# Breath-Actuated Nebulizer Versus Small-Volume Nebulizer: Efficacy, Safety, and Satisfaction

The breath-actuated nebulizer (BAN, AeroEclipse, Trudell Medical International, London, Ontario, Canada) has been available as an aerosol delivery option for several years. This small-volume jet nebulizer is primarily designed to generate aerosol during inspiration in response to the patient's inspiratory flow triggering the opening valve.[1,2] Some studies report that BAN provides smaller particles and greater dose delivery efficiency than continuous jet nebulizers.[2–5] This increased drug efficiency is associated with decreased release of aerosol to the atmosphere, but comes at the cost of increased treatment time, by 2–3-fold with standard unit doses.[2] Despite an increasing interest in use of the BAN in hospitals, clinical studies comparing use of BAN with other nebulizers are limited. In a study in this issue of RESPIRATORY CARE, Arunthari and colleagues compared BAN to the standard continuous small-volume nebulizer (SVN) in terms of safety, efficacy, and satisfaction. This is the first study examining not only the safety and efficacy of BAN and SVN in adults with obstructive airway diseases, but also patient and respiratory therapist (RT) satisfaction with these nebulizers.[6]

This study employed a randomized cross-over design, which is increasingly popular in clinical research, due to its advantage of randomly assigning 2 arms of the study (BAN and SVN) to each subject. This design exposes each patient to each alternative device, and unbalanced groups are less of an issue.

### Efficacy and Safety

While cross-over design provides a balanced utilization of each nebulizer, distribution of patients receiving single (albuterol alone) versus combined (ipratropium bromide and albuterol) treatment were not matched or even tracked. In addition, drug dose concentration and volumes used with each type of nebulizer using both single and combined treatment were different. These particulars with a relatively small sample size present some challenges in comparing the 2 primary treatment groups. Therefore, to say that there is equivalent efficacy and safety may be an oversimplification.

For the albuterol only treatment, the doses compared were the standard label dose of 0.083% (2.5 mg in 3 mL of normal saline) with the standard continuous SVN, and the 0.5% solution (2.5 mg in 0.5 mL) with the addition of 0.5 mL normal saline for a 1 mL total volume with the BAN.

This difference greatly impacts the available dose to the patient. If we assume that both nebulizers have a residual drug volume of 0.8 mL remaining at the end of dose, then the standard SVN will emit 2.2 mL of formulation as aerosol, while the BAN will emit only 0.2 mL. If we assume an inspiratory/expiratory ratio of 1:2, the 0.2 mL emitted dose from the BAN would require 2–3 min with an inhaled dose of 500 $\mu$g. In contrast, the 2.2 mL SVN would require 9 min, with 33% of the emitted dose (0.73 mL) inhaled (603 $\mu$g). With BAN the emitted dose is equivalent to inhaled dose; in contrast, with an inspiratory/expiratory ratio of 1:2, only one third of the emitted dose is inhaled with the SVN.

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This dynamic inhaled dose changes dramatically with the larger dose used with the BAN for combined therapy, adding ipratropium with albuterol, increasing the dose volume from 1.0 mL to 1.75 mL. Subtracting the 0.8 mL residual drug, the inhaled dose volume increases from 0.2 mL to 0.95 mL (containing 1,357 $\mu$g), with the dosing time increased by $>$ 4-fold, likely requiring 8 min for the complete treatment. With a reported treatment time of 4.1 min, it is likely that a relatively small percentage of BAN treatments were administered the combined ipratropium/albuterol therapy. Consequently, the 2 BAN regimens could alter inhaled albuterol from 500 $\mu$g with the 1 mL dose volume, to 1,357 $\mu$g with the 1.75 mL dose volume, if both are run to sputter. This greater prevalence of the smaller dose with BAN may account for the reported trend toward greater incidence of palpitations and tremor (commonly associated with larger doses of albuterol) reported with the SVN group.

Pre/post heart rate and respiratory rate obtained from BAN and SVN were almost the same, and showed no significant difference between nebulizers. However, it must be noted that the treatment time of the BAN in this study is 4.1 min, as opposed to 9.9 min with SVN, so monitoring of pulse immediately after administration with BAN might precede the development of a significant increase in heart

rate, as pulse rate change typically begins 5 min after the treatment, as shown by Lin and Huang.[5] While peak expiratory flow significantly increased with both BAN and SVN after the treatment, no significant difference on peak expiratory flow was found between the 2 nebulizers.[6]

We know that the dose-response curve with albuterol is rather steep, with most patients responding to inhaled doses of 200 $\mu$g or less of albuterol from a metered-dose inhaler, with a flattening of dose response above that level. However, while increased dosing may not result in greater bronchodilator response, it is associated with increased adverse effects and decreasing serum potassium levels.[7] Lower occurrences of adverse effects such as nausea, vomiting, palpitations, and tremor with the BAN versus SVN may be due to a reduction in fill volume with BAN, which decreases the amount of inhaled drug and leads to fewer adverse effects after the treatment.

A more apple to apple comparison might be to compare the same dose of 0.5 mL of 0.5% solution with dose volume of 1.5 mL for the SVN. This would reduce dosing time for the emitted dose of 0.7 mL to 3.3 min and provide an inhaled dose of 625 $\mu$g. One would then need to ask if the 1−2 min greater dosing time with SVN justifies the greater cost of the BAN versus SVN.

It is meaningful that the higher concentration of albuterol used with the BAN was well tolerated by patients. Use of 0.5% albuterol is approved for use when mixed with 2.5 mL normal saline. Clinicians should be aware that even the 0.25% albuterol used with the BAN in this study is a considerably higher concentration than the drug label. This report suggests that use of this higher than label concentration was well tolerated in this patient population. Other countries, such as Taiwan, have standard unit doses with 5 mg in 2.5 mL, which have supporting safety data, but, nonetheless, this concentration has not been approved in this country. Administration of the undiluted 0.5% albuterol solution as aerosol has been reported without incidence; however, safety and tolerance have not been extensively studied in the United States.[7]

If time of administration and optimizing dose in the acute care setting is of importance, such as in the emergency department for treatment of acute airway obstruction, using a dose of 1 mL of 0.5% solution (5 mg) with a standard SVN could deliver an inhaled dose of 330 $\mu$g (representing 33% of the 0.2 mL of formulation emitted, which is 6.6% of the 5 mg dose) in a 1-min treatment. The cost of the additional dose of 2.5 mg of albuterol, up to $1 United States, might provide a clinically viable alternative to the more expensive BAN versus SVN.

That said, safety is not just about the patient. Aerosol spewing indiscriminately into the air provides unintended secondhand exposure to care providers and others in the vicinity. Standard SVNs release two thirds of the emitted aerosol into the atmosphere. Despite concerns of ambient contamination of aerosols, the vast majority of SVNs are not used with expiratory filters. The BAN reduces ambient aerosol by $>$ 85%, compared to SVN with no filters. This attribute reduces risk to care providers; this reduced risk, along with the cost benefit of this aerosol technology, should justify RT preference for the BAN.

### Satisfaction

Patient and RT satisfaction with each aerosol device was determined using 2 different types of survey. While patient satisfaction includes drug delivery time and overall satisfaction, RTs evaluated each nebulizer based on overall performance, ease of use, and duration of treatment.

The findings of this study show that the majority of patients were more satisfied with the BAN than SVN in terms of delivery time, but had no real preference in terms of overall satisfaction.[6] Duration of treatments may be an adherence factor for patients receiving aerosol therapy. Shorter is better. It is not surprising that this would be the case for RTs at the bedside as well. In contrast, RTs ranked BAN superior in all dimensions, compared to standard SVN.[6] If the surveys used in this study were more comprehensive it might have been possible to gain greater insights on the reasons behind their satisfaction with BAN beyond just time savings. The 19 RTs who participated in this study were 42.6 $\pm$ 2.6 years old and had 7 years of experience on average, much of that using the SVN as their primary aerosol device. One might be more skeptical of veteran (as opposed to relatively novice) staff RTs assessing any new device in comparison with older standard of care devices.

In conclusion, Arunthari and colleagues advance our understanding of the use of BAN versus SVN by addressing very important research questions. Their findings provide insights for the necessity of future research. Such studies should compare more similar dosing rationales between devices and provide greater definition of the efficacy, safety, and satisfaction measures of BAN and SVN in other patient populations.

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The authors have disclosed no conflicts of interest.

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DOI: 10.4187/respcare.01995

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