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Efficiency of Aerosol Therapy Through Jet Nebulizer, Breath-Actuated Nebulizer, and
Pressurized Metered Dose Inhaler In A Simulated Spontaneous Breathing Adult

By

Abdullah Saad ALQarni

A Thesis

Presented in Partial Fulfillment of Requirements for the

Degree of

Master of Science

In

Health Sciences

In

The Department of Respiratory Care

In

Byrdine F. Lewis School of Nursing & Health Professions

Georgia State University

Atlanta, Georgia

2011

ACCEPTANCE

This thesis, EFFICIENCY OF AEROSOL THERAPY THROUGH JET NEBULIZER, BREATH-ACTUATED NEBULIZER, AND PRESSURIZED METERED DOSE INHALER IN A SIMULATED SPONTANEOUS BREATHING ADULT, by Abdullah Saad ALQarni was prepared under the direction of the Master's Thesis Advisory Committee. It is accepted by the committee members in partial fulfillment of the requirements for the degree Master of Science in Byrdine F. Lewis School of Nursing & Health Professions, Georgia State University.

The Master's Thesis Advisory Committee, as representatives of the faculty, certifies that this thesis has met all standards of excellence and scholarship as determined by the faculty.

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ABSTRACT

BACKGROUND: Aerosol therapy using albuterol is one of the most prescribed asthma treatments. The most frequently used methods of aerosol delivery are pneumatic jet nebulizer (JN), pressurized metered-dose inhaler (pMDI), and breath-actuated nebulizer (BAN). Choosing among these devices is usually not based on thorough comparison of efficiency or cost. We compare the efficiency of these three devices using a spontaneously breathing adult model.

METHODS: We connected each aerosol generator—JN, BAN, or pMDI with a valved holding chamber (VHC)—to the face of an adult teaching manikin. Below the bifurcation, an elbow adaptor was connected to a corrugated tube and was angled to be at a lower level than the collecting filter to prevent droplets from dripping directly into the collecting filter. From the collecting filter, another corrugated tube was connected to a prevention filter, which was then connected to an adult breathing simulator. Spontaneous breathing parameters were V_T 450 ml, RR 20/min, and I: E ratio 1:2. First, we compared JN, BAN (2.5 mg/3 ml), and pMDI (4 puffs); second, we compared JN and BAN 2.5 mg/0.5 ml plus 0.5 ml normal saline. Data were analyzed using spectrophotometry (276 nm). One-way ANOVA and independent sample t-tests were used ($p < 0.05$).

RESULTS: There were no differences in inhaled mass percentage ($p = 0.172$) JN, BAN, and pMDI in the first experiment. Treatment time with BAN was significantly longer ($p = 0.0001$) than with JN or pMDI. In the second experiment, BAN delivered more medication ($p = 0.004$) than jet nebulizer. Treatment time was significantly less with JN

($p=0.010$). There was no difference in residual volume among JN and BAN in both experiment ($p=0.765$, $p=0.115$).

CONCLUSIONS: All the devices that were compared using a 3 ml or 4 pMDI puffs delivered comparable amount of medication with no significant difference. However, BAN using 1 ml fill volume delivers more drug compared to JN. Additionally, treatment time was longest with BAN. Even with reduction of its filling volume, BAN delivers a higher amount of medication to that of pMDI but was not statistically significant.

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ABBREVIATIONS

AARC: American Association for Respiratory Care

ANOVA: Analysis of Variance

BAN: Breath Actuated Nebulizer

CCP: Common Canister Protocol

CDC: Centers for Disease Control

CFC: Chlorofluorocarbon

COPD: Chronic Obstructive Pulmonary Diseases

DPI: Dry Powder Inhaler

ED: Emergency Department

FEV1: Forced Expiratory Volume in the first second

HFA: Hydrofluoroalkane

Hr.: Hour

ICU: Intensive Care Unit

JN: Jet Nebulizer

L: Liter

ML: Milliliter

Mg: Milligram

Min: Minute

NHLBI: National Heart, Lung and Blood Institute

NZ: New Zealand

Nm: Nanometer

PEFR: Peak Expiratory Flow Rate

PSI: Pound per Square Inch

RCT: Randomized Clinical Trial

RT: Respiratory Therapist

SD: Standard Deviation

SVN: Small Volume Nebulizer

SaO₂: Arterial Oxygen Saturation

VC: Vital Capacity

VHC: Valved Holding Chamber

pMDI: Pressurized Metered Dose Inhaler

µg: Microgram

\$: United State Dollar

CHAPTER I

I. INTRODUCTION

Background and Problem

Aerosolized medications can be delivered by many means, with pneumatic jet nebulizer (JN), pressurized metered-dose inhaler (pMDI), and breath-actuated nebulizer (BAN) being the three most frequently used methods. Choosing among these three devices is sometimes confusing and may not be grounded in evidence-based medicine. Without looking at the whole picture, the selection of one device over the others could impose significant costs that could be easily minimized by switching to a different delivery device. The JN is considered the cheapest; however, wasted medication is highest with this device. In fact, the deposited amount in the lung represents approximately 15–17% of the total nebulized dose (Rau, Ari, & Restrepo, 2004). In addition, the nebulization time using this method ranges from 9 to 11 minutes. On the other hand, the BAN is more expensive, but since it only nebulizes during inhalation, it can increase the deposited drug amount up to 38%. However, this device can increase the nebulization time to be approximately 14 minutes. In contrast to these two devices, the pMDI, especially with a valved holding chamber (VHC), are considered costly when comparing it with the previous two devices. However, the amount of drug deposited has been demonstrated to be comparable to that of JN (Wildhaber, Dore, Wilson, Devadason, & LeSouef, 1999). More importantly, this method requires a shorter nebulization time, which can decrease the labor intensity when compared with the two other devices.

Significance

Several studies have either compared the performance of different nebulizers or have compared certain nebulizers to pMDIs; however, no studies were found that have compared the amount of drug deposited using the following three delivery devices: a JN, a BAN, and a pMDI. This study fills this gap in the literature by providing a thorough comparison of these three methods in terms of the amount of medication delivered. Such a comparison can help to guide clinicians and decision makers in choosing the optimum method for aerosol delivery. In addition, this study provides reliable and consistent comparisons of three of the most widely used methods of delivering aerosol therapy.

Purpose

The purpose of this in vitro study is to compare the amount of drug deposition, treatment time, and residual volume that results from using pMDI-HFA with VHC, the BAN and the JN in a spontaneously breathing adult model.

Research Questions

The following research questions provide the framework for this study:

1. What are the differences in the amounts of drug deposited in the lung between the pMDI+VHC, JN, and BAN models?
2. What are the differences in treatment time between the pMDI +VHC, the JN, and the BAN?
3. What are the differences in residual volume between the JN, and the BAN?

CHAPTER II

II. REVIEW OF LITERATURE

Pneumatic Jet Nebulizer (JN)

A small volume jet nebulizer is a small, pneumatically powered device used to generate aerosol. It is one of the most frequently used methods to deliver medication via inhalation route. It works by delivering a compressed gas through a jet that causes regional negative pressure (Hess, 2000, 2008). The solution is then nebulized by being drawn up (updraft) into a gas stream, before being sheared into smaller particles. These particles can be further broken down by means of a baffle.

Because this device has many advantages it is quite popular. It can be used by any age group and for any disease, and it allows nebulization of more than one drug (Geller, 2005). Moreover, patients using nebulizers have the advantage of normal tidal breathing with no breath coordination or breath-holding required (Ari, Hess, Myers, & Rau, 2009). On the other hand, a JN has many disadvantages including longer treatment time, the possibility of contamination, less portability, waste of medication during exhalation, and the need for an external source of compressed gas (Ari, et al., 2009; Geller, 2005).

Breath-Actuated Nebulizer (BAN)

BAN, also referred to as a dosimetric nebulizer, was developed to decrease the loss of aerosolized medication during exhalation, which is a major disadvantage with the conventional JN. This new design generates aerosol only during inspiration, which enables the BAN to deliver more medication. An example of a BAN is the AeroEclipse® (Monaghan Medical Corporation, Plattsburgh, NY), which is considered a mechanically

breath-actuated nebulizer. This nebulizer has a breath-actuated valve that can be activated by the patient's inspiratory effort. When a patient has entrained enough inspiratory flow (more than 8 L/m), an actuator-piston moves down, which allows aerosol to be generated during the inspiratory phase only. On expiration, the piston moves up to its resting position, causing cessation of aerosol production during this phase (Leung, Louca, & Coates, 2004).

While such a design may preserve a significant amount of medication, it requires a longer time for nebulization because it nebulizes medication during the inspiratory phase only. Furthermore, BAN is more expensive than the conventional JN. Since it requires an inspiratory effort to trigger the spring-loaded valve, this device may be appropriate only for older children and adults (Ari, et al., 2009).

Pressurized Metered Dose Inhaler (pMDI)

The pMDI is a small pressurized canister that is commonly used to administer aerosolized medications. The pMDI has many components that play major roles in the function of the pMDI. The components are a canister, active drugs, propellants, a metering valve, and an actuator (S. P. Newman, 2005). Once the canister is depressed into the actuator, it releases the propellant-drug mixture, which then expands and vaporizes to convert the liquid medication into an aerosol. The initial vaporization of the propellant cools the aerosol suspension. The canister aligns the hole in the metering valve with the metering chamber when it is pressed down. Then, the high propellant vapor pressure forces a premeasured dose of medication out of this hole and through the actuator nozzle. Releasing the metering valve refills the chambers with another dose of

the drug-propellant mixture(Ari, et al., 2009).

Compared to conventional jet nebulizer, the pMDI has numerous benefits. It is a portable, small, compact, and easy to use device. Conveniently, pMDIs can deliver reproducible, multidoses within a significantly short period of time. Moreover, no drug preparation is required and little contamination is likely to occur. The pMDI, however, does have limitations. One of the major limitations is that the pMDI-delivered dose is highly dependent on the patient understanding the technique. This technique includes breath initiation, proper inspiratory pattern, breath-hold, and complex hand-breath coordination. Patients with poor coordination may have trouble properly using the pMDI, which can significantly impact the amount of drug deposited. In addition, a large amount of the aerosolized drug is deposited in the oropharyngeal airway; as a result, less drug is deposited in the lung. Moreover, the pMDI has fixed drug doses that cannot be changed. Finally, some patients have negative reactions to the propellant, particularly when using old chlorofluorocarbon (CFC) pMDIs.

An In Vitro Comparison

In an in vitro model, Rau et al. (2004) compared the performance of five nebulizer models: two with constant-output (a Misty-Neb and a SideStream), one breath-enhanced nebulizer (Pari LCD), and two dosimetric nebulizers (Circulaire and AeroEclipse). The results showed that the inhaled drug percentages were highest with the AeroEclipse (38.7%) versus with the Misty-Neb (17.2%) and with the SideStream (15.8%). The percentage of drug lost to the ambient air was highest with the Misty-Neb (26.8%) and lowest with the AeroEclipse (6.6%). Duration of nebulization was shortest with the

Circulaire (7 min) and longest with the AeroEclipse (14.4 min). According to Rau et al., nebulizers differ considerably, and the dosimetric AeroEclipse resulted in the largest inhaled drug deposition and the lowest loss to ambient air.

An In Vivo Comparison

Many in vivo studies compare the clinical efficacy when using a nebulizer versus using a pMDI+VHC. Wildhalber, et al. (1999) compared lung deposition in 17 stable, asthmatic children, using a nebulizer and pMDI+VHC. Body and lung deposition of radiolabeled salbutamol was assessed with a gamma camera after children inhaled the medication from a nebulizer and a pMDI+VHC. They found that for the same age groups, there were comparable percentages of total lung deposition of radiolabeled salbutamol aerosolized using either a nebulizer or a pMDI+VHC. However, they found that the delivery rate per minute and the total dose of salbutamol deposited were considerably higher for the nebulizer.

Blake, et al. (1992), in a double-blinded, randomized, crossover design, evaluated different doses of albuterol administered either by JN or by pMDI. They used histamine bronchoprovocation as a bioassay for the amount of drug reaching the beta 2 receptors in the lung. Their results indicated that the higher doses of the nebulizer solution delivered more drug to the lung than the lower doses from the pMDI. They also estimated that 10 puffs from the pMDI (0.9 mg) would deliver approximately the same amount of albuterol to lung receptors as 2.5 mg of the nebulizer solution. They concluded that differences in dose, administration technique, nebulizer system efficiency, and severity of airway

obstruction could alter the amount of drug reaching the beta 2 receptors in the lungs and, thus, the clinical response.

Poole, et al. (2004) conducted a randomized, crossover trial that included 24 COPD patients with severe exacerbation. The authors investigated whether there were differences in pulmonary function and in the perception of breathlessness when a bronchodilator was administered via nebulizer or via a pMDI with a spacer. Their findings showed that the subjects were significantly less breathless after 5 minutes of salbutamol administration by nebulizer; however, after 45 minutes, both treatments resulted in equivalent relief. Additionally, there was no difference between the two treatments in terms of forced expiratory volume in one second (FEV1) and vital capacity (VC). Despite the early improvement during the first 5 minutes of breathlessness after the JN was used, the authors concluded that these findings were not enough to justify the frequent or routine use of a JN to treat patients with severe COPD.

Newman, et al. (2002) conducted a large, prospective, nonblinded, nonrandomized study of adult asthmatic patients to compare the efficacy of albuterol administered by a pMDI with a spacer versus a nebulizer. They reported that the peak expiratory flow rate (PEFR) and the arterial oxygen saturation (SaO₂) were higher after the administration of pMDI compared to postnebulization. Moreover, they found a significant reduction in the time patients spent in the emergency department when a pMDI was used. Additionally, they observed significant lower relapse rates among patients who used the pMDI. However, the latter could be the result of researchers' bias,

non-randomization, and the effect of corticosteroid that was given during the phase of the pMDI.

Clinical Efficacy Conclusion

Cates, et al. (2008) conducted a systematic review to evaluate the effects of VHCs versus nebulizers for the delivery of beta₂-agonists for acute asthma. The study included 27 randomized controlled trials (RCTs) of adults (n=614) and children (n=2295) over more than two years in the emergency department (ED) and community settings. Additionally, they reviewed another six trials of adult (n=28) and children (n=28) from an inpatient setting. They concluded that a pMDI with a spacer produced outcomes that were at least equivalent to nebulizer delivery. They also stated that pMDIs with spacers might have some advantages compared to nebulizers for children with acute asthma.

In a meta-analysis, Dolovich, et al. (2005) compared the clinical efficacy of nebulizers versus pMDIs with and without a spacer/VHC versus a dry powder inhaler (DPIs) for several clinical settings and patient populations. This meta-analysis covered 59 RCTs between years 1982 and 2001 that primarily tested beta₂-agonists. Their results showed no significant difference between devices in term of efficacy of any patient group for each of the four clinical settings that were investigated: ED, intensive care unit (ICU), outpatient, and inpatient.

Castro-Rodriguez, et al. (2004), in another meta-analysis, compared the efficacy of beta-agonists given by a pMDI with a VHC or a nebulizer to children under 5 years of age with moderate to severe acute exacerbations of wheezing or asthma in the ED setting.

They reviewed six RCTs (n=491) that were published between 1966 and 2003. The results showed a significant reduction in the admission rate for patients who received beta-agonists via a pMDI with a VHC compared with those who received them by nebulizer. Additionally, the pMDI with VHC group showed a significant improvement in clinical scores compared to those who used a nebulizer.

Cost–Benefit Comparison of JN Versus pMDI With VHC

Based on many of the studies that have been presented in this paper as well as the high cost of respiratory care services, many hospitals have begun to move to more cost-effective methods such as the pMDI to deliver aerosolized medication. In light of this change, several researchers have compared the two approaches—JN and pMDI with a VHC—in an attempt to determine whether the use of a pMDI is cost effective.

In an in-patient setting, Jasper, et al. (1987) compared the use of JN administered by a respiratory therapist (RT) to the self-administered pMDI among 34 COPD patients. They found that both methods were clinically equivalent. Additionally, they calculated the cost of such therapy based on their 1985 complete audit of aerosol therapy. They found the annual cost of JN to be \$299,193, which included annual equipment costs (\$16,495) and medication and labor costs (\$47,038). Also, assuming that all treatments could be given by inhaler, they calculated the total cost of using a pMDI with a spacer to be \$45,706 per year, which included the cost of instruction, the cost of the spacer, and the cost the pMDI itself. Making the assumption of possible total replacement, they reported that the direct cost saving would be around \$253,000 annually. This included the

medication and the labor costs for one year. However, their assumption of the absolute total replacement of JN is not achievable.

In 1992, Bowton, et al. evaluated the impact of routine substitution of a pMDI for nebulizer therapy in a 700-bed hospital. Using data from the time-management studies at their institution, they estimated the therapist's time spent administering each treatment, which included initial setup, patient instruction, and follow-up visits. Based on this time estimate and the therapist's hourly wage of \$13.70, the costs of aerosol delivery were calculated. In addition, they calculated the equipment and the drug costs (albuterol pMDI canister cost \$7, spacer cost \$4.50, JN including daily change cost \$1, and unit-dose of albuterol cost \$0.54 per treatment). Total patient charges were calculated to be \$13 per JN treatment, \$16.50 for the initial pMDI treatment, and \$5 for pMDI treatment follow-up. After the hospital had achieved an approximately 60% substitution of pMDI for nebulizer, they reported a significant reduction in the total cost to deliver aerosol therapy, from \$27,600 to \$20,618. They stated that their hospital could achieve a potential cost savings of \$83,000 annually.

In 1996, Turner, et al. over a 6 week period, evaluated the cost of aerosol therapy (with pMDI, nebulization, or both) administered to 95 patients at four preselected hospital wards. Of these 95 patients, 6.3% received a pMDI, 70.5% received nebulization, and 23.2% received both. Salbutamol and ipratropium bromide doses, frequency, and delivery methods—either pMDI or nebulizer—were recorded for the 95 patients treated with aerosolized bronchodilators. The authors determined direct costs for

medications and hourly wages including benefits and equipment. They used time and motion studies to identify time allocated to pMDI and nebulization delivery and sensitivity analyses to test assumptions that could significantly affect treatment costs, especially assumptions about medications, labor, and spacer devices. Their results showed that the delivery of aerosol therapy using a pMDI was the least expensive method.

Another RCT by Leversha, et al. (2000) compared the cost and effectiveness of albuterol delivery administered via a pMDI+VHC versus a nebulizer to 60 children with moderate to severe asthma who presented to the emergency department. They calculated the cost of the medication, equipment (which included a spacer, masks, and a nebulizer bowl), the ED presentation, and, for those requiring admission, the cost of the resulting hospital admission. Their management unit provided cost estimates that included the fixed costs, human resources, and investigation and treatment costs. Their hospital benchmark estimates in 1996 (presented in New Zealand Dollar) were NZ\$190 (roughly, US\$148.751) for each ED presentation and NZ\$1814 for each hospital admission for asthma. They found that the mean total cost was NZ\$825 (roughly, US\$645.892) for the holding chamber group (n=30) and NZ\$1282 (roughly, US\$1,003.68) for the nebulizer group.

Dhuper, et al. (2008), in a prospective randomized double-blind study, compared the efficacy and cost using a pMDI with a spacer and a nebulizer among 60 acute asthmatic patients who presented to the ED. As previous studies concluded, they found

no differences between the two groups in terms of efficacy. Their cost analysis was based only on treatments with albuterol and did not include placebo administration. Payroll costs (including fringe benefits) for a respiratory therapist in their institutions was on average \$40.94 per hour. They estimated that it took the therapist approximately 10 minutes to instruct the patient on how to use the pMDI with a spacer, and this had to only be done once throughout the entire emergency department stay. For the nebulizer group, each treatment took approximately 12 minutes of the therapist's time. Thus, the cost for the respiratory therapist's time represented the biggest difference in cost between the two groups, with a constant \$6.82 per patient among the pMDI with spacer group and a median cost of \$16.38 for the nebulizer group. There was a one-time cost per patient for the delivery system of \$2.95 for the LiteAire spacer and \$1.50 for the nebulizer. More importantly, the total cost for using the pMDI with a spacer was significantly lower (median of \$10) compared to the nebulizer cost (\$18). They concluded that a pMDI with a spacer could offer an economical alternative to nebulization for aerosol delivery.

Conversions to pMDI Protocols: Success and Failure

While the substitution of a pMDI for nebulizer treatment could save money by allowing staff time to be reallocated, which would in theory increase productivity, such a policy needs proper planning and careful implementation. Like any process, pre-planning for implementation of such a change is the cornerstone of success.

In a pediatric hospital, Salyer, et al. (2008) introduced their approach to switch from using a nebulizer to using a pMDI with VHC. At the beginning, they formed a team

to promote the implementation of this conversion. Their intervention comprised four parts: a literature review, products selection, policy and operational changes, and staff training. After the literature review and products selection were completed, they revised the policy and procedures for the respiratory care department to ensure that pMDI+VHC was the initial method to be used with patients. Respiratory therapists and nurses were trained and informed of the conversion. Physicians were notified and the default mode of delivery was changed to pMDI in their computerized physician order entry system. After 3 months of processing and implementation, their respiratory care department was able to increase the usage of pMDI+VHC from 25% to 77% among all non-ICU patients, and from 10% to 79% among patients with asthma only. These results indicate a huge success while emphasizing that a complete conversion was not expected. They acknowledged that pMDI is not appropriate for every case.

In the respiratory therapy section, at Cleveland Clinic Foundation, Orens, et al. (1991) implemented a policy to change from a small volume nebulizer (SVN) to a pMDI. A general rule was announced that a pMDI should be prescribed whenever possible. Over two years (1988–1990), they were able to increase pMDI use from 5% to 18%. Obstacles that hindered more widespread conversion included the inability of some patients to use a pMDI and the unavailability of some medications in a form that could be used with a pMDI. The authors also touched on another obstacle that hindered further conversion: Some physicians continued to order the use of a SVN because they were under “a persisting misimpression” that it was more effective than a pMDI.

In 1992, Bowton, et al. evaluated the success and effect of the routine conversion to pMDI in a 700-bed tertiary hospital. Before implementation, they educated the RTs and medical staff about the perceived benefits of such a conversion. Then, they implemented a policy that stated that all beta₂-agonist nebulization orders were to be administered via pMDIs. The accepted exceptions to this rule were if a physician ordered that no substitution take place, if a patient was not cooperative, or if the respiratory therapist, using his or her judgment, recommended an SVN. They were able to achieve a conversion of more than 60% to pMDIs. They attributed their success mainly to the comprehensive educational programs directed at respiratory therapists and physicians that took place before the substitution was implemented.

Hendeles et al. (2005) reported another conversion experience. Their initial effort to change to pMDIs for the administration of albuterol, ipratropium bromide, or a combination of two took place in their surgical ICU for mechanically ventilated patients. They formed a committee that recommended the change in two phases. In the first phase, physicians were asked by respiratory therapists to change the orders for each patient to pMDI+VHC. In the second phase, after acceptance of their policy, the committee approved a pilot program that allowed automatic conversion in all adult ICUs, whether they were ventilated or not. Exclusion criteria included the need for continuous nebulization and the need for more than four doses per hour. Patients were also excluded from this policy if other drugs such as N-acetylcysteine were mixed with the bronchodilator or if a physician ordered that no substitution be made. At the end of the 6-

month pilot program, conversion was extended throughout the hospital and also began to encompass children. At the end of the first 6 months, there was a decline in SVN treatment of around 30% and approximately a 53% increase in pMDI usage. In non-ICU areas, however, the authors found that none of the patients had been switched, not because any of the exclusion criteria had been met, but rather because of a lack of adherence to the policy. They concluded “a policy to switch patients from SVN to pMDI+VHC for administration of bronchodilator was met with limited success.” (Hendeles, Hatton, Coons, & Carlson, 2005, p. 1060).

Economical Evaluation

Economic evaluation refers to the comparison of alternative courses of action, such as switching to a pMDI, in terms of their costs and consequences (Douglas & Normand, 2005). With introduction of new procedures or new drugs, it is crucial to assess its impact on two axes: the clinical and the economic outcomes. Since clinical outcomes of conversion to pMDI use have been sufficiently assessed and results have demonstrated it to be equal to other methods of delivery, it is imperative to evaluate its impact on cost. A variety of techniques can be used to conduct an economic evaluation. For example, in a cost-minimization analysis, which is the simplest form of economic evaluation, the researcher would evaluate the cost differences between two or more products or procedures that have been deemed by the literature to be equivalent (Douglas & Normand, 2005). Hence, the purpose of such an evaluation is to determine which substitute would result in the use of fewer health care resources (and thus would lower

costs) (Douglas & Normand, 2005). That type of analysis is often confused with cost-effectiveness analysis, in which different outcomes of two different interventions are expected.

Additionally, as Camargo et al. (2000) have shown, there are many types of costs. The authors categorized costs as either direct or indirect, with *direct costs* representing the expenditure for goods or services. Examples of this type of cost include labor, equipment, and medication. In contrast, *indirect costs* are other expenses that usually result from loss of productivity. For example, patients may be unable to work because of an asthma attack.

Economic evaluation of aerosol therapy must include all related costs. The initial setup, equipment, medication, and labor must all be considered. Labor, which plays a major role in reducing the cost when switching from nebulization to pMDI+VHC, must be assessed very carefully. While many studies have recorded labor as a variable cost (i.e., based on each treatment) it should really be treated as a fixed cost (Camargo & Kenney, 2000). This means that labor does not change proportionally with volume change in the short term. “Determining the labor cost per minute and multiplying that figure by the number of minutes expended on a therapy ignores that a hospital’s labor payments are fixed in the short term” (Camargo & Kenney, 2000, p. 761).

CHAPTER III

III. METHODOLOGY

Bench Model

The bench model consisted of JN, BAN, or pMDI+VHC connected to an air flow compensated Thorpe flow meter; the pMDI+VHC was attached to the face of an adult teaching manikin. A mouthpiece was connected to the face of the manikin. Below the bifurcation, an elbow adaptor was connected to a corrugated tube and was angled to be at a lower level than the collecting filter to prevent droplets from dripping directly into the collecting filter. From the collecting filter, another corrugated tube was connected to a prevention filter, which was then connected to an adult breathing simulator. An adult breathing simulator (Harvard Apparatus Dual Phase Control Respirator Pump, LSU Medical Center, Shreveport, LA) was used to simulate adult spontaneous breathing cycles. Tidal volume (V_T) was set at 450 ML, the respiratory rate (RR) at 20 breaths/min, and the inspiratory to expiratory ratio (I:E) was 1:2. V_T was assessed multiple times using the Wright Spirometer (Harris Lake Inc., Cleveland, OH) and 450 ml was verified with each breath. Figure 1 shows the experimental model with the three aerosol delivery devices used in this study.

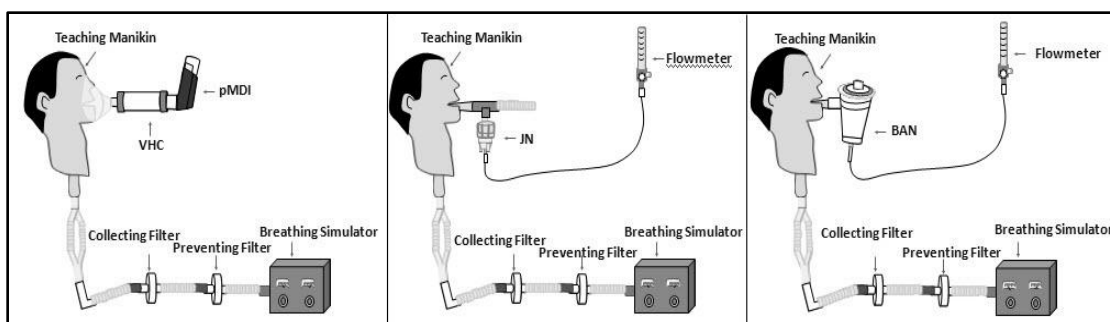


Figure 1 Experimental Setup with the three aerosol delivery devices used in this study

Efficiency of JN, BAN and pMDI+VHC Using 3 ml or 4 Puffs

This experiment compared three aerosol generators: JN, BAN, and pMDI+VHC.

The two nebulizers were tested using a simulated spontaneous adult breathing pattern.

(1) The Salter Labs 8900 nebulizer (Salter Labs, Arvin, CA) is a constant-output pneumatic jet nebulizer. (2) The AeroEclipse (Monaghan Medical Corp, Plattsburgh, NY) is a mechanical breath-actuated nebulizer. First, each nebulizer aerosolized the unit-dose of albuterol sulfate solution of 2.5 mg with a 3 mL total fill volume (Nephron Pharmaceuticals, Orlando, FL). No additional diluents were added to either nebulizer. Both nebulizers were powered by 50-psi of oxygen at 8 l/min. and operated until the onset of sputter, with no tapping of the nebulizer, and the time to sputter was recorded with a stopwatch.

The ProAir Inhaler (Teva Specialty Pharmaceuticals, Horsham, PA) is an HFA-based pMDI that contains albuterol sulfate. The 108- μ g ProAir (equivalent to 90 μ g from the mouth piece) was used with the AeroChamber Plus (Monaghan Medical, Plattsburgh, NY), which is a VHC with antistatic properties. After shaking, the pMDI

was primed with three actuations, and then pMDI+VHC was actuated four times with a 30-second waiting time between actuations. Each actuation was done in synchrony with a beginning of the inspiratory phase, and the same investigator actuated the pMDI to ensure the consistency of medication delivery.

Efficiency of JN, and BAN Using 1 ml

In this experiment, two nebulizers were compared: a JN and a BAN. Salter Labs 8900 nebulizer (Salter Labs, Arvin, CA) is a constant-output pneumatic jet nebulizer. The AeroEclipse (Monaghan Medical, Plattsburgh, NY) is considered a mechanical breath-actuated nebulizer. Each nebulizer aerosolized a concentrated dose of albuterol sulfate solution (Nephron Pharmaceuticals, Orlando, FL) of 2.5 mg/ 0.5 ml with an additional volume of 0.5 ml for a total fill volume of 1 ml per nebulizer. Each of the nebulizers was powered by 50-psi of oxygen at 8 L/min. and operated until the onset of sputter, with no tapping of the nebulizer, and the time to sputter was recorded with a stopwatch.

Measurement of Drug

Each experiment was repeated three times (n=3) using a simulated spontaneous adult breathing pattern. In each trial, the total aerosol drug mass was measured based on the amount of drug deposited in the collecting filter. All drug amounts were analyzed via spectrophotometry (Beckman Instruments, Fullerton, CA) at a wavelength of 276 nm. Collecting filters were washed with hydrochloric acid (JT Baker Company, Phillipsburg, NJ) for one minute with gentle agitation. The spectrophotometer was calibrated prior to the trials using a holmium oxide filter (Beckman Instruments,

Fullerton, CA) to determine wavelength accuracy and it was set to zero using the solvent alone before each analysis.

Data Analysis

Means and standard deviations were calculated for each component of the inhaled mass percentage, treatment time, and residual volume. In the comparison of JN, BAN, and pMDI, we used one-way ANOVA to compare the inhaled mass percentage, and treatment time of the three devices. Multiple follow-up comparisons were performed if the p value was significant. In addition, we used independent t test to compare the residual volume of the nebulizer. In the comparison of JN, and BAN (1 ml fill volume), however; independent t test was used to compare the inhaled mass percentage, treatment time, and residual volume. Differences were considered statistically significant when $p < 0.05$. To identify differences among aerosol generators, all statistical calculations were performed using commercially available software (SPSS v.18, Chicago, IL).

CHAPTER IV

I. RESULTS

Efficiency of JN, BAN and pMDI+VHC Using 3 ml or 4 Puffs

The first experiment, which used 3 ml/ four puffs of albuterol, showed no statistically significant differences in the inhaled mass percentage among the three aerosol generators ($p=0.172$) (Table 1). However, there was a statistically significant difference among the delivery times ($p=0.000$). BAN required eight times the nebulization time of the pMDI. Post hoc analysis showed a significant difference in treatment time between the BAN and the pMDI ($p=0.0001$) and between the BAN and the JN ($p=0.0001$) but no significant difference between the JN and the pMDI ($p=0.196$). Additionally, the BAN and the JN showed no statistically significant difference in residual volume ($p=0.765$).

Table 1 *Efficiency of Aerosol Generator, JN(Jet Nebulizer),BAN (Breath-Actuated Nebulizer), and pMDI(pressurized metered dose inhaler),used in this study.*

	First Experiment With 3 ml or 4 Puffs			Second Experiment With 1 ml	
	JN	BAN	pMDI	JN	BAN
Inhaled Mass (%)	15.83± 2.08	23.63± 6.55	18.32 ± 3.53	5.76±1.28	17.25± 3.05
Treatment Time (Min)	2.35 ± 0.18	11.19 ± 0.93	1.42 ± 0.03	0.143 ± 0.05	1.77 ± 0.62
Residual Volume (ml)	1.57 ± 0.55	1.44 ± 0.43	NA	0.86 ± 0.058	0.68 ± 0.145

Efficiency of JN, and BAN Using 1 ml

The second experiment showed that the BAN was more efficient than the JN ($p=0.004$). Additionally, comparisons of delivery time ($p=0.010$) and residual volume ($p=0.115$) showed no statistically significant differences between the JN and the BAN.

CHAPTER V

II. DISCUSSION

This study aimed to measure the amount of drug deposited in the lungs by different aerosol delivery methods. Finding of this study showed no significant difference in the inhaled mass percentages among JN, BAN, and pMDI when a fill volume of 3 ml or 4 puffs were used. While BAN delivered more medication than JN with 1 ml, the residual volume of the BAN was the same as JN. Regardless of the fill volumes used in this study, the treatment time with BAN was longer than JN and pMDI.

Aerosol Generator Efficiency

First Experiment With A Fill Volume of 3 ml or 4 Puffs

The JN delivered the smallest amount of drug, approximately 16%, which is comparable to results of previous studies (Rau, et al., 2004). Although the BAN delivered the highest medication percentage (24%) of the three devices in this study, it was approximately 15% less than what Rau et al. found in their study (approximately 39%). One explanation for this big difference may be the models used. In Rau et al.'s experimental model, they connected the nebulizer directly to a collecting filter and to the lung simulator, which caused less aerosol particles impaction. The model in this study was designed to mimic the human anatomy, resulting in greater aerosol particles impaction and less deposition of drug in the filter. Although the BAN delivered the highest percentage of medication, it did not reach a statistically significant level. However, aerosol deposition with BAN using 3 ml is higher than pMDI although it is not

statistically significant. What is more important is that the BAN's delivery time was as much as five times that of the JN and as much as eight times that of the pMDI. Moreover, the residual volume with the BAN was comparable to that of the JN with no statistically significant difference.

Efficiency of JN, and BAN Using 1 ml

This experiment provides crucial and helpful information for practicing respiratory therapists. The BAN delivered as much as three times the amount of the drug that the JN delivered and in less than two minutes. In fact, it delivered more than the amount of drug deposited by the JN when a 3 ml fill volume was used in the first experiment. Also the BAN with 1 ml delivered nearly the same amount of albuterol as the pMDI. Surprisingly, the JN reached sputter in about 14 seconds, which reveals the poor effectiveness of the device. An even more unexpected result was that the JN left a dead volume of nearly 87% of the original fill volume compared to 67% with BAN.

Limitations

Like any other study, this study has limitations. First, the impact of changing breathing parameters should be explored to determine how aerosol deposition would be affected by different patient conditions and diseases. Second, the in vitro lung model used in this study was not configured to precisely match the human airway, which may have affected the aerosol deposition and subsequently the results. Because the lung model collected aerosol prior to the lung (filter at the level of bronchi), we could not determine aerosol deposition past this point.

Conclusion

All aerosol devices that were compared using a 3 ml fill volume delivered comparable inhaled mass percentage with no significant differences. When a 1 ml fill volume was used, the BAN delivered more drug than the JN. The BAN, however, had the longest treatment time. When the BAN fill volume was reduced to 1 ml, the pMDI delivered approximately the same amount of medication as the BAN using a fill volume of 1 ml. Future studies should explore the impact of the different aerosol delivery device and treatment on the cost of aerosol therapy.

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