The Impact of High-Flow Nasal Cannula Device, Nebulizer Type, and Placement on Trans-Nasal Aerosol Drug Delivery

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BACKGROUND: Aerosol delivery via high-flow nasal cannula (HFNC) has been increasingly used in recent years. However, the effects of different HFNC devices, nebulizer types, and placement on aerosol deposition remain largely unknown. METHODS: An adult manikin with anatomically correct upper airway was used with a collection filter placed between the manikin's trachea and a breathing simulator, composed of a dual-chamber model lung driven by a critical care ventilator. Three HFNC device configurations were compared, with vibrating mesh nebulizer and small-volume nebulizer placed at the humidifier (inlet for Optiflow and outlet for Airvo 2) and proximal to the nasal cannula at gas flows of 10, 20, 40 and 60 L/min, in quiet and distressed breathing patterns. Albuterol (2.5 mg) was nebulized for each condition (no. = 3). The drug was eluted from the collection filter and assayed with ultraviolet spectrophotometry (276 nm). RESULTS: At all settings, except when a nebulizer was placed proximal to the nasal cannula with the Optiflow and when the HFNC flow was set at 60 L/min, the vibrating mesh nebulizer generated a higher inhaled dose than did the small-volume nebulizer (all $P < .05$). With the exception of distressed breathing at an HFNC flow of 10 L/min, the inhaled dose with the vibrating mesh nebulizer placed at the humidifier was greater than with the vibrating mesh nebulizer placed proximal to the nasal cannula (all $P < .05$), Optiflow provided a higher inhaled dose than did Airvo 2 with either AirSpiral or 900PT501 circuits with the vibrating mesh nebulizer placed at the humidifier (all $P < .05$). CONCLUSIONS: During transnasal aerosol delivery, the vibrating mesh nebulizer generated a higher inhaled dose than did the small-volume nebulizer when the nebulizer was placed at the humidifier. With the vibrating mesh nebulizer placed at the humidifier and an HFNC flow > 10 L/min, the inhaled dose was higher than with the vibrating mesh nebulizer placed proximal to the nasal cannula, and the inhaled dose was higher with Optiflow than with Airvo 2. *Key words: high-flow nasal cannula; aerosol therapy; nebulizer.* [Respir Care 2022;67(1):1–8. © 2022 Daedalus Enterprises]

Introduction

High-flow nasal cannula (HFNC) has demonstrated its clinical efficacy in improving oxygenation and avoiding intubation for patients with acute hypoxemic respiratory failure.[1,2] During HFNC therapy, patients may require aerosolized medications for treating pulmonary pathologies, such as bronchoconstriction[3-5] or pulmonary hypertension.[6,7] In vitro and in vivo studies have demonstrated that clinically effective dosages of pulmonary medications, such as inhaled albuterol or epoprostenol can be delivered transnasally by using HFNC.[3-8] A recent worldwide survey among clinicians in adult ICUs reported a wide variety of clinical practices to provide aerosol via HFNC: 40% of the respondents used vibrating mesh nebulizer, whereas 28% placed a small-volume jet nebulizer (small-volume nebulizer) in-line with an HFNC.[9] Currently, no consensus has been achieved for delivering transnasal aerosol.

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Several studies have been conducted to compare the efficacy of using a small-volume nebulizer versus a vibrating mesh nebulizer to provide transnasal aerosol delivery.[10-12] In an adult in vitro study with HFNC gas flow set at 30 L/min, the inhaled mass at the cannula outlet was similar between a vibrating mesh nebulizer and 2 small-volume nebulizers (Micromist nebulizer, Hudson RCI, Teleflex, Morrisville, NC and Micro cirrus nebulizer, Intersurgical, Wokingham, UK).[10] However, in the scintigraphy study with 6 healthy adult volunteers with the same gas flow setting, Dugernier et al[11] found a higher inhaled dose with a vibrating mesh nebulizer than a small-volume nebulizer (Opti-Mist Plus Nebulizer, ConvaTec, Bridgewater, NJ). Similarly, in the systemic bioavailability study by Madney et al[12] with 12 subjects with COPD, the urinary salbutamol excretion with a vibrating mesh nebulizer was higher than that with a small-volume nebulizer after inhaling albuterol via an HFNC at gas flow of 5 L/min, which suggests a higher drug delivery. All of these studies compared the nebulizers at one single gas flow with one breathing pattern.[10-12] The ratio of gas flow to patient inspiratory flow was found to play a crucial role in transnasal aerosol delivery[13]; however, the question of whether delivery efficiency of a vibrating mesh nebulizer is superior to a small-volume nebulizer at different flow settings and breathing patterns remains unknown.

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Several devices are available to provide HFNC treatment, in which Optiflow and Airvo 2 (both from Fisher and Paykel Healthcare, Auckland, New Zealand) are commonly used in the United States and worldwide. The Optiflow uses an external air-oxygen blender and a separate humidification unit, whereas the Airvo 2 is an integrated system. Due to the different designs, nebulizer placement is different between the systems. The Optiflow allows nebulizer placement at both the inlet (dry side) and the outlet (wet side) of the humidifier as well as between the circuit and the nasal cannula (proximal to the nasal cannula). In contrast, nebulizer placement with the Airvo 2 was initially limited to proximal to the nasal cannula before the recent release of a nebulizer T-adapter at the outlet of the humidifier.[5] An in vitro study reported a lower inhaled dose with a nebulizer placed proximal to the nasal cannula than when placed at the inlet of the humidifier[10]; however, only one gas flow (30 L/min) was used, and the inhaled mass was measured at the nasal prong rather than distal to the trachea.[10] Thus, little has been reported about the aerosol delivery efficiency distal to the trachea with different nebulizer placements via an HFNC with various flow settings used in the adult population, particularly with the Airvo 2 system.

Different circuits are available for use with the HFNC devices. The Optiflow is used with the RT219 circuit, the Airvo 2 was introduced with a 900PT501 circuit, with a newer circuit

QUICK LOOK

Current knowledge

Aerosol delivery via high-flow nasal cannula (HFNC) has been increasingly used in recent years. In vitro and in vivo studies in both adult and pediatric populations have demonstrated that clinically effective dosages of pulmonary medications, such as inhaled albuterol or epoprostenol, can be delivered transnasally by using an HFNC. However, the effects of different HFNC devices, nebulizer types, and placement on aerosol deposition remain largely unknown.

What this paper contributes to our knowledge

During transnasal aerosol delivery, a vibrating mesh nebulizer generated a higher inhaled dose than did a small-volume jet nebulizer in most scenarios. With an HFNC flow > 10 L/min, an inhaled dose was higher with a nebulizer placed at the humidifier than placement proximal to the nasal cannula. With a vibrating mesh nebulizer placed at the humidifier, the inhaled dose was higher with Optiflow than with Airvo 2.

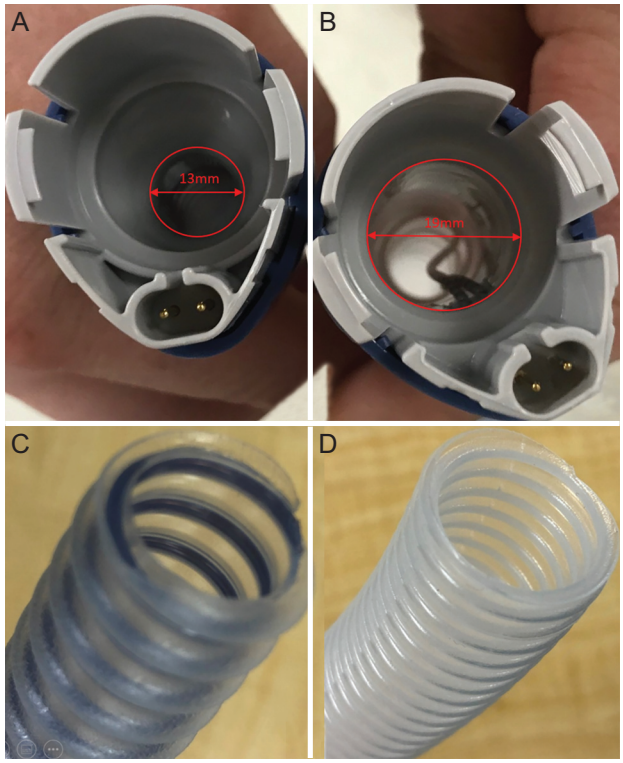

Fig. 1. A comparison of Airvo 2 circuits: AirSpiral (A and C) versus 900PT501 (B and D). Compared with the traditional 900PT501, the AirSpiral has a smaller inner diameter (19 vs 13 mm) and smoother interior surface, where the heating spiral and insulating spiral are molded together, and results in higher thermal efficiency.

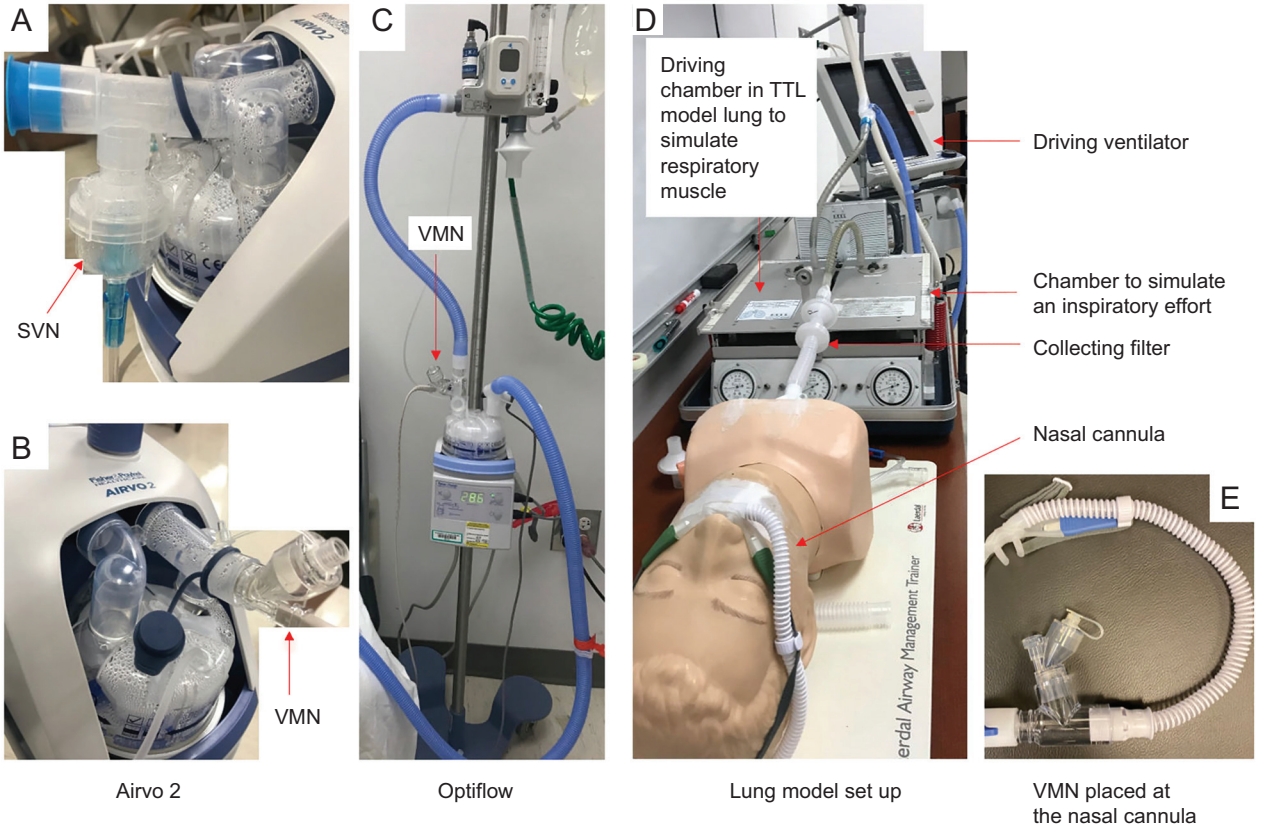

Fig. 2. Experiment setup. The lung model setup was composed of an adult manikin, a collection filter, and a spontaneous breathing simulator (D), which was created by the dual-chamber TTL model lung and a critical care ventilator. In this study, the Optiflow (C) and the Airvo 2 (A and B) were compared; the vibrating mesh nebulizer (VMN) (B) and the small-volume nebulizer (SVN) (A) were compared. In the Optiflow configuration, the nebulizers were placed at the inlet of the humidifier (C), whereas, in the Airvo 2 configuration, the nebulizers were placed at the outlet of the humidifier (A and B). The placement of the humidifier was compared with the placement of the nebulizers proximal to the nasal cannula (E).

(AirSpiral) recently introduced (All three circuits were from Fisher and Paykel Healthcare, Auckland, New Zealand). This new circuit has a smaller interior diameter and smoother interior surface compared with the traditional circuit (Fig. 1). However, little is known about the impact of this new circuit on transnasal aerosol delivery. Therefore, we aimed to investigate the impact of different HFNC devices, circuits, nebulizer type, and placements on aerosol delivery via an HFNC for adult patients when using different flow settings and breathing patterns. We hypothesized that the inhaled dose would be higher with a vibrating mesh nebulizer placed at the humidifier than proximal to the nasal cannula, and no differences would be found between the circuits.

Methods

Experimental Design

An adult manikin (adult airway management trainer, Laerdal Medical AS, Stavanger, Norway) with anatomically correct upper airway proportions was used in this experiment. The manikin's mouth was taped so that inspiration was limited to the nose. Breaths were generated by a critical care ventilator (PB840, Medtronic, Minneapolis, Minnesota) connected to 1 chamber of a 2-chamber model lung (TTL, Michigan Instruments, Grand Rapids, Michigan). The 2 chambers were connected by a metal bar so that a positive-pressure breath into the ventilated chamber raised the other chamber to generate a simulated spontaneous breath (Fig. 2). A collection filter (Respirgard 303, CareFusion, San Diego, California) was connected with the chamber and the trachea of the manikin. The tidal volume was measured by using a NICO2 monitor (Respironics, Murrysville, Pennsylvania). Distressed breathing (tidal volume 700 mL, breathing frequency 30 breaths/min, and inspiratory time 1.0 s) was compared with quiet breathing (tidal volume 500 mL, breathing frequency 15 breaths/min, and inspiratory time 1.0 s).

Comparisons

HFNC Devices and Circuits. We compared 3 HFNC configurations of heated-wire circuits, Optiflow with the RT219

Table 1. Comparison of Inhaled Doses with Different HFNC Setups by Using a Vibrating Mesh Nebulizer

Nebulizer Placement	Breathing Pattern	HFNC Flow, L/min	Inhaled Dose, mean ± SD %			*P*
			Optiflow	Airvo 2 with the Air Spiral Circuit	Airvo 2 with the 900PT 501 Circuit	
At the humidifier	Quiet	10	19.8 ± 0.8*†	15.9 ± 0.2	12.8 ± 0.6	<.001
		20	16.5 ± 0.8*†	12.0 ± 0.3	10.9 ± 0.5	<.001
		40	8.8 ± 1.0*†	5.2 ± 0.5	5.8 ± 0.3	.001
		60	6.3 ± 0.2*†	2.7 ± 0.3	3.1 ± 0.2	<.001
	Distressed	10	17.5 ± 1.0	18.6 ± 0.8†	16.2 ± 0.5	.03
		20	17.8 ± 0.2†	19.8 ± 1.0†	14.5 ± 0.9	.001
		40	16.5 ± 0.3*†	9.1 ± 0.3†	5.7 ± 0.3	<.001
		60	9.8 ± 0.7*†	8.2 ± 0.3†	4.5 ± 0.1	<.001
Proximal to the nasal cannula	Quiet	10	12.0 ± 0.2*†	10.1 ± 0.3	10.2 ± 0.3	<.001
		20	6.7 ± 0.4†	6.8 ± 0.2†	5.7 ± 0.3	.006
		40	3.9 ± 0.3†	3.8 ± 0.2	3.3 ± 0.06	.03
		60	2.0 ± 0.1	2.0 ± 0.1	2.1 ± 0.2	.44
	Distressed	10	17.8 ± 0.5†	18.5 ± 0.5†	13.6 ± 0.4	<.001
		20	13.6 ± 0.2*†	10.6 ± 0.1†	8.0 ± 0.3	<.001
		40	8.2 ± 0.6*†	6.8 ± 0.4	5.9 ± 0.5	.004
		60	3.8 ± 0.1*	3.2 ± 0.1	3.7 ± 0.1*	.002

* $P < .05$, when compared with the Airvo 2 with the AirSpiral circuit.
† $P < .05$, when compared with the Airvo 2 with the 900PT501 circuit.
HFNC = high-flow nasal cannula

circuit, Airvo 2 with the 900PT501 circuit, and Airvo 2 with the AirSpiral circuit (Fisher and Paykel Healthcare) with internal diameters of 22, 19, and 13 mm, respectively. These devices were operated at 4 gas flows (10, 20, 40, and 60 L/min) with the humidifier temperature set at 37°C.

Nebulizers. A single unit of a vibrating mesh nebulizer (Aerogen Solo, Aerogen, Galway, Ireland) and a single unit of a small-volume nebulizer (AirLife 002446; CareFusion) were compared. The small-volume nebulizer was attached with a flow meter and operated at 8 L/min, and the HFNC set gas flow was adjusted to achieve the total gas flow of 20, 40, and 60 L/min. The small-volume nebulizer was not tested at 10 L/min due to the inability of the low gas flow (2 L/min) passing through the humidifier to provide sufficient levels of heat and humidity.

Nebulizer Placement. Per manufacturer's recommendation, the nebulizer was placed at the inlet of the humidifier for Optiflow and the outlet of the humidifier for Airvo 2 (with adapter), and proximal to the nasal cannula with both systems. For each condition, 2.5 mg of albuterol was used, with a fill volume of 1 mL for the vibrating mesh nebulizer (2.5 mg/mL) and 3 mL (0.83 mg/mL) for the small-volume nebulizer. The collection filter was removed 1 min after the nebulization was completed and was eluted with a 10-mL solution of 0.1 M HCl mixed with 20% ethanol. The elution was assayed with ultraviolet spectrophotometry (276 nm). Each condition was repeated 3 times (no. = 3).[13,14]

Statistical Analysis

The inhaled dose was calculated as a percentage of the amount of albuterol captured by the collection filter to the nominal dose (2.5 mg), and was expressed as mean ± SD for each experiment setting with different gas flow, breathing pattern, HFNC device and circuit, nebulizer type, and placement. The independent *t*-test was used to compare the differences of the inhaled doses between 2 nebulizers (vibrating mesh nebulizer vs small-volume nebulizer) and 2 positions (at the humidifier vs proximal to the nasal cannula), whereas an analysis of variance test was used to compare the differences of inhaled doses with 3 HFNC configurations, whereas post hoc corrections for all pairwise multiple comparisons were performed by using the Bonferroni method. A *P* value of <.05 was considered statistically significant. Data analysis was conducted with SPSS statistical software (SPSS 26.0 for Windows; SPSS, Chicago, Illinois).

Results

HFNC Devices and Circuits

When the vibrating mesh nebulizer was placed in-line with the HFNC, the Optiflow provided a higher inhaled dose than did the Airvo 2 with the 900PT501 circuit at both nebulizer positions and during both quiet and distressed breathing patterns with all HFNC flows (all $P < .05$), with the exceptions of 10 L/min with the vibrating mesh

Table 2. Comparisons of Inhaled Doses with the Small-Volume Nebulizer and the Vibrating Mesh Nebulizer

HFNC Device and Circuit	Nebulizer Placement	Breathing Pattern	HFNC Flow, L/min	Inhaled Dose, mean ± SD %		*P*
				Vibrating Mesh Nebulizer	Small-Volume Nebulizer	
Airvo 2 with the Air Spiral circuit	At the humidifier	Quiet	20	12.0 ± 0.3	6.7 ± 0.6	<.001
			40	5.2 ± 0.5	3.4 ± 0.4	.009
			60	2.7 ± 0.3	2.9 ± 0.4	.58
		Distressed	20	19.8 ± 1.0	14.1 ± 0.3	.001
			40	9.1 ± 0.3	6.4 ± 0.7	.004
			60	8.2 ± 0.3	3.9 ± 0.3	<.001
	Proximal to the nasal cannula	Quiet	20	6.8 ± 0.2	6.4 ± 0.1	.02
			40	3.8 ± 0.2	2.9 ± 0.2	.002
			60	2.0 ± 0.1	2.3 ± 0.3	.24
		Distressed	20	10.6 ± 0.1	7.3 ± 0.5	<.001
			40	6.8 ± 0.4	5.3 ± 0.3	.006
			60	3.2 ± 0.1	4.1 ± 0.2	.002
Optiflow	At the humidifier	Quiet	20	16.5 ± 0.8	6.7 ± 0.5	<.001
			40	8.8 ± 1.0	4.2 ± 0.2	.01
			60	6.3 ± 0.2	3.3 ± 0.2	<.001
		Distressed	20	17.8 ± 1.0	8.2 ± 0.7	<.001
			40	16.5 ± 0.3	8.9 ± 0.7	<.001
			60	9.8 ± 0.7	7.3 ± 1.0	.03
	Proximal to the nasal cannula	Quiet	20	6.7 ± 0.4	6.6 ± 0.5	.73
			40	3.9 ± 0.3	3.8 ± 0.4	.58
			60	2.0 ± 0.1	3.3 ± 0.1	<.001
		Distressed	20	13.6 ± 0.2	6.0 ± 0.4	<.001
			40	8.2 ± 0.6	5.8 ± 0.1	.02
			60	3.8 ± 0.1	3.8 ± 0.2	.83

HFNC = high-flow nasal cannula

nebulizer placed at the humidifier during distressed breathing and 60 L/min with the vibrating mesh nebulizer placed proximal to the nasal cannula during quiet breathing (Table 1). With the Airvo 2, the AirSpiral circuit achieved a higher inhaled dose than did the traditional (900PT501) circuit, particularly with the vibrating mesh nebulizer placed at the humidifier during distressed breathing (all $P < .05$).

Nebulizers

Regardless of the HFNC devices, breathing patterns, and flow settings, the vibrating mesh nebulizer generated a higher inhaled dose than did the small-volume nebulizer (all $P < .05$), except when the nebulizer was placed proximal to the nasal cannula with the Optiflow and when the HFNC flow was set at 60 L/min (Table 2).

Nebulizer Placement

When the vibrating mesh nebulizer was placed at the humidifier, the inhaled dose was greater than with the vibrating mesh nebulizer placed proximal to the nasal cannula with all HFNC devices at all flow settings in both breathing patterns (all $P < .05$), except distressed breathing at 10 L/min (Fig. 3A). When the small-volume nebulizer was placed at the inlet of the Optiflow humidifier, the inhaled dose was higher than with the small-volume nebulizer placement proximal to the nasal cannula during distressed breathing (all $P < .05$), but no differences were found during quiet breathing (Fig. 3B).

HFNC Flow Settings and Simulated Breathing Patterns

When the nebulizers (vibrating mesh nebulizer and small-volume nebulizer) were placed proximal to the nasal cannula or when the nebulizers were placed at the humidifier with quiet breathing, the inhaled dose decreased as the HFNC flow increased (Table 2). However, when the nebulizers were placed at the humidifier with distressed breathing, the inhaled dose peaked at 20 L/min with a vibrating mesh nebulizer in the Optiflow and the Airvo 2 with the AirSpiral circuit.

Discussion

We found that the Optiflow outperformed the Airvo 2 when the vibrating mesh nebulizer was placed at the

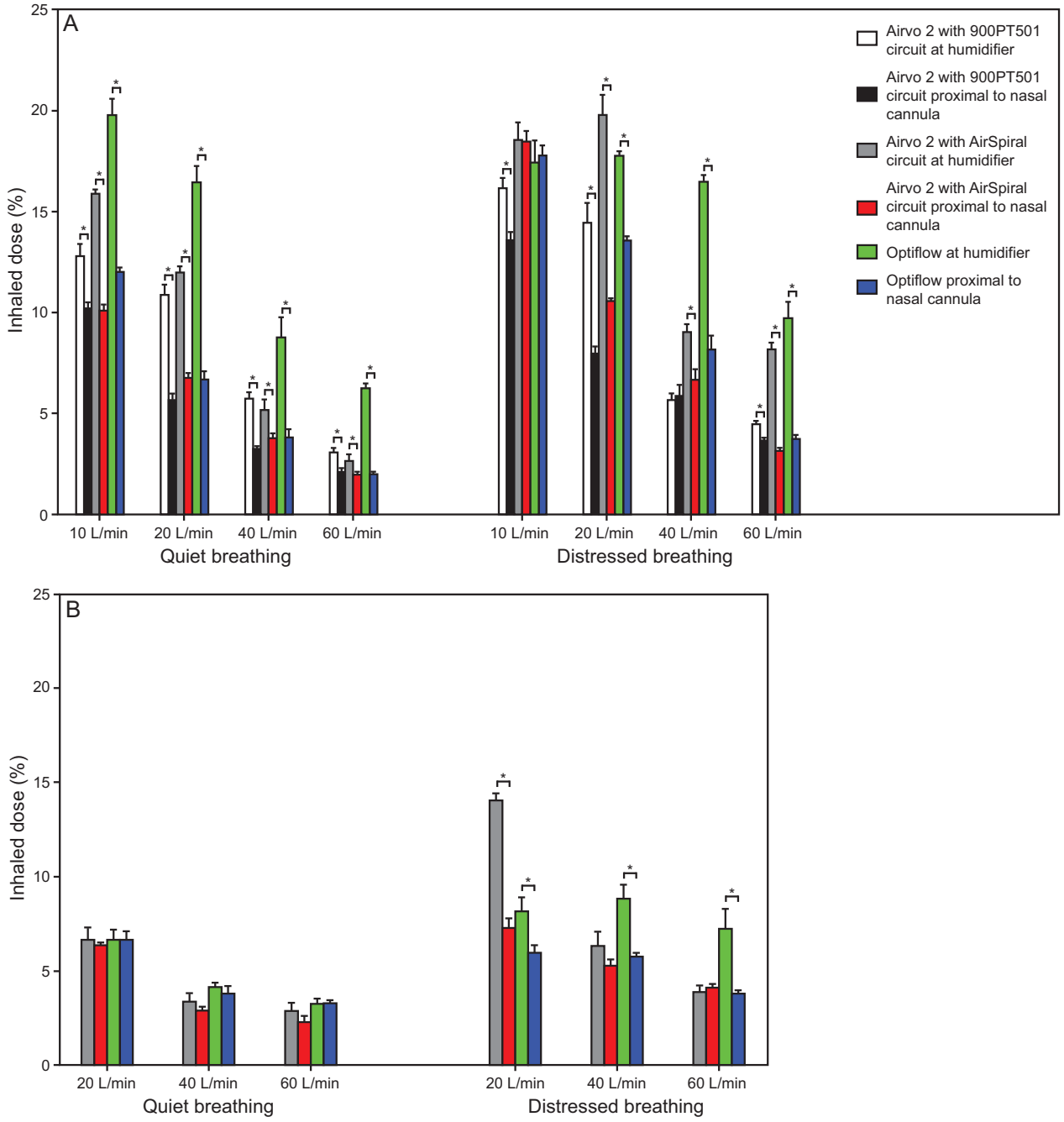

Fig. 3. A comparison of the inhaled dose with the nebulizer placed at the humidifier versus proximal to the nasal cannula. When the vibrating mesh nebulizer was used via HFNC (A), the inhaled dose was higher with the vibrating mesh nebulizer placed at the humidifier than placed proximal to the nasal cannula during quiet breathing at all flows (left). During distressed breathing (right), the inhaled dose was higher with the vibrating mesh nebulizer placed at the humidifier than placed proximal to the nasal cannula, with the exception of HFNC flow at 10 L/min by using the Airvo 2 with the AirSpiral circuit and at 40 L/min by using the Airvo 2 with the 900PT501 circuit. When the small-volume nebulizer (SVN) was used (B), the inhaled dose was higher with the SVN placed at the humidifier than when placed proximal to the nasal cannula with the Airvo 2 and the AirSpiral circuit during distressed breathing (right) as well as with the Optiflow and the HFNC flow at 20 L/min.* $P < .05$.

humidifier and with an HFNC flow > 10 L/min in this first in vitro study, to our knowledge, to report the impact of different HFNC configurations on aerosol deposition. Our findings were also consistent with previous reports of a vibrating mesh nebulizer versus a small-volume nebulizer and their placement, despite those studies being limited to a single HFNC flow,[10-12] and the aerosol was collected at the level of the nose rather than at the

trachea.[10] Our study validated those findings when using the same setup, breathing patterns, and flow settings.[10]

Nebulizer Type and Placement

When nebulizers were placed at the humidifier and the HFNC flow was set at 20–60 L/min, the inhaled dose with the vibrating mesh nebulizer was 1.5–2 times greater than with the small-volume nebulizer in both quiet and distressed breathing. This finding was consistent with previous in vivo studies[11,12] and may be explained in part by the little to no residual drug volume (<0.1 mL) with a vibrating mesh nebulizer, in contrast to the high-residual volume (>1.0 mL) with a small-volume nebulizer.[8] In this study, we tapped the small-volume nebulizer until no aerosol was seen, which resulted in a slightly higher inhaled dose with the small-volume nebulizer than when the nebulizer was not tapped at the bedside by a busy clinician.

Moreover, the small-volume nebulizer requirement of compressed gas flow, usually 6–8 L/min and anhydrous from the tank or the wall, may impact the final F_{IO_2} that is delivered to the patient when it is placed in-line with an HFNC. This requires caution when treating patients with stringent F_{IO_2} requirements, for example, those with COPD.[8] At gas-flow settings of 15–30 L/min, a standard-label dose of albuterol (2.5 mg) delivered by a vibrating mesh nebulizer with an HFNC has been proven to elicit similar bronchodilation effects as conventional aerosol devices with conventional oral interfaces.[3,5] However, in some resource-limited areas, where a vibrating mesh nebulizer is not available and a small-volume nebulizer is the only choice, increasing the nominal dose by 1–2-fold should be considered, especially for patients who do not respond to the initial label dose.[3]

When the vibrating mesh nebulizer was used, the inhaled dose with placement at the humidifier (inlet or outlet) was 1.5–2 times that with the vibrating mesh nebulizer placed proximal to the nasal cannula. This finding agreed with previous in vitro studies.[10,14] Putting the vibrating mesh nebulizer at the humidifier transforms the humidifier chamber and the circuit to act as a reservoir to store the continuous aerosol generated by the vibrating mesh nebulizer, which results in less waste during exhalation.[14] This mechanism may explain our finding of a higher inhaled dose with the vibrating mesh nebulizer placed at the humidifier.

Moreover, putting the nebulizer proximal to the nasal cannula has been associated with the collection of obstructing liquids (rainout) at the airway, and maintaining the nebulizer in a vertical orientation to generate aerosols may be difficult. Also, the additional weight of the nebulizer between tubing and prongs may apply additional pressure on the nares and possibly dislodge the nasal cannula. Consequently, it is recommended that the nebulizer be placed at the humidifier rather than proximal to the nasal cannula.[8] At this writing (April, 2021), the nebulizer adapter for the Airvo 2 is not available in the United States market, which limits nebulizer placement proximal to the nasal cannula. A higher nominal dose needs to be considered to achieve the appropriate lung dose, especially at high gas-flow settings.

HFNC Device and Circuit

When the vibrating mesh nebulizer was placed at the humidifier, the inhaled dose with the Optiflow was approximately 1.5–2 times of the inhaled dose with the Airvo 2 with the 900PT501 circuit, especially at quiet breathing or an HFNC flow ≥ 40 L/min during distressed breathing. This finding could be explained by the difference in nebulizer locations within the 2 devices. Due to the design of the nebulizer adapter, the vibrating mesh nebulizer could only be placed at the outlet of the humidifier with the Airvo 2, in contrast to the placement of the inlet of the humidifier with the Optiflow. The difference is the volume of the humidifier chamber, which functions as a reservoir to collect continuous aerosol generated by the vibrating mesh nebulizer.[10]

With the same nebulizer position with the Airvo 2, a higher inhaled dose was found with the AirSpiral than with the 900PT501 circuit. We speculated that it might be due to the smooth interior surface with the AirSpiral circuit, which might avoid forming turbulence and reduce the effects of inertial impaction, despite the narrower internal diameter. Clinically, when switching patients from one HFNC device to another, we might closely monitor patient's response to the inhaled medication, and consider adjusting the nominal dose based on the patient's response,[3] due to the different performance of transnasal aerosol delivery between devices and circuits.

Similar to our previous findings, the ratio of HFNC gas flow to a patient's inspiratory flow plays the most important role in the aerosol deposition.[13] For a vibrating mesh nebulizer, the inhaled dose could be increased by 2–5-fold with the reduction of gas flow to be ~50% of the patient's inspiratory flow.[13,14] Besides a vibrating mesh nebulizer, in the current study, a small-volume nebulizer placed in-line with the HFNC was also found to be affected by an increased flow. This finding has meaningful clinical implications, especially in the settings with limited resources that the HFNC device, nebulizer type, and position could not be optimized; titrating HFNC gas flow might be a simple, realistic, and feasible solution without increasing the nominal dose.

However, reducing the flow below a patient's inspiratory flow might sacrifice HFNC benefits; thus, the unit dose with a high concentration is recommended[8] to shorten the duration of flow reduction for transnasal aerosol delivery and to minimize the potential harms. It needs to be noted that no commercial device is currently available to measure a patient's inspiratory flow breath by breath. An alternative might be by titrating the HFNC flow based on the patient's real-time clinical response to

the inhaled medication.[6] In general, 15–20 L/min for adult patients who are stable,[3] 20–30 L/min for adult patients with distressed breathing,[6] and 0.25–0.5 L/kg/min for pediatric patients[15] were found to improve aerosol deposition during transnasal aerosol delivery.

This study had some limitations. As with other in vitro studies, the manikin we used to serve as the breathing model could not replicate the actual results of a human being due to the lack of physiologic structures and functions. We only used one of each nebulizer in our study, and the performance of individual nebulizers may vary. More importantly, our model could not quantify the inhaled dose absorbed by nasal membranes, with their rich blood supply, to assess the impact of nasal deposition. Future in vivo studies are needed to address this concern. Even though we studied 2 breathing patterns with a range of flow settings, only one-size nasal cannula and manikin were investigated.

Conclusions

In this in vitro model with an HFNC flow > 10 L/min, the inhaled dose was higher with the vibrating mesh nebulizer placed at the humidifier than proximal to the nasal cannula. With the vibrating mesh nebulizer placed at the humidifier and HFNC flow > 10 L/min, the Optiflow outperformed the Airvo 2 with either AirSpiral or 900PT501 circuits. The vibrating mesh nebulizer generated a higher inhaled dose than a small-volume nebulizer in most scenarios. These findings cannot be extrapolated to other systems or models of different age groups.

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