients who are on short or long-acting bronchodilator medication.

Finally, it is expected that the findings of this study could serve as guideline for the management of BA with electrophysical agents and would further support the cost-benefit of asthma management in Nigeria and other low-income countries.

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