Obstructive Sleep Apnea Treatment with EPAP Nasal Devices: Physiological Principles and Limitations

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Abstract

Expiratory Positive airway pressure (EPAP) devices such as Provent have been used for treatment of obstructive sleep apnea without discussing their limitations. In this short review we discuss the physiological limitations of EPAP devices during inspiration and during expiration. During spontaneous breathing, when EPAP is excessive, the patient would have difficulty breathing in because lung compliance decreases at higher volumes. Furthermore excessive EPAP could lead to progressive trapping of air in the lungs. An ideal EPAP device should allow the patient to adjust the resistance to a comfortable level that would provide EPAP without a progressive buildup in pressure, without compromising tidal volume, without causing CO2 retention, and without disturbing sleep. The use of EPAP devices with adjustable resistance is essential for best results in treatment of obstructive sleep apnea and snoring.

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Introduction:

The preferred therapy for obstructive sleep apnea (OSA) is continuous positive airway pressure (CPAP). A new expiratory resistance device called Provent was introduced by Ventus Medical in 2008 (Belmont, CA) as an option for OSA treatment. Provent consisted of a miniature two-way valve that fits against the opening of the nostril and is fixed in place with adhesive material to provide a seal. The valve allows a patient to breathe in with minimal resistance and breathe out through a narrow hole with high resistance, thus generating an expiratory positive airway pressure (EPAP). This device simulated experiments that were published in 1983 by Mahadevia et al concluding that increased pressure during expiration is in itself sufficient to treat OSA. Provent was cleared by the Food and Drug Administration (FDA) as an EPAP device for treatment of OSA with all severities. The effectiveness and safety of Provent was validated through several published clinical trials demonstrating significant reductions in apnea-hypopnea index, oxygen desaturation, and daytime sleepiness. Wu et al and Riaz et al reviewed, in detail, most of the studies that used Provent, and the reader is referred to such reviews. Others have also reviewed the literature and, in general, gave favorable opinions about use of Provent as an EPAP device for treatment of OSA. It remains unclear why Provent is not effective in some patients. Provent was usually more effective in patients with mild to moderate OSA than in patients with severe OSA. One study attempted to identify if other factors determine which patient is likely to benefit from Provent but did not add to our understanding of EPAP devices. The idea of offering Provent with different levels of expiratory resistance was insightful and was necessary. The scientists at Provent realized that level of resistance in the device plays a critical factor to the success of therapy. Indeed one patient may be more comfortable with a Provent with low resistance while another may prefer a Provent with a high resistance, but the reason remains unclear. Using Provent with a fixed resistance, is somewhat arbitrary; the resistance may be too little which makes the device ineffective or may be too excessive which causes difficulty breathing. There are physiological reasons that determine how much resistance is appropriate for a patient but were not discussed previously. One may be misled by the simple notion that a device with a higher resistance may work better for a patient because it could potentially generate more EPAP. There are factors related to physiology of lung and chest wall mechanics that place limits on how much resistance should be used. In a recent publication we discussed the theoretical changes in pressures in the nasopharyngeal region and in lung volume that are generated during CPAP or BiPAP and compared it to EPAP but did not discuss the limitations of EPAP devices.

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below and it may become clear how to better match an OSA patient with an EPAP device for a more successful treatment. Indeed there are limitations during inspiration and to expiration that will be discussed,

**Limitations during Inspiration:**

The pressure-volume relationship of the respiratory system (lungs and chest wall) exhibits a curvilinear shape. The relationship is linear in the low pressure range, but the slope (compliance) decreases at higher pressure and therefore, becomes more difficult to inhale a given volume of air. The pressure range where lung compliance ($\Delta$Volume/$\Delta$Pressure) begins to decrease is about the same, regardless of size of the lungs. Fig 1 illustrates the curvilinear relationship between pressure and volume in the lungs of a patient with large lungs (Fig 1a), or a patient with smaller lungs (Fig 1b). Zero on the Y-axis represents lung volume at the end of normal expiration (Functional Residual Capacity). Transpulmonary pressure is the distending pressure in the lungs (alveolar pressure-pleural pressure) and zero on the X-axis represents the transpulmonary pressure at end of normal expiration which is approximately 5 cmH2O. The figure illustrates the changes in pressure and volume as the pressure at end expiration increases due to an increase in expiratory resistance such as by using an EPAP device. In most healthy individuals, the slope remains linear until a pressure of approximately 10 to 15 cmH2O is reached. Therefore inspiration remains relatively easy until such pressure is exceeded. During sleep, the low level of neural drive to the inspiratory muscles increases the transpulmonary pressure by 5 cmH2O and lung volume by about 500 ml (Fig 1a, yellow shaded area). Dynamic inflation and deflation curves during tidal breathing are represented by the red loops at the different levels of

![Fig 1: Schematic representation of the Pressure-Volume relationship in the lung. Zero on the Y-axis represents lung volume at the end of normal expiration and zero on the X-axis represents the transpulmonary pressure at the end of normal expiration. The solid blue line represents the static relationship while the red loops represents the dynamic changes during tidal inhalation and exhalation while breathing against different expiratory resistances. Slope of the line is lung compliance ($\Delta$volume/ $\Delta$Pressure), which remains linear until the pressure exceeds 16 cmH2O above the pressure at FRC.](Fig1.png)
end expiratory pressure. When expiratory resistance is increased such that the pressure at end expiration increases to 7 cmH2O, inhalation remains relatively easy, and the neural drive to the inspiratory muscles will be sufficient to increase lung volume (Fig 1a, pink shaded area) the same as before. However a further increase in resistance causes pressure at end expiration to increase beyond the linear portion of the curve, where compliance decreases (e.g. > 15 cmH2O) (Green shaded area). When end expiratory pressure exceeds 15 cmH2O, compliance of the lungs decreases, and the neural drive to the inspiratory muscles would increase lung volume only by 300 ml. Therefore in a person who is asleep, there is an expiratory resistance level above which, the lungs become more difficult to inflate, and consequently inhaled tidal volume will be decreased. Thus the patient would hypoventilate. A similar phenomenon would occur in a patient with a smaller lung volume (Fig 1b). Hypoventilation causes CO2 retention leading to an increase in respiratory drive \(^{16}\), and perhaps to awakening of the patient. It is important to emphasize that because the shape of the pressure-volume curves are nearly comparable in all healthy adults, it is likely that the pressure where lung compliance begins to decrease falls within a narrow range. Therefore in a spontaneously breathing patient during sleep, end expiratory pressure should remain within the linear portion of lung compliance curve by using the appropriate expiratory resistance so the patient can continue to breathe normally. Compared to EPAP devices where the patient inhales entirely spontaneously, patients can tolerate higher pressure during CPAP or bi-level positive airway pressure (> 20 cmH2O), because the pressure support during inspiration makes inhalation easier and thus hypoventilation is less likely to happen.

In conclusion, during sleep, expiratory resistance can be increased up to a certain level (optimum resistance) without compromising the volume of air that a patient can inhale. When optimum resistance is exceeded, inhalation becomes more difficult and ventilation may be compromised leading to CO2 retention. An increase in expiratory resistance, would cause the pressure at end expiration to rise, but as long as it remains on the linear portion of the lung compliance curve (< 15 cm H2O), it is likely to be tolerated by most patients without causing hypoventilation and CO2 retention. A mild increase in CO2 may be well tolerated by some patients without waking up. Excessive increase in expiratory resistance would cause severe CO2 retention and may awaken the patient. Therefore, successful therapy with EPAP devices depends on choosing the appropriate resistance that allows the patient to continue breathing normally without significant CO2 retention. If necessary, end tidal CO2 can be monitored with capnography to determine if the patient is hypo-ventilating.

**Limitations during Expiration:**

The studies with Provent (having a fixed resistance), show that the device generated a wide range of EPAP (5 to 23 cmH2O) among patients \(^{13}\). The reason why some patients generated low EPAP while others generated much higher EPAP was not explained. Differences in EPAP level among patients are related to elastic recoil properties of the respiratory system (lungs and chest wall). Exhalation during sleep is a passive process, driven only by elastic recoil of the respiratory system. Figure 2a illustrates the effect of a gradual increase in expiratory resistance, using an EPAP device, on flow profile during expiration of one breath. The normal expiratory flow profile without expiratory resistance is represented by the solid line (#1) (somewhat triangular in shape). Peak flow rate during passive exhalation at rest is approximately 0.8 l/sec for an average size man, and expiratory time is about 2 sec. The integrated area under the curve represents the exhaled tidal volume which would be 0.4 to 0.5 liter. When resistance increases slightly, the shape of the
curve would change as shown by the dotted line #2 becoming more square in form, but the area under the curve (exhaled tidal volume) would remain unchanged. As the expiratory resistance increases further, the flow profile approaches line #3 with the flow profile becoming more square in form, and with the area under the curve remaining equal to that as curve #1. At some point, increasing expiratory resistance further would cause the area under the curve to decrease indicating that the exhaled tidal volume was smaller (line #4), which leads to air trapping in the lungs, and progressive pressure build-up preventing the patient from breathing normally. Therefore curve #3 represents the flow profile with the highest resistance (optimum resistance) that can be tolerated without compromising ventilation. With excessive expiratory resistance, not only inhalation becomes difficult as explained earlier, but exhalation also becomes impeded, either or both of which lead to hypoventilation, CO2 retention, and patient disturbance.

The expiratory positive airway pressure (EPAP) in the naso-pharyngeal region during such step increases in expiratory resistance is illustrated in Fig 2b. During normal breathing with no expiratory resistance, the nasal pressure becomes slightly positive but remains close to zero (solid blue line #1). As the expiratory resistance increases slightly, EPAP would increase as illustrated with curves #2. When optimum resistance is reached, EPAP would increase as shown by red line #3. Increasing the resistance beyond the optimum resistance will not cause EPAP to rise any further (curve #4), but instead, expiratory flow rate will be reduced (line #4 in Fig 2a). Therefore curve #3 represents the maximum EPAP that this patient can generate and tolerate while asleep. This maximum EPAP is determined by the expired flow rate generated by the passive elastic recoil of the lungs. Therefore optimum resistance is the expiratory resistance that generates maximum EPAP without compromising exhaled tidal volume.

Fig 2: Fig 2a: Exhaled flow profile during one breath in the same person while using different levels of expiratory resistance. Areas under the curves under all conditions is equal to exhaled tidal volume which decreases only at the highest level of resistance. Fig 2b: The pressure profile during exhalation while using different levels of expiratory resistance.
How much EPAP a person can generate?

Optimum resistance that can be tolerated varies among patients, however all healthy adults generate approximately a similar level of EPAP. Figure 3 compares two patients with different lung volumes. A person with large lungs would have perhaps twice the average flow rate during expiration compared to a person with smaller lungs (expiratory time being equal). Therefore a person with large lungs is likely to generate more EPAP against a given resistance than a person with smaller lungs (Pressure=Flow rate x Resistance). Exhaled air flow profiles for one breath are represented by the solid lines (Fig 3a); Solid blue line A for the larger lungs, and solid red line B for the smaller lungs. Increasing expiratory resistance to optimum resistance would change the flow profiles as shown in Fig 3a; dotted blue line A’ for the person with large lungs, and dotted red line B’ for the person with small lungs. The area under the curve (Tidal volume), as expected would be larger for the larger lungs, however, because the optimum resistance was not exceeded, the area under each curve remains unchanged in both patients.

The EPAP profile for the two patients are illustrated in Fig 3b. Without expiratory resistance, the pressure becomes slightly positive during expiration but remains close to zero in both patients (red and blue solid lines A and B). With their respective optimal resistance, both patients will generate about a comparable EPAP as illustrated with profiles A’ and B’ (e.g. 15 cmH2O). In the person with larger lungs, expiratory flow rate is higher but optimal resistance would be lower, while in the person with smaller lungs, expiratory flow rate is lower but optimum resistance would be higher. Therefore the product of Flow rate and Resistance (which equals

Fig 3: Fig 3a: Exhaled flow profile during one breath in an adult that has a large tidal volume compared to an adult with a smaller tidal volume. When optimum expiratory resistance is used, the flow profile changes but the area under the curve remains unchanged in both individuals, indicating the exhaled tidal volume remained unchanged. Fig 3b: The pressure profile during expiration in the two adults in panel a. The maximum pressure in both adults is about same despite the difference in tidal volume.
pressure) would be about comparable in both individuals. Because optimum resistance was not exceeded, both patients would continue to breathe normally without hypoventilation or CO2 retention. Furthermore, neither person in this example would be able to generate more than the maximum EPAP of approximately 15 cmH2O while asleep. If the expiratory resistance is increased above optimum resistance, EPAP will not increase but exhaled volume will be restricted and more air will be trapped in the lungs. In the example shown in Figure 3, the average expiratory flow rate in these two patients are approximately 0.4 l/sec and 0.16 l/sec (these represent realistic range of numbers), the optimum resistance required to generate 15 cmH2O can be calculated (Resistance=Pressure/Flow rate), and would be 15 cmH2O divided by 0.4 /sec (= 37.5 cmH2O/L/sec) for the person with larger lungs and 15 cmH2O divided by 0.16 l/sec (= 93.75 cmH2O/l/sec) for the person with small lungs. The optimum resistances were vastly different in these two patients but the maximum EPAP that they can generate were comparable. In contrast, using Provent with a fixed resistance of 50 cmH2O/l/sec in these two individuals would generate 0.4 l/sec x 50 cmH2O/l/sec (= 20 cmH2O) for the large lungs, and 0.16 l/sec x 50 cmH2O/l/sec (= 8 cmH2O) for the smaller lungs. This may explain the wide range in pressures that were reported while using Provent. With a device that provides an adjustable and appropriate resistance, a patient is likely to get the most benefit for treating OSA and snoring without the risk of hypoventilation and CO2 retention. With a device that has a fixed expiratory resistance, it is possible that the resistance may be adequate for one patient, or perhaps maybe too excessive for another patient that it would cause gradual pressure build-up, hypoventilation and CO2 retention. Therefore it would be ideal to have an EPAP device where the expiratory resistance can be adjusted easily to provide optimum resistance that would generate a maximum EPAP for every patient every time. As mentioned earlier, maximum EPAP is likely to fall within a narrow range for all patients, and may be adequate to resolve OSA fully such as in mild to moderate OSA, but it also may be less than adequate for some patients with severe OSA. Nevertheless, an EPAP device that provides optimum resistance would always provide the most benefit for the patient. The majority of OSA patients have mild to moderate OSA and most patients are usually treated with a CPAP much less than 15 cmH2O. The pressure that can be generated by an EPAP device is likely to be well tolerated by most patients as long as optimum resistance is not exceeded and as such EPAP devices maybe suitable for the majority of OSA patients. It is misleading to suggest that increasing the expiratory resistance would make the EPAP device more effective. Too much resistance, beyond optimum resistance, does not help, and in fact, it may only lead to hypoventilation, CO2 retention and sleep disturbance. Using less resistance than optimal resistance will generate less than maximum EPAP, and that may be adequate for a patient with primary snoring or with mild OSA. In general, a smaller resistance is more appropriate for a patient with a large lung volume, while a larger resistance may be more appropriate for a patient with a small lung volume.

Conclusions:

In summary, an ideal EPAP device should be able to provide an optimum resistance that leads to an increase in EPAP without compromising ventilation. A small decrease in ventilation with a small increase in CO2 may be tolerated by some patients and may help stimulate respiratory drive, and would be acceptable only if it does not disturb sleep or wake up the patient. In general however, an increase in CO2 retention while using EPAP devices, is a signal that expiratory resistance is excessive and should be reduced. An ideal EPAP device should increase the expiratory pressure without a buildup in pressure, without compromising tidal volume, without causing CO2 retention, and
without disturbing sleep. We stated earlier that all healthy adults generate approximately a similar level of maximum EPAP, however, it is possible that a small difference may exist among patients. For example one patient may generate 8 cmH2O of maximum EPAP, while another may generate 12 cmH2O, in which case the EPAP device may treat a higher level of OSA in the latter. EPAP devices with a fixed resistance may be inappropriate for some patients, and the notion that one size resistance fits all, should be reconsidered. Providing the appropriate expiratory resistance is extremely essential for the success of OSA therapy with EPAP devices. Such an EPAP device with adjustable resistance has recently been introduced and promises to improve the acceptance of EPAP devices.

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References:


