

EXCELLENCE IN RESPIRATORY CARE

PAST – PRESENT – FUTURE California State Regional Conference

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Disclosures

None

 The opinions expressed during this presentation are those of the speaker, and not necessarily those of MemorialCare, the CSRC, Association or any vendor or sponsor referenced or in attendance.





ex·cel·lence 'eks(ə)ləns/ *noun* noun: **excellence**

1. The quality of being outstanding or extremely good.

synonyms: an outstanding feature or quality. plural noun: **excellences**

Note: Excellence is NOT perfection

EXCELLENCE IN RESPIRATORY?

- Leadership with vision who are:
 - Not afraid to take risks and lead
- Engaged Staff who are:
 - Competent, Passionate, Respectful and Caring Respiratory Therapists
- Protocols that are:
 - Patient Centered, Collaborative and Evidenced Based
- Equipment:
 - Adequate supply and in good
 working condition!

Paradigm Shift Drives Care Transformation

0



The First 3 Initiatives

- Decrease Average Length Of Stay / Prevent Admissions Altogether:
 - Decrease to GMLOS / Stay Home
- Reduce Contract Labor:
 - Decrease or Eliminate Agency & Travelers
- Maximize Efficiency and Throughput
 - FCOTS and Block Utilization Operating Room, PFT, Sleep, Neurodiagnostics

Types of Aerosol – Variation on Particle size



Sneeze



Plant Spores



Flu Virus



Dust

The Micron in Context



Why particle size important?



Best deposition occurs between 2 – 6_{um}



AeroEclipse® BAN - this shows the medication getting deep into your lungs.

Conventional Nebulizer - this shows the large particles from a conventional nebulizer ending up in your stomach, not your lungs.

Example of breathing pattern of a 10-month-old child while **awake** (left) and **asleep** (right)



Janssen JM et al. Aerosol therapy and the fighting toddler: Is administration during sleep an alternative? J Aerosol Med 2003, 16: 4: 395-400

Agitation Reduces Lung Deposition



• Murakami et al Ann Allergy 1990; 64: 383-7

Needs Change with Age: Interface is Critical to Aerosol Delivery

CHOOSINC FC				
	< 4 Years	≥4 Years	≥ 5 years	≥9 years
Aerosol Generator	Nebulizer or pMDI + VHC	pMDI + VHC or DPI	pMDI, BAN , Breath actuated pMDI ↓ All Devices	All Devices
nterface	Mask, Hood, or HFNC	Mask ↓ Mouthpiece or HFNC	Mouthpiece	Mouthpiece

Facemask and Aerosol Delivery In Vivo



FIG. 1. Drug deposition of radiolabeled Salbutamol in a young child (A) inhaling with a pMDI/spacer through a non-tightly fitted facemask, (B) inhaling with a nebulizer through a non-tightly fitted facemask, (C) inhaling with a pMDI/spacer through a tightly fitted facemask, screaming during inhalation, (D) inhaling with a nebulizer through a tightly fitted facemask, screaming during inhalation, (E,F) inhaling with a pMDI/spacer through a tightly fitted facemask, quietly inhaling, and (G,H) inhaling from a nebulizer through a tightly fitted facemask, quietly inhaling.

Erzinger S et al. JAM 2007 Suppl S78 – S84.

Hyperpolarized Helium-3 Magnetic Resonance Imaging

- Hyperpolarized Helium-3 Magnetic Resonance Imaging (³He MRI) was used to
 - Produce detailed images of patient ventilation (airway function)
 - Identify unventilated areas (gas trapped and/or blocked airways)
 - Understand how/where gas distribution was improving

³He MRI is a unique imaging tool for patients with COPD





Hyperpolarized Helium-3 Magnetic Resonance Imaging

Healthy Lungs

Lung with COPD



Study 1 Aerobika* Oscillating PEP in COPD

OBJECTIVE

 Clinical evaluation of the Aerobika* OPEP device in patients with different stages of COPD (non-phenotyped)

METHODOLOGY

- n=14; longitudinal 8 week cross-over study
- 73 (±6) years old; 6 male, 8 female all with COPD
- **Aerobika*** Oscillating PEP (4 weeks)/No device (4 weeks)

EVALUATION POINTS

- Bi-weekly: spirometry, plethysmography, Six Minute Walk Test, St. George's Respiratory Questionnaire (SGRQ), 4x daily OPEP administration, Symptom diary
- Start/Cross-Over/Finish: Hyperpolarized Helium-3 (³He) Magnetic Resonance Imaging (MRI)

Study 1 Aerobika* Oscillating PEP in COPD

Pre-Oscillating PEP



Post-Oscillating PEP



- Reduced breathlessness
- Improved ease of bringing up sputum
- Increased gas distribution to previously unventilated areas
- Reduced hyperinflation (gas trapping)

Study 2 Aerobika* OPEP in COPD and Bronchiectasis

OBJECTIVE

- Clinical evaluation of the *Aerobika** Oscillatory PEP device in patients with bronchiectasis and COPD
 - Only COPD patients with chronic bronchitis and/or chronic sputum production were selected

METHODOLOGY

- *n*=29; longitudinal 6 week cross-over study
- 67 (±10) years old; 13 male, 16 female
 - COPD (n=15, aged 65±9, 9 male/6 female)
 - Bronchiectasis (*n*=14, aged 69±10, 4 male/10 female)
- Aerobika* Oscillating PEP (3 weeks)/No device (3 weeks)

EVALUATION POINTS

 Each Clinic Visit: spirometry, plethysmography, Six Minute Walk Test, St. George's Respiratory Questionnaire, 4x daily OPEP administration, Symptom diary, ³He MRI

Study 2 Aerobika* OPEP in COPD and Bronchiectasis



Pre-Oscillating PEP

Post-Oscillating PEP

Aerobika* Oscillating PEP in COPD and Bronchiectasis

COMBINED STUDY RESULTS

Numerous patient outcomes were shown to be statistically improved following use of Aerobika* OPEP

- Breathlessness (dyspnea)
- Quality of Life (SGRQ measures)
- Cough Frequency
- Ability to Exercise
- Ease of Bringing up Sputum
- Lung Function
 - Resulting from decreased airway obstruction (improved Slow Vital Capacity_{%pred})

³He MRI revealed changes in lung ventilation

- Increase in air transfer from previously unventilated areas
- Decrease in gas trapping (hyperinflation)

No adverse events were recorded

Post Implementation of Aeroeclipse and Aerobika







Aerosol and Ventilators : Invasive and Noninvasive



		2				4	Ą	5	
			Ŷ	9	h			10	h
9	· ·	/		0	Intubo	7 - 40d	Nonin	iv ,	_
					Subje	cts	Sul	bjects	
Administered radioactivity		activity	5	.75 ± 1.	3 mCi	6.53 ±	0.4 mCi	_	
	Percent o dioactiv	f administe vity in:	ered ra-			. 01 0		0.107.0	
	of en	a (includes dotracheal	tube in		1.6 ± 1.	1%"	0.3 ±	0.1%*	
Lung parenchyma Stomach Oral cavity			2.9 ± 0.1	7% ^b	11.9 ±	2.2% ^b			
			_		7.3 ±	2.05%			
			_		$15.0 \pm$	13%			
	Nebuliz	zer circuitr	у		—		65.5 ±	16%	_

Macintyre Crit Cre Med 1985



Fuller et al. 1990. ARRD 141:440-444.

Clinical response to pMDI during CMV



Dhand R AJRCCM 154;388:1996

Dose response in mechanically ventilated patients with COPD.

MDI-spacer & albuterol

 Similar decline in airway resistance with 4, 8 and 16 puffs of albuterol.

Toxicity

Increase in heart rate after 28 puffs of MDI albuterol.

AJRCCM 1996;154:388

 Ventricular ectopy and SVT developed after 3-6 times normal nebulizer dose.

Am Rev Resp Dis 1993;148



Drug deposition

CFC formulated albuterol



HFA formulated albuterol



Fink et al. AJRCCM 1999: 159; 63-67

Vibrating Mesh Nebulizers









https://www.youtube.com/watch?v=J5G OPTE6bEo&pp=ygURYWVyb2dlbiBuZWJ1b GI6ZXI%3D



Four types of aerosol generators in 3 positions during CMV with no bias flow





Ari et al. Respiratory Care 2010; 55 (7): 837-844.



Neb Position	Pos 1 - Between ETT & Y		Pos 2 - 6 in from Y		Pos 3 - 6 in from Vent	
Ventilator Circuit	Heated	Unheated	Heated	Unheated	Heated	Unheated
JN	4.66 (0.5)	7.62 (0.9)	3.61 (0.2)	9.66 (1.5)	5.98 (0.1)	14.66 (1.5)
VM	12.82 (0.5)	14.54 (1.0)	16.79 (2.6)	30.24 (1.0)	8.39 (2.1)	24.20 (1.2)
UN	10.07 (3.9)	10.70 (1.5)	16.53 (4.3)	24.68 (4.4)	4.59 (2.0)	10.51 (0.3)
pMDI	7.6 (1.3)	22.1 (1.5)	17 (1.0)	27.8 (3.3)	2.5 (0.8)	7.9 (1.5)

Ari et al, Respir Care 2010


	ADULT STUDY	PEDIATRIC STUDY
Mode	Volume Control	Volume Control
Tidal Volume	500 ml	100 ml
Respiratory Rate	20/min	20/min
PEEP	5 cmH ₂ O	5 cmH ₂ 0
Waveform	Descending	Descending
Bias Flow	2 and 5 lpm	2 and 5 lpm
Ari et al Resr	piratory Care 2010: 55 (7)	· 845-851

With Bias Flow A VM and JN more Efficient Placed Prior to Humidifier

> As Bias flow Increases deposition decreases

> > VM > JN



Ari et al. Respiratory Care 2010; 55 (7): 845-851.



For HFOV: Place Neb between circuit and ETT



Aerosol Deposition 10.25±6.0%

Demers et al. ATS San Diego, 2005

AEROSOL LUNG DEPOSITION USING A VIBRATING MESH NEBULIZER DURING HIGH FREQUENCY OSCILLATORY VENTILATION IN AN ADULT LUNG MODEL OF ARDS

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Background: Lung deposition of aerosolized medication during high frequency oscillatory ventilation (HFOV) in adults has not been thoroughly quantified. We measured simulated lung deposition in an adult lung model during HFOV using a vibrating mesh nebulizer (VMIN).

Method: A VMN (Aeroneb Solo, Aerogen) was placed between the 3100B (Viasys) ventilator "Y" and a Ballard Trach Care double swivel elbow inline suction catheter. The suction catheter was connected to a 7.5mm endotracheal tube inserted into a bifurcated trachea model and the cuff was inflated. Bacteria filters were positioned at the distal ends of each bronchial lumen and connected via a "Y" adapter to a single compartment of a test lung (TTL, Michigan) set at a compliance of 20 mL/cm H20. The ventilator was set to amplitude of 90 cm H2O, mean airway pressure of 34 cm H2O, 33% inspiratory time, with bias flow of 40 L/min. The VMN was filled with a 3 mL (2.5 mg) dose of albuterol and nebulized continuously until empty. A total of 3 runs each were performed at frequencies of 4 Hz, 8 Hz, and 12 Hz. Albuterol was eluted from the filters and analyzed with UV spectrophotmetry (276 nm) and reported as percent of total dose.

Results: The percent of albuterol delivered distal to the mainstem bronchi in a bifurcated trachea model was 8.7 ± 0.78 % at 4 Hz, 15.1 ± 6.9 % at 8 Hz,frequency. The average deposition across all frequencies tested was 13.8%.

Conclusion: During HFOV in an adult lung model of ARDS, simulate lung deposition of drug aerosolized with the VMN is consistent with th range of dose efficiency reported with conventional ventilation (Ari et a Resp Care July 2010). During HFOV, drug delivery appears to increase wit higher frequencies. Further investigation of lung deposition, penetration, an clinical response to aerosol medication delivery during HFOV in adu patients with ARDS is warranted.





A STUDY TO EVALUATE THE MAXIMAL DOSE ADMINISTRATION AT TWO DIFFERENT LOCATIONS IN TWO DIFFERENT VDR 4 HIGH FREQUENCY PERCUSSIVE VENTILATOR (HFPV) CIRCUITS



AUTHORS: <u>Heltborg, Jeff L.</u>¹; Kobza, Beth S.¹; Nilson, Ace ¹ INSTITUTIONS: 1. Respiratory Therapy, Legacy Health System, Portland, OR, United States

Background: The purpose of this study was to determine if the positioning of an Aerogen® Aeroneb solo nebulizer at different locations in two different VDR4 ventilator circuits would result in differing dose administrations. Determining the location with the maximal dose administration could allow clinicians to deliver more medication. We hypothesize that placement near the endotracheal tube will provide greater dose deposition.

The VDR4 is a high frequency ventilator that combines a convective and percussive high frequency rate. The Aerogen® nebulizer is a low velocity vibrating mesh nebulizer.

Methods: The VDR4 ventilator was used with the Hudson RCI Double or Single Limb Circuit connected to an 8.0 ETT tube with a collecting filter attached to a passive lung with these settings: PIP 30, PEEP 12, Convective rate 15, Tinsp 2 seconds, Texp 2 seconds, High frequency rate 500.

Humidification was provided by the Hudson RCI Concha-Therm Neptune Humidifier. Administration of the dose was done through the Aerogen® nebulizer placed in-line with the ventilator circuit either before the humidifier or between the endotracheal tube and the VDR 4's Phasitron. A unit dose of 0.5 mg / 2.5mL of Albuterol was delivered until complete for the trials. Each trial was performed three times.

After the medication was delivered to the test lung, the filters were sent to a lab where the mass of the drug was eluted from the filters using a UV spectrophotometer at 276nm. Using this data, the percent dose delivered was calculated. Data validation was measured with standard deviation.

Disclosures: There are no presenter conflicts of interest and there was no research funding, sponsorship or financial support for this study.

Double limb

circuit







RANDALL CHILDREN'S HOSPITAL

Single limb circuit

circuit showed contrasting results, with greater deposition when the nebulizer was placed near the endotracheal tube (3.65%), as compared to the placement pre-humidifier (2.62%). Particle size was shown to be at 4.6-4.9 VMD.

> **Conclusions:** Maximal dose was achieved between the two circuits when the Aerogen was placed before the humidifier using the double limb circuit. The results were unexpected; we anticipated that the proximity of the medication to the test lung with either VDR 4 circuit would increase medication deposition. We hypothesize now that releasing the medication into the circuit where the air is already saturated with water may possibly decrease the uptake of medication.

> **Results:** With the double limb circuit, the deposition to

the end of the endotracheal tube was greater when the

nebulizer was placed before the humidifier (8.6%), rather

than near the endotracheal tube (5.2%). The single limb

Aerosol Delivery via High Flow Nasal Cannula



	Infant cannula		Pediatric cannula		Adult cannula	
	No Harvard lung	Harvard lung	No Harvard lung	Harvard lung	No Harvard lung	Harvard lung
Aerosol output dose (%) delivery time (min)	8.4 ± 2.3 13.1 ± 2.5	18.6 ± 4.0 10.8 ± 0.7	18.1 ± 4.2 13.0 ± 0.0	25.4 ± 1.7 10.9 ± 1.4	25.1 ± 5.0 12.5 ± 0.4	26.9 ± 4.9 12.1 ± 0.8

Bhashyam et al. JAM 2008

Aerosol Delivery with High Flow Nasal Cannula Pediatric Cannula

GAS/FLOW	3 LPM	6 LPM	p-values between Flow Rates
Heliox (80/20%)	11.41 ± 1.54	5.42 ± 0.54	p=0.028
Oxygen (100%)	10.65 ± 0.51	1.95 ± 0.50	p=0.002
p-values between Heliox and Oxygen	p=0.465	p=0.01	

Vt – 100 mL RR – 30 BPM



Ari, Dailey, Fink , Peds Pulm, 2011

Humidifier

Research Question

 The impact of different HFNC systems on Trans-nasal aerosol delivery.



Results

Flow (L/min)	Inhaled dose (%) of different HFNC devices, Mean ± SD					
	Hamilton C1	Optiflow	Airvo2	V60 Plus	Vapotherm	
5 (L/min)	NA	NA	NA	NA	2.5 ± 0.4	
10 (L/min)	16.8 ± 0.6	18.2 ± 1.2	15.0 ± 1.2	8.5 ± 0.8	1.8 ± 0.3	
20 (L/min)	13.5 ± 0.4	12.6 ± 1.9	12.8 ± 1	6.4 ± 0.3	1.5 ± 0.1	
40 (L/min)	10.9 ± 0.5	7.7 ± 0.6	3.7 ± 0.5	5.1 ± 0.3	0.9 ± 0.5	
60 (L/min)	8.8 ± 0.3	6.0 ± 0.5	2.2 ± 0.2	NA	NA	
80 (L/min)				1.7 ± 0.7		



Discussion

Inhaled dose & high-velocity nasal cannula

Elem I /min	Inhaled of	lose (%)	
Flow, L/min	Vapotherm	Airvo2	- p
20	1.3 ± 0.1	12.9 ± 0.9	0.05
40	0.8 ± 0.1	5.0 ± 0.2	0.05
60	NA	3.4 ± 0.1	NA

Table 1. Inhaled dose of VMN via Vapotherm and Airvo2 at different flow settings.

VMN, vibrating mesh nebulizer; NA, not available (Vapotherm does not operate at 60 L/min).

Li J, A Alolaiwat A, J Harnois L, et al. Mitigating Fugitive Aerosols During Aerosol Delivery via High-Flow Nasal Cannula Devices. Respir Care. 2022;67(4):404-414.



Perry SA, Kesser KC, Geller DE, Selhorst DM, Rendle JK, Hertzog JH. Influences of cannula size and flow rate on aerosol drug delivery through the Vapotherm humidified high-flow nasal cannula system. Pediatr Crit Care Med 2013;14(5):e250–e256



COMPARISONS OF THE RAM CANNULA WITH HIGH FLOW NASAL CANNULA ON AEROSOL DRUG DELIVERY IN A SIMULATED NEONATAL LUNG MODEL



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1. Georgia State University, Atlanta, GA, USA, 2. Chang Gung University, Taoyuan, Taiwan,

3. Seattle Children's Research Institute, Seattle, WA, USA 4. Lucile Packard Children's Hospital at Stanford, Palo Alto, CA.

Background:

Aerosol delivery through HFNC has been described with in vitro models. The RAM cannula, which is used for support of ventilator-dependent patients, has not been characterized for aerosol delivery. The purpose of this study is to compare HFNC with RAM cannula on aerosol delivery in a simulated neonatal lung model.

Methods

Lung Model: An in-vitro airway/lung model, using the DiBlasi newborn upper airway model attached to a collecting filter and test lung, was passively ventilated using the RAM cannula (Premie RAM Cannula, Neotech) or during active simulated spontaneously breathing newborns using a sinusoidal breathing pump with a HFNC (Fisher& Paykel) placed in the nares of the model (Figure 1).

Figure 1. Experimental set-up of the study.



Methods

Breathing Parameters Used with HFNC: RR 50, Vt 8ml, and I:E ratio 1:2.

<u>Ventilator Parameters Used with RAM</u>: Based on the RAM manufacturer's recommendations, two ventilator settings were utilized: Initial & Maximum

	PIP	PEEP	т	RR
Initial	15 cmH ₂ O	5 cmH ₂ O	0.5 sec	40/min
Maximu m	30 cmH ₂ O	8 cmH ₂ O	1 sec	48/min

Data Collection: A vibrating mesh nebulizer (Aeroneb Solo, Aerogen) was placed at the inspiratory inlet of a heated humidifier (Fisher&Paykel) in which the temperature was held constant at 37 °C.

Albuterol sulfate (2.5mg/3mL) was administered through either HFNC and the RAM cannula connected to the HFNC and ventilator circuit, respectively.

Data Analysis: Drug deposited on a filter distal to the model's trachea was eluted and analyzed via spectrophotometry. Independent and paired sample t-test were used for data analysis (p<0.05).

Results

Deposition of inhaled dose (expressed as mean mass and % of nominal dose \pm SD) is shown in the table below.

Comparisons of the RAM cannula with HFNC showed that the RAM cannula delivers significantly less aerosols than HFNC at both 3 lpm (p=0.002) and 6 lpm (p=0.022).

Using minimum setting with the RAM cannula increases dose efficiency (p=0.033) during mechanical ventilation. Decreasing flow rate from 6 to 3 L/min increases aerosol delivery with HFNC (p=0.119).

Cannulae Type	RA	M	HFNC				
Settings	Minimum	Maximum	3 lpm	6 lpm			
Inhaled mass (mcg)	16.53 ± 2.9	10.03 ± 2.0	39.96±5.5	28.63 ± 8.6			
Inhaled mass Percent (%)	0.66 ± 0.1	0.4 ± 0.08	1.60 ± 0.2	1.14±0.3			
	Conclusion						

Regardless of the settings, aerosol delivery via HFNC is more efficient than the RAM cannula in a simulated neonatal lung model.

Evaluation of the Solo performance during Nasal High Flow - Adult



EVALUATION OF VIBRATING MESH NEBULIZER PERFORMANCE DURING NASAL HIGH FLOW THERAPY

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INTRODUCTION

The efficiency of lang-targeted serosid delivery during Nasal High Flow therapy (NHF) was evaluated in this study

There is an increasing adoption of NH² main and flexible and noninvesive method of positive pressure verification across instant and each projection in both the homeone and distinguished by a sub-transformed provide the distinguished by a sub-transformed provide the distinguished by a sub-transformation of a surrow flow the negligible transformation is the method of the bar implicative presentation of a surrow flow the sub-table to bar bar implicative presentation of the sub-table to bar bar implicative presentation of the surrow flow and barrow flow the sub-table to bar bar implicative presentation of the sub-table to bar bar implicative presentation of the sub-table to bar and barrow flow the sub-table to bar barrow flow the sub-table to bar barrow flow the sub-table to bar barrow flow the sub-table to barrow flow table to barrow

The Answerk & Bols vibrating mesh relations, was selected for concurrent assessing prevention during this sensitive intervention. The Answerk Solo vibrating mesh reducine to down not introduce additional additional app flows or primations and to down not intrifere with the priand gas from rates being deleved to the perfect. This reduces the hall of adverse wide affects such as bact- and wide houses, magnetized by intrifered board of interference with the gas flow rate halps matriation the inside/wij leniner flows expected in the circuity, further increasing affects and assess the paper.

The use of concurrent second delivery during NHF can be exploited to facilitate delivery of a variety of physicien generotized medications for intelation. These include but are by no means limited to hypothesis earlier and p-agreests.

METHODS

Two measures of serosol performance were evaluated, i.e. Emitted Dose (dose evaluate for inhelation) and Respirable Dose (dose delivered to the lung).

Adult high flow name cannula were used (Op85ov^{IM}, Faher & Peyke), 3.0 mL of Abuberol subptile (2regifm), were net/Alized as a marker awread using the Aeroneb Solo (Aerogen), a single patient use device, with an everage MMAD of 3.4 microne (as measured at 28.3 UPM using the Andreson Caesade Incoactor).

Emitted Done at each gas flow rate under teal (15, 30, 45 LPM) was recorded on an abeclute filter (Respirgerd 303, Backer) placed at the exit of the cannula (n+3), see Figure 1.

A loweshing simulator (ASL5000, Ingmer) was used to generate the adult breath ([SH4 15, VI 500 mL, 12 1.1, as per EN15544-1) and Respirable Dose at each gas flow rate under test (5, 30, 45 LPM) was recorded disbit to the LUCY adult sinvey motel (in-3), see Figure 2.

The mean of drug eluted from the fitters was determined using spectrophotometry (at 276 rm) and interpolation on a standard ourve of Abuterol Subhate concentrations (200 µg/mL to 3.125 µg/mL).

Results were expressed as a percentage of the nonlinel dose placed in the netulizer's medication cup, Time to delivery of a full 3.0 mL dose was also recorded.



Figure 1: Emitted Done test setup



Figure 2: Respirable Done test setup

REPULTS

The results of testing are presented in Table 1. Time to delivery of a full 3.0 mL does of Abstanci Subjects was recorded at approximately 7 minutes for each run (equating to approximately 0.85 mg/min served output rate and 0.426 mL/min metolower flow rate).

	EMITTED	EMITTED DOSE		RESPIRABLE DOSE	
Gas Flow Rate (LPM)	Average (%)	SD	Average (%)	SD	
15	64.50	2.00	22.90	1.15	
30	50.74	7.20	13.69	4.12	
45	34.44	3.91	6.53	1,20	

Table 1: Results for Emiliad Dose and Respirable Dose (9D + standard deviation) (n+2).

DISCUSSION

As expected, higher gas flow rates were associated with reduced efficiency of delivery of drug through this model of a humidified aduit nase high flow therapy system.

In relation to both Einsteind Dose and Respirative Dose, this is likely due to impectional losses within the distall tableg and upper alweight of the LUCY model, respectively, with greater losses seen at higher ges flow inter due to potentially turtuident gas flow, and concombant greater interplotential for each second clogist.

A near 3-bid difference was noted between minimum and maximum gas flow relax for Emitted Dows, and a near 3.5-bid difference was noted between minimum and maximum gas flow rates for Respirable Dows.

At all gas flow rates Respirable Dose efficiencies are comparable to those reported in the Startbare with vibrating mesh rebuildons during both investve T and non-investve mechanical vertilation R.

These results provide further proof of principle for concurrent and highly efficient serosol delivery during a nasal high flow therapy intervention.

REFERENCES

[1] Adau A et al., Evaluation of seriosi generator devices at 3 locations in humidified and nonhumidified discuts during soult mechanical vertilation. Respir Care. 2010 Jul 59(7):537-44.
[2] White CC at al., Bronchedilator Delivery During Simulated Pediatic Noninvesive Vertilation. Respir Care. 2013 Feb 5.

Aerogen

		OSE	RESPIRABLE DOSE		
Gas Flow Rate (LPM)	Average (%)	SD	Average (%)	SD	
15	64.50	2.00	22.90	1.16	
30	50.74	7.20	13.69	4.12	
45	34.44	3.91	6.53	1.20	



Nebulizer position



International: +353-91-540400

1-540400 WWW.aerogen.com

Aerosol Delivery with High Flow Nasal Cannula with Adult Cannula

	10 lpm	30 lpm	50 lpm
02	27.1%	12.03%	3.6%
80%Heliox	27.9%	14.4%	5.6%



FIGURE 4-44 In vitro setup for testing aerosol delivery with a heated humidifier through a nasal cannula. The nebulizer is placed at the inlet of the humidifier, and the cannula is attached to a T-piece that allows aerosol to collect on filter 1 and condensate to collect on filter 2. This device can be used in infants, children, and adults.

Ari, Dailey, Fink 2009

Aerosol Delivery and NIV

- Aerosols delivered by pMDI and spacer and facemask or nebulizer and facemask
- Efficiency of aerosol delivery is low due to air leaks in the mask and circuit
- Ventilatory parameters, position of air leak in the circuit, and particle size influence efficiency of drug delivery



Aerosol Delivery and NIV – place neb between leak and patient



- Drug delivery influenced by:
 - Nebulizer position
 - Breathing frequency
 - IPAP/EPAP settings

Chatmongkolchart S et al Crit Care Med 2002;30:2515-2519.

Bench Study: Pediatric aerosol delivery during noninvasive ventilation with the NIVO



Comparison of aerosol delivery with the NIVO and the Aeroneb Solo during non-invasive ventilation

White CC, 2013. Bronchodilator delivery during simulated pediatric noninvasive ventilation. Respiratory Care. Published ahead of print February 5, 2013, doi:10.4187/respcare.02171

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NICU

- Term CDH (Congenital Diaphragmatic Hernia) delivered in our Newborn Resuscitation Room . Right sided defect diagnosed early in utero.
- Infant placed on mechanical ventilation, UAC and UVC placed. Fluids and electrolytes started.
- First Gas: UAC- PH= 6.97, CO2= 110, Po2=47, HCO3=14
- Patient on maximum conventional settings. <u>No</u> right side lung is visible on x-ray. All stomach contents appear to be elevated into the right lung.
- What to do?

Day 1 NICU

- Patient doing very poorly. Placed on HFOV and nitric oxide. CO2 remains > 100.
- Cardiac ECHO shows severe Persistent Pulmonary Hypertension (PPHN). Infant is not a candidate for ECMO with this severe of defect.
- Survival rate for this child is quoted at 12% to parents.

Day 2 NICU

- Current UAC ABG is: PH-7.07, CO2-92, PO2-48, HCO3=21
- Patient is stuck on Oscillator at MAP of 16, amplitude of 50, HZ of 8, 100% FiO2 and 10 ppm of NO.
- We decide to use the VDR:
- 1 hour post VDR UAC: PH= 7.20, CO2= 60, PO2= 54 FiO2=90%
- Patient somewhat stable now but parents told will probably not survive.

1 Week Later

- Patient more stable but still on VDR, NO, multiple pressers and has severe PPHN.
- Surgeons will not operate at this time because PPHN is too severe and patient is on too large of vent settings.
- What to do?
- Cardiologist queried fellow cardiologists around the country regarding various strategies to decrease PPHN.
- It was decided to try aerosolized Veletri.
- How DO you do that?

Combination of Veletri (Inhaled Epoprostenol), VDR and Nitric

- Multidisciplinary meeting to discuss this option and agreed to try.
- Aerogen placed in line with VDR and Nitric Oxide.
- Patients Sa02 increases from 88% to 93% in 10 minutes.
- Cardiac ECHO is done the next day with slight improvement in PPHN that was not seen before.
- 5 days later PPHN has improved by over 30% since introduction of Veletri with Aerogen.
- Vent settings have improved also.
- Surgeons have never done surgery on VDR and Veletri and Nitric Oxide.

ANYTHING IS POSSIBLE

- Surgeons agree to do surgery while on Veletri, Nitric Oxide and VDR.
- Surgery went tremendously well. Lung tissue was available when chest opened up.
- Infant improved tremendously post surgery!!!
- 5 weeks later infant left NICU with no requirement for O2 or special needs.
- Without ability to use Aerogen to deliver Veletri not sure if patient would have survived to have surgery!
- Mom is a hospital employee and always comments about miraculous save of her child!



Aerosolized lloprost is a Viable Alternative to Inhaled Nitric Oxide in Post **Cardiothoracic Surgery Patients**



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Background

Inhaled nitric oxide (iNO) is widely used "off label" to reduce pulmonary hypertension and right ventricular afterload in adult post cardiothoracic surgery patients. Aerosolized iloprost is a stable prostacyclin analogue which has FDA approval for use in adult patients with pulmonary hypertension. Iloprost has appeal in relation to iNO because it has a longer half life, is much less expensive, doesn't require special equipment and it doesn't have potentially toxic biological pathways in the body(figure 1 is a general depiction of the NO pathways). We sought to determine if aerosolized lloprost could be a viable alternative to iNO in this patient population.



Results



Figure 3

Conclusion

The use of lloprost was safe and an effective alternative to iNO for controlling pulmonary artery pressures and reducing right ventricular afterload in this group of cardiothoracic surgery patients.

Methods

We established lloprost delivery guidelines and received IRB approval to do a retrospective review of mechanically ventilated patients who were switched from iNO therapy to aerosolized Hoprost in our adult cardiothoracic ICU. Our quidelines recommended 10 mcg lloprost Q3h X 3 then PRN. The decision to switch over to lloprost was, in all cases, made by the cardiothoracic ICU team. A vibrating mesh nebulizer (Aeroneb Solo, Aerogen Ltd. Galway, Ireland) was used to deliver the lloprost (figure 2). The initial time period cited in the abstract was October 2009 to March 2011 and included 64 patients. Data collection however, did continue up until October 2011 and included 87 patients. We assessed tolerance to aerosolized lloprost and whether or not the patients had to be switched back to iNO prior to extubation.

Results

Out of the 87 patients who received aerosolized lloprost.7 (8%) were switched back to iNO. Reasons for the switch back to iNO included the following; a return trip to the operating room (3), hemodynamic instability (3) and a bed side percutaneous tracheostomy (1). The patient populations are depicted in figure 3. The red bars indicate the number of patients that were switched back to iNO. There were no adverse events associated with the use of lloprost.



Effect of inhaled iloprost in 12 children with postoperative congenital heart disease. Iloprost lowered mean pulmonary artery pressure (mPAP) without lowering mean systemic blood pressure (mSBP). Limsuwan et al



Conversion from inhaled nitric oxide to inhaled epoprostenol reduces costs of inhaled pulmonary vasodilator therapy in critically ill patients

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HARVARD MEDICAL SCHOOL TEACHING AFFILIATE VE RI TAS



Background

Inhaled nitric oxide (iNO) and inhaled epoprostenol (iEPO) are potent pulmonary vasodilators that have been given off label as rescue therapy for severely hypoxic, critically ill patients

Limited data exists evaluating the efficacy of these agents in a diverse cohort of critically ill patients

Purpose

To describe process and associated costs for inhaled epoprostenol use

Methods

Retrospective, single-center analysis of adult mechanically ventilated (MV) patients receiving iNO or iEPO for pulmonary vasodilation

Patients were enrolled between January 1, 2009 and October 31, 2010

This study was approved by our institutional IRB
 Inclusion criteria

- □ ≥ 18 years old
- Admitted to an intensive care unit at Brigham and Women's Hospital
- Received either iNO or iEPO

Exclusion criteria

Received > 2 hours of concomitant iNO and iEPO

Therapy Duration				
	Inhaled Nitric Oxide (N=53)	Inhaled Epoprostenol (N=52)	p value	
Duration of Shute	3.5±2.7*	3.2 ± 2.6*	0.88	
Duration of Study Therapy, days	2.3 (0.6-4.8)†	2.0 (0.9-4.3)†	0.83	
Amount of Study	83.3 ± 90.0*	72.7 ± 85.4*	0.54	
his	54.4 (15-115.5)†	47.9 (20.9-102.6)†	0.63	
1 Median (IQR) MeantSD				

	Cost			
	NO (N=53)	IEPO (N=82)	p value	
Total Cost, USD*				
Low INO Contract Price Mean INO Contract Price High INO Contract Price	206,945 405,775 749,190	43,995	< 0.0001 < 0.0001 < 0.0001	
Cost of Therapy Per Patient, USD*				
Low INO Contract Price Mean INO Contract Price High INO Contract Price	3,930 ± 4,210 9,250 ± 9,910 14,240 ± 15,255	838 ± 997	< 0.0001 < 0.0001	

USD = U.S. Dolar "Based off University HealthSystem Consortium (UHC) survey of nitric oxide contract pricing range

Site

Legacy Emanuel Medical Center Randall Children's Hospital at Legacy Emanuel

Aim statement

To reduce the use and expense of nitric oxide for the treatment of pulmonary hypertension with inhaled Epoprostenol delivered via the Aerogen TM, vibrating mesh aerosol delivery system.

Context

Patients with severe hypoxemic respiratory failure can have subsequent pulmonary hypertension. A common treatment that can reduce pulmonary hypertension is the use of either inhaled nitric oxide or an inhaled prostacyclin, such as Epoprostenol.

Epoprostenol has been shown to be as effective as inhaled nitric oxide in reducing pulmonary hypertension and is significantly less expensive when compared to Nitric Oxide.

Epoprostenol produces vasodilation in low resistance vascular beds in the lungs with improvement in oxygenation in patients with Acute Respiratory Distress Syndrome (ARDS), whereas traditional treatment with optimal ventilator support and positional therapy has been unsuccessful. Epoprostenol has also been successful in the treatment of Persistent Pulmonary Hypertension (PPHN) by reducing V/Q mismatching and shunt in the lung.

Strategies for change / Quality improvement tools

As with all clinical changes both the PDSA model and CQI were implemented. The care of any patient that required this therapy was monitored by all disciplines to include pharmacy, respiratory, nursing and physicians. All respiratory therapists were trained and in-serviced on the use of this medication and delivery via all mechanical ventilators. Pharmacy approved and researched the mixing, proper storage and efficacy of medication.

Careful monitoring to patient response and delivery technique were applied with clinical response similar to the effectiveness of nitric oxide while providing meaningful therapy with significant reduction in expense to the patient.

Measurement / results

In 2013 the use of inhaled Epoprostenol was implemented in the face of the drastically increasing cost of Nitric Oxide (Approximately 100% increase over previous year). Inhaled Epoprostenol costs on average \$9.50 per hour to deliver. In contrast, Nitric Oxide averaged \$128 per hour during CY 2014 and 2015 and is forecast to increase to more than \$170 per hour in 2016. If these patients had been treated with Nitric Oxide vs. Epoprostenol, the expense to our organization would have been > \$1.8M.



Conclusions / lessons learned

Inhaled Epoprostenol provides a safe, effective and significantly less expensive alternative to inhaled nitric oxide for the treatment of ARDS and PPHN.

Team members
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Limitations to Delivery of Prostacyclincs in the ICU/OR

- Iloprost and Treprostinil are only drugs approved for treatment pulmonary hypertension for inhalation in adults, but not readily available for use in the ICU
- Flolan is not approved for inhalation
 - Has short half life -2 3 minutes, requiring continuous aerosol delivery
- In general it is better to use drugs approved for inhalation when they are available.
- Difficult to translate between devices to determine comparable dosing.
- Currently there are no alarms available

Medications via Aerosol to Intubated Patients

- Bronchodilators
- Anti-infectives
- Prostanoids
- Anticoagulants Heparin
- Diuretics
- Insulin
- Perfluorocarbons (PFCs)

RESEARCH



Open Access

Nebulized heparin is associated with fewer days of mechanical ventilation in critically ill patients: a randomized controlled trial

Barry Dixon^{1*}, Marcus J Schultz², Roger Smith¹, James B Fink³, John D Santamaria¹, Duncan J Campbell^{4,5}

Abstract

Introduction: Prolonged mechanical ventilation has the potential to aggravate or initiate pulmonary inflammation and cause lung damage through fibrin deposition. Heparin may reduce pulmonary inflammation and fibrin deposition. We therefore assessed whether nebulized heparin improved lung function in patients expected to require prolonged mechanical ventilation.

Methods: Fifty patients expected to require mechanical ventilation for more than 48 hours were enrolled in a double-blind randomized placebo-controlled trial of nebulized heparin (25,000 U) or placebo (normal saline) 4 or 6 hourly, depending on patient height. The study drug was continued while the patient remained ventilated to a maximum of 14 days from randomization.

Results: Nebulized heparin was not associated with a significant improvement in the primary end-point, the average daily partial pressure of oxygen to inspired fraction of oxygen ratio while mechanically ventilated, but was associated with improvement in the secondary end-point, ventilator-free days amongst survivors at day 28 (22.6 \pm 4.0 versus 18.0 \pm 7.1, treatment difference 4.6 days, 95% Cl 0.9 to 8.3, *P* = 0.02). Heparin administration was not associated with any increase in adverse events.

Conclusions: Nebulized heparin was associated with fewer days of mechanical ventilation in critically ill patients expected to require prolonged mechanical ventilation. Further trials are required to confirm these findings.

Trial registration: The Australian Clinical Trials Registry (ACTR-12608000121369).



Figure 3 Rate of freedom from mechanical ventilation. Over the first 28 days among surviving patients, the rate of freedom from mechanical ventilation was higher in patients administered heparin. Median times of ventilation were 5 days in the heparin group (n = 20) and 8 days in the placebo group (n = 21) (P = 0.01) (log-rank test).

Delivery of inhaled amikacin during mechanical ventilation targets the lung without systemic toxicity



Pulmonary Drug Delivery System for Drug Development



ADULT ECMO for H1N1patient

- 36 Y/O male that our mobile ECMO team retrieved and placed on ECMO from another hospital and brought back to Legacy Emanuel.
- Patient remained on ECMO for several days "resting" with severe pulmonary hypertension noted.
- Lungs finally started to open up and wanted to wean off of ECMO.
- PPHN was a big concern for patient.
- Our ECMO physicians want to try Veletri (Epoprostenol) and they want to aerosolize it!
- Can we do this?






Rotoflow console

pump head



Rotoflow console

pump head

r

oxygenato







OR RN



TRN OR RN

Perfusion •





TRN OR RN RRT

perfusior

surgeon

Driver -





ANYTHING IS POSSIBLE

- YES we can!
- Patient placed on Veletri through the VDR seamlessly.
- Right heart pressures decrease after application of Veletri.
- With the application of the VDR and aerosolized Veletri we were able to wean this patient off mechanical ventilation.
- During H1 N1 season in 2013 and 2014 we had many patients that improved with aerosolized Veletri. We would also give them bronchodilators and hypertonic saline to help breakup debris and again the Aerogen delivered this flawlessly.

Legacy Health ECMO Transport



Respiratory Rescue Team



What about treatment strategies before ECMO

- 1. ARDS network
- 2. Proning
- 3. APRV / Bi-level
- 4. Delivery of nitric oxide or an inhaled prostacyclin (Veletri or Iloprost).
- 5. high frequency ventilation (HFPV not HFOV)

Proning Anyone?



Positional Therapy

Strategies for Skin Protection



High Frequency Percussive Ventilation VDR 101 Case Studies





HFPV STUDY

- 1. To determine if early use of High Frequency Percussive Ventilation (HFPV) reduces need for Veno-Venous ECMO (V-V ECMO) in patients who have failed conventional modes of ventilation and were referred and accepted for ECMO Treatment at our facility.
- 2. The majority of patients referred to our facility for V-V ECMO have severe Refractory Hypoxemic Respiratory Failure . They have failed traditional treatment and conventional modes of ventilation including ARDSnet, APRV, PCV, HFOV, prone positioning and inhaled Nitric Oxide and / or Epoprostenol.
- 3. Patients are considered for ECMO when the P/F ratio is <100 and have a treatable and reversible cause. Patients found to be unstable or in extremis upon arrival to the referring hospital were not considered candidates for HFPV alone. These candidates were immediately placed on ECMO

<u>Aim statement</u>

In an effort to provide good health to our community, we investigated if early use of High Frequency Percussive Ventilation (HFPV) reduces the need for Veno-Venous Extracorporeal Membrane Oxygenation (V-VECMO) in patients who have failed conventional modes of ventilation and were accepted or met the criteria for ECMO at our facility.

Context

Traditional ventilator support in ECMO patients involves use of minimal ventilator settings to allow complete lung rest. However, this frequently results in worsening of radiographic findings and lung derectuitment by not allowing the lung some level of expansion and participation in gas exchange. By using lung recruitment with HEPV early with these refractory patients, we can, in some cases, eliminate the need for ECMO.

Patients referred to our facility for V-VECMO consideration have severe refractory hypoxemic respiratory failure. They have failed traditional treatments such as prone positioning and inhaled Nitric Oxide and/or Epoprostenol, and conventional modes of ventilation, including ARDSnet, APRV, PCV and HFOV,

The PaO₂/FioO₂ ratio is used to determine severity of hypoxemia. Patients are considered for ECMO when the P/F ratio is <100 and they have a treatable and reversible cause. Patients found to be unstable or in extremis upon arrival to the referring hospital were not considered candidates for HFPV alone. These candidates were immediately placed on ECMO and stabilized for transfer to Legacy Emanuel Medical Center.

We reviewed calendar years 2014 and 2015 to compare patients accepted for ECMO, but were placed on HFPV first, before determining further need for extracorporeal support. We found that 15% of patients in 2014 and 44% of patients in 2015 were treated with HFPV alone and were not placed on ECMO.

We exclusively use the Percussionaire VDR-4 high frequency percussive ventilator (HFPV) on all patients requiring ECMO, or patients transferred for respiratory failure, who have failed conventional ventilator modes. For transport, we use the Percussionaire Sinusoidal Bronchotron TM (this is the transport version of the VDR-4).

Strategies for change / Quality improvement tools

Quality improvements are continuously assessed by using CQI and PDSA. This is done using all disciplines involved in the care of these patients including ECMO Surgeons, Critical Care Medicine (CCM) Physicians, RT, RN and Perfusionists.



Referrals 2014/2015



In some cases (15% in C Y14 and **44%** in C Y15) we were able to avoid the need for ECMO by early application of HFP V even though the patient met criteria for ECMO. This substantiates findings of the CESAR trial. Cite: Peek G, Elbourne D, Truesdale A, et al. Randomized controlled trial and parallel economic evaluation of conventional ventilatory support versus extracorporeal membrane oxygenation for severe adult respiratory failure (CESAR). *Health Technology Assessment* [serial online]. January 2010; 14(55):1-74 74p. Available from: CINAHL Complete, Ipswich, MA. Accessed November 27, 2015.

Conclusions / Lessons Learned

Good financial stewardship is sought by identifying patients with severe hypoxemic and/or hypercapnic respiratory failure who can benefit from early implementation of HFPV. These patients have qualified for extracorporeal support, and in some cases can be managed with HFPV without ECMO. By doing this, we avoid the inherent mortality risks associated with extracorporeal support, decrease overall hospital length of stay and ventilator days. We also contribute to a significant reduction in ECMO associated costs. This led to a combined savings for calendar years 2014 and 2015 of \$3.98 million.

Average per case direct costs associated with ECMO	\$248,591
Average per day direct costs associated with ECMO	\$6,631
Combined savings 2014/2015	\$3.98 million

Team members

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Adult Respiratory Failure Program

Patients accepted for ECMO at Legacy, but were placed on HFPV first:

2014: 20% of patients rescued with HFPV alone

2015: **44%** of patients rescued with HFPV alone and were not placed on ECMO.

2016: **35%** of patients rescued with HFPV avoided ECMO



Referrals 2014/2015

Early implementation of HFPV in patients with Severe Hypoxemic and/or Hypercapnic Respiratory Failure who have qualified for extracorporeal support, could be managed with HFPV without ECMO in some cases. By doing this, we avoid the inherent mortality risks associated with extracorporeal support, decrease overall hospital length of stay and ventilator days. We also contribute to a significant reduction in ECMO associated costs. A combined savings for calendar years 2014 and 2015 of \$3.98 million.



Referrals 2014/2015

SURVIVAL TO DISCHARGE



ELSO international average survival to d/c is 55%

Conclusions

- ARDS continues to affect many patients and as respiratory therapists we can greatly affect the outcome of these patients by early detection and identification of disease.
- Respiratory Therapists must use treatment strategies quickly and efficiently to include: ARDS network, Proning, APRV, inhaled prostacyclin's and if they are not working consider aggressive strategies such as HFPV and ECMO!
- WE CAN MAKE A DIFFERENCE

Wrap Up

- Anything IS possible
- Health Care Transformation is upon us
- We are now <u>REWARDED for QUALITY</u> patient care
- Gone are the days of counting how many widgets you can do in a given day
- Decreasing readmissions is key
- Thinking outside of the box and trialing new forms of therapy will help the profession of Respiratory Care survive!

Bonus Case Study – Time permitting...



Will an ambulance fit in a C-130? Can you do that?



Yes it will... NO... YOU Can't!!!



But it's Christmas Eve...













