



Original Contribution

Comparison of bronchodilator administration with vibrating mesh nebulizer and standard jet nebulizer in the emergency department

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ABSTRACT

Introduction: Projects comparing bronchodilator response by aerosol devices in the ED are limited. Evidence suggests that the vibrating mesh nebulizer (VMN) provides 5-fold greater aerosol delivery to the lung as compared to a jet nebulizer (JN). The aim of this project was to evaluate a new nebulizer deployed in an Emergency Department. **Methods:** A quality improvement evaluation using a prospectively identified data set from the electronic medical record comparing all ED patients receiving aerosolized bronchodilators with the JN during September 2015 to those receiving aerosolized bronchodilators with the VMN during October 2015.

Results: 1594 records were extracted, 879 patients received bronchodilators via JN and 715 patients via the VMN. Admission rates in the VMN group were 28.1% and in the JN group at 41.4%. The total albuterol dose administered was significantly lower in the VMN group compared to the JN ($p < 0.001$). No patient in the VMN group required >5 mg albuterol to control symptoms (85% of the VMN group received only 2.5 mg) whereas dosing in the JN group was higher in some patients (with 47% receiving only 2.5 mg). The use of VMN was also associated with a 13% (37 min) reduction in median length of stay in the ED.

Conclusions: The VMN was associated with fewer admissions to the hospital, shorter length of stay in the ED and a reduction in albuterol dose. The device type was a predictor of discharge, disposition and amount of drug used. Randomized controlled studies are needed to corroborate these findings.

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1. Introduction

Asthma and chronic obstructive pulmonary disease (COPD) are among the top twenty diagnoses associated with ED visits with albuterol being one of the most commonly administered medications and nebulizer therapy accounting for approximately 4 million ED procedures annually in the US [2].

Historically, inhaled bronchodilators have been administered with jet nebulizers (JN) ranging in lung delivery efficiency of between 5 and 12% inhaled dose [3,4,6]. Advancements in aerosol delivery devices have improved aerosol delivery to the lung. The vibrating mesh nebulizer with the valve-adaptor (VMN) (Aerogen Solo with Ultra, Aerogen Ltd., Ireland) has been reported in simulated breathing models to provide greater aerosol inhaled mass with 2 L/min oxygen flow via

mouthpiece (VMN; $15.42 \pm 1.4\%$) compared to a JN with 2 L/min oxygen flow ($7.7 \pm 0.62\%$) [5].

Scintigraphy data also demonstrates greater drug delivery efficiency. In a crossover-study of 6 healthy adults comparing radio-tagged aerosol deposition using VMN (Aerogen Solo with Ultra, Aerogen, Galway, Ireland) and JN, the VMN resulted in 5-fold greater aerosol delivered to the lungs than JN, expressed as a percentage of the nominal dose of radio-tagged solution placed in the device ($22.8\% \pm 9.83$, $4.5\% \pm 1.35$), respectively [1].

Based on these studies demonstrating greater efficiency of drug delivery, we expected that a higher dose of bronchodilator would be delivered in patients with acute respiratory distress with the VMN [1,5,7]. This project was designed to help evaluate a new nebulizer that the hospital was considering expanding the use of. Often hospital equipment choices have little input from the clinicians. The hospital had been using vibrating mesh nebulizers on the ventilators for many years and was evaluating a change in the nebulizers used for acute care. The aim

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of the project was to determine whether the type of bronchodilator delivery device would have an effect on any patient related factors.

2. Methods

This was a quality improvement project assessing the introduction of a new nebulizer into the Emergency Department. The VMN was substituted for JN for an evaluation period of 30 days for all patients receiving inhaled bronchodilator therapy in the ED. This project was reviewed by the IRB waiving as an exempt quality assurance project.

Respiratory therapy (RT) staff were trained in the use of the handheld VMN. The RT was responsible for administering all aerosol treatments and recording the data in the patient EMR (Cerner, Firstnet™) per hospital protocol.

Prior to initiation of the project, a data set from Cerner, Firstnet™, was identified for the evaluation of the device. At the completion of the 30-day period, the predetermined data set which included age, disposition, chief complaint, total amount of albuterol delivered, final diagnosis and length of stay in the ED, was retrieved from the clinical EMR of all ED patients receiving aerosol bronchodilator treatments with the standard of practice JN in September 2015 and with the VMN in October 2015. Only the prospectively identified data set was utilized for evaluation, there was no ad-hoc retrospective chart review. This data extraction plan was designed to reduce bias inherent to many projects that use existing data. The population included all patients (adult and pediatric) who presented to the ED and received bronchodilator aerosol therapy. Protected Health Information (PHI) was not included in the data extracted.

2.1. Nebulizers utilized

A jet nebulizer (JN; VixOne, Westmed, Inc., Tucson, AZ) and a vibrating mesh nebulizer with a valved-adaptor (VMN; Aerogen Solo with Ultra, Aerogen Ltd., Galway, Ireland) were the two devices compared. The JN was operated with oxygen from a 50-psi source at 8 L/min with a mouthpiece or an aerosol mask. Selection of mask or mouthpiece was RT driven and based upon the ability of the patient to co-ordinate a proper mouthpiece treatment.

For patients using VMN and the valved-adaptor, a mouthpiece treatment with no added flow was the method of choice, with an option for use of a valved-mask for those patients who were too young or unable to coordinate a mouthpiece treatment. Minimal added oxygen flow was used with the valved-mask as per device label (pediatric; minimum/maximum flow 1 L/min/2 L/min, adult; minimum/maximum flow 2 L/min/6 L/min).

2.2. Medication

Patients admitted to the ED were administered an initial dose of albuterol sulfate (0.083% 2.5 mg/3 mL solution) as prescribed by the attending ED physician. The dose was titrated up based on physician order. Patients were only administered the higher doses if felt to be clinically indicated by the treating physician.

2.3. Statistical analysis

Statistical analysis included descriptive statistics, regression testing, Pearson chi square tests of independence and Mann-Whitney analysis. ($p < 0.05$) was considered significant using SPSS v22, IBM, Chicago, IL. Multinomial logistic regression was used to predict the effect the device would have on disposition, controlling for both diagnosis and age. Pearson chi-square test of independence was used between group and total albuterol dose (z-proportion tests comparing column proportions) to compare the populations, which were not normally distributed for total dose. The Mann-Whitney test was used to compare median LOS in the ED for each device.

3. Results

A total of 1594 patient consecutive encounters were extracted (879 JN and 715 VMN). Statistical review of populations showed similar demographic characteristics across both groups (Table 1) although the mean age was slightly lower in the VMN group. Patient disposition data are presented in Table 2. Admission rate for the VMN group was 32% lower (a 13.3 percentage point difference) than the JN group admission rate (Fig. 1), coinciding with a JN discharge rate that was 30% higher (a 13.1 percentage point difference) compared to the VMN discharge rate (Fig. 2). Furthermore, the total albuterol dose administered was significantly lower in the VMN group ($p < 0.001$) (Table 3). No patient in the VMN group required >5 mg albuterol to control symptoms (85% of the VMN group received only 2.5 mg) (Fig. 3). A small number of patients in the JN group (<1%) required a continuous infusion of inhaled albuterol to control their symptoms (400 mg of albuterol in an infusion bag prepared and issued by pharmacy and connected to a JN and titrated until symptomatic relief). Unfortunately, for these patients the portion of the total dose delivered was not recorded in the EMR and these patients were excluded as outliers from the analysis in Table 3.

Controlling for age and diagnosis, the VMN group was 1.5 times more likely to be discharged than the JN group (OR = 1.5, $p < 0.001$), respectively and the JN group was 1.7 times more likely to be admitted than the VMN group (OR = 1.77, $p < 0.001$). (Table 4). Patients older than 19 treated with the VMN had significantly lower admission rates; patients younger than 19 years of age showed no significant difference in admission rates (Table 2, Fig. 4). A breakdown of the patients 65 years and older showed a 76% admission rate for the JN group as compared to a 61% admission rate for the VMN group (Fig. 6). The reduction of admission rates associated with the VMN in the 65 years and older group was 15.5% (−0.154912 to be exact) with a 95% confidence interval of 4.5% to 26.5% and a (p -value = 0.006).

The median length of stay in the ED was 37 min shorter (13% reduction) with the VMN group (4 h and 10 min) than with the JN group (4 h 47 min; ($p = 0.0001$)) (Fig. 5). Length of stay was defined by electronic health record time points, specifically the initial quick registration time to the time of discharge from the emergency department.

Heart rate post treatment decreased in the JN group and increased post treatment in the VMN group. There was no difference in respiratory rates pre and post treatment in the JN or VMN group. (Table 5).

4. Discussion

Patients in acute respiratory distress from reversible bronchoconstriction remain a serious challenge in the emergency medicine setting. The recent development of VMN technology has been well received in the ICU setting with widespread use, but little has been documented regarding potential impact of such technology in the emergency department.

Prior to our project no clinical outcome comparisons between VMN and JN had been reported. However, scintigraphy data had suggested greater efficiency of drug delivery associated with the VMN as compared to JN [1,7].

Table 1
Baseline demographics of patients who received either JN or VMN nebulization.

| | JN | VMN | P value |
|----------------------------------|----------------|----------------|---------|
| N | 879 | 715 | |
| Gender | | | 0.337 |
| Female sex No. (%) | (51.8) | (54) | |
| Male sex No. (%) | (48.2) | (46) | |
| Age (mean(SD)) | 42.23 (25.75) | 36.86 (25.04) | <0.001 |
| Pre Heart Rate (mean (SD)) | 102.43 (26.60) | 100.37 (25.60) | <0.001 |
| Pre Respiratory Rate (mean (SD)) | 19.25 (6.30) | 22.88 (6.51) | <0.001 |

Pearson Chi-square and independent sample-*t*-test.

Table 2
Frequencies and percentages for patient disposition by intervention group stratified by age.

| | Group | | | | | | | | χ^2 |
|------------------------------|--------------|------|--------|------|---------------|------|--------|------|------------|
| | JN (N = 879) | | | | VMN (N = 715) | | | | |
| | n | % | 95% CI | | n | % | 95% CI | | |
| | | | LL | UL | | | LL | UL | |
| Ages 0 to 2 years | | | | | | | | | |
| Admit - ER | 7 | 14.9 | 4.3 | 25.5 | 6 | 13.0 | 2.9 | 23.2 | NS |
| Discharge | 35 | 74.5 | 61.5 | 87.4 | 34 | 73.9 | 60.7 | 87.1 | NS |
| OBS - PEDS | 5 | 10.6 | 1.5 | 19.8 | 6 | 13.0 | 2.9 | 23.2 | NS |
| Ages 3 to 18 years | | | | | | | | | |
| Admit - ER | 20 | 12.7 | 7.4 | 17.9 | 20 | 12.1 | 7.1 | 17.2 | NS |
| Discharge | 121 | 76.6 | 69.9 | 83.3 | 136 | 82.4 | 76.6 | 88.3 | NS |
| OBS - PEDS | 17 | 10.8 | 5.9 | 15.6 | 9 | 5.5 | 2.0 | 9.0 | NS |
| Ages 19 to 50 years | | | | | | | | | |
| Admit - ER | 86 | 29.7 | 24.4 | 34.9 | 50 | 19.8 | 14.8 | 24.7 | $p < 0.05$ |
| Discharge | 164 | 56.6 | 50.8 | 62.3 | 162 | 64.0 | 58.1 | 70.0 | NS |
| OBS - CDU | 40 | 13.8 | 9.8 | 17.8 | 41 | 16.2 | 11.6 | 20.8 | NS |
| Ages 51 or more years | | | | | | | | | |
| Admit - ER | 248 | 65.6 | 60.8 | 70.4 | 122 | 50.2 | 43.9 | 56.5 | $p < 0.05$ |
| Discharge | 56 | 14.8 | 11.2 | 18.4 | 65 | 26.7 | 21.1 | 32.4 | $p < 0.05$ |
| OBS - CDU | 74 | 19.6 | 15.6 | 23.6 | 56 | 23.0 | 17.7 | 28.4 | NS |

Admit-ER, admission from ER into hospital.
Discharge, discharge home for the ER.
OBS - CDU, under observation in the Clinical Decision Unit.
Pearson Chi-square.

A review of various meta-analyses and RCTs (involving 394 trials) comparing clinical outcomes of inhaled drugs (beta agonist, anticholinergic and corticosteroid) with nebulizers, pMDI, pMDI with spacer and DPI (dry powder inhalers) showed no difference between devices in efficacy outcomes in any patient group, including the ED [8]. Several other randomized, controlled trials have since been published comparing different aerosol delivery devices in the acute care setting [9–12]. In a randomized, controlled trial of 54 adults in the ED comparing bronchodilator administration via JN and breath-actuated nebulizer (BAN) (AeroEclipse, Monaghan Medical, Plattsburgh, New York), Parone, et al. found no significant difference in clinical outcomes, in respect of the total number of treatments, respiratory rate, modified Borg Scale (MBS), and peak expiratory flow rate (PEFR) between groups [9]. The authors concluded that the BAN group had longer treatment times at a higher cost which did not justify the use of the BAN in their ED. In contrast, in our project we found substantial outcome differences probably relating to the greater inhaled dose associated with VMN.

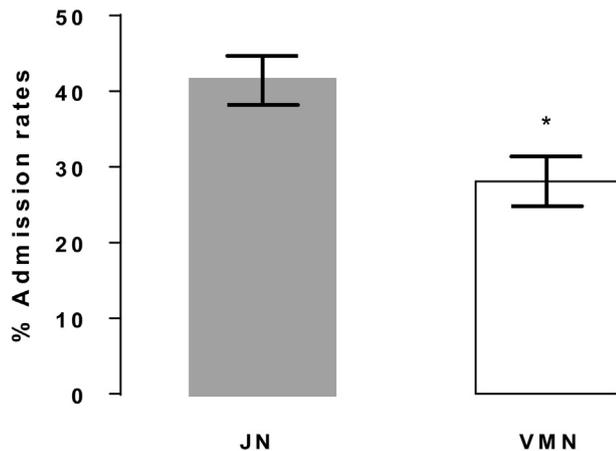


Fig. 1. Admission Rates for all age groups demonstrating a 13.3 percentage point decrease in admission rates with VMN equating to a 32% lower admission rates compared to JN admission rates. * $p < 0.05$ as compared to JN group.

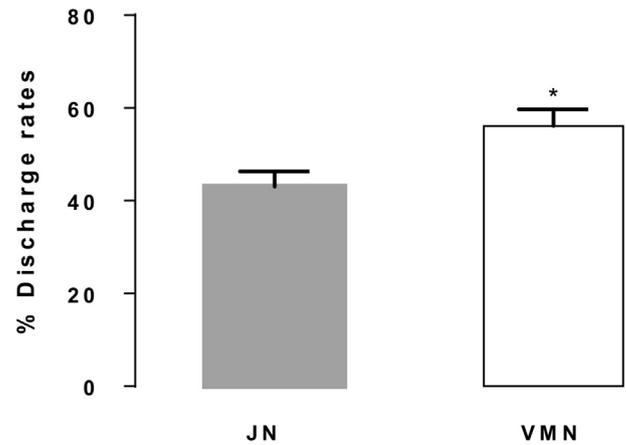


Fig. 2. Discharge rates for all age groups demonstrating a 13.1 percentage point increase in discharge rates with VMN equating to a 30% higher discharge rates in VMN compared to JN discharge rates. * $p < 0.05$ as compared to JN group. Mann Whitney 95% CI.

Haynes compared JN and BAN in COPD patients, reporting a higher inspiratory capacity (IC) with a lower respiratory rate in the BAN group but no difference in LOS and resting dyspnea measured by the Borg scale [11]. This suggests some additional benefit from the greater inhaled dose with BAN, but no improvement in LOS or, surprisingly, patient symptoms despite the improved IC. In our project, we showed a modest reduction of LOS. However, length of stay can be impacted by factors other than improvement in the respiratory condition of the patient as some patients have difficulty with transport and getting additional medication before discharge from the ED. However, this is the reality of throughput problems in a large ED and it would have been difficult to collect any other meaningful data for this from the EMR without introducing bias.

Noting the inherent potential for a breath activated system to be more efficient in medical delivery over free-flowing nebulization, Sabato and colleagues reported a randomized controlled study in 149 pediatric asthma patients in the ED comparing bronchodilator aerosol administered with standard small volume JN (SVN), large-volume JN (LVN) and use of a BAN [12]. While LOS in the ED was not reduced, patients in the BAN group showed a greater improvement in clinical asthma score, respiratory rate and a significantly lower admission rate with the BAN 38% vs. 57%, ($p = 0.03$) [12]. In an editorial review of this article, Ari & Fink identified a few confounding variables between the groups (SVN vs. LVN vs. BAN) [12,13]. The authors of the editorial concluded that the method of delivering the dose probably had a direct impact on the outcomes of the study.

Greater total dose can translate into more time spent administering care in the ED and there is mounting evidence that β_2 -agonist use leads to an increased risk of cardiovascular events and risk of sudden death in patients with COPD [14,15]. This is of special concern in the elderly

Table 3
Frequencies and percentages of amount of albuterol used by group.

| Albuterol dosage | Group | | | | χ^2 | p | Cramer's V |
|--------------------------|--------------|-------------------|---------------|-------------------|----------|--------|------------|
| | JN (N = 869) | | VMN (N = 641) | | | | |
| | n | % | n | % | | | |
| Amount of albuterol used | | | | | 264.54 | <0.001 | 0.419 |
| 2.5 mg | 416 | 47.9 ^a | 548 | 85.5 ^b | | | |
| 5.0 mg | 250 | 28.8 ^a | 93 | 14.5 ^b | | | |
| 7.5 mg or higher | 203 | 23.4 ^a | 0 | 0 ^b | | | |

Note: For each row category, pairs of column proportions with different superscripts differed significantly, $p < 0.05$. 10 patients in the JN group who received continuous infusion of albuterol up to 400 mg were excluded as outliers because a precise dosage was not recorded for these patients in the EMR.

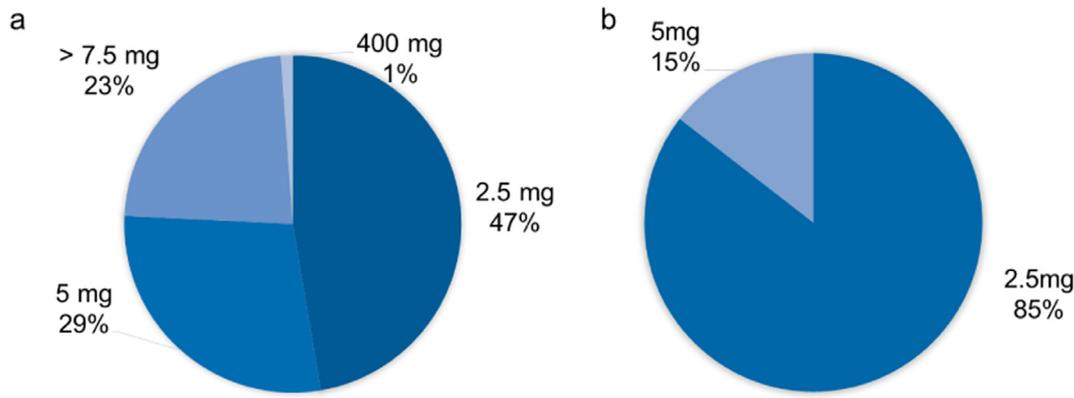


Fig. 3. Total albuterol dosage for all age groups for patient treated with JN (a) or VMN (b) ($p < 0.001$).

COPD patient with cardiovascular co-morbidities. In our project, total albuterol dose given was reduced significantly with the VMN ($p < 0.001$) compared to the JN and significantly more patients in the VMN group had their symptoms controlled with only 2.5 mg of albuterol ($p < 0.05$).

Improvement in ED throughput and cost containment has become a critical focus for most hospitals. Poor door-to-discharge times cause ED waiting rooms to back up with patients resulting in overcrowding, delays in diagnosis and intervention. The Joint Commission, Centers for Medicare and Medicaid Services (CMS), and some third-party payers have taken increased interest in organizational and ED patient flow and the latter two have begun assessing penalties when the ED LOS goals are not met [16]. Revenue is dependent on an ED's patient case mix, insurance mix, local contractual agreements with insurers and insurance contribution margin for reimbursement [17]. In our project, we not only observed significantly improved discharge rates but this was associated with a shorter LOS in the ED.

Another important factor affecting hospital reimbursement is the CMS pay-for-performance system that either provides a financial reward or penalty based on patient experience [18,19]. Although we did not measure patient satisfaction, getting more rapid treatment in the ED may result in a better patient experience. An ED backed up with patients waiting for treatment and long LOS in the ED can be a strong patient dissatisfier.

With the CMS focus on readmission rates combined with ED overcrowding, any improvement in treatment of asthma and COPD patients in the ED could have an impact on hospitals and healthcare systems. Our project showed a 15.5% decrease in the admission rate of the 65 and older group most likely to be covered by Medicare and susceptible to lost reimbursement due to 30-day readmission [20]. In this project the analysis of the patient cohort eligible for Medicare (i.e. older than 65 years of age) indicated a reduction in patient admission rates of 15.5% ($p = 0.006$) for the subgroup treated using VMN. Almost certainly some of those September 2015 JN admissions would have been readmissions.

Asthma exacerbations are also associated with an economic burden and enormous healthcare expenditure. A systematic review of studies

assessing direct and indirect costs of asthma, identified hospitalizations and medications as the most important cost drivers of direct costs [21]. The reduction in hospital admissions and LOS experienced in our project may result in associated savings and makes the case for an ED asthma management program inclusive of VMN.

The project was prompted by an interest in a new nebulizer, all patients requiring a nebulized bronchodilator in the ED were included. A single nebulizer device was used during each month. It is possible that there was a dilution of the effect experienced by patients with acute moderate to severe respiratory disease. The overall effect of the type of device still demonstrated a significant difference. The size of effect observed between treatment groups in this project may help to determine appropriate sizing and power calculation for future randomized clinical trials for patients with moderate to severe respiratory disease.

This is the first clinical project to show that the type of aerosol device utilized in bronchodilator delivery to patients in the emergency department impacts both patient disposition and length of stay in the ED. Our evaluation has demonstrated how the use of a more efficient device for bronchodilator administration resulted in significantly lower total albuterol dose, fewer admissions and shorter LOS. These results could potentially reduce patient inconvenience and improve patient satisfaction while reducing overall treatment costs for the hospital. This project suggests that there may well be a correlation between better delivery of aerosolized drug to the lung and improved clinical outcomes.

5. Limitations

This project is designed to evaluate a change in nebulizer device on all comers in an ED requiring aerosolized bronchodilators. The project

Table 4
This is the overall numbers for disposition by group.
Frequencies and Percentages of Patient Disposition by Group

| Disposition | Group | | | | | | | | χ^2 |
|-------------|--------------|------|--------|------|---------------|------|--------|------|----------|
| | JN (N = 879) | | | | VMN (N = 715) | | | | |
| | n | % | 95% CI | | n | % | 95% CI | | |
| | | LL | UL | LL | UL | LL | UL | p | |
| Admit - ER | 362 | 41.4 | 38.2 | 44.7 | 199 | 28.1 | 24.8 | 31.4 | <0.001 |
| Discharge | 376 | 43.0 | 39.7 | 46.3 | 397 | 56.1 | 52.4 | 59.7 | |
| OBS - CDU | 136 | 15.6 | 13.2 | 18.0 | 112 | 15.8 | 13.1 | 18.5 | |

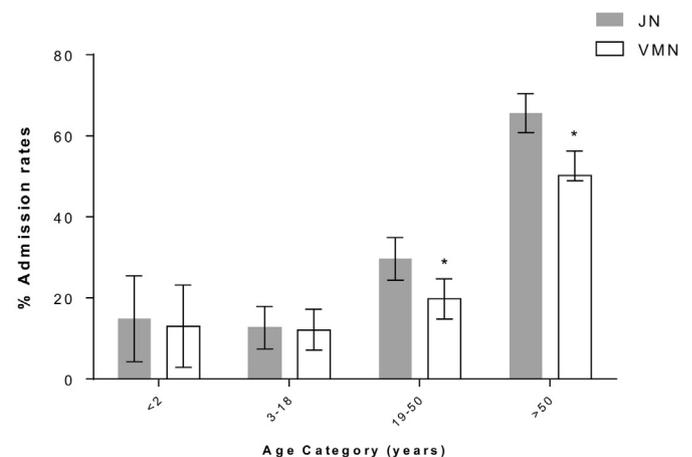


Fig. 4. Admission rates stratified by age group for both patients treated with JN and VMN. * $p < 0.05$ compared to JN.

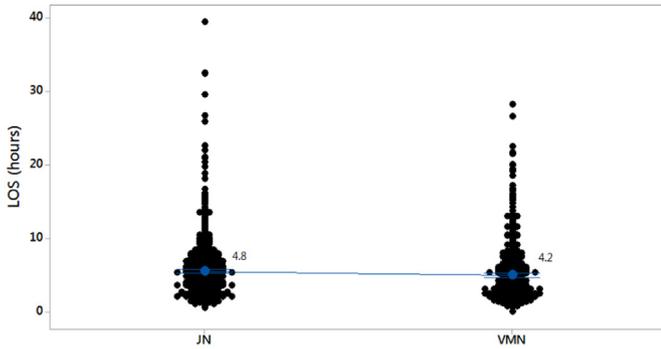


Fig. 5. Length of stay in ED: 37 min (13%) median reduction in length of stay observed per patient with VMN (4.2 h) compared to JN (4.8 h). * $p = 0.0001$ as compared to JN group.

evaluated all patients prescribed aerosol bronchodilators, including patients ranging from minimal to severe respiratory disease. This may have diluted the effect seen between the groups but is typical of how nebulizers are used in an ED setting. Due to the large variety of listed primary diagnoses it was not possible to look at treatment effects in carefully defined diagnostic groups (e.g. asthma and COPD). It is recommended that this be studied further in prospective randomized controlled studies, with specific inclusion and exclusion criteria. Impact on costs from lower admission and readmission rates and faster throughput of subgroups should be studied.

6. Conclusions

When compared to the JN, the VMN was associated with increased discharge rate to home, fewer admissions to the hospital from the ED and shorter LOS in the ED with a substantial reduction in total albuterol dose required. The device type was a strong predictor of discharge, disposition, LOS and total amount of drug, regardless of age or diagnosis. The reduction experienced in admissions, increased patient discharges, LOS, and total drug used should all translate to cost savings and should be prospectively studied. Future randomized controlled studies are required to determine the undiluted effect of device type on sub

Table 5

Pre and post heart rate and respiratory rate of patients who received either JN or VMN nebulization

| | JN | VMN | P value |
|-----------------------------------|----------------|----------------|---------|
| N | 879 | 715 | |
| Pre Heart Rate (mean (SD)) | 102.43 (26.60) | 100.37 (25.60) | <0.001 |
| Post Heart Rate (mean (SD)) | 89.69 (25.75) | 109.17 (29.89) | <0.001 |
| Pre Respiratory Rate (mean (SD)) | 19.25 (6.30) | 22.88 (6.51) | <0.001 |
| Post Respiratory Rate (mean (SD)) | 18.76 (5.87) | 22.23 (7.72) | <0.001 |

Pearson Chi-square and Independent sample-t-test.

populations of patients with primary respiratory disease such as asthma and COPD, and for prospective cost data collection.

The Authors wish to thank Patricia Dailey, BS, RRT for background on the technical aspects of vibrating mesh nebulizer and Sara Brady Phd at elite research for statistical review.

Author contributions

RD and SS conceived the project to evaluate a new device that the hospital was already using. RD identified the data from the electronic health record that would be extracted. SS trained the respiratory therapists. RD did initial analysis and arranged for independent statistical review. RD drafted the manuscript, and both authors contributed substantially to its revision. RD takes responsibility for the paper as a whole.

Industry support

Some of the Aerogen controllers, vibrating mesh nebulizers and adapters were supplied by Aerogen, Ltd. who also provided financial support for independent statistical review. Funding for meeting attendance was also provided.

Meetings

Portions of this data were presented at the 2016 American Association of Respiratory Care Meeting and at the 2016 ACEP Research Forum.

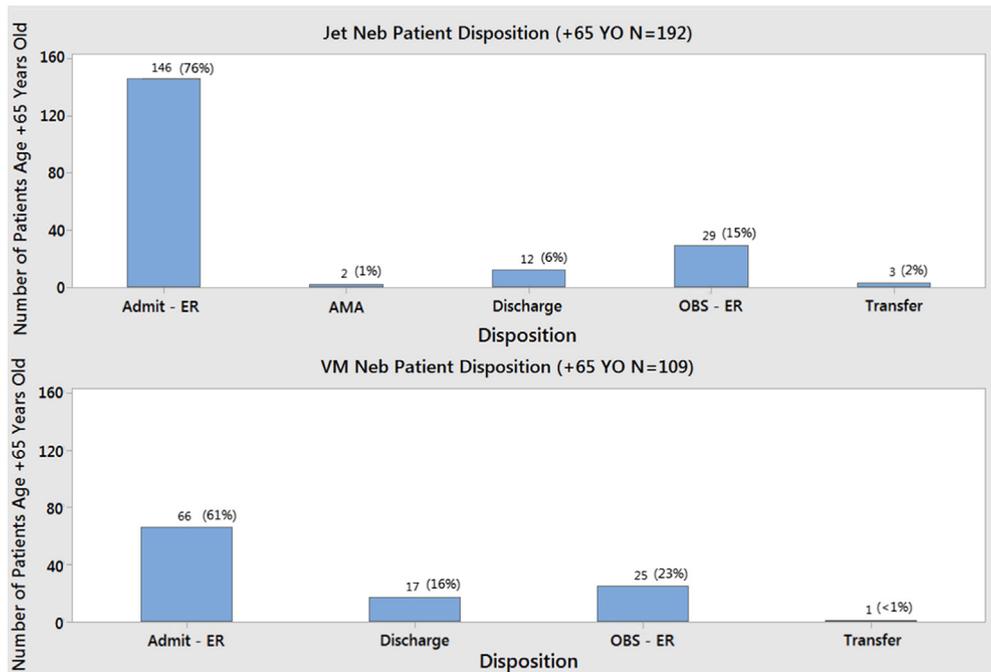


Fig. 6. Breakdown of disposition for patients 65 years and older for the JN group and for the VMN group.

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