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Comparison of expiratory pressures generated by four different EPAP devices in a laboratory bench setting

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ABSTRACT

Objective/background: Expiratory positive airway pressure (EPAP) has been a treatment option for patients with obstructive sleep apnea (OSA). ULTepap is a new FDA-cleared EPAP device that seals the nares with a nasal pillow interface. Comparisons of expiratory pressures generated by ULTepap and other EPAP devices like Provent, Bongo Rx, and Theravent are not available. We aimed to compare the backpressures created by these devices in an in vitro laboratory bench setting.
Methods: A test rig was designed and fabricated to test the expiratory pressures generated by ULTepap, Provent, Bongo Rx, and Theravent. Airflow was generated by a linear actuator-driven piston in a syringe, and a range of flow rates was provided by varying the voltage input to the actuator. The resulting expiratory and inspiratory pressures were measured and resistances were calculated.
Results: The backpressures generated by ULTepap and Provent were comparable at all flow rates. For flow rates at 99/142/212 ml/s, the expiratory pressures were 3.5/7.5/13.8 cmH2O for ULTepap and 4.5/8.5/14.5 cmH2O for Provent. Bongo Rx and Theravent devices produced substantially lower backpressures compared to ULTepap devices (0.8/1.8/3.5 cmH2O for Bongo Rx and 0.9/2.2/5.3 cmH2O for Theravent at flow rates of 99/142/212 ml/s). All four devices presented very low inspiratory flow resistance, with all generating 0.5 cmH2O or less at all flow rates.
Conclusion: Not all FDA-cleared EPAP devices produce similar expiratory pressure profiles. ULTepap generated backpressures closest to that of Provent. Clinical trials comparing the efficacy, tolerance, and adherence of these EPAP devices in patients with OSA are warranted.

1. Introduction

1.1. Background

Obstructive Sleep Apnea (OSA) is now considered a common community problem affecting up to 1 in every 5 middle-aged adults and is associated with cardiovascular complications [1–8]. There are degrees of expression and variations in the consequences resulting from chronic intermittent hypoxemia and sympathetic hyperactivity associated with fragmented sleep [9,10]. Continuous Positive Airway Pressure (CPAP) was introduced in 1981 and over the years has become the standard, initial OSA treatment with strong evidence of efficacy in those who are adherent [10–13]. However, many fail to tolerate CPAP, and the overall adherence is roughly around 30–70% [14].

In 1983, Mahadevia and Lopata studied 9 patients with OSA one week apart without and with expiratory positive airway pressure (EPAP) of 10 cm H2O and noted that EPAP could reduce apnea index, apnea duration, and oxygen desaturation index (ODI) during sleep [15]. Moreover, they found that EPAP significantly improved sleep quality by decreasing the relative time spent in Stages N1 and N2 sleep and increasing the relative time spent in Stage N3. This study demonstrated that EPAP in itself is sufficient to improve OSA

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and sleep quality to some extent, but at that point, the institution of therapy was cumbersome requiring a tight-fitting face mask that contained an inspiratory valve and an expiratory valve that was attached to a threshold resistance to apply EPAP.

1.2. EPAP devices and their valving systems

Fast forward to today, several devices have been developed that focus on generating a positive pressure only in expiration rather than a pressure throughout the respiratory cycle, with the advantage of being relatively non-intrusive. At the time of this study, there were three FDA-cleared EPAP devices to treat OSA (ULTepap, Bongo Rx, and Provent) and one FDA-cleared device to treat snoring (Theravent). All four devices utilize some kind of resistance valve in the breathing path. When the patient inhales, there is minimal resistance, but upon expiration, the patient is forced to breathe through a partially restricted fixed opening which in turn increases airway pressure. This creates therapeutic backpressure (i.e., EPAP), which is maintained until the start of the next inspiration.

Provent (Ventus Medical, Belmont, CA), the first commercially available EPAP device, was cleared by the FDA for treatment of OSA of all severities in 2009 but was discontinued in June 2020. Provent is a disposable, single-use disc-shaped bandage type and one-size-fits-all patch, which adheres externally under each nostril. There is a small one-way flap valve in each disc, which acts as a bi-resistor valve. The efficacy of Provent EPAP to treat OSA has been investigated and confirmed in several studies [16–23].

Theravent (Ventus Medical, Belmont, CA), using a similar bandage design with “MicroValve technology” for creating EPAP, was cleared by FDA for over-the-counter treatment of snoring in 2012, but was also discontinued in 2020 as Provent. The valving system is somewhat different, in that there are four parallel vent slits on either side of a fixed orifice in the center. More recently, Bongo Rx (AirAvant Medical, Deerfield Beach, Florida) was cleared by the FDA for treatment of mild to moderate OSA in 2018. Bongo Rx is a reusable EPAP device that seals inside the patient's nares and may be used with supporting headgear. Its valving system is very similar to that of Provent, in that there is a small flap valve under each nasal pillow, which opens on inhalation and closes on exhalation, requiring the patient to breathe through two fixed orifices in each flap-valve, thus creating backpressure during the expiratory phase of breathing.

ULTepap (BRYGGS Medical, Avon, Ohio), the latest EPAP device on the market, was cleared by FDA for treatment of mild to moderate OSA in 2020. ULTepap is a reusable EPAP device that seals around the patient's nares similar to conventional CPAP nasal pillow interfaces (Fig. 1a). Under each pillow is a proprietary “flow cartridge” (Rashidi-Sleeper valve) that contains a collapsible silicon thin-walled shell (Fig. 1b). The shell collapses on inhalation and expands on expiration, forcing the patient to exhale through a small fixed diameter lumen.

1.3. Research question

Our research question was “Are expiratory threshold therapy devices equivalent in generating backpressures in an expiratory direction?” We, therefore, compared the expiratory pressures created by ULTepap, Provent, Bongo Rx, and Theravent systems in an in vitro laboratory bench setting. We also measured and compared the non-therapeutic pressures generated on inhalation and calculated inspiratory and expiratory resistance.

2. Materials and methods

2.1. Bench test rig design

To test the inspiratory and expiratory pressures generated by ULTepap, Provent, Bongo Rx, and Theravent over a range of flow rates, we designed and fabricated a test rig specifically (Fig. 2). The test rig included a 1-L piston-driven calibration syringe (Spirometrics, Grey, ME) that created airflow at selectable different rates using a linear actuator (Zsxuianda XDHA12-300, Guangdong, China) driven by a 12-V DC motor, controlled by a triple output DC power supply (Agilent® Model E3631A, Santa Clara, CA).

2.2. Manifold configuration and pressure measurement

The expiratory and inspiratory pressures were measured by a Respironics digital pressure manometer (Philips-Respironics, Murrysville, PA) from a nipple mounted to each manifold as shown in Fig. 3. Each manifold had a flat surface on one end with two holes roughly designed to replicate a person's nares opening, and a pipe thread on its other end attached to the calibration syringe's discharge end.

1. For ULTepap, the airflow cartridges were mounted and hermetically sealed directly over the holes onto its manifold.
2. For Provent, each disc was mounted with the devices' adhesive surface directly over the holes of its corresponding manifold.
3. For Bongo Rx, the device was inserted directly into the holes of its manifold, secured, and hermetically sealed with adhesive.
4. For Theravent, the device was mounted with the devices' adhesive surface covering both holes of its corresponding manifold.

All four devices were tested to ensure that they were securely attached to the manifold without air leaks around the adhesive's surfaces using magnified visual inspection and soap-bubble leak-detecting liquid. Each manifold was then attached to the calibration syringe by securely tightening the manifold's pipe thread into the calibration syringe and further sealed with plumber's putty (Oaty Stain Free plumber's putty). All connection points were also tested with soap liquid to ensure hermetically sealed connections at all joints.

Before each test, the digital manometer was calibrated to zero using the manometer's zero adjust dial, and the triple output DC power supply was adjusted using the voltage adjust dial to the required voltage to a tolerance of 0.00. The calibration syringe required no calibration as the flow was a calculated value using the fixed area of the syringe piston.

Each test began with the linear actuator fully retracted. A manifold with one of the devices was threaded into the calibration syringe and sealed with plumber's putty. The power supply was initially set at 12 V which resulted in a calculated flow rate of 260 ml/s. Upon the activation of the power supply, the linear actuator rod pushed the syringe piston from its fully retracted position (syringe fully filled with air) to its fully compressed position (syringe empty of air). During this time, the backpressure being produced by each respective device was displayed on the pressure manometer and recorded. The polarity of the power supply was then reversed, and the linear actuator rod pulled the syringe piston until the rod was fully retracted. The negative pressures measured during this phase were also recorded, which represent the resistance to inspiration. This cycle was repeated three times for each voltage at 5, 6, 7, 8, 9, 10, 11, and 12 V. This entire process was then repeated for each of the other three devices.

2.3. Flow rate and resistance calculation

The flow rate for each test was calculated as follows: $Q = A \times V$, where Q is the airflow rate (ml/sec), A is the cross-sectional area of the piston in the syringe (cm2), and V is the piston's speed

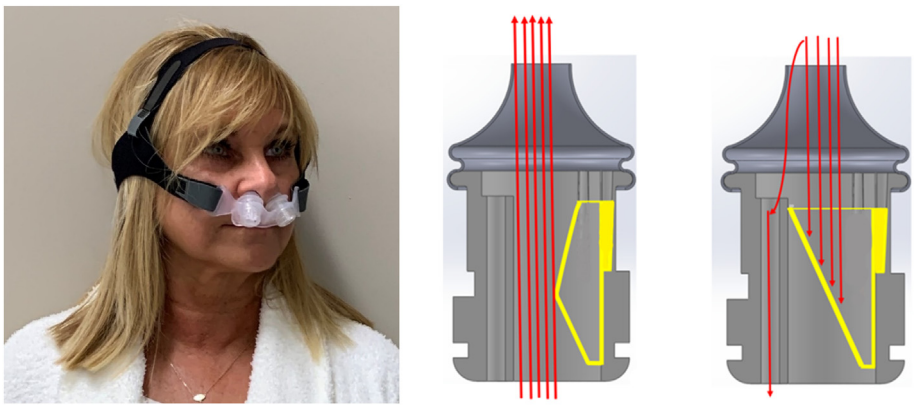

Fig. 1. (a) ULTepap device on a model; (b) Flow cartridge (Rashidi-Sleeper valve) that contains a collapsible silicon thin-walled shell. Inhalation (on the left) with the contracted flexible shell (yellow), and exhalation (on the right) with the expanded flexible shell (yellow). The airflow direction is shown with red arrows.

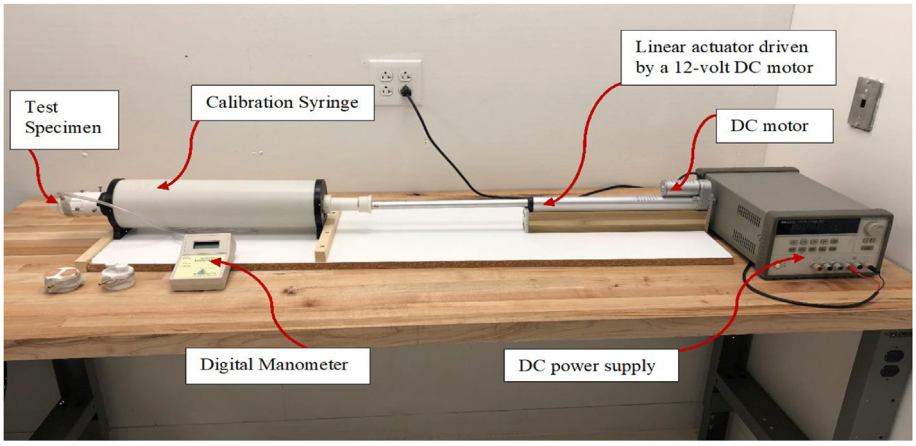

Fig. 2. The test rig designed and used in this study. The test rig consists of a piston-driven calibration syringe, a linear actuator, a DC motor, and a DC power supply. The expiratory and inspiratory pressures were measured by a digital pressure manometer from a nipple mounted to each manifold.

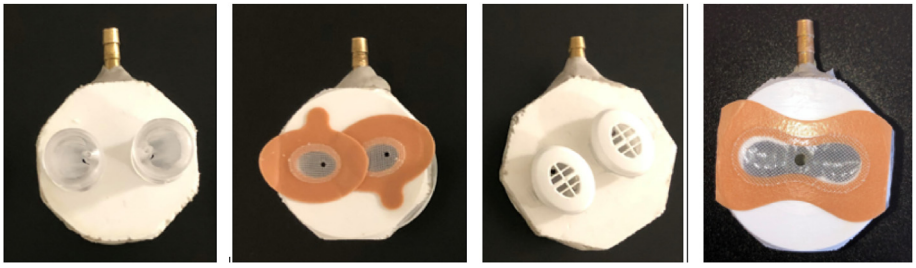

Fig. 3. Manifolds' configurations designed and used in this study. From left to right: ULTepap, Provent, Bongo Rx, and Theravent.

produced by the linear actuator (cm/sec). To determine V, the rod of the actuator was marked at both ends (fully extended and fully retracted), which represented the known distance D. Then the total travel time (t) was measured using the iPhone timer app. Thus, the speed was determined by dividing the distance by the time ($V = D/t$).

The backpressures generated during the expiratory phase represent the level of therapeutic pressures created by the four devices. The negative pressures generated during the inspiratory phase indicate the resistance that a patient would experience during inhalation. The resistance (R) can be calculated from the expression shown below

$$R = P/Q$$

where P is the negative inspiration pressure and Q is the flow rate.

2.4. Statistical analysis

All statistical analyses were conducted using SAS®, Version 9.4 (SAS Institute Inc, Cary, NC). Generalized linear models were used to compare the differences of expiratory pressures and resistances generated by the four devices. A p-value less than 0.05 indicates that expiratory pressures and resistances generated between two comparison devices are significantly different across various flow rates.

3. Results

3.1. Expiratory and inspiratory pressures

The means of expiratory and inspiratory pressures produced by ULTepap, Provent, Bongo Rx, and Theravent EPAP devices at various flow rates are summarized in Table 1. The expiratory pressures generated by ULTepap and Provent were comparable ($p = 0.6448$), with ULTepap being slightly lower at all flow rates consistently. Bongo Rx and Theravent devices produced substantially lower backpressures than Provent ($p < 0.0001$, and $p < 0.0001$, respectively) and ULTepap ($p < 0.0001$, and $p < 0.0001$, respectively), with Bongo Rx being significantly lower than Theravent at higher flow rates ($p < 0.0001$) (Fig. 4).

3.2. Expiratory and inspiratory resistances

Table 2 contains the means of calculated expiratory and inspiratory resistances at various flow rates for the four devices tested. Similarly, the expiratory resistances generated by ULTepap and Provent were comparable ($p = 0.1317$), with ULTepap being a bit lower at all flow rates. Bongo Rx and Theravent devices produced significantly lower resistances than Provent ($p < 0.0001$, and $p < 0.0001$, respectively) and ULTepap ($p < 0.0001$, and $p < 0.0001$, respectively), with Bongo Rx being lower than Theravent ($p < 0.0001$).

All four devices presented very low inspiratory pressures and resistances, with all generating 0.5 cmH2O or less at all flow rates.

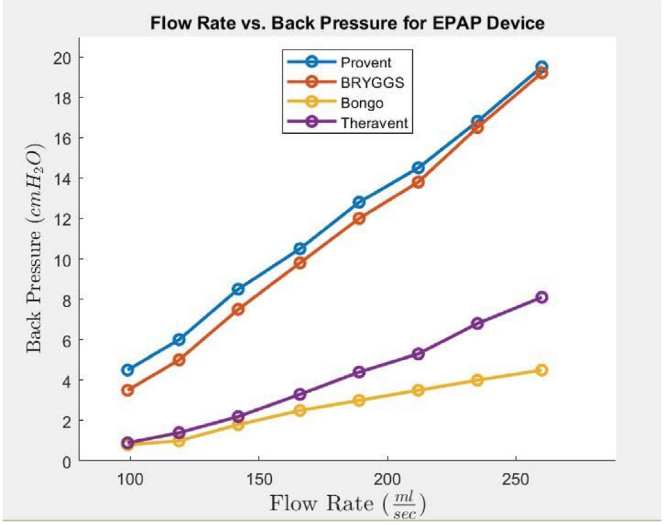

Fig. 4. The backpressure-flow relationship of the four devices at various flow rates.

4. Discussion

4.1. Emerging OSA treatment options

Innovative therapeutic alternatives for OSA management have been rapidly emerging. In the past decade, we have witnessed the rise of nasal EPAP, new positional devices, negative intra-oral pressure therapy, and hypoglossal nerve stimulation. New novel sleep technologies continue to grab our attention but there remains a lack of rigorous scientific validation on the efficacy, adverse effects, acceptance, tolerance, and adherence of these therapeutic devices [24,25].

4.2. Summary of findings

This laboratory bench study is the first step to investigate the performance of ULTepap, an innovative nasal EPAP device using a "flow cartridge" that has an appearance of a nasal pillow mask. This study demonstrated that ULTepap can generate backpressures comparable to that of Provent, and substantially higher than the pressures generated by Bongo Rx and Theravent at various flow rates in an in vitro bench setting.

4.3. Earlier nasal valve EPAP research

Colrain et al. first exploited a novel nasal expiratory resistance valve that can be inserted into each nostril and demonstrated that a simple nasal EPAP valve can improve breathing during sleep in OSA patients [26]. The authors tested the valve in 24 OSA patients (6 severe, 7 moderate, 11 mild OSA cases) and showed that nasal EPAP can significantly decrease both apnea-hypopnea index (AHI) and ODI and increase the percentage of the night spent above 90% saturation. Several studies subsequently evaluated Provent, the first commercialized nasal EPAP device, and confirmed its efficacy in treating patients with OSA [16–20,23]. Riaz et al. performed a systematic review and meta-analysis to quantitatively evaluate the effectiveness of Provent on PSG variables and sleepiness in OSA patients and concluded that Provent reduced AHI by 53%, ODI by 42%, and improved SpO2 nadir by 3% [22]. There were no major adverse effects, but minor adverse events including difficulty breathing, exhaling, and sleeping, dry mouth, nasal congestion/drainage/discomfort, itching, and headaches were reported. Exclusion criteria varied with studies and included conditions such as prior use of CPAP or oral appliance, history of upper airway surgery, poorly treated severe nasal allergies/sinusitis/nasal occlusion, uncontrolled hypertension, severe cardiovascular, respiratory, or neuromuscular diseases, hypoventilation, severe nocturnal

Table 1
Mean expiratory and inspiratory pressures generated by the four devices at various flow rates. No standard deviations were presented due to no or very little variation among the repeated measurements at each flow rate.

Input Voltage (Volts)	Flow rate (ml/sec)	ULTepap Expiratory Pressure (cm H_2O)	Provent Expiratory Pressure (cm H_2O)	Bongo Rx Expiratory Pressure (cm H_2O)	Theravent Expiratory Pressure (cm H_2O)	ULTepap Inspiratory Pressure (cm H_2O)	Provent Inspiratory Pressure (cm H_2O)	Bongo Rx Inspiratory Pressure (cm H_2O)	Theravent Inspiratory Pressure (cm H_2O)
5	99	3.5	4.5	0.8	0.9	- 0.1	- 0.3	- 0.0	−0.2
6	119	5.0	6.0	1.0	1.4	- 0.1	- 0.3	- 0.0	- 0.2
7	142	7.5	8.5	1.8	2.2	- 0.1	- 0.4	- 0.1	- 0.2
8	166	9.8	10.5	2.5	3.3	- 0.1	- 0.4	- 0.1	- 0.3
9	189	12.5	12.8	3.0	4.4	- 0.1	- 0.4	- 0.1	- 0.3
10	212	13.8	14.5	3.5	5.3	- 0.2	- 0.4	- 0.1	- 0.3
11	235	16.5	16.8	4.0	6.8	- 0.2	- 0.5	- 0.0	- 0.3
12	260	19.2	19.5	4.5	8.1	- 0.2	- 0.5	- 0.0	- 0.3

Table 2
– **Mean expiratory and Inspiratory resistances generated by the four devices at various flow rates.** No standard deviations were presented due to no or very little variation among the repeated measurements at each flow rate.

Input Voltage (Volts)	Flowrate (ml/sec)	ULTepap Expiratory Resistance (cm H2O/ml/sec)	Provent Expiratory Resistance (cm H2O/ml/sec)	Bongo Expiratory Resistance (cm H2O/ml/sec)	Theravent Expiratory Resistance (cm H2O/ml/sec)	ULTepap Inspiratory Resistance (cm H2O/ml /sec)	Provent Inspiratory Resistance (cm H2O/ml /sec)	Bongo Rx Inspiratory Resistance (cm H2O/ml /sec)	Theravent Inspiratory Resistance (cm H2O/ml /sec)
5	99	0.0354	0.0455	0.0081	0.0091	0.0010	0.0030	0.0000	0.0020
6	119	0.0420	0.0504	0.0084	0.0118	0.0008	0.0025	0.0000	0.0017
7	142	0.0528	0.0599	0.0127	0.0155	0.0007	0.0028	0.0007	0.0014
8	166	0.0590	0.0633	0.0151	0.0199	0.0006	0.0024	0.0006	0.0012
9	189	0.0661	0.0677	0.0159	0.0233	0.0005	0.0021	0.0005	0.0011
10	212	0.0651	0.0684	0.0165	0.0250	0.0009	0.0019	0.0005	0.0014
11	235	0.0702	0.0715	0.0170	0.0289	0.0009	0.0021	0.0000	0.0013
12	260	0.0738	0.0750	0.0173	0.0312	0.0008	0.0019	0.0000	0.0012

oxygen desaturation, and comorbid sleep disorders. Although there was no clear predictor as to which patients will respond favorably to Provent, patients with positional OSA, mild to moderate OSA, and those without significant nasal obstruction were felt to be better candidates [16–23].

Braga et al. investigated the mechanisms of how Provent nasal EPAP improves OSA. MRI was used with and without nasal EPAP to estimate the functional residual capacity and measure the upper airway (UA) cross-section area to examine the EPAP effect during wakefulness in 10 patients with sleep-disordered breathing [27]. Provent produced an end-expiratory pressure of 4–17 cmH2O which caused significant hyperinflation, consistent with an increase in tracheal traction and a decrease in UA collapsibility. Direct MDI imaging effects on the UA were less consistent, but there was a trend to dilatation. In addition, significant hypoventilation with a rise in end-tidal PCO2 was noted on EPAP during wakefulness and sleep. These three mechanisms probably contribute to the therapeutic effect of nasal EPAP on OSA.

4.4. Recent nasal valve EPAP research

Currently, Bongo Rx and ULTepap are the only two FDA-cleared EPAP devices for the treatment of OSA. Lanford recently reported an industry-sponsored, prospective, non-randomized, open-label, single-center trial for the assessment of Bongo Rx in an abstract form. Full face CPAP mask users, mouth breathers, and subjects with nasal congestion, and uncontrolled serious illness including severe respiratory disorders, pneumothorax, and severe heart disease were excluded. Twelve subjects with mild to moderate OSA were recruited with two subjects subsequently withdrawing. Results in 10 subjects showed a significant reduction of AHI from 15.7 ± 6.4 to 7.1 ± 4.2 ($p = 0.0093$) [28]. Two adverse events (chest discomfort in one patient and nasal abrasion in another) were reported [29]. Gay et al. evaluated Bongo Rx in a laboratory bench setting to determine the inspiratory and expiratory resistance and expiratory work of breathing. Airway pressure measurements were taken applying the Bongo Rx device to the nasal fixture to the airway port of the breathing simulator. The authors found at flow rates of 10/20/30 L per minute, the average expiratory resistance was 17.4/34.1/49.1 vs 59.0/76.9/83.1 cmH2O/L/sec for Bongo Rx vs Provent (all $p < 0.0008$) and concluded that Bongo Rx may result in a more comfortable EPAP therapy for patients with OSA [30].

Most recently, Hakim et al. compared the expiratory resistance of the Bongo Rx, Theravent, and OptiPillows (a device recently cleared by the FDA for treatment of snoring) in a laboratory experimental setup. They showed that expiratory resistances of Theravent and Bongo Rx are equivalent (at 100 ml/s, the calculated resistance were 12.76 and 13.21 cm H2O/L/sec, respectively; at 200 ml/s, the calculated resistance were 28.44 and 28.89 cm H2O/L/sec, respectively). The pressures generated during expiration were also equivalent in Theravent and Bongo Rx at both tidal volumes of 200 ml and 400 ml [31].

Our bench testing confirmed that Bongo Rx is associated with lower expiratory resistance than Provent, which is likely due to its design that has two fixed orifices in each flap valve as opposed to one orifice in each flap-valve in Provent. While Bongo Rx may be more comfortable due to its lower expiratory resistances, it may not be as efficacious as Provent or ULTepap in treating OSA due to its low backpressures. It may thus be rational to consider using ULTepap as a rescue measure in those who tolerate Bongo Rx but fail to achieve adequate OSA control.

4.5. Strengths and limitations

One important strength of this study is that we directly compared four different devices including Provent and illustrated the effects of each device on expiratory and inspiratory pressures produced through the valves in the range of human resting breathing at different flow rates. Also, we cautiously inspected the experiment set-up and performed equipment calibration before each test to ensure the accuracy of our data. There are, however, important limitations of this study. First, this is a laboratory experimental testing, in which airflow and pressure measured may not mimic spontaneous tidal breathing. Further in vivo physiological testing with measurement of pressure and airflow in patients with OSA during wakefulness and in sleep is warranted as the actual EPAP levels may be different with state and posture affecting upper airway mechanics. Second, this study did not provide pivotal clinical information including efficacy, tolerance, and adherence in actual patients. As various EPAP devices may generate different backpressure profiles, the tolerance, adherence, and time required for acclimatization may vary significantly among them. These metrics need to be examined and compared in future clinical trials.

5. Conclusions

In sum, clinicians must discern that not all FDA-cleared EPAP devices produce similar mechanical profiles. We demonstrated that there are fundamental differences concerning the expiratory pressures and resistances generated due to different valve designs. Further clinical trials comparing short-term and long-term efficacy, acceptance, optimal acclimatization duration, patient satisfaction, and adherence are warranted.

CRediT author contributions statement

Geoffrey Sleeper: Conceptualization, Methodology, validation, Investigation, Resources, Data curation, Writing-original draft,

Project administration, Visualization, **Majid Rashidi:** Conceptualization, Methodology, Validation, Investigation, Writing-review & editing, Visualization, **Kingman Strohl:** Conceptualization, Methodology, Validation, Writing-review & editing, **Neda Najimi:** Visualization, Writing-original draft, **Pai-Lien Chen:** Formal analysis, Writing-review & editing, **Rawad El Ghoul:** Writing-original draft, **Ambrose Chiang**: Conceptualization, Methodology, Writing-original draft; Writing-review & editing, Visualization, Supervision.

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Declaration of competing interest

Dr. Majid Rashidi is the inventor of ULTepap and a partner of BRYGGS Medical. Geoffrey Sleeper is the co-inventor of ULTepap and the president of BRYGGS Medical. Drs. Kingman Strohl, Neda Najimi, Pai-Lien Chen, Rawad El Ghoul, and Ambrose Chiang have no financial conflicts of interest.

References

[1] Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increase prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013 May 1;177(9):1006–14. https://doi.org/10.1093/aje/kws342.

[2] Gami AS, Howard DE, Olson EJ, Somers VK. Day-night pattern of sudden death in obstructive sleep apnea. N Engl J Med 2005;352(12):1206–14. https://doi.org/10.1056/NEJMoa041832.

[3] Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med 2009;6(8):e1000132. https://doi.org/10.1371/journal.pmed.1000132.

[4] Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep-disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep 2008;31(8):1071–8. https://doi.org/10.5665/sleep/31.8.1071.

[5] Marin JM, Agusti A, Villar I, Forner M, Nieto D, Carrizo SJ, et al. Association between treated and untreated obstructive sleep apnea and risk of hypertension. JAMA 2012;307(20):2169–76. https://doi.org/10.1001/jama.2012.3418 PMID: 22618924.

[6] Gottlieb DJ, Yenokyan G, Newman AB, O'Connor GT, Punjabi NM, Quan SF, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure. Circulation 2010;122(4):352–60. https://doi.org/10.1161/CIRCULATIONAHA.109.901801.

[7] Arzt M, Young T, Finn L, Skatrud JB, Bradley TD. Association of sleep-disordered breathing and the occurrence of stroke. Am J Respir Crit Care Med 2005;172(11):1447–51. https://doi.org/10.1164/rccm.200505-702OC.

[8] Marin JM, Carrizo SJ, Vicente E, Agusti AGN. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. Lancet 2005;365(9464):1046–53. https://doi.org/10.1016/S01406736(05)71141-7.

[9] Prabhakar NR, Peng YJ, Nanduri J. Hypoxia-inducible factors and obstructive sleep apnea. J Clin Invest 2020 Oct 1;130(10):5042–51. https://doi.org/10.1172/JCI137560.

[10] Gottlieb DJ, Punjabi NM. Diagnosis and management of obstructive sleep apnea: a review. JAMA 2020 Apr 14;323(14):1389–400. https://doi.org/10.1001/jama.2020.3514.

[11] Sullivan CE, Issa FG, Berthon-Jones M, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1981 Apr 18;1(8225):862–5. https://doi.org/10.1016/s0140-6736(81)92140-1.

[12] Weaver TE, Mancini C, Maislin G, Cater J, Staley B, Landis JR, Ferguson KA, George CF, Schulman DA, Greenberg H, Rapoport DM, Walsleben JA, Lee-Chiong T, Gurubhagavatula I, Kuna ST. Continuous positive airway pressure treatment of sleepy patients with milder obstructive sleep apnea: results of the CPAP Apnea Trial North American Program (CATNAP) randomized clinical trial. Am J Respir Crit Care Med 2012 Oct 1;186(7):677–83. https://doi.org/10.1164/rccm.201202-0200OC. Epub 2012 Jul 26.

[13] Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet 2014 Feb 22;383(9918):736–47. https://doi.org/10.1016/S0140-6736(13)60734-5.

[14] Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proc Am Thorac Soc 2008 Feb 15;5(2):173–8. https://doi.org/10.1513/pats.200708-119MG.

[15] Mahadevia AK, Onal E, Lopata M. Effects of expiratory positive airway pressure on sleep-induced respiratory abnormalities in patients with hypersomnia-sleep apnea syndrome. Am Rev Respir Dis 1983 Oct;128(4):708–11. https://doi.org/10.1164/arrd.1983.128.4.708.

[16] Rosenthal L, Massie CA, Dolan DC, Loomas B, Kram J, Hart RW. A multicenter, prospective study of a novel nasal EPAP device in the treatment of obstructive sleep apnea: efficacy and 30-day adherence. J Clin Sleep Med 2009 Dec 15;5(6):532–7.

[17] Walsh JK, Griffin KS, Forst EH, Ahmed HH, Eisenstein RD, Curry DT, Hall-Porter JM, Schweitzer PK. A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-adherent with continuous positive airway pressure. Sleep Med 2011 Feb;12(2):147–52. https://doi.org/10.1016/j.sleep.2010.06.011. Epub 2011 Jan 21.

[18] Patel AV, Hwang D, Masdeu MJ, Chen GM, Rapoport DM, Ayappa I. Predictors of response to a nasal expiratory resistor device and its potential mechanisms of action for treatment of obstructive sleep apnea. J Clin Sleep Med 2011 Feb 15;7(1):13–22.

[19] Berry RB, Kryger MH, Massie CA. A novel nasal expiratory positive airway pressure (EPAP) device for the treatment of obstructive sleep apnea: a randomized controlled trial. Sleep (Basel) 2011 Apr 1;34(4):479–85.

[20] Kryger MH, Berry RB, Massie CA. Long-term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea (OSA). J Clin Sleep Med 2011 Oct 15;7:449–453B. https://doi.org/10.5664/JCSM.1304.

[21] Wu H, Yuan X, Zhan X, Li L, Wei Y. A review of EPAP nasal device therapy for obstructive sleep apnea syndrome. Sleep Breath 2015 Sep;19(3):769–74. https://doi.org/10.1007/s11325-014-1057-y. Epub 2014 Sep. 23.

[22] Riaz M, Certal V, Nigam G, Abdullatif J, Zaghi S, Kushida CA, et al. Nasal expiratory positive airway pressure devices (provent) for OSA: a systematic review and meta-analysis. Sleep Disord 2015 Dec 21;2015:734798.

[23] To KW, Chan TO, Ng S, Ngai J, Hui DSC. Role of nasal positive end-expiratory pressure valve as an alternative treatment for obstructive sleep apnoea in Chinese patients. Respirology 2016 Apr;21(3):541–5. https://doi.org/10.1111/resp.12703.

[24] Kezirian EJ, Simmons M, Schwab RJ, Cistulli P, Li KK, Weaver EM, Goldberg AN, Malhotra A. Making sense of the noise: toward rational treatment for obstructive sleep apnea. Am J Respir Crit Care Med 2020 Dec 1;202(11):1503–8. https://doi.org/10.1164/rccm.202005-1939PP.

[25] Chiang AA, Miller J, Bhargava S, Schutte-Rodin S, Deak M. On behalf of the AASM Emerging Technology Committee. Emerging sleep technologies: novel obstructive sleep apnea treatment alternatives. AASM Montage, fall 2021: p14–5.

[26] Colrain IM, Brooks S, Black J. A pilot evaluation of a nasal expiratory resistance device for the treatment of obstructive sleep apnea. J Clin Sleep Med 2008 Oct 15;4(5):426–33.

[27] Braga CW, Chen Q, Burschtin OE, Rapoport DM, Ayappa I. Changes in lung volume and upper airway using MRI during application of nasal expiratory positive airway pressure in patients with sleep-disordered breathing. J Appl Physiol 1985;111(5):1400–9. https://doi.org/10.1152/japplphysiol.00218.2011. 2011 Nov.

[28] Lankford A, Kram J. A novel EPAP device for the treatment of mild to moderate obstructive sleep apnea. Sleep 2019 April 1;42:A218. https://doi.org/10.1093/sleep/zsz067.544.

[29] https://clinicaltrials.gov/ct2/show/results/NCT02878590?term=NCT02878590&draw=2&rank=1&view=results.

[30] Gay P, Lankford A, Diesem R, Richard R. A comparison of two nasal expiratory PAP devices for the treatment of OSA. Chest 2019 Oct 1;156(4):A1063–4. https://doi.org/10.1016/j.chest.2019.08.982.

[31] Hakim TS, Bonnetti M, Bosco G, Camporesi EM. EPAP devices optipillows, Bongo Rx, and theravent: flow resistance and the pressures they generate. J Sleep Med Disord 2021 Apr;7(1):1119.