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PERFORMANCE OF HOME-BASED HIGH FLOW THERAPY DEVICES IN MUCUS CLEARANCE AND HYGROMETRY

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High-flow therapy (HFT) has emerged as a promising option to improve oxygenation and comfort acute respiratory failure patients (1). By generating positive end-expiratory pressure (PEEP), enhancing dead space washout, and reducing airway resistance, HFT has demonstrated benefits for respiratory mechanics (2,3). Furthermore, it provides controlled humidity and temperature, which promotes tracheobronchial clearance, critical for managing chronic respiratory disease (4,5). Recognizing these advantages, home-based HFT devices have been developed for patients with chronic conditions, using either integrated blower-humidification systems similar to positive airway pressure devices or non-invasive ventilators (NIV) with an HFT mode. This study aimed to compare mucus clearance, humidification performance, and respiratory mechanics between dedicated HFT devices and adapted NIV (6,7).

We conducted a high-fidelity bench study connecting an ASL 5000 mechanical lung, a 15cm silicone rubber trachea, and a 3D-printed airway model (8-10) (Figure 1).

Two respiratory profiles were tested: obstructive (RawI 20 $cmH_2O \cdot s/L$, RawE 25 $cmH_2O \cdot s/L$, compliance 50 mL/cmH_2O) and restrictive (RawI 8 $cmH_2O \cdot s/L$, RawE 5 $cmH_2O \cdot s/L$, compliance 30 mL/cmH_2O). Functional residual capacity was set at 0.5 L, respiratory rates ranged from 14 to 18 bpm, and inspiratory effort was standardized to a P0.1 of 2 cmH_2O (11). Humidity and temperature were measured at the trachea using Vaisala HMP110 sensors. Airflow was recorded with a Fleisch pneumotachograph and a Validyne pressure transducer. For mucus clearance assessment, 5mL of artificial mucus (2% polyethylene glycol-based) were applied 5cm distal to the trachea (12,13). We tested two dedicated devices: Airvo2 (Fisher & Paykel Healthcare, Auckland, NZ) and LumisHFT (ResMed, San Diego, CA, USA), and two NIV with HFT mode: EO-150 (EOVE, Pau, FR) and PrismaVent-50C (Löwenstein Medical, Bad Ems, DE), paired with a MR810 humidifier (Fisher & Paykel Healthcare) as per manufacturer recommendations. All devices used M-size nasal cannulas (Fisher & Paykel Healthcare) covering 70% of the nares.

Experiments were conducted without any HFT device (control condition) and with each device set at 30 L/min and 37°C, with the mannequin's mouth closed to minimize leaks. Mucus movement was recorded over eight hours (ImageJ software, NHS), with velocity and displacement measured. Positive and negative movement indicates displacement towards the mouth and the lungs, respectively. Humidification and respiratory mechanics were assessed under different flow rates (10–60 L/min), temperatures (31, 37°C) and open or closed-mouth scenarios.

Both dedicated and adapted devices promoted significantly greater mucus displacement compared to spontaneous breathing (26.03 [14.97; 37.91] mm and 16.72 [12.10; 20.94] mm vs. -6.72 [-12.87; -1.73] mm; $p<0.001$), with dedicated devices being more effective ($p=0.03$). Mucus velocity did not differ significantly between devices (dedicated: 0.062 [0.041; 0.229] mm/min and adapted: 0.041 [0.008; 0.235] mm/min). However, velocities were significantly higher compared to spontaneous breathing (-0.024 [-0.056; 0.003] mm/min; $p = 0.002$ and $p = 0.007$; respectively). (figure 2A). Mucus displacement remained stable over the time without differences between devices (figure 2B).

Humidification showed higher maximum and mean relative humidity (RH_{mean}) for dedicated devices ($p<0.001$). Dedicated devices delivered an 11.72% higher RH_{mean}. At higher flow rates (50 and 60 L/min), RH_{mean} decreased, while higher temperatures (37°C) and closed-mouth conditions improved RH_{mean}. Mean absolute humidity (AH_{mean}) levels were similar between devices, though dedicated devices achieved slightly higher AH_{mean} (+1.5 mgH_2O/L). Temperature decreased by -1.80 °C with open-mouth conditions ($p<0.0001$), whereas flows above 50 L/min were correlated with higher temperatures (β 2.45 °C; $p<0.001$).

Respiratory mechanics showed no significant differences between device types. However, higher flow rates were associated with increased PEEP and reduced WOB.

This study overcomes some limitations in assessing mucus clearance, which often rely on surrogate endpoints. Hasani et al. (14) demonstrated the positive impact of HFT on mucociliary clearance in bronchiectasis patients, but aerosol deposition techniques may lack specificity. Our artificial mucus model, validated in critical care

settings (12,13), enabled an objective evaluation of mucus velocity, a key parameter that may be impaired by humidity or temperature fluctuations, leading to bronchoconstriction and reduced ciliary function (15). These changes are particularly detrimental in chronic respiratory conditions like COPD and bronchiectasis, where compromised mucociliary clearance increases the risk of infection and hospitalization (2,16). Furthermore, Diaz et al. (17) reported that mucus plugs in lung segments correlate with increased mortality in COPD patients, with the risk rising as the number of affected segments increased. Enhanced clearance observed in our study suggests that HFT devices may contribute to reducing occurrence of exacerbations, and potentially improving long-term outcomes in these patients.

Optimal duration of HFT to enhance mucociliary clearance remains uncertain. In our study, an increase in mucus velocity was observed within the first 30 minutes, aligning with Kelly et al. (5). Their in-vitro study demonstrated a 15% increase in mucus velocity (9.8 ± 0.2 mm/min, $p<0.05$) within 15 minutes of HFT at 20 L/min with nebulized isotonic saline, strongly correlated with airway surface liquid height ($R^2=0.93$). Similarly, our study showed higher mucus velocity with dedicated devices between 6 and 8 hours (Airvo2: 0.06 mm/min; LumisHFT: 0.07 mm/min). These findings are supported by Nagata et al. (18), where patients using HFT for 7.3 ± 3.0 hours daily experienced reduced exacerbation rates (adjusted mean difference [95% CI]: 2.85 [1.48–5.47]) and prolonged exacerbation-free periods. This reduction may be attributed to improved mucus clearance, further corroborating our results.

Scant evidence exists regarding optimal AH levels in non-invasive respiratory supports, especially for HFT. A bench study by Delorme et al. showed AH for Airvo2 ranging from 41.8±3.9 mgH_2O/L at 10–15 L/min to 38.8±1.0 mgH_2O/L at 50–60 L/min (19). The differences between their findings and ours may stem from wider compliance and resistance ranges, diverse clinical scenarios, and higher leaks (open vs. closed mouth) simulated in our study, which directly impacted hygrometry and complicated comparisons. Notably, our results align closely with Lellouche et al., who reported AH of 29.4±1.9 mgH_2O/L without leaks and 27.7±2.7 mgH_2O/L with leaks during NIV in healthy subjects (20), confirming the reproducibility of our bench model.

This bench study has limitations. First, we did not simulate varying inspiratory efforts, which could influence mucus clearance. Second, the simplified tracheal model does not consider the physiological complexities of distal airways, ciliary function, or regional humidity and temperature variations. Additionally, despite using the highest temperature settings, we recorded lower temperatures. This may result from heat loss in the bench model. Finally, we used room air (F_IO_2 0.21) but different gas mixtures may affect humidification performance. These findings require validation in clinical settings.

In conclusion, dedicated HFT devices demonstrated superior mucus clearance compared to adapted NIV devices with HFT mode, highlighting the importance of device selection in optimizing patient outcomes. Dedicated devices also maintained better humidity and temperature control, although respiratory mechanics were similar across devices. Our artificial mucus model offers a novel approach to objectively assess HFT's impact on mucus clearance. These findings may inform clinical strategies for managing chronic respiratory diseases.

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Authors' Contributions: Study concept and design: EF, MP; Acquisition of data: RMA, EF; Analysis and interpretation of data: RMA, EF, ML, GP, MP; Statistical analysis: RMA, EF; Drafting of the manuscript: RMA, EF; ML; Critical revision of the manuscript for important intellectual content: ML, GP, MP.

EF has full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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FIGURES:

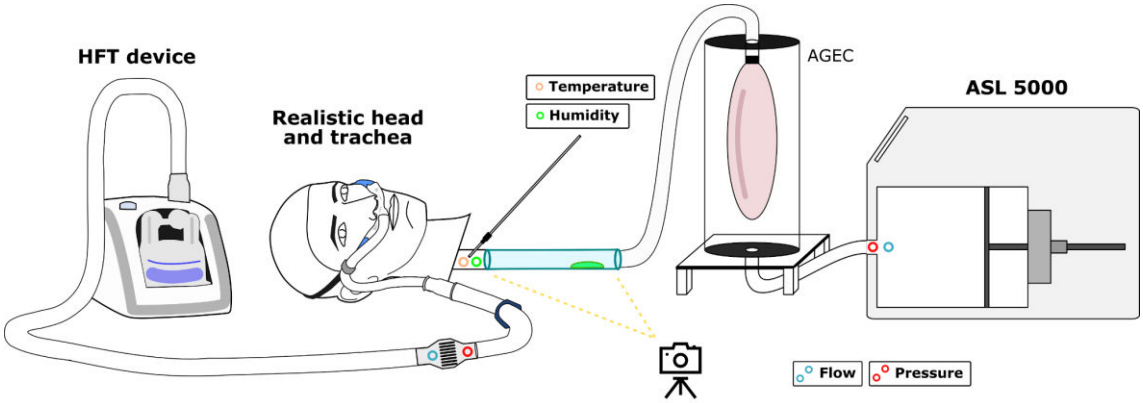
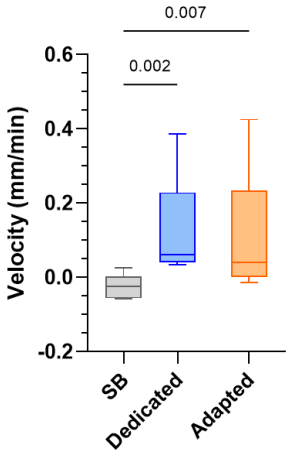


Figure 1: Bench experimental setup. From left to right: HFT device to be tested, flowmeter and pressure sensor on the circuit, manikin head with nasal cannula, silicone trachea with hygrometric sensors and synthetic mucus, AGEC protective balloon, mechanical lung.

2A)



2B)

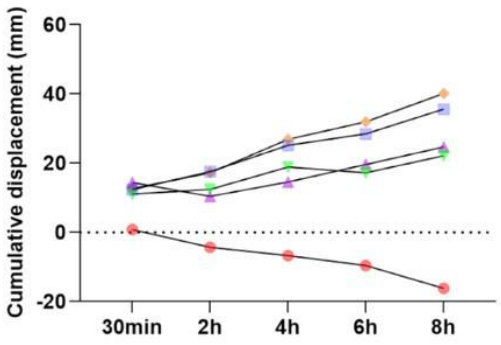


Figure 2: Mucus velocity (mm/min) (2A) assessed during spontaneous breathing, treatment with dedicated devices and adapted non-invasive ventilation devices, and cumulative mucus displacement (mm) per device (2B). mm/min: millimeters per minute; SB: spontaneous breathing.