Effect on Airflow of a Vibrating Mesh Nebulizer Compared to a Jet Nebulizer for Delivery of Bronchodilator Therapy to Acute Severe Asthma Patients in an Emergency Department

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Study Title: Effectiveness of the Aeroneb Compared to a Jet Nebulizer for the Delivery of Bronchodilator Therapy of Acute Severe Asthma

I. Aim and Hypotheses

Acute exacerbations of asthma remain a frequent cause of emergency department (ED) visits and hospital admissions. About one-fifth to one-third of ED patients have poor short term responses to bronchodilator therapy and require admission to the hospital. The initial response to bronchodilator is an important indicator of favorable outcomes. The response to bronchodilator therapy is determined by patient-specific factors but it is also possible that the delivery method of bronchodilator therapy could be playing a role in the response to bronchodilator. Aeroneb system utilizes vibrating mesh technology to generate consistently sized particles with greater lung deposition. It may provide greater benefits in acute asthma exacerbations.

Aim: To study whether Aeroneb nebulizer is more effective than small volume jet nebulizer in delivering bronchodilators in severe asthma exacerbation

Hypothesis: Compared to small volume jet nebulizer, the Aeroneb nebulizer is more effective than a small volume jet nebulizer for delivering bronchodilator therapy in patients with acute severe asthma.

We hypothesize that the mean of PEFR percentage of predicted at 30 minutes after the initial bronchodilator treatment in the Aeroneb group will be 10 points higher than the mean of PEFR percentage of predicted at 30 minutes after the initial bronchodilator treatment in the small volume jet nebulizer group.

II. Background and Rationale

A. **Background**:

Acute exacerbations of asthma remain a frequent cause of emergency department (ED) visits and hospital admissions. About one-fifth to one-third of ED patients have poor short term responses to bronchodilator therapy and require admission to the hospital[1]. The presence of peak expiratory flow rate (PEFR) < 40% is an indicator of severe asthma [2]. In patients with peak flow <50% ~~severe asthma~~, the improvement in PEFR at 30 minutes after the initial bronchodilator treatment is associated with favorable outcomes [3,]. Initial response to bronchodilators may be affected by patient-specific factors such as duration of symptoms and frequency of beta agonist use prior to ED admission. It is also possible that the method of delivering bronchodilator therapy in the ED impacts outcome.

The effectiveness of aerosol delivery systems in this clinical setting depends upon the capacity to generate particles that reach the small airways of the lower respiratory tract, which is the site of disease in acute asthma. Jet nebulizers, which are often used in the ED treatment of asthma, are inexpensive systems that deliver aerosols of varying particle size and have been shown to be unreliable in delivering the bronchodilator drugs[8]. Vibrating mesh technology, which is employed in the Aeroneb system, produces consistently sized respirable particles of 3.4 μm mass mean aerodynamic diameter [6]. This improvement in aerosol delivery technology translates into greater lung particle deposition in both animal studies and in normal humans [7]. Therefore, the Aeroneb nebulizer may be more effective that small volume jet nebulizer in the management of asthma exacerbations.

The Aeroneb Nebulizer System is a portable medical device for single patient use that is intended to aerosolize physician-prescribed solutions for inhalation to patients on and off ventilation.

The Aeroneb Adapter is an accessory specific to the Aeroneb Nebulizer. It facilitates intermittent and

continuous nebulization and optional supply of supplemental oxygen to adult patients in hospital use environments via a mouthpiece or aerosol mask. The Aeroneb Nebulizer System and Adapter are FDA approved devices for nebulizing solutions including bronchodilators (albuterol and ipratropium).

B. **Rationale**:
Aeroneb system has advantages over the small volume nebulizer as mentioned above. These advantages may make it more efficient system to deliver the bronchodilator therapy and to treat the asthma exacerbations more effectively.
This is the first study that we are aware of that will look at the use of Aeroneb system to deliver bronchodilator therapy in asthma exacerbations.
The study will provide novel data to demonstrate whether the use of Aeroneb system to deliver bronchodilator therapy is advantageous to patients with severe asthma exacerbations.
If the hypothesis is proven to be correct this will mean improved patient's outcomes in severe asthma exacerbations and potentially shorter ER stay, reduction in the hospitalization rate and cost of care.

III. Research Plan

A. Experimental design:

This is a prospective, single blinded, parallel, single center, randomized controlled clinical trial (n=68). Upon entry into the study, patients will be randomized to two groups:
Treatment group: All the bronchodilator therapies during the ER visit (albuterol and ipratropium) will be delivered via Aeroneb nebulizer system. The asthma management will be as per the adult asthma protocol in the ER.
Control group: All the bronchodilator therapies (Albuterol and ipratropium) will be delivered via small volume jet nebulizer system, which is currently the standard nebulizer device used in the emergency department at Tufts Medical Center. The asthma management will be as per the adult asthma protocol in the ER.

B. Sample size and statistical analysis(es):

Upon entry into the study patients will be randomized at a 1:1 ratio with permuted block design of 6 to one of the 2 groups. Randomization will be conducted using a computerized randomization scheme and secured in a sealed envelope for allocation.

For a power calculation to determine the sample size, historical data was utilized from prior clinical study that examined the effect of bronchodilator (B2-agonist) treatment on the improvement of the peak flow measurement after 30 minutes of the initial bronchodilator treatment[4]. In this study, the mean PEFR improved from 27% to 39% at 30 minutes after the initial bronchodilator treatment. We hypothesize that mean PEFR of the intervention group at 30 minutes of the bronchodilator therapy will be at least 10 points higher than the control group (i.e. mean PEFR ≥ 49% at 30 minutes of the initial bronchodilator therapy). Group sample sizes of 34 and 34 is required to achieve a power > 80% to reject the null hypothesis of equal means when the groups mean difference is 10.0 with a standard deviation for both groups of 14.4 and with a significance level (alpha) of 0.050 using a two-sided two-sample equal-variance t-test.

Taking into consideration the screen failures the disqualification and drop-outs, we are anticipating enrolling around 110 patients in order to have 68 patients who will complete the study objectives.

For the statistical analysis treatment evaluations will be performed on the principle of intention to treat (ITT) using the data collected from all randomized participants who completed the study procedures including the two parts of the informed consent form (ICF). Demographics and baseline characteristics of patients will be summarized for each group. Continuous variables will be reported as mean ± standard deviation, with minimum, median, and maximum values.

Categorical variables will be reported as n and %. All statistical testing will be two-sided with alpha=0.05.
For the primary outcome, mean PEFR at 30 minutes post-bronchodilator treatment, analysis of covariance (ANCOVA) with adjustment for baseline PEFR will be utilized.
ANCOVAs with adjustment for baseline values, and incorporating repeated measures where appropriate, will be utilized for the following secondary outcomes: absolute value of PEFR (L/Min) at 30 minutes, PEFR percentage of predicted at 60 minutes and 180 minutes, FEV1 percentage of predicted as well as absolute FEV1 (L/Sec) at 30 minutes, 60 minutes and 180 minutes, Borg dyspnea score at 30 minutes, 60 minutes and 180 minutes, accessory muscle use score at 30 minutes, 60 minutes and 180 minutes, and heart rate at 30 minutes, 60 minutes and 180 minutes.

The outcomes which are measured at different time points will be averaged for each group and plotted to visualize the trajectory of those outcomes.

Differences in length of stay (hours) in the ER and the total doses of albuterol and ipratropium will be compared using T-tests or non-parametric methods (e.g., Mann-Whitney test) as depending on the distribution of the data. The proportion of patients in each group who require hospitalization will be compared using a Chi-square test.

C. Subject Characteristics

1. Subject criteria:
   The study will be conducted at the emergency department at Tufts Medical Center.

   a) Inclusion criteria:
   -Acute asthma exacerbations presenting to the emergency room
   -Peak expiratory flow rate at presentation <50%~~40%~~ of predicted
   -Enrolment within 90 minutes of the arrival to the ER
   -Age 18-55 years old

   b) Exclusion criteria:

   -History of chronic obstructive pulmonary disease
   -Clinical evidence to suggest a non-asthmatic cause of bronchospasm as determined by the treating physician
   -Clinical evidence of acute coronary syndrome
   -Respiratory failure requiring mechanical ventilation either invasive or non-invasive
   -Tachyarrhythmia other than sinus
   -Agitated or uncooperative
   -Inability to provide informed consent

   c) Withdrawal/Termination criteria:
   The subject will be withdrawn from the study if any of the following:
   -The subject develops respiratory failure requiring mechanical ventilation (invasive or non-invasive)
   -The subject becomes unable to perform peak flow measurement at the pre-specified time points
   -The treating physician determines that it is not clinically advisable to continue with the study.
   -The subject opts to decline to sign the second part of the informed consent form. In this case, the data collected may not be used for the study.

A study participant will have the right to withdraw from the study at any point of the study.

A study participant may not participate in another research study while participating in this study.

D. **Risk/benefit assessment**:

1. **Physical risk**:
   Patients in both the intervention and control arms are at risk for developing respiratory failure as a result of severe asthma exacerbation and it is unknown if the risk of such complications is higher in any arm. It is possible that the Aeroneb group patient my experience more frequent side effects related to potentially more albuterol and ipratropium delivery and those side effects may include tremor and arrhythmias.

2. **Psychological risk**:
   There is no increased psychological risk to the study participants from the study for either arm

3. **Social risk**:
   There is no increased social risk to the study participants from the study for either arm

4. **Economic risk**
   There is no increased economic risk to the study participants from the study for either arm.

5. **Benefit of participating in the study**:
   a) Patients randomized to the intervention group may benefit from the increased bronchodilator delivery by Aeroneb system

   b) Future asthma patients may benefit from this study if Aeroneb system is proven to be more effective in treating severe asthma exacerbation

E. **Specific methods and techniques used throughout the study**:

1. **Laboratory tests**:
   No additional laboratory test is required in the study.

2. **Study Procedures**:
   -The patient presenting with acute severe asthma exacerbations to the emergency room will be screened by the PI, co-investigator or research coordinator to determine their eligibility based on the inclusion and exclusion criteria.

   -The required treatment must not be delayed for a research related reason and patients will still be eligible for enrollment after receiving the treatment as long as their PEFR<50%~~40%~~ of predicted and the enrollment occur within 90 minutes of the ER arrival time.

   - The initial part of the consenting process will cover the essential elements of the informed consent in a concise manner to ensure timely process

   -Eligible patient will be randomized using the method mentioned above to either the intervention arm or the control arm. The randomization should take place within 90 minutes of the ER arrival, however, every effort will be made to enroll the patient as soon as possible; patients will be enrolled as long as their PEFR is less than 50% ~~40%~~ of predicted regardless of the number of bronchodilator treatment they received prior to the randomization.

-The assignment will be blinded to the recording investigator and the treating physician but not to the patient or the nurse or respiratory therapist who is administering the nebulization. In order to avoid any delay in administering the treatments, the sets of Aeroneb nebulizer and small volume jet nebulizer will be stored in identical boxes and will be readily available in the ER.
In order to blind the treating physician and the recording investigator, a sign "treatment in progress" will be displayed at the outdoor of the ER room when the patient is getting the bronchodilator treatment. The nebulizer devices will be placed in the box between the bronchodilator treatment sessions. The physician and the recording investigator will be asked if possible to see the patients only when the sign is taken off the outdoor.

-Once assigned, all the bronchodilator treatments in the ER will be administered using the nebulizer device assigned to that patient.

-The Peak flow and FEV1 will be measured using Spirometer (micro I). Both values will be obtained through the same exhalation maneuver.

-Patient will be treated and managed according to the asthma ER adult protocol or as directed by the ER physician who is in charge of patient's care

-After the study procedures have been performed and the subject is determined to be in stable condition and have the capacity to make medical decisions, the investigator will approach the subject again and review all the elements of the ICF again with the subject. The collected data will be used only if the subject signs both parts of the informed consent.

-Within two weeks of the subject participation, the research team will attempt to conduct a phone interview with the subject to obtain their feedback on the study procedures and mainly on the informed consent process. The phone interview questionnaire is included in the supplement

-The research team will report to the IRB the progress of the study including the consent process after enrolling the first 10 patients.

3. **Subject Timeline**:
During the study several data will be recorded, most of them are standard hospital recording, which are conducted frequently. These data will be collected at baseline and at multiple points after the initial bronchodilator therapy (at 30±10 minutes, 60±10 minutes, at 180 ± 10 minutes and upon disposition from the ER). All recorded data are obtained through noninvasive measurements. No samples of any body component will be taken that it not part of the normal standard hospital protocols.
The results that will be collected are summarized in table 1.

3.1 Baseline readings
Once patient is enrolled in the study, baseline characteristics such as gender, age, height, weight, BMI and race will be collected, as well as smoking history and past medical history including prior ER visits for asthma exacerbations, prior intubation for asthma exacerbation and the use of any respiratory therapy at home will be investigated and data will be collected. Clinical data such as respiratory and heart rate, blood pressure, O2 sat and FIO2 will be recorded. Peak flow and FEV1 will be measured by spirometer micro I during the same exhalation maneuver and they will be recorded.

The dyspnea will be graded with Borg score[9] as outlined in figure 1 and the accessory respiratory muscle[10] use will be graded as outlined in figure 2. Cough will be recorded as present or absent.

0 1 2 3 4 5 6 7 8 9 10	No difficulty Moderately hard Hard Very hard Very, very hard	Score 0 – 6: Moderate respiratory distress Score 7 – 10: Severe respiratory distress

Fig. 1 Borg Scale to assess Dyspnea

0	No visible tonic or phasic use of neck muscles
1	Neck muscles taut but with no respiratory modulation (i.e., tonic activity)
2	Mild respiratory modulation in neck muscle contraction
3	Moderate phasic activity (no supraclavicular or intercostal indrawing)
4	Vigorous phasic activity with indrawing
5	Vigorous phasic activity with abdominal paradox

Fig. 2 Accessory muscle use

Baseline readings upon enrolment	**Routine test**	**Study test**
Gender	•	
Age	•	
Height		•
Weight		•
BMI		•
Race		•
Smoking history (Number of pack years)	•	
Respiratory medications (home medication list)	•	
History of prior intubation for asthma exacerbation		•
Number of hospitalization for asthma exacerbations in the last year		•
Bronchodilator treatment in the EMT		•
Respiratory rate	•	
Heart rate	•	
Systolic/diastolic blood pressure	•	
O2 sat	•	
FIO2	•	
Dyspnea score		•
Cough		•
Respiratory accessory muscle use		•

Peak flow (percentage from predicted)	•	
Peak flow (L/Min)	•	
FEV1 (percent of predicted)		•
FEV1 (Liter)		•
At (30±10) minutes after nebulizer treatment		
Respiratory rate	•	
Heart rate	•	
Systolic/diastolic blood pressure	•	
O2 sat	•	
FIO2	•	
Dyspnea score		•
Cough		•
Respiratory accessory muscle use		•
Peak flow (percentage from predicted)	•	
Peak flow (L/Min)	•	
FEV1 (percent of predicted)		•
FEV1 (Liter)		•
At (60±10) minutes after nebulizer treatment		
Respiratory rate	•	
Heart rate	•	
Systolic/diastolic blood pressure	•	
O2 sat	•	
FIO2	•	
Dyspnea score		•
Cough		•
Respiratory accessory muscle use		•
Peak flow (percentage from predicted)	•	
Peak flow (L/Min)	•	
FEV1 (percent of predicted)		•
FEV1 (Liter)		•
At (180±10) minutes after nebulizer treatment		
Respiratory rate	•	
Heart rate	•	
Systolic/diastolic blood pressure	•	
O2 sat	•	
FIO2	•	
Dyspnea score		•
Cough		•
Respiratory accessory muscle use		•
Peak flow (percentage from predicted)	•	
Peak flow (L/Min)	•	
FEV1 (percent of predicted)		•
FEV1 (Liter)		•
Upon disposition from the ER		
Disposition (Home, floor or ICU)		•
Length of stay in the ER (from ER arrival time to disposition order placement time)		•
Intubation in the ER (Yes or No)		•
Need for NIV ventilation		•
Number of total albuterol treatment during the ER stay		•
Total accumulative dose of albuterol during the ER stay		•
Number of total ipratropium treatment during the ER stay		•
Total accumulative dose of ipratropium during the ER stay		•
Total dose of steroid (prednisone equivalent in mg)		•

3.2 During the study
The following variables (respiratory rate, heart rate, BP, O2 sat, FIO2, Dyspnea Borg score, cough, respiratory accessory muscle, peak flow and FEV1) will be recorded at the following time points after initial bronchodilator therapy (30±10 minutes, 60±10 minutes, 180±10 minutes and at the disposition from the ER). If the patient is discharged from the ER within 3 hours from the initial bronchodilator therapy then the data collection at 3 hours mark will be waived.

3.3 Upon disposition from the ER
The following data will be collected: the disposition location (home, floor or ICU), length of stay in the ER (from ER arrival time to the disposition order placement time), intubation in the ER, need for NIV ventilation, number and total doses of albuterol treatments in the ER and number and total doses of ipratropium in the ER.

F. Assessment of Subject Safety and Development of a Data and Safety Monitoring Plan

1. Definition of Serious Adverse Event (SAE) and Adverse Event (AE) for this study:
For the purposes of this study a SAE is a serious adverse event that is life-threatening or results in death, hospitalization or prolonged hospitalization, significant disability/incapacitation, congenital anomaly or birth defects, or may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other listed outcomes. A SAE does not necessarily have to have a causal relationship with the study treatment. SAE may not be uncommon in the study due to the acute nature of patients presenting with severe asthma exacerbations that may be enrolled into the study. The study will be conducted in the emergency room, which provides a high level of monitoring and is capable of managing SAE in this acute patient group. It is possible that the Aeroneb group patients may experience more frequent side effects related to potentially more albuterol and ipratropium delivery and those side effects may include arrhythmia and tremor. Those side effects will be monitored closely and patients will be placed on continuous cardiac monitoring during the ER visit to capture any arrhythmia.

2. Reporting timeframe for SAEs and AEs:
SAEs will be reported to the IRB within five business days of the event occurring. The investigators will record and track any SAE or AE that might occur during the study. If a disproportionate number of events occur in either of the groups, then the study will be stopped. A "disproportionate number" is defined as one showing a statistically significant difference in SAEs and AEs occurrence after the recruitment of half the sample size (34 patients).

3. Accountability procedures as they relate to drugs, devices, and data:
The Principal Investigator Dr. Nicholas Hill and the research team member Haval Chweich, MD will be accountable for the study and interface with Aerogen, the study sponsor.

4. Data and Safety Monitoring Plan:
We do not anticipate serious complications attributable to the device, but will monitor patients for potential adverse effects such as discomfort or cough. Any serious adverse events that occur during use are more likely due to the underlying disease than the device itself, but will be reported promptly to the IRB by the investigators per the reporting timeframes described above.

The Research team will report to the IRB the process of the informed consent after enrolling 10 patients (if this occurs before the study continuing review).

G. Subject Participation

1. **Recruitment**:
   Patients presenting with severe asthma exacerbation to Tufts Emergency Room will be recruited on to the study. Patients who meet any exclusion criteria will not be screened for possible enrollment. Patients will be approached at their bedside by the PI, co-investigator or research coordinator. No advertisements will be used.

2. **Registration**:
   Patients, that can potentially take part in the study, will be assessed by the PI or the co-investigator for their ability to fulfill the eligibility criteria and meet the exclusion criteria, as listed above.

3. **Screening Interview/questionnaire**: Not applicable

4. **Transportation**: Not applicable

5. **Informed consent process and timing of obtaining of consent**:

   The participant must have the full mental capacity to provide the consent. The consenting process will be two steps process, each step will involve face-to-face meeting with one of the study investigators at bedside in the ER room

   1-The first part of the consent will cover all the essential elements of the informed consent. Given the acuity of the medical condition, it is anticipated that the total amount of time given to this step of the informed consent will be no longer than10 minutes. No study related procedures will be conducted until this step of the informed consent is signed off by the subject. Permission will also be obtained from the primary provider for the participation of the patient in the study before a discussion with the patient regarding consent occurs.

   The patient will be provided with a copy of the consent form to read and all questions will be answered prior to their signing the first part of the consent. In order to determine the subject's understanding of the study, the subject will be asked to describe his understanding of the study back to the investigator obtaining the consent. The subject will be encouraged to call the investigator with any questions. No study procedures will be performed other than chart review to determine eligibility prior to obtaining informed consent. The investigators recognize the potential vulnerability of the patient in this setting (i.e., being acutely ill) and thus will terminate the consent discussion in any situation where the patient appears to be uncomfortable or apprehensive about providing consent for participation in the study.

   2-The second part of the informed consent will take place after the study procedures have been performed and the patient condition has been stabilized. The investigator will meet face-to-face with the subject and review the ICF again with the subject in more detailed manner. The subject will be asked to sign a separate section of the ICF re-consenting that they agreed to participate in the study.

   Subjects who do not sign the second part of the ICF will be withdrawn from the study and data collected on those subjects may not be used for the study.

   It will be explained that if they refuse to be in the study it will not affect their care or medical treatment outside of the study.

If non-English speaking persons will be enrolled, state the informed consent process for enrolling the subjects, including who will conduct the consent interview, use of interpreters, translated documents, etc.: Only English speaking persons will be enrolled as it will be difficult to communicate with non-English speaking patients about the PEFR maneuvers and the dyspnea scoring. Timely assistance from the interpreter service personnel may not be feasible given the acuity of the cases. Interpreter phone will not be sufficient as it would be hard to demonstrate the maneuver though phone interpretation.

6. **Location where study will be performed**:
   The study will be performed at the Emergency Room at Tufts Medical Centre. Study records will be kept in a locked filing room.

7. **Personnel who will conduct the study, including**:
   a. **Present during study procedure(s) and their proximity during the study**:
      The PI, co-investigator or the research coordinator will oversee the study procedure. Normal clinical care of patients will be performed by the patient's assigned nurse, respiratory therapist and doctor in the emergency room.

   b. **Primary responsibility for the following activities**:

      i. **Obtaining informed consent**:
      The principal investigator and the co-investigators will be responsible for obtaining the informed consent from the patients.

      ii. **Providing on-going information to the study sponsor and the IRB**:

      Dr. Nicholas Hill and Dr. Haval Chweich will be responsible for providing on-going information to the study sponsor and the IRB.

      iii. **Maintaining participant's research records**:

      Dr. Chweich will be responsible for maintaining the participant's research records. The records will be maintained up to 7 years as per the IRB policy.

8. **Subject fees**:
   There will be no fees paid to subjects for the study. It is part of their emergency visit care treatment

9. **Study results**:

   Study results will not be given to patients.

10. **Procedures to protect subject confidentiality**:

    Patient confidentiality will be maintained under normal emergency room procedures which are in compliance with the HIPPA rules.

11. **Confidentiality**:

    a. **Certificate of Confidentiality**:

    Certificate of confidentiality is not relevant for this research study

    b. **How data will be coded, recorded, and stored to protect confidentiality**:

    Study participants will be allocated a study number, which will be used as a study identifier on all study forms. The study data and records will be kept locked.

    c. **Parties who will have access to the date, including the key to the identity code**:

    The study PI, Dr. Nicholas Hill and research team member Dr. Haval Chweich will have access to the study data and the identity codes.

    d. Parties who will have access to research records:

    The study PI, Dr. Nicholas Hill and research team member Dr. Haval Chweich will have access to the study data.

12. **Collaboration**:

    This is not a collaborative study.

13. **Alternatives**:

    Patients not participating in this study will receive usual ER care as determined by the ER.

14. **How new information will be conveyed to the study subject and how it will be documented**:

    In the event new information is discovered about the study, a letter describing the new information will be mailed to the contact address for each subject who participated in the study.

15. **Payment, including a prorated plan for payment**:

    There will be no payment for participants. The study is part of Emergency Room care that a patient is receiving as part of their visit.

16. **Payment for a research-related injury**:

Aerogen (the study sponsor) agrees to reimburse the site for the costs of the care and treatment of any illness or injury to a subject directly resulting from his or her participation in the Study; provided, however, that such illness or injury is not a result of the negligence or misconduct of Site, Principal Investigator or any of Site's employees.

I. **Outcomes**:

The expected outcome of the study is that the Aeroneb system arm will have higher PEFR after treatment with bronchodilator as compared with the small volume jet nebulizer arm. It is also expected that the improvement in the PEFR in the Aeroneb arm will translate in improvement in the respiratory outcomes like dyspnea, accessory muscle use, length of ER stay and need for hospitalization.

Primary outcome: the mean of PEFR percentage of predicted at 30 minutes after the initial bronchodilator treatment in the Aeroneb group will be 10 points higher than the mean of PEFR percentage of predicted at 30 minutes after the initial bronchodilator treatment in the small volume jet nebulizer group.

Secondary outcomes:

- Change in the absolute value of PEFR (L/minute) at 30 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-Change in the PEFR percentage of predicted at 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-Change in the FEV1 percentage of predicted at 30 minutes, 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-Change in the absolute FEV1 (L/Second) at 30 minutes, 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-The Borg dyspnea score at 30 minutes, 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-The accessory muscle use score at 30 minutes, 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-The heart rate at 30 minutes, 60 minutes and 180 minutes after the initial bronchodilator treatment in the Aeroneb group compared to the small volume jet nebulizer group
-Length of stay in the ER
-Percentage of patients requiring hospitalization
-The total dose of albuterol used in each group
-The total dose of ipratropium used in each group

J. **Tissue banking considerations**: Not applicable

VULNERABLE POPULATIONS:

The study will recruit patients with severe acute asthma exacerbations. These patients are vulnerable due to the severity of their illness. The risk of providing this alternative method of bronchodilator delivery is not greater than minimal to the patient as this device has been FDA approved for the delivery of bronchodilator.

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