High Flow Therapy and Humidification:
A Summary of Mechanisms of Action,
Technology and Research

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INTRODUCTION

Vapotherm, Inc. is the market leader in high-flow, thermally-controlled, humidification systems for respiratory therapy. Currently, these medical devices are indicated for use in adding warm moisture to breathing gases to infant, pediatric and adult patients in the hospital, sub-acute institutions and home settings. Vapotherm devices are approved for delivery of breathing gases by nasal cannula at flow rates of up to 8 lpm in infants and 40 lpm in adults, providing what is known as high flow therapy (HFT).

WHAT IS HIGH FLOW THERAPY (HFT)?

HFT is defined as flow rates that exceed patient inspiratory flow rates at various minute volumes. Historically, high flow therapy has been used with face masks, where the high flows flush the mask volume to facilitate high inspiratory oxygen fractions. While effective in supporting oxygenation, mask therapy can be limited by factors including ability to eat/drink and communicate, as well as feelings of claustrophobia, leading to poor patient compliance.

The standard nasal cannula has been the standby for better compliance and patient comfort. Cannulae provide supplemental oxygen, are comfortable for long periods and allow patients to eat and talk without interruption of the therapy. However, higher flows (over 2 lpm in neonates or 6 lpm in adults) needed to meet inspiratory requirements without allowing entrainment of room air are not possible with conventional nasal cannula therapy. This limitation to conventional cannula therapy is a result of the discomfort and irritation caused by delivering cold, dry gas to the nasal passages. Vapotherm’s technology has transformed conventional cannula therapy through optimal conditioning of breathing gas. Proprietary heating and humidification technology allows for breathing gases to be delivered at high flow rates while maintaining body temperature and up to 99.9% relative humidity.

RESPIRATORY PHYSIOLOGY AND ALVEOLAR VENTILATION

In order to understand the mechanisms behind HFT, it is helpful to review some fundamental respiratory physiology. Under normal breathing conditions, approximately 30% of an inspired tidal volume represents anatomical dead space. At the start of an inspiration, this dead space is filled with end-expiratory gas remaining from the previous expiration. While this anatomical dead space volume is essential to 1) inspiratory gas warming and humidifying and 2) conducting gas to the thorax and dispersing to lung regions, the contribution of dead-space (end-expiratory gas) to a new breath does impact breathing efficiency.
In a healthy person, alveolar oxygen concentrations are lower than ambient air and alveolar carbon dioxide concentrations are greater than ambient air. This difference between ambient and alveolar gas is a function of alveolar ventilation as well as blood gas content. Alveolar ventilation differs from the more familiar term minute ventilation as a function of dead space.

**Minute ventilation = tidal volume x respiratory rate**

**Alveolar ventilation = (tidal volume – dead space) x respiratory rate**

Based on the relationship between ventilation parameters, a reduction in dead space volume results in lower minute ventilation required to achieve adequate alveolar ventilation. Therefore, dead space volume directly impacts tidal volume and/or respiratory rate requirements, and thus breathing effort, even in healthy people. In this regard, HFT via cannula can enhance respiratory efficiency by flushing nasopharyngeal anatomical dead space and supporting respiratory work. But first, ideal gas conditioning must be achieved.

**IMPORTANT OF GAS WARMING AND HUMIDIFICATION**

The mucosal tissue of the nasopharyngeal space is designed to warm and humidify breathing gas prior to entering the lower respiratory tract\(^4\). This is accomplished anatomically by achieving a large surface area to interact with inspiratory gas. As such, exposing the nasopharyngeal tissues to greater than a normal minute ventilation rate flow of gas that is below body temperature and the water vapor saturation point (i.e., below 100% relative humidity) can overload these tissues. Such an overload of the nasopharyngeal tissues results in significant dysfunction, drying and damage to the nasal mucosa\(^5-8\), which likely also contributes to staphylococcal sepsis\(^9\). Even at low flows, conventional nasal cannula therapy is uncomfortable and raises numerous patient complaints, particularly related to dry nose and mouth\(^10\).
Ideally, inspiratory gas should be warmed to body temperature (37°C) and humidified to 100% relative humidity. Furthermore, humidification with vapor versus aerosolized water is the least likely to cause airway and lung injury by latent heat loss and deposition of water droplets. Vapotherm membrane technology facilitates the passage of water into the breathing gas in a vapor phase, and as demonstrated in a bench test by Waugh and Granger, provides respiratory gases at body temperature and 99.9% relative humidity throughout the designated flow range up to 40 lpm.

**THE TECHNOLOGY BEHIND OPTIMAL GAS CONDITIONING**

Vapotherm devices incorporate a patented vapor transfer cartridge system that allows water vapor to diffuse into the respiratory gas stream while heating the gases to the prescribed temperature (typically 37°C). This system is fundamentally different from the conventional heated plate humidifier systems. The Vapotherm devices also employ a triple lumen “jacketed” delivery tube and proprietary nasal cannulae optimized to maintain temperature and to minimize condensation (rainout). These later two features protect the state of respiratory gases so that the gas reaches the patient at the same temperature and humidification state that was achieved in the membrane cartridge.

In a randomized crossover study, Woodhead and colleagues evaluated the impact of Vapotherm compared to conventional HFT on the nasal mucosa of preterm infants post extubation. Thirty infants received either Vapotherm or conventional HFT for 24 hours, and then switched to the opposite modality (conventional or Vapotherm) for an additional 24 hrs. Using a blinded scoring system accounting for nasal erythmia, edema, thick mucus and hemorrhage ranging from 2 to 10, Vapotherm infants had much better tolerance compared to conventional humidification (2.7 ± 1.2 vs 7.8 ± 1.7; p < 0.001).

**HOW DOES HFT IMPACT BREATHING?**

Because Vapotherm technology allows respiratory gases to be delivered to the patient truly at body temperature and saturation, high flow is now feasible via nasal cannula. In this regard, HFT is effective because of a number of basic physiologic mechanisms that improve the efficiency of breathing, independent of any specific disease state.

**CO₂ VENTILATION**

By supplying flows that exceed patient demand, HFT results in a washout of nasopharyngeal dead space. As with any reduction in anatomical or physiological dead space, this therapy contributes to establishing improved fractions of alveolar gases with respect to carbon dioxide as well as oxygen. Therefore, whereas low flow nasal cannula therapy is only thought to facilitate oxygenation, HFT impacts CO₂ elimination as well.

**EFFICIENT OXYGENATION**

HFT via nasal cannula works under the same principles as HFT through a face mask to achieve high inspired oxygen fractions by eliminating room air entrainment during inspiration. However, because HFT via nasal cannula reduces anatomical dead space by using the nasopharynx as a gas reservoir, it has the potential to improve alveolar oxygen fractions beyond mask therapy based on the equation for alveolar ventilation. Therefore, patients can often maintain better oxygenation or require a lower FiO₂ compared to conventional mask or cannula therapies.

**WORK OF BREATHING**

The distensible nature of the nasal mucosa that facilitates physiologic gas condition also results in significant resistance on inspiration efforts relative to expiratory efforts. Because HFT provides enough flow to match or exceed a patient's
inspiratory flow, HFT most likely minimizes the inspiratory resistance associated with the nasopharynx. This change in resistance translates to a change in resistive work of breathing.

In addition, adequate warming and humidification of the conducting airways by delivery of warm, humid gas is associated with improved conductance and pulmonary compliance compared to dry, cooler gas. Furthermore, Fontanari and colleagues showed that receptors in the nasal mucosa respond to cold and dry gas to elicit a protective bronchoconstrictor response in both normal subjects and asthmatics. Therefore, delivery of breathing gases at body temperature and saturation promotes an ideal respiratory mechanical response.

**ENERGY COST OF GAS CONDITIONING**

The nasal air passages expend energy to warm inspiratory air from ambient to 37°C and vaporize water to humidify the incoming air to 100% relative humidity. Whereas many of the factors involved in this process are unclear or not easily definable, we believe that it can be ascertained that there is some significant energy cost to the process of gas conditioning. This energy cost is alleviated when gas is delivered at body temperature and saturated.

**RELATIONSHIP BETWEEN FLOW AND PRESSURE**

More than fifteen years ago, Dr. Locke and colleagues demonstrated that, even with low flows, positive airway pressure can be inadvertently generated with the use of nasal cannula when the prongs are large relative to the size of the nares. In fact, low flow nasal cannulae have been widely used for CPAP generation in the NICU setting by using relatively large nasal prongs (relative to the nare internal dimensions) and a closed mouth to create up to 8 cmH₂O of pharyngeal pressure. These historical perspectives have been cause for concern over what nasopharyngeal pressure could be with high flow nasal cannula.

A number of bench and clinical studies have now clarified that the pressure development in the nasopharynx and airways is determined by leak around the nasal prongs and position of the mouth. In this regard, when Vapotherm HFT is applied as recommended with nasal prong no larger than ½ the diameter of the nares with the mouth free to open, pressure generation is at best mild. Dr. Saslow and colleagues at Cooper University Hospital (Camden, NJ) have shown that distending pressures generated by HFT up to 8 lpm in infants was not more than that produced by 6 cmH₂O of CPAP, and in some cases significantly less (at 5 lpm; p = 0.03). Dr. Kubicka and colleagues showed that in 27 neonates receiving cannula flows up to 5 lpm, oral pressure never exceeded 5 cmH₂O. Dr. Wilkinson and colleagues showed that nasopharyngeal pressures were relatively mild in infants during HFT, and predictable when flows were normalized to body weight.

Nonetheless, studies that have evaluated high flow therapy in an effort to develop distending airway pressure with the mouth closed found that typically only mild positive pressures develop. Vapotherm devices are not Continuous Positive Airway Pressure devices and are not designed to deliver set pressure. The technology is designed to deliver conditioned gas flows in an open system via simple nasal cannula.
References
