Is the delivery of supplemental oxygen via the Vapotherm 2000i (Vapotherm, Inc., Stevensville, MD) superior to delivery via standard nasal cannula in the treatment of postoperative hypoxemia, defined as an \( \text{SaO}_2 < 94\% \) on room air?

A Study Design

By

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A Master’s Paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health in the Public Health Leadership Program.

Chapel Hill

2005

Advisor

Second Reader

Date
ABSTRACT

Surgical patients commonly experience postoperative, post-extubation hypoxia, which may require re-intubation. Endotracheal intubation and mechanical ventilation are associated with a number of complications, such as laryngotracheal injury, patient discomfort, ventilator-associated pneumonia and ventilator-associated lung injury. Avoiding reintubation postoperatively would help to prevent these complications in hypoxemic postoperative patients.

There is some evidence that noninvasive ventilation, particularly continuous positive airway pressure (CPAP), is effective in treating postoperative hypoxemia. The Vapotherm 2000i (Vapotherm, Inc., Stevensville, MD) is a new, noninvasive device that delivers high-flow, warmed and humidified oxygen via nasal cannula in a way that mimics CPAP. Recent evidence supporting the use of CPAP in the treatment of postoperative hypoxemia suggests that Vapotherm might also be effective in select postoperative patients, allowing them to avoid reintubation. The following paper includes a systematic review of the literature dealing with the use of noninvasive ventilation to treat postoperative hypoxemia, as well as the literature concerning the Vapotherm 2000i.

A research plan is described for a pilot study examining the safety and feasibility of using the Vapotherm 2000i in relatively healthy adults with postoperative hypoxemia, in preparation for future studies of the effectiveness of this device in a broader population of postoperative patients. A discussion of issues involved in testing a new device follows.
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INTRODUCTION

Surgical patients commonly experience postoperative, post-extubation hypoxia that, while generally transient, may require re-intubation. There is some evidence that noninvasive ventilation, particularly continuous positive airway pressure (CPAP), is effective in treating postoperative hypoxemia. The Vapotherm 2000i (Vapotherm, Inc., Stevensville, MD) is a new, noninvasive device that delivers high-flow, warmed and humidified oxygen via nasal cannula. While not a ventilator itself, the Vapotherm mimics CPAP in its mode of oxygen delivery. Recent evidence supporting the use of CPAP in the treatment of postoperative hypoxemia suggests that Vapotherm might also be effective in select postoperative patients, allowing them to avoid re-intubation. Because of its ability to warm and humidify, the Vapotherm can deliver oxygen at higher tolerable flow rates than CPAP. Additionally, the warming feature, unavailable with CPAP, allows the use of Vapotherm in the treatment of postoperative hypothermia. The ability to deliver flow rates of oxygen higher than those tolerable with CPAP, traditional nasal cannula or face mask could make the Vapotherm a superior treatment for postoperative hypoxemia. This paper presents a systematic review of the literature to inform a research plan for a pilot study examining the feasibility of using the Vapotherm 2000i to decrease the rate of re-intubation among relatively healthy adult patients at UNC Hospitals who experience postoperative hypoxemia.
SYSTEMATIC REVIEW OF THE LITERATURE

Methods for Literature Review

A PubMed search was conducted March 31, 2005 using the search terms “noninvasive positive pressure ventilation” and “postoperative hypoxemia.” It was limited to humans and included all years for which PubMed has data. This search returned only one result. A second search using the same limits and the search terms “noninvasive positive pressure ventilation” and “postoperative respiratory failure” returned 11 articles. The majority of articles addressed the use of noninvasive positive pressure ventilation (NIPPV) in patients with acute respiratory failure secondary to chronic disease, such as COPD or asthma. However, review of those papers and their reference lists revealed a number of articles regarding the use of NIPPV in patients with postoperative respiratory failure. References to abstracts alone were excluded. The search yielded a total of 5 articles, which are summarized in Table 1 in the Appendix. Another PubMed search using the term “Vapotherm” returned 2 articles. One of those was an equipment investigation. The other is summarized in Table 2 in the Appendix.

Additionally, 31 abstracts, published in the November, 2004 issue of Respiratory Care, were presented in December 2004 at the International Congress of the American Association for Respiratory Care. These abstracts were provided by personal communication with Kathleen Short, RRT, RN, Director of Respiratory Care at UNC Hospitals. Ten were related to Vapotherm. Of those, 7 were case reports and 3 were reports of equipment investigations. The case reports are summarized in Table 2 in the Appendix.
Results of Literature Review (see Appendix Tables 1 – 2)

Postoperative Hypoxemia

"Hypoxemia" can be defined by a number of measurements taken on room air, such as partial pressure of oxygen (PO$_2$) $\leq$ 60 torr, arterial oxygen saturation (SaO$_2$) $\leq$ 90%, or arterial partial pressure of oxygen / fraction of inspired oxygen ratio (PaO$_2$/FiO$_2$) $\leq$ 200. The hypothesized explanations for postoperative hypoxemia include the loss of functional alveolar units due to atelectasis, as well as ventilation/perfusion mismatch.$^{1,2}$ Estimates of the incidence of postoperative hypoxemia vary, partly because more inclusive outcomes such as postoperative pulmonary complications may include a number of more specific processes such as atelectasis, pneumonia, and pulmonary embolism.$^3$ The incidence of postoperative pulmonary complications has been estimated to be 5-10% among all surgical patients and 4-22% among abdominal surgical patients.$^3$ Postoperative hypoxemia is estimated to occur in 30-50% of patients undergoing abdominal surgery and 8-10% of those patients may require intubation and mechanical ventilation.$^{1,2}$ Some authors distinguish between early postoperative arterial hypoxemia (EPAH), which occurs within hours after surgery, and late postoperative arterial hypoxemia (LPAH). Among all surgical patients, the incidence of EPAH is 41-55%. The incidence of LPAH is 41-50% among patients who have undergone major abdominal or thoracic surgery.$^4$
Complications of Intubation and Mechanical Ventilation

Endotracheal intubation and mechanical ventilation are associated with a number of complications, such as laryngotracheal injury, patient discomfort, ventilator-associated pneumonia (VAP) and ventilator-associated lung injury (VALI).\textsuperscript{5-7} VALI includes: 1) barotrauma, which may lead to pneumothorax, pneumoperitoneum, or pneumomediastinum; 2) volutrauma, which may lead to pulmonary edema; 3) atelectrauma, and 4) biotrauma, which results in release of inflammatory mediators.\textsuperscript{6} Thus, avoiding prolonged intubation or reintubation postoperatively would help to prevent these complications in hypoxemic postoperative patients.

Noninvasive Positive Pressure Ventilation (NIPPV)

A number of alternatives to intubation and mechanical ventilation exist. The International Consensus Conferences in Intensive Care Medicine defines the term noninvasive positive pressure ventilation (NIPPV) as “any form of ventilatory support applied without the use of an endotracheal tube.”\textsuperscript{8} This definition includes continuous positive airway pressure (CPAP), volume- and pressure-cycled systems, proportional assist ventilation (PAV), as well as the use of therapies such as helium-oxygen gas mixtures.\textsuperscript{8} Extensive research has documented the effectiveness of NIPPV in the treatment of acute respiratory failure (ARF) due to a number of causes, such as chronic obstructive pulmonary disease (COPD), asthma, and cardiogenic pulmonary edema.\textsuperscript{9} This literature is

Considering the evidence supporting the use of NPPV to treat ARF resulting from chronic disease, it follows that NIPPV could be effective in the treatment of postoperative respiratory failure. Unfortunately, few studies have been conducted specifically looking at postoperative patients. The existing literature is reviewed below.

**Studies of NIPPV in Postoperative Patients**

**Randomized Controlled Trials of Continuous Positive Airway Pressure (CPAP)**

A recent randomized controlled trial conducted in Italy supports the use of NIPPV in postoperative respiratory failure. Squadrone et al. (2005) randomized 209 postoperative patients to either a control treatment, oxygen via Venturi mask at an \( \text{FiO}_2 \) of 0.5, or the intervention, oxygen at an \( \text{FiO}_2 \) of 0.5 plus CPAP at 7.5 cm H\(_2\)O. The subjects were elective abdominal surgery patients who developed hypoxemia in the postoperative period, defined by a \( \text{PaO}_2/\text{FiO}_2 \) ratio less than 300 after extubation and a one-hour screening test breathing supplemental oxygen through a Venturi mask at an \( \text{FiO}_2 \) of 0.3. Thus, these authors drew an arterial blood gas (ABG) on each subject.

Squadrone et al. defined extensive exclusion criteria for their study population (Appendix Table 1), thus limiting their trial to relatively healthy patients without significant underlying cardiovascular or respiratory disease.
Specifically, patients with a history of asthma or COPD were excluded. The primary outcome in this trial was incidence of intubation. Secondary outcomes included length of stay in the ICU, length of hospital stay, and incidences of pneumonia, infection, sepsis and mortality. The trial showed that the rate of intubation was higher in the control group (10%) than in the CPAP group (1%) (p=0.005). In fact, the trial was stopped early because the efficacy of CPAP was superior to that of oxygen alone. Patients treated with CPAP also had lower incidences of pneumonia (RR 0.19; 95% CI 0.01-0.76), infection (RR 0.27; 95% CI 0.07-0.94) and sepsis (RR 0.22, 95% CI 0.04-0.99), and spent less time in the intensive care unit (1.4 days compared to 2.6 days, p=0.09).

The strengths of this study include the fact that it was a well-designed randomized, controlled, unblinded study with concealed allocation and well-defined inclusion and exclusion criteria. Despite being conducted at several centers, differences in treatment by center were minimized by defining protocols for operative anesthesia, postoperative pain control and uniform delivery of CPAP. Analysis was conducted on the basis of intention-to-treat and subjects were followed throughout their hospital stay. Unfortunately, masking is nearly impossible in a study of this type where the treatment is visible and obvious. The internal validity of this study is strong. The external validity is limited for several reasons. First, the trial was conducted in Italy, where patients and procedures may differ from those in the United States. Second, the extensive exclusion criteria limit the applicability of the results to relatively healthy patients who have undergone elective abdominal procedures. Patients with co-morbid disease or
those who have other types of surgery may be at higher risk for respiratory failure and CPAP may work differently in those patients. On the other hand, patients who undergo abdominal procedures may be at higher risk for respiratory failure due to mechanical impairment.¹²

Carlsson et al.¹³ conducted a randomized controlled trial comparing supplemental oxygen by face mask with CPAP delivered by the same face mask as prophylactic treatment for pulmonary complications after abdominal surgery. They randomized twenty-four healthy patients undergoing elective open cholecystectomy to receive either pre-warmed, moistened oxygen at 30%, or CPAP with 30% pre-warmed, moistened oxygen. None of the patients had underlying lung disease. Outcome measures included pre- and post-operative measurements of arterial blood gases and vital capacity, as well as pre- and post-operative chest x-rays. The investigator measuring vital capacity and collecting samples for ABG was not masked to treatment group as the treatment is visible. The investigator interpreting chest x-rays was, however, masked to treatment group.

Carlsson et al. found that 3 out of 13 patients in the CPAP group and 1 out of 11 patients in the comparison group had changes in their chest x-rays. Patients in the CPAP group showed an average of 44% decrease in vital capacity after surgery, while the control group had an average decrease of 38%. After surgery, PaO₂ values were slightly higher in the CPAP group. While the authors do not give specific values, they state that none of these differences between groups were statistically significant.
There are a number of problems with this trial. First, the sample size is small. Second, the only inclusion criterion was having undergone elective open cholecystectomy. Third, the authors state that none of the patients had known lung disease, but they do not define any other exclusion criteria. Fourth, no statistical values are given. Finally, subjects were only followed through 24 hours after surgery. Adverse outcomes which can occur after 24 hours postoperatively and which may be related to intubation and mechanical ventilation, such as pneumonia, are not discussed.

Stock et al.\textsuperscript{14} conducted a small randomized study comparing three modes of respiratory therapy in postoperative patients: CPAP by face mask, incentive spirometry (IS) and cough/deep breathing (CDB). They randomized 38 adults scheduled for elective cardiac surgery to one of the three treatments. Therapy was started 2 hours after extubation. Outcomes included postoperative functional residual capacity (FRC), forced vital capacity (FVC), forced expiratory volume in one second (FEV\textsubscript{1}), FEV\textsubscript{1}/FVC ratio, chest x-ray and body temperature. Lung function tests were conducted 2, 24, 48 and 72 hours after extubation. Chest x-rays were taken 24 and 72 hours postoperatively. Body temperature was measured every 6 hours for 72 hours after surgery.

The results showed no differences between any of the groups in mean FRC, FVC, FEV\textsubscript{1}, or FEV\textsubscript{1}/FVC. There also were no differences in x-ray evidence of atelectasis, PaO\textsubscript{2}, PaCO\textsubscript{2}, arterial pH, or in the incidence of body temperature above 38.5°C (an indication of possible pneumonia).
This study had a small sample size and poorly defined inclusion and exclusion criteria. The authors do not address whether investigators were masked to treatment, but the absence of masking is likely since it is difficult to mask an investigator when respiratory therapies are involved. Subjects were followed for 72 hours after extubation. Follow-up throughout the hospital stay may have provided more data regarding late outcomes related to intubation and mechanical ventilation, such as pneumonia. One possible explanation of the findings in this study is that the patients were treated prophylactically, instead of after the development of hypoxemia or respiratory failure. It is possible that one or more of these modes of therapy might be more effective in patients who have already developed respiratory difficulty.

Case Series of CPAP

Dehaven et al.\textsuperscript{15} report a case series in which they treated 27 patients with postoperative hypoxemia with CPAP via face mask at an FIO\textsubscript{2} of 0.45. All of the patients came from the general surgery service and had undergone major thoracic or abdominal surgery either electively or for trauma. They all developed post-extubation hypoxemia that was resistant to chest physical therapy, incentive spirometry and continuous high-flow oxygen by face mask. Criteria for exclusion in the series included recent esophageal or gastric anastomoses, basilar skull fracture, laryngeal injury, and severe maxillofacial injury. Outcomes measures were pre- and post-treatment arterial blood gases, respiratory rate, heart rate and
mean arterial blood pressure, as well as duration of treatment and incidence of intubation.

The authors report that PaO₂, PaO₂/FIO₂, and respiratory rate improved significantly in all patients after initiation of treatment (p<0.0005). Heart rate and mean arterial blood pressure did not change significantly after treatment. The mean duration of treatment with CPAP was 23 hours. Two of 27 patients required intubation: one for excessive secretions and one for *Pseudomonas* pneumonia.

One of the strengths of this study is that patients served as their own controls since arterial blood gases, respiratory rate and heart rate were measured prior to initiation of treatment. Nevertheless, the lack of a traditional control group limits the interpretation of the results. The authors describe some inclusion and exclusion criteria, but they do not mention the health status of the subjects prior to surgery. The patients in their sample may have been healthier or sicker than patients in other studies, which may have contributed to their finding of significant improvement in oxygenation after treatment with CPAP. Another problem with the internal validity of this study is that the authors do not describe how subjects were selected for inclusion in the study from among all general surgery patients. They mention that the included patients were enrolled over an 18-month period and that they represent 8% of all patients extubated during that period. The authors do not state that the subjects were consecutive patients or identify who selected them for inclusion. Finally, the authors state that the mean
duration of treatment was 23 ± 14 hours, but they do not define total follow-up time.

Another case series is reported by Smith et al. (1980). These investigators treated with CPAP by face mask 44 patients with mild-to-moderate acute respiratory insufficiency. Subjects were both postoperative and trauma patients. Inclusion criteria included acute respiratory insufficiency and progressive deterioration of arterial oxygenation that was resistant to oxygen therapy, coughing, deep breathing and chest physical therapy. Patients had to be awake, cooperative and breathing spontaneously. They also had to be either normo- or hypocapnic, have stable cardiovascular status, and demonstrate a PaO₂/FIO₂ ratio less than 300. Exclusion criteria are not described. Outcomes were pre- and post treatment arterial blood gases and respiratory rate, as well as incidence of intubation.

All patients showed an increase in PaO₂ after treatment with CPAP. The mean PaO₂/FIO₂ ratio increased from 171 ± 42 to 300 ± 68. One patient was intubated after developing respiratory academia. There were no significant changes in arterial pH or respiratory rate.

This study included both postoperative and trauma patients and, unfortunately, the authors do not mention how many were postoperative, which limits the applicability of this study to patients with postoperative hypoxemia. There is significant potential for selection bias as the authors do not describe the process of selecting subjects for inclusion in the series, nor do they describe exclusion criteria or duration of follow-up.
**Studies of Vapotherm (please see Appendix for a picture of the device)**

The Vapotherm 2000i is neither a ventilator nor a CPAP machine, but its mechanism of oxygen delivery mimics CPAP. Other devices cannot deliver oxygen or air at rates above 6 liters per minute (lpm) because such high flow is uncomfortable for the patient, dries out the airway, and can damage the airway epithelia. The Vapotherm 2000i, on the other hand, can safely and comfortably deliver gases up to 50 lpm. In addition to providing high flow, the Vapotherm 2000i is capable of humidifying and warming the delivered gases up to 100% humidity and above body temperature. These characteristics of the device allow its use in the treatment of a variety of disease processes.

High flow optimizes gas exchange and reduces work of breathing in chronic lung disease, such as COPD, while humidity and warmth improve oxygenation in conditions such as croup, asthma, and cystic fibrosis. The Vapotherm is able to deliver warm air directly to the body core, which is valuable in the treatment of hypothermia. Based on these attributes, the device has potential as a treatment for postoperative hypoxemia. A number of abstracts and case reports have been published about the benefits of the Vapotherm in various settings. However, the role of the Vapotherm is still being explored and no large trials have been conducted.

One published pilot study examined the feasibility of using the Vapotherm MT-3000 to treat radiation-induced xerostomia. Criswell and Sinha randomized 8 patients to the standard treatment for xerostomia, a bedside cool air humidification system, or hyperthermic, supersaturated humidification via nasal
cannula from the Vapotherm MT-3000. After 2 weeks on the devices, subjects underwent a 1-week washout period and then crossed over to the other device for a 2-week treatment trial. Outcomes included objective assessment of xerostomia symptoms by physical exam, as well as patient-reported subjective assessment of symptoms using the Walizer Mouth Dryness Questionnaire. The authors found no significant differences between the two devices. The relevance of this study to the use of the Vapotherm in postoperative hypoxemia is limited for several reasons. First, the Criswell study used a different model of Vapotherm. Second, their study was very small and dealt with a different disease process. Third, the devices were being operated at home by patients, as opposed to being used in a more controlled setting and operated by trained personnel. Finally, the authors report that adherence to the study protocol was poor. Nevertheless, Criswell and Sinha do not report any adverse events resulting from use of the Vapotherm, other than dislike of the device’s noise and “being tethered to the nasal cannula.”

A number of abstracts and case reports describe the benefits of Vapotherm in various settings. The first case series describes four patients treated with Vapotherm. The patients included: 1) a 16 month-old with respiratory distress secondary to pneumonia who would not tolerate an oxygen mask; 2) a 14 year-old with respiratory distress due to severe asthma for whom standard treatment with Albuterol was ineffective; 3) a 3 month-old extubated after cardiac surgery who developed severe atelectasis; and 4) a 2 ½ year-old with respiratory syncytial virus (RSV) and bronchiolitis who was initially treated with BiPAP but could not expectorate because of the mask. The goal for each patient was treatment of their
respiratory distress while avoiding intubation. All patients showed improved markers of respiratory distress (heart rate, respiratory rate, and SaO₂), as well as improved comfort and decreased work of breathing. No patient required intubation.

The second abstract comes from investigators in the UNC Hospitals Burn Unit. Cairns et al. describe the case of a 12 month-old female with 8% cutaneous burns and inhalation injury who developed respiratory distress after extubation. In order to avoid re-intubation, she was placed on Vapotherm delivering 50% oxygen at 15 lpm. Her heart rate, respiratory rate and breath sounds improved rapidly, as did her sedation requirements. She was weaned to room air over five days and discharged.

Martinez-Gomez and Lefkowitz state that Vapotherm is used in the neonatal intensive care unit (NICU) at Wilford Hall Medical Center. They report the case of a 3 month-old former 25-week infant who developed respiratory distress after extubation. Multiple therapies were initiated, including blow-by, hood, mask CPAP and standard CPAP, but none was successful and re-intubation was considered. The infant was found to have significant swelling, as well as a vocal cord granuloma, resulting in an airway only 1x2 mm wide. Vapotherm treatment was initiated with 100% oxygen at 6 lpm. The infant remained extubated and, at the time of publication, had been extubated for one month and was on standard nasal cannula ready for discharge.

Manning et al. report the use of Vapotherm in a 64 year-old male with a history of COPD and stage III large cell carcinoma who developed pulmonary
edema, dyspnea, increased SaO\textsubscript{2}, and high respiratory rate on post-operative day 3 after a left pneumonectomy. His respiratory distress did not improve on a double-aerosol mask, nor on a non-rebreather mask with nasal cannula in series at 6 lpm. The patient was placed on Vapotherm nasal cannula with 100% oxygen at 20 lpm and subsequently developed improved oxygen saturation. He remained extubated and was later weaned to nasal cannula at 3 lpm.

Sanchez and Sabato (2004)\textsuperscript{23} present the successful use of Vapotherm in a series of seven neonates with respiratory failure who were failing treatment with nasal continuous positive airway pressure (nCPAP). These authors report commonly using nCPAP in neonates at their institution and describe the complications associated with the therapy, including nasal septal trauma and the need for sedation. Infants entered in their trial were failing nCPAP, defined by at least one of the following criteria: 1) SPO\textsubscript{2} < 88 despite nCPAP > 8 cm H\textsubscript{2}O on FiO\textsubscript{2} > 0.60; 2) agitation believed to be caused by the nCPAP device and requiring increased sedation; 3) unacceptable work of breathing while on nCPAP; or 4) nasal trauma or breakdown. All patients were started on FiO\textsubscript{2} of 0.60 at 5 lpm. Flow was then adjusted based on work of breathing and respiratory rate. FiO\textsubscript{2} was weaned to maintain the SpO\textsubscript{2} between 88-96%.

The authors found that 7 neonates, ranging in gestational age from 26-38 weeks (all but one premature), required decreased FiO\textsubscript{2} and less sedation, and showed decreased PaCO\textsubscript{2}. The authors report that the Vapotherm nasal cannula was not associated with nasal trauma. They also report one 710 gram infant who failed Vapotherm treatment, but did well with nCPAP.
Hewitt et al. (2004) report the use of Vapotherm to rewarm a previously healthy 50 year-old male construction worker who, in January of 2004, fell 20-25 feet into a ditch where he then lay for approximately 2 hours in 40-45 degree water. Upon arrival in the Emergency Department, a Foley catheter probe revealed his body temperature to be 95°F. The patient was treated with a Bair Hugger warming device and warmed IV fluids. However, after 1 hour, his temperature had only risen to 95.8°F. He was then placed on the Vapotherm delivering 30 lpm at an FiO₂ of 21% and heated to 102°F, keeping the Bair Hugger in place. Warmed IV fluids were discontinued. After 45 minutes, the patient’s body temperature had increased to 98.1°F. Throughout treatment, the patient did not complain of discomfort from the warmed, high flow gas. He was treated with Vapotherm for 2 hours and was discharged 3 days later following work-up and observation for his injuries.

Brennan et al. (2004) report using Vapotherm as an alternative to nCPAP in the treatment of obstructive sleep apnea and nocturnal oxygen desaturation in an obese 52 year-old male with a BMI of 50.3 and a history of noncompliance with nCPAP. The patient was placed on the Vapotherm nasal cannula at 40 lpm 35% blended FiO₂, and 100% relative humidity. During 7.5 hours overnight, the patient had an average SaO₂ of 96% and his SaO₂ was greater than 90% during 99% of the time for which data was collected. He experienced 6 episodes of apnea and 28 episodes of hypopnea. The patient reported being much more comfortable using the Vapotherm system than with nCPAP.
**Equipment Investigations**

Waugh and Granger\(^{26}\) conducted an equipment investigation comparing the temperature and relative humidity of gases delivered by two nasal cannula/humidifier devices – the Vapotherm 2000i and the Salter Labs (Salter Labs, Arvin, CA) non-heated nasal cannula and bubble humidifier. Humidity and temperature measurements were collected by a digital psychrometer from each unit set at 5, 10 and 15 lpm. They found that the Vapotherm 2000i delivered gases at 99.9% relative humidity at 37°C and the Salter Labs device delivered gases between 72.5 - 78.7% relative humidity at room temperature. The Salter Labs device does not have a heating mechanism and therefore delivers gases at ambient temperature. Waugh and Granger concluded that both devices meet the equipment humidification standards set by the American Association for Respiratory Care and both are acceptable options for high-flow oxygen therapy.

Several abstracts have been published describing various equipment investigations involving Vapotherm. Walsh (2004)\(^{26}\) attached the Neopuff system, used to deliver controlled flow and pressure to infants, to the Vapotherm system in order to warm and humidify the air delivered by the Neopuff. He found that combining the systems allowed warming and humidification of gases, without interfering with the Neopuff's function.

Polston (2004)\(^{27}\) used the Vapotherm to deliver Heliox, a mixture of 70% helium and 30% oxygen, and found that attaching the Vapotherm did not affect Heliox tank life but allowed delivery of the gases at body temperature and saturated humidity. Newhart (2004)\(^{28}\) experimented with combining Vapotherm
with the Datex-Ohmeda INOvent, a device used to deliver inhaled nitric oxide and used for patients with pulmonary hypertension and refractory hypoxemia. He found that addition of the Vapotherm did not interfere with INOvent function at flow rates up to 30 lpm. Newhart suggests that higher flow rates or smaller cannulas could lead to excessive pressure in the INOvent system.

**RESEARCH PLAN**

There is strong evidence supporting the use of noninvasive ventilation in the treatment of acute respiratory failure due to chronic disease, but there are limited data regarding its use to treat postoperative hypoxemia. Vapotherm is a mode of noninvasive ventilation similar to CPAP, but because it is so new, there is little data supporting its use in any form of respiratory failure. However, considering that CPAP and other forms of NIPPV are effective at treating hypoxia related to complex chronic diseases, which involve multiple mechanisms of respiratory compromise, it seems logical that NIPPV might be effective for treating postoperative respiratory failure, which is usually due to transient processes such as airway compromise and/or atelectasis. There is some evidence that this is true, particularly the recent study by Squadrone et al., which showed that CPAP reduced the rate of re-intubation in postoperative patients. The Vapotherm 2000i delivers high-flow, warmed and humidified oxygen non-invasively in a way that mimics CPAP and involves only a nasal or trans-tracheal cannula. The proposed study seeks to test the safety and feasibility of using the Vapotherm 2000i in relatively healthy adults with postoperative hypoxemia, in
preparation for future studies of the effectiveness of this device in a broader population of postoperative patients.

Research Design

Patient Population

Sample Size

The target sample size for this study will be 90 subjects. This is based on a calculation seeking to achieve a confidence level of 95% and 90% power to detect a 4% difference in oxygen saturation. Using a goal of 95% confidence and 80% power, the sample size would be 68 subjects.

Inclusion Criteria

Criteria for enrollment in this study will include postoperative, post-extubation respiratory distress, defined by an \( \text{SaO}_2 < 94\% \) on room air, measured by pulse oximetry. Subjects will be between the ages of 18 and 80 and will have undergone general anesthesia. There will not be a protocol for induction and maintenance of anesthesia. Rather, the type of anesthesia will be at the discretion of the anesthesiologist. Patients will have undergone elective (non-emergency) surgery and will come from the following services: general surgery, orthopedics, gynecological, urological and plastic surgery.

Exclusion Criteria

Criteria for exclusion from the study will include: 1) chronic respiratory disease such as COPD or asthma; 2) Sleep disorders such as obstructive sleep
apnea; 3) sepsis and/or preoperative infection; 4) BMI > 40; 5) tracheostomy; 6) trauma to the face or neck; 7) chest wall abnormalities; 8) history of congestive heart failure, unstable angina, syncope or myocardial infarction within the previous 6 months; 9) emergency surgery; and 10) other conditions identified during the preoperative evaluation that are believed to be potentially life-threatening or capable of causing respiratory failure.

**Recruitment and Consent**

The Department of Anesthesiology at UNC conducts preoperative evaluations on all inpatient surgical patients, as well as high-risk outpatient surgical patients. Lower risk patients who are not in-house are evaluated by their surgeon. In order to recruit patients who meet inclusion and exclusion criteria, surgeons from the general surgery, orthopedics, gynecological, urological and plastic surgery services will be asked to recommend eligible patients for the study during preoperative visits. At the conclusion of the visit, a trained research assistant will ask if the patient is interested in participating in the study. If so, the patient will be screened for eligibility based on the inclusion and exclusion criteria described above. Eligible subjects will be consented and enrolled.

**Intervention**

Postoperative patients will have an initial arterial oxygen saturation (SaO₂) measured on room air and then continuously monitored during their stay in the post-anesthesia care unit (PACU). Patients whose SaO₂ falls below 94% at any
time during their stay in the PACU will be randomized to either the intervention, oxygen via the Vapotherm 2000i, or the control treatment, standard oxygen therapy via nasal cannula at 2 lpm, which corresponds to an FiO₂ between 28-30%. The primary difference between these two therapies is that the Vapotherm device delivers warmed, humidified gases at higher flow rates. All patients will be followed throughout their hospital stay in order to monitor re-intubation and other outcome measures.

**Criteria for Intubation**

Patients will be intubated and mechanically ventilated if, at any time during the study, intubation is clinically indicated for one or more of the following reasons: 1) airway protection (in the case of seizure, coma, etc.); 2) management of secretions; 3) hemodynamic instability; 4) the patient is expected to require long-term ventilatory support, such as in the development of ARDS; or 5) other emergent conditions judged by the PACU team to indicate intubation.

**Outcome Measures**

The primary outcome measures will be the change in SaO₂ measured by pulse oximetry and the incidence of re-intubation. Secondary outcomes will include ICU stay length (if applicable), hospital stay length, and incidences of pneumonia, infection, sepsis and mortality. Adverse events will be documented for both groups.
**Statistical Analysis**

The sample size calculation was done using the “rule of thumb” for sample size calculation for studies about means in two groups described by Dawson and Trapp.\(^{29}\) In this calculation based on a 95% confidence level, the ratio of the standard deviation to the difference to be detected \(\frac{\sigma}{\mu_1 - \mu_2}\) is squared and multiplied by a number corresponding to the desired power of the study. For a study with 90% power, the multiplier is 20 and for 90% it is 15.

Based on the oxyhemoglobin dissociation curve, the desired clinically significant difference in oxygen saturation was 4%. The standard deviation for \(\text{SaO}_2\) used was 6%.\(^{30}\)

Patient demographic variables and outcome variables will be analyzed as depicted in Tables 1 and 2 below. Differences in demographic variables between groups will be analyzed by comparing means and standard deviations for age, and by percentages of the total for gender, smoking status, body mass index, ASA physical status and surgical service. The outcome variables will be analyzed for differences between the control (\(\text{O}_2\) via nasal cannula) and intervention (Vapotherm) using t-tests and 95% confidence intervals.
Results

Table 1. Patient Demographics.

<table>
<thead>
<tr>
<th>Patient Variable</th>
<th>Vapotherm</th>
<th>O₂ via nasal cannula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years; mean ± SD)</td>
<td></td>
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<tr>
<td>Gender (%)</td>
<td></td>
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<tr>
<td>Male</td>
<td></td>
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<tr>
<td>Female</td>
<td></td>
<td></td>
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<tr>
<td>Smoking Status (N, %)</td>
<td></td>
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<tr>
<td>Body Mass Index (mean ± SD)</td>
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<tr>
<td>ASA Physical Status (%)</td>
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<tr>
<td></td>
<td>II</td>
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<tr>
<td></td>
<td>III</td>
<td></td>
</tr>
<tr>
<td></td>
<td>IV</td>
<td></td>
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<tr>
<td>Surgical Service (N, %)</td>
<td>General</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gynecology</td>
<td></td>
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<tr>
<td></td>
<td>Orthopedic</td>
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<tr>
<td></td>
<td>Plastic</td>
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<td></td>
<td>Urology</td>
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</tbody>
</table>

Table 2. Outcome Measures.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Vapotherm</th>
<th>O₂ via nasal cannula</th>
</tr>
</thead>
<tbody>
<tr>
<td>Change in SaO₂ (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incidence of re-intubation (N, %)</td>
<td></td>
<td></td>
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<tr>
<td>ICU stay length (days)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hospital stay length (days)</td>
<td></td>
<td></td>
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<tr>
<td>Incidence of pneumonia (N, %)</td>
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<td></td>
</tr>
<tr>
<td>Incidence of infection (N, %)</td>
<td></td>
<td></td>
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<tr>
<td>Mortality (N, %)</td>
<td></td>
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</tbody>
</table>
DISCUSSION

This study will examine the feasibility and effectiveness of the Vapotherm device, compared with standard oxygen therapy via nasal cannula, at treating postoperative hypoxemia and preventing re-intubation in relatively healthy surgical patients. The proposed study will track more outcomes than previous investigations, ranging from oxygen saturation measured by pulse oximetry to mortality, and will follow subjects for adverse events until they are discharged from the hospital. While there is limited evidence supporting the use of the Vapotherm in specific settings, it is FDA-approved and is very similar to standard oxygen therapy via nasal cannula. The main difference is that the Vapotherm is able to warm and humidify gases, which allows increased flow rates.

In any investigation of a new device there is the possibility of equipment failure. In the case of the Vapotherm, there are three ways that the device might fail. These include failure of the warming mechanism, failure of the humidification mechanism, and disconnection or failure of the oxygen delivery system. Oxygen delivery by standard nasal cannula is limited to 6 lpm, as higher flow rates can cause drying and cooling of the airway.\textsuperscript{31} The Vapotherm, on the other hand, can comfortably deliver up to 40 lpm.\textsuperscript{17} Should the warming or humidification mechanism fail, the patient would be exposed to oxygen delivered at a high flow rate, which could result in discomfort from drying of the airway and could damage airway epithelia. While this would be unpleasant, it is not life-threatening. If the oxygen delivery system were to fail, the patient would be transiently deprived of supplemental oxygen, which could be life-threatening.
However, this complication is equally likely with other forms of NIPPV, including nasal cannula and face mask. Additionally, like all postoperative patients, the subjects in this study will be closely monitored by the PACU staff. They will be cared for by a nurse or resident with experience caring for postoperative patients and their oxygen saturation will be monitored constantly until discharge from the PACU.

Several additional safety measures are built into the study design. First, a protocol will be in place which specifically defines criteria for re-intubation so that any patient may be intubated if the physician believes that the subject’s respiratory status is compromised. Second, the selection of 94% as the cut-off $\text{SaO}_2$ maximizes patient safety by identifying early those patients at risk of progressing to severe hypoxemia. Most clinicians consider an $\text{SaO}_2$ less than 90% to indicate hypoxemia. This level of hemoglobin saturation corresponds to an arterial $\text{PO}_2$ of 60 torr at normal body temperature and pH. The choice of an $\text{SaO}_2$ of 90% or a $\text{PO}_2$ of 60 torr as the cut-off point is based on the oxyhemoglobin dissociation curve. This curve is influenced by numerous parameters, including body temperature, pH, $\text{PCO}_2$, and 2,3-DPG concentration. However, when those parameters are within the normal range, the curve is S-shaped and flattens out at about 90% saturation. This means that above 90% hemoglobin saturation, very large increases in $\text{PO}_2$ are required to make small changes in hemoglobin saturation. On the other hand, below 90%, the curve has a steep slope such that small changes in $\text{SaO}_2$ indicate larger changes in $\text{PO}_2$. This means that once a patient’s $\text{SaO}_2$ reaches 90%, they are in danger of rapidly
progressing to severe hypoxemia. Choosing 94%, where the curve is still relatively flat, as the cut-off for this study provides more safety for the subjects by catching at-risk patients before they reach the steep, rapidly falling part of the curve.

The use of SaO\textsubscript{2} as the measure of oxygenation raises certain issues. Many studies of ventilation, such as that by Squadrone et al., use the PaO\textsubscript{2}/FiO\textsubscript{2} ratio or PaO\textsubscript{2} as the outcome measure. This requires drawing an arterial blood sample for blood gas analysis. While this might be simple in patients who already have an arterial line in place for surgery, it would subject other patients to an additional, painful, invasive procedure that is accompanied by its own risks of infection and bleeding. Since the subjects for this study will be relatively healthy, they are less likely to need an arterial line for monitoring during surgery and would thus require an additional arterial puncture in the PACU. An arterial blood gas analysis would provide more data on oxygenation than an SaO\textsubscript{2} since it includes PO\textsubscript{2}, PCO\textsubscript{2}, pH and HCO\textsubscript{3}⁻, but it is more invasive, while SaO\textsubscript{2} is a reliable, non-invasive measure of oxygenation.

As with any study, the use of a measurement tool such SaO\textsubscript{2} introduces the possibility of inter-observer variability. The sensitivity and specificity of pulse oximetry are 98-100% and 52-67%, respectively, and depend on the particular model of pulse oximeter. Additionally, factors such as patient movement, low perfusion, and low signal strength can alter the reliability of pulse oximetry.\textsuperscript{32} Despite these possible problems, pulse oximetry is the standard measure of arterial oxygenation in postoperative patients.
The validity of this study could potentially be threatened by selection bias. It is designed such that the surgeons initially recommend subjects for the study, rather than the anesthesiologists who will be taking care of the patients postoperatively and making decisions about oxygenation and the need for re-intubation. This presents several issues. First, the surgeons are less invested in the study since its results are not related to their work or the way that they treat patients. Postoperative hypoxemia affects their patients, but it is the anesthesiology team that identifies and treats problems with oxygenation and ventilation in the postoperative period. As a result, surgeons will likely be less motivated to identify and recommend subjects than would an anesthesiologist. Second, because the surgeons are probably less familiar with the treatment of postoperative hypoxemia and with the Vapotherm in particular, they might be hesitant to enroll their patients in the study. This could lead to an overall small sample or to the recruitment of only the healthiest, lowest risk patients. Third, there might be a difference between surgeons from the different departments in how interested and motivated they are to recommend subjects. Motivating surgeons to identify and suggest potential subjects to the research assistant will be an important step in the start-up phase of this study.

Selection bias could also be introduced by the physicians and nurses in the PACU. While a study team member will identify subjects eligible for the study based on \( \text{SaO}_2 \), the ultimate decision about patient care lies with the PACU staff. This presents the opportunity for those doctors and nurses to choose not to enroll patients based on their perception of the patient’s status or their own familiarity.
with the Vapotherm. For example, a team member might decide not to enroll a patient with a low SaO₂ because he or she is not familiar with the Vapotherm device, is worried about the patient’s respiratory status, or is more comfortable using a standard nasal cannula. Appropriate training regarding use of the Vapotherm and the study protocol among the PACU staff will be imperative for the success of this study.

The proposed study seeks to determine the feasibility of the use of Vapotherm in the treatment of postoperative hypoxemia. While there is little existing evidence supporting use of the Vapotherm in specific settings, there are abstracts reporting its successful use to treat various conditions, including environmental exposure-related hypothermia and respiratory distress secondary to infection, chronic disease, inhalation injury and postoperative atelectasis. These reports do not provide sufficient evidence to change current standards of care, nor will the proposed study. However, this feasibility investigation may help to further define the role of the Vapotherm, specifically in the treatment of postoperative hypoxemia.

Should the results show a benefit of the Vapotherm among relatively healthy subjects with postoperative hypoxemia, future studies could evaluate its effectiveness among an expanded patient population at higher risk of postoperative respiratory distress, such as those with chronic lung diseases like COPD and asthma. Other studies might further investigate the use of the Vapotherm to treat acute respiratory failure secondary to chronic disease. There is good evidence supporting the use of CPAP in that setting and the Vapotherm
may also have a role in the treatment of acute exacerbations of chronic respiratory illness.
REFERENCES


system to rewarm a nonintubated hypothermic trauma patient. *Respir Care.* 2004;49:1368.


# Appendix

## Table 1. Studies of CPAP in Postoperative Patients

<table>
<thead>
<tr>
<th>Author</th>
<th>Study Type</th>
<th>Intervention</th>
<th>Population</th>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
<th>Outcomes</th>
<th>Main Results</th>
<th>Statistical Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>[Squadrone V, 2005 #1]</td>
<td>RCT</td>
<td>Control – O₂ via Venturi mask at FiO₂=0.5. Intervention – O₂ at FiO₂=0.5 plus CPAP=7.5 cm H₂O</td>
<td>209 patients s/p elective abdominal surgery from Piedmont Intensive Care Units Network (Italy)</td>
<td>Elective abdominal surgery requiring laparotomy and &gt;90min. viscera exposure. PaO₂/FiO₂ ≤300 after extubation and 1-hour screening test breathing through a Venturi mask at FiO₂ = 0.3.</td>
<td>Age &gt;80 or &lt;18; NYHA functional class II, III or IV; valvular heart disease, h/o dilated cardiomyopathy; implanted pace maker; unstable angina; MI or cardiac surgery within 3 months; h/o COPD, asthma, or sleep disorders; pre-op infection, sepsis, or both; BMI&lt;40; tracheostomy, facial/neck/chest wall abnormalities; required emergency surgery; undergone AAA repair, chemotherapy, or immunosuppressive therapy within previous 3 months; If pre-randomization arterial pH &lt;7.30 with arterial CO₂ &gt;50mmHg; arterial O₂ sat.&lt;80% on maximal FiO₂; signs of acute MI; SBP&lt;90mmHg under optimal fluid therapy; presence of criteria for ARDS; Hgb&lt;7; serum albumin &lt;3; creatinine&gt;3.5; or Glasgow Coma Score&lt;l2.</td>
<td>1- rate of intubation. 2- ICU stay length, hospital stay length, incidences of pneumonia, infection, sepsis, and mortality</td>
<td>Rate of intubation higher in control group (10 patients, 10%) than in CPAP group (1 patient, 1%).</td>
<td>P = 0.005</td>
</tr>
<tr>
<td>Author</td>
<td>Study Type</td>
<td>Intervention</td>
<td>Population</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Outcomes</td>
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<td>Statistical Significance</td>
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<tr>
<td>Carlsson C, 1981</td>
<td>RCT</td>
<td>Face mask CPAP v. control. Both groups received 30% pre-warmed and moistened O₂</td>
<td>24 healthy pts undergoing elective open cholecystectomy with no known lung disease</td>
<td>Elective open cholecystectomy</td>
<td>None described</td>
<td>Pre- and post-op ABG, chest x-ray, vital capacity</td>
<td>3/13 CPAP pts and 1/11 control pts had post-op x-ray changes. 44% ↓ in VC in CPAP group and 38% ↓ in VC in control group. CPAP pts. had slightly higher ↑ in PaO₂ in 4 hrs after surgery</td>
<td>No sig. difference bwn groups in incidence of x-ray changes, decrease in VC, or increase in PaO₂. Authors don't give statistical values.</td>
</tr>
<tr>
<td>Stock MC, 1984</td>
<td>Case series/cohort</td>
<td>CDB (cough &amp; deep breathing), IS (incentive spirometry) or face mask CPAP</td>
<td>38 adults s/p elective cardiac surgery</td>
<td>Adults s/p elective cardiac surgery</td>
<td>None described</td>
<td>FRC, FVC, FEV₁, FEV₁/FVC, chest x-ray, body temp.</td>
<td>No difference between groups in mean FRC, FVC, FEV₁, FEV₁/FVC, x-ray evidence of atelectasis, PaO₂, PaCO₂, arterial pH, incidence of body temp. &gt;38.5°C.</td>
<td>No p values given.</td>
</tr>
<tr>
<td>Dehaven CB, 1985</td>
<td>Case series/cohort</td>
<td>Face mask CPAP at FIO₂=0.45</td>
<td>27 post-op patients from general surgery service who had undergone major thoracic or abdominal surgery electively or for trauma</td>
<td>Postextubation hypoxemia resistant to chest PT, incentive spirometry, and continuous high-flow O₂ by face mask</td>
<td>Recent esophageal or gastric anastomoses, basilar skull fracture, laryngeal injury, severe maxillofacial injury</td>
<td>ABG, RR, HR, mean arterial BP, duration of treatment, intubation</td>
<td>2 patients intubated (1 for excessive secretions, 1 for Pseudomonas pneumonia). PaO₂ ↑ in all pts. PaO₂, PaO₂/FIO₂, RR improved in all pts. Mean treatment duration = 23 hrs.</td>
<td>P=0.0005 for difference in pre- and post-treatment, PaO₂, PaO₂/FIO₂, and RR</td>
</tr>
<tr>
<td>Author</td>
<td>Study Type</td>
<td>Intervention</td>
<td>Population</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Outcomes</td>
<td>Main Results</td>
<td>Statistical Significance</td>
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<tr>
<td>Smith RA, 1980</td>
<td>Case series</td>
<td>Face mask CPAP</td>
<td>44 trauma and post-op pts w/ mild-mod. acute respiratory insufficiency (ARI)</td>
<td>ARI and progressive deterioration of arterial oxygenation resistant to (O_2) coughing, deep breathing, and chest PT. Awake, cooperative, spontaneously breathing, normo- or hypocapnic, (PaO_2/FIO_2&lt;300), stable cardiovascular status</td>
<td>None described</td>
<td>ABG, (PaO_2/FIO_2), RR, intubation</td>
<td>1 pt intubated for acidemia, (PaO_2)↑ in all pts. (PaO_2/FIO_2)↑ from 171±42 to 300±68. No significant change in pHa or RR.</td>
<td>(P&lt;0.005) for change in (PaO_2/FIO_2)</td>
</tr>
<tr>
<td>Author</td>
<td>Study Type</td>
<td>Intervention</td>
<td>Population</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Outcomes</td>
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<tr>
<td>Criswell MA, 2001</td>
<td>Randomized, controlled, crossover pilot study</td>
<td>Standard cool air bedside humidification system v. hyperthermic, supersaturated humidification via nasal cannula (Vapotherm MT-3000)</td>
<td>8 ENT pts with h/o head/neck cancer</td>
<td>Age ≥ 18; capable of completing 3 clinic visits; completion of ≥ 5000 cGy external beam radiation to oral cavity or oropharynx ≥ 4 months before study entry; persistent, symptomatic radiation-induced xerostomia.</td>
<td>Stating that xerostomia was not a problem; life expectancy &lt; 3 months; planned radiotherapy, chemotherapy or surgery during study; active disease limiting ability to participate.</td>
<td>Physical exam using objective xerostomia scale; subjective assessment of xerostomia (Walizer Mouth Dryness Questionnaire); VAS measuring dryness, speaking and swallowing; patient reports of overall impression of devices.</td>
<td>No significant differences between devices.</td>
<td>n/a</td>
</tr>
<tr>
<td>Frick J, 2004 (abstract)</td>
<td>Case Series</td>
<td>NIPPV via Vapotherm</td>
<td>Pt. A – 16 m/o w/respiratory distress 2° to pneumonia, would not tolerate O₂ mask. Pt. B – 14 y/o w/ respiratory distress 2° severe asthma, baseline therapy (cont. Albuterol) ineffective. Pt. C – 3 m/o Post-op/post-extubation cardiac patient w/ severe atelectasis. Pt. D – 2.5 y/o w/ respiratory distress 2° to RSV, bronchiolitis, unable to expectorate 2° to BPAP mask</td>
<td>n/a</td>
<td>Intubation, markers of respiratory distress (HR, RR, O₂ sat), comfort, work of breathing</td>
<td>No patient was intubated, all showed improved markers of respiratory distress, improved comfort, decreased work of breathing.</td>
<td>n/a</td>
<td></td>
</tr>
<tr>
<td>Author</td>
<td>Study Type</td>
<td>Intervention</td>
<td>Population</td>
<td>Inclusion Criteria</td>
<td>Exclusion Criteria</td>
<td>Outcomes</td>
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<tr>
<td>Cairns B, 2004</td>
<td>Case Report</td>
<td>NIPPV with Vapotherm</td>
<td>12 m/o female with 8% cutaneous burns and inhalation injury, developed respiratory distress after extubation.</td>
<td>n/a</td>
<td>n/a</td>
<td>intubation</td>
<td>Patient was not re-intubated, weaned to room air after 5 days of treatment and discharged.</td>
<td>n/a</td>
</tr>
<tr>
<td>Martinez-Gomez R, 2004 (abstract)</td>
<td>Case Report</td>
<td>NIPPV with Vapotherm</td>
<td>&gt;3 m/o former 25-week twin failed extubation to blow-by, hood, mask CPAP or standard CPAP and required re-intubation. Vapotherm treatment started at 6 lpm and 1.0 FiO₂. Infant remained extubated.</td>
<td>n/a</td>
<td>n/a</td>
<td>intubation</td>
<td>Patient remained extubated.</td>
<td>n/a</td>
</tr>
<tr>
<td>Manning L, 2004 (abstract)</td>
<td>Case Report</td>
<td>NIPPV with Vapotherm</td>
<td>64 y/o male with h/o COPD, stage III large cell carcinoma s/p L pneumonectomy, developed pulmonary edema, dyspnea, decreased SaO₂, and high RR on post-op day 3, did not improve with double-flow aerosol mask or NRB mask with NC in series at 6 lpm. Patient placed on Vapotherm NC 20 lpm, 37°C, 100% FiO₂.</td>
<td>n/a</td>
<td>n/a</td>
<td>intubation</td>
<td>Patient was not intubated, weaned to traditional NC 3 lpm within 48 hours.</td>
<td>n/a</td>
</tr>
<tr>
<td>Sanchez F, 2004 (abstract)</td>
<td>Case Series</td>
<td>NIPPV with Vapotherm</td>
<td>7 neonates (26-38 weeks gestation) with respiratory failure who failed standard treatment with nCPAP.</td>
<td>Failing therapy with nCPAP</td>
<td>n/a</td>
<td>FiO₂, sedation requirements, ABG</td>
<td>All required decreased FiO₂, less sedation, and showed decreased PaCO₂.</td>
<td>n/a</td>
</tr>
<tr>
<td>Hewitt MJ, 2004 (abstract)</td>
<td>Case Report</td>
<td>NIPPV with Vapotherm</td>
<td>50 y/o previously healthy construction worker who fell 20-25 feet into a ditch and lay for 2 hours in 40-45° water, failed treatment with warmed IV fluids and Bair Hugger</td>
<td>n/a</td>
<td>n/a</td>
<td>Body temperature</td>
<td>Body temperature increased from 95.8° to 98.1° after 45 minutes.</td>
<td>n/a</td>
</tr>
<tr>
<td>Brennan T, 2004 (abstract)</td>
<td>Case Report</td>
<td>NIPPV with Vapotherm</td>
<td>52 y/o male with h/o OSA, BMI=50.3, noncompliant with nCPAP</td>
<td>n/a</td>
<td>n/a</td>
<td>SaO₂, episodes of apnea and hypopnea</td>
<td>Average SaO₂=96%, 6 episodes of apnea, 28 episodes of hypopnea</td>
<td>n/a</td>
</tr>
</tbody>
</table>
Vapotherm 2000i