Effectiveness of Salbutamol Administration by Nebulizer versus Metered Dose Inhaler in Acute Asthma in Children in Suez Canal University Hospital Emergency Department: A Randomized Control Trial

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Study Protocol

Study design

Single-blinded randomized control trial.

Study location

Pediatric Emergency Department in Suez Canal University Hospital.

Study population

This study includes patients presenting with an acute exacerbation of asthma at the Pediatric Emergency Department in Suez Canal University Hospital.

Inclusion criteria:

- Children ranging from 2 – 14 years old.
- Both genders will be included.
- Patients with an acute exacerbation of asthma who were previously diagnosed with asthma.

Exclusion criteria:

- Patients with arrhythmia and cardiac diseases.
- Patients with thyroid diseases.
- Patients with bronchiolitis or pneumonia.
- Patients with status asthmaticus requiring immediate pediatric intensive care unit hospitalization.

Sampling

All children fulfilling the inclusion criteria will be included consecutively until the calculated sample size had been reached.

Sample size

The sample size was calculated using the following formula:

$$n = 2\left[\frac{\left(Z_{\alpha/2} + Z_{\beta}\right) * \sigma}{\mu_1 - \mu_2}\right]^2$$

Where:

n= sample size

$\mathbf{Z_{\alpha/2}}$ = 1.96 (The critical value that divides the central 95% of the Z distribution from the 5% in the tail)

$\mathbf{Z_{\beta}}$ = 0.84 (The critical value that separates the lower 20% of the Z distribution from the upper 80%)

σ = the estimate of the standard deviation = 1.5

$\mathbf{\mu_1}$= mean in the nebulizer group = 4.4

$\mathbf{\mu_2}$ = mean in the metered-dose inhaler group = 3.3

Therefore, by calculation, the sample size was equal to 30 cases per group, giving a total sample size of 60 cases.

Methods of data collection

Infants and children known to have asthma coming to the Pediatric Emergency Department of Suez Canal University Hospital and fulfilling the inclusion criteria will be assessed according to the following clinical respiratory score:

Assess	Score 0	Score 1	Score 2
Respiratory Rate	<2 months <50 2-12 months <40 1-5 years <30 >5 years <20	<2 months 50-60 2-12 months 40-50 1-5 years 30-40 >5 years 20-30	<2 months >60 2-12 months >50 1-5 years >40 >5 years >30
Auscultation	Good air movement, expiratory scattered wheezing or loose rales/crackles	Depressed air movement, inspiratory and expiratory wheezes or rales/crackles	Diminished or absent breath sounds, severe wheezing, or rales/ crackles or marked prolonged expiration
Use of Accessory Muscles	Mild to no use of accessory muscles, mild to no retractions **OR** nasal flaring on inspiration	Moderate intercostals retractions, mild to moderate use of accessory muscles, nasal flaring	Severe intercostals and substernal retractions, nasal flaring
Mental Status	Normal to mildly irritable	Irritable, agitated, restless	Lethargic
Room Air SpO2	> 95%	90-95%	<90%
Color	Normal	Pale to normal	Cyanotic, dusky

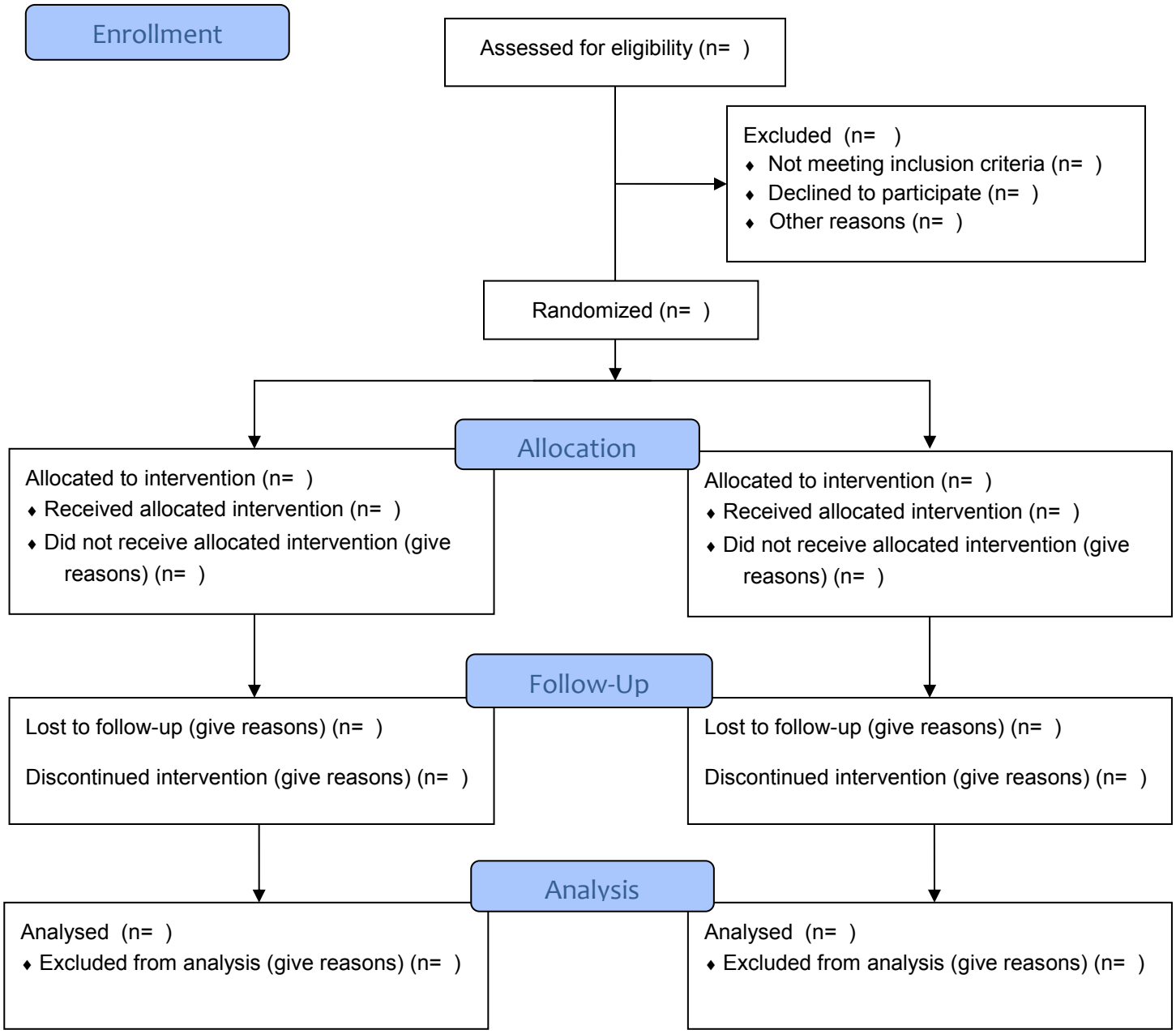
(Mild 0-3 moderate 4-7 severe 8-12)

The target population are patients who presented with moderate to severe wheezing (score 4-12).

Randomization will take place through a box that contained 60 thick envelopes, in which either nebulizer or spacer are written on 30 each, and each time an envelope is picked out by the assistant nurse in the emergency room to avoid any selection bias till our sample is fulfilled.

The assessment of the respiratory score before and after the treatment will be performed by an independent pediatrician resident who isn`t involved in the decision-making and randomization of treatment. This physician will be asked to assess initially and then reassess after the equipment had been removed to avoid any bias.

CONSORT Flow Diagram to be filled in during the study:



Dosage and administration:

The nebulizer group will receive salbutamol aerosol solution (Farcolin® 0.121 gm/20ml solution) in a dose of 0.15 mg/kg weight, up to a maximum of 5 mg in 3.5 ml of normal saline solution. Aerosol is generated by jet nebulizers (Afnor oxygen flow meter) powered by oxygen and delivered via a face mask till the whole solution is vaporized every 20 min during the first hour (a maximum of three nebulization /hr). A flow rate of 7 L/min is used. (Liu, Covar, and Leung, 2016)

The metered dose inhaler with spacer group will receive two puffs of salbutamol (Ventolin® evohaler 100 mcg/puff) every 10 min 5 times over 1 hr with a maximum of 10 puffs/hr, using a spacer device with a face mask (Smart care chamber 500ml volume). Following each puff, the children will take 7 breaths from the spacer device held in place. (Rubilar, Castro-Rodriguez and Girardi, 2000)

Assessment:

Patients will be reassessed after each treatment, if improved we can stop treatment and follow up after 2 hrs. Score <4 is considered a success while score>4 is failure of therapy. If not improved, we continue till the maximum number of treatment mentioned above.

Patients will be compared together according to the following characteristics: duration of treatment (preparation and delivery time), clinical outcome, patient satisfaction after treatment and hospitalization rate.

Each patient will have a form: Page 1 is an informed consent to be signed before randomization of treatment. Page 2 includes the following items that will be filled by parents after receiving the treatment;

1-personal data (name, age, address and telephone number). In addition, the researcher's phone number will be accessible to the patients.

2- Medical history (other illnesses, medications and degree of asthma either intermittent or persistent)

3-Clinical assessment (clinical respiratory score before and after treatment)

4-Patient satisfaction with given modality on a Likert scale from 1-5. This will be asked by the blinded assessor and included questions regarding:

- Comfort with modality used
- Duration of modality used
- Ease of administration
- Confidence in repeating treatment on their own at home if required

Statistical analysis of the data (Kotz et al, 2006)

Data will be fed to the computer and analyzed using IBM SPSS software package version 20.0**. (**Armonk, NY: IBM Corp**)** (Kirkpatrick, Feeney, 2013). Qualitative data will be described using number and percent. The Kolmogorov-Smirnov test is used to verify the normality of distribution. Quantitative data will be described using range (minimum and maximum), mean, standard deviation and median. Significance of the obtained results will be judged at the 5% level.

The used tests will be

1 - Chi-square test

For categorical variables, to compare between different groups (gender, address, satisfaction, admission)

2 - Fisher's Exact or Monte Carlo correction

Correction for chi-square when more than 20% of the cells have expected count less than 5

3 - Student t-test

For normally distributed quantitative variables, to compare between two studied groups (delivery and preparation time)

4 - Mann Whitney test

For abnormally distributed quantitative variables, to compare between two studied groups (age, percentage of improvement of clinical respiratory score and satisfaction).

Ethical Considerations

- An informed consent will be obtained from legal guardian of all patients included in this study after full explanation of the aim of the study, benefits and hazards of the procedures.
- Standardized protocols are used for evaluation.
- The legal guardians have the right to withdraw without affecting the medical care expected to be offered to them.
- Confidentiality of all data and test results of all the study population will be preserved.
- The new modality introduced is a well-established form of administration and is not expected to cause any side effects that would not happen with the standard mode of administration (nebulizer).