Humidified High-Flow Nasal Oxygen Utilization in Patients with Cancer at Memorial Sloan-Kettering Cancer Center

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Abstract

Background: Respiratory signs and symptoms are commonly encountered by physicians who care for cancer patients. Supplemental oxygen (SO₂) has long been used for treatment of hypoxic respiratory insufficiency, but data reveal mixed efficacy results. The use and outcome patterns of technologically advanced oxygen delivery devices, such as humidified high-flow nasal oxygen (HHFNO₂), are incompletely understood.

Methods: Institutional database search of the number of patient cases in which the current HHFNO₂ device was used, and abstraction of 183 patient medical records for usage characteristics.

Results: Patients have been treated with HHFNO₂ at Memorial Sloan Kettering Cancer Center (MSKCC) since 2008. Of the 183 patients randomly selected for our study, 72% received HHFNO₂ in the intensive care unit (ICU) because of hypoxia. Patients usually improved (41%) or remained stable (44%) while on the device, whereas 15% declined. At study completion, 45% of patients were living, and 55% had died. The median time on HHFNO₂ was 3 days (range: 1–27). A do not resuscitate (DNR) order was present in 101 (55%) patients, either before (12%) or after (43%) device utilization. The majority (78%) of these 101 patients died at MSKCC.

Conclusion: Dyspnea is a common and important symptom in cancer patients for which SO₂ traditionally has had no clear basis except in select cases of hypoxia and patient preference. Our institutional experience with HHFNO₂ contributes to the understanding of the applications and challenges surrounding the use of new medical devices in the cancer population. Physiologic and quality-of-life benefits of HHFNO₂ compared with traditional oxygen delivery methods should be studied prospectively.

Introduction

DYSPNEA IS A COMMON AND MULTIFACTORIAL SYMPTOM, particularly in advanced illnesses including cancer,¹ and can be distressing for patients, families, and caregivers. Physicians are ethically obligated to recognize, evaluate, and consider treatment for dyspnea.² Supplemental oxygen (SO₂) represents one such treatment modality and is utilized widely in institutional settings as well as at home.³ Possible benefits include symptomatic and functional improvement, as well as the perception that oxygen is life-sustaining. Patients with underlying hypoxia are more likely to benefit⁴; however, in certain settings there is no significant dyspnea reduction between hypoxic and nonhypoxic patients.⁵ Two randomized double-blind cross-over studies^{6,7} comparing air versus oxygen in cancer patients with dyspnea, as well as a consecutive cohort study⁸ and a metaanalysis⁹ in dyspneic patients, all

failed to demonstrate a symptom benefit, even when oxygen saturation improved. Most recently, a randomized-controlled double-blind multinational trial of oxygen versus room air, both via nasal cannula, in 239 outpatients with refractory dyspnea revealed no significant differences in the palliation of breathlessness.¹⁰

Additionally, disadvantages of SO₂ therapy include mobility reduction, barriers to acquiring equipment, complexities of framing goals of care, and factors such as noise, irritation of the nasal mucosa, and discomfort associated with SO₂ devices. Guidelines from medical societies^{11,12} therefore consistently recognize the lack of data to support the use of SO₂ in the treatment of dyspnea and recommend individualizing care to specific situations, including hypoxia. The need for individualizing SO₂ and awareness about available resources is supported by variations in patients' reported experiences with dyspnea, and their expectations of physician involvement.^{13,14}

Physicians also have varying opinions and practices regarding SOx.^{15,16}

Technologically advanced oxygen delivery devices, such as humidified high-flow nasal oxygen (HHFNOx) have gained increased acceptance over the last decade. HHFNOx can deliver up to 50 to 60 L/min with low-level positive airway pressure,¹⁷ and has led to anecdotal improvements in functioning and palliation of dyspnea.¹⁸ These devices also offer the advantage of supplying patients with heated humidified oxygen and the potential to reduce mouth and throat dryness.¹⁸ Larger series have been reported more recently in adults, including 20 patients with acute respiratory failure treated with HHFNOx after face mask oxygen,¹⁹ as well as a randomized trial of face mask oxygen versus HHFNOx in the postextubation adult setting,²⁰ with both studies demonstrating improved tolerability with HHFNOx. The non-randomized study showed improved oxygenation and lower respiratory rate with HHFNOx, whereas the randomized investigation revealed no difference in these physiologic differences, and only a trend toward improved comfort with HHFNOx.

Nonetheless, the majority of the HHFNOx literature remains in the pediatric population; and, in the adult oncology population, the technology has not been described. As a new device in the complex and heterogeneous oncology population, it may compound existing ethical issues and organizational intricacies in patient care.²¹ We have experienced both the benefits (e.g., comfort, and ability to eat and talk while on the device) and disadvantages (e.g., complication of hospital discharge planning for patients wanting to stay on the device) of HHFNOx in patients treated at our institution. Our goal for this study was to document the prevalence of HHFNOx use at our tertiary cancer center and to analyze individual case characteristics relating to HHFNOx initiation, discontinuation, and consistency with patient goals of care.

Patients and Methods

We queried the Memorial Sloan-Kettering Cancer Center (MSKCC) Institutional Database (IDB) data search engine (DAVINCI) to identify patients in whom HHFNOx has been used. DAVINCI is an MSKCC web-based application that enables independently run data queries. DAVINCI data are updated daily and consist of demographics, diagnosis and procedure codes, pathology reports, hospital and outpatient encounters, dispensed medications, and laboratory results.

The HHFNOx device (Fig. 1) currently used at MSKCC is Optiflow™ (Fisher & Paykel Healthcare, CA). After coding for HHFNOx began at MSKCC in 2008, the device has been ordered in 353 patients (63 in 2008, 152 in 2009, and 138 through August 2010). Of the 353 patients, we randomly selected 183 to further analyze.

Utilizing the DAVINCI results, we manually abstracted patient medical records, including admission notes, discharge summaries, ICU and floor ventilatory and vital sign records, advance directives, and daily clinician progress notes. Characteristics of HHFNOx usage included malignancy diagnosis, presence of underlying cardiopulmonary disease, reason for HHFNOx initiation (hypoxia or dyspnea), duration of HHFNOx therapy, reported HHFNOx impact (recorded patient subjective impressions and clinician documentation), reason for discontinuation (stable, declined, or expired), pa-

FIG. 1. Schematic of an HHFNOx device.¹⁷

tient outcome (discharge, code and vital statuses), and if applicable, dates of do not resuscitate (DNR) orders and death. Oxygen devices used before and after HHFNOx, with associated oxygen saturation (SaO₂) percentile range subsets (70s, 80s, 90s, etc.), were also recorded. All information was recorded in a standard data software program (Microsoft® Excel® 2007; ©2006 Microsoft Corporation, Redmond, WA) for basic statistical analysis (percentages, means, and ranges).

Results

The median age (years) of the 183 patients at first HHFNOx order was 67 (range: 20–95). Patients treated with the device had a variety of malignancies, including hematologic (29%), lung (17%), gastrointestinal (15%), sarcoma (6%), head, neck, and central nervous system (CNS) (5%), breast (4%), and other tumors (24%). The majority of patients were administered HHFNOx for hypoxia (98%; includes 37 postoperative or postprocedure patients) and had underlying cardiopulmonary disease (93%, including contributing thromboembolic and neurologic diseases).

HHFNOx was used in the ICU in 72% of cases and otherwise, on the hospital ward alone or after an ICU stay. Objective clinical outcomes (documented patient comfort and SaO₂ on the device, as well as “step-up” or “step-down” grading to other oxygen support devices or care settings) of patients on HHFNOx varied: 41% improved while on the device, whereas 44% remained stable and 15% declined. Subjectively, patients appeared to tolerate the device well, and complaints were seldom reported. Two patients requested removal of the device due to nasal discomfort and were successfully transi-

tioned onto a face-tent oxygen device. Pre- and post-HHFNOx SaO₂ and oxygen delivery devices varied (Table 1) but a majority of patients (66%) appeared to benefit indirectly from HHFNOx as it acted as a step-up or step-down device between more intensive/invasive ventilation and lower oxygenation, or vice versa. This resulted in a recorded pre- and post-HHFNOx saturation that was maintained within the normal range (90%–100% SaO₂). Patients saturating at the low end of this range (low 90s SaO₂) were commonly transitioned from room air or nasal cannula to HHFNOx in an attempt to improve saturation. Common devices for patients who were transitioned off HHFNOx included nasal cannula (40%), face or nonrebreather mask (18%), and intubation (12%). At the time of the chart abstraction, 45% of patients were still alive, 33% had died at MSKCC, and 22% had died outside of

TABLE 1. OXYGEN INTERVENTION PRE- AND POST-HHFNOx TREATMENT AND ASSOCIATED OXYGEN SATURATION^a

Oxygen saturation (SaO ₂ % range)	Oxygen device Room air	Patient no. (%)
<i>Pre-HHFNOx</i>		
40s	Room air	1 (0.5)
70s	Room air	6 (3.3)
	Nasal cannula	2 (1.1)
	Face mask	1 (0.5)
80s	Room air	10 (5.4)
	Nasal cannula	7 (3.8)
	Face mask	2 (1.1)
	Nonrebreather mask	3 (1.6)
90s	Room air	19 (10.4)
	Nasal cannula	44 (24)
	Face mask	46 (25)
	Face tent	1 (0.5)
	Nonrebreather mask	15 (8.1)
	CPAP	2 (1.1)
	BiPAP	16 (8.7)
100	Face mask	3 (1.6)
	Nonrebreather mask	2 (1.1)
	CPAP	1 (0.5)
	BiPAP	2 (1.1)
<i>Post-HHFNOx</i>		
60s	Room air	1 (0.5)
70s	BiPAP	1 (0.5)
80s	Nonrebreather mask	1 (0.5)
90s	Room air	16 (8.7)
	Nasal cannula	71 (38.8)
	Face mask	17 (9.3)
	Face tent	3 (1.6)
	Nasopharyngeal airway	1 (0.5)
	Nonrebreather mask	16 (8.7)
	CPAP	5 (2.7)
	BiPAP	12 (6.5)
	Intubated	23 (12.6)
	Expired on HHFNOx device	14 (7.6)
100	Nasal cannula	2 (1.1)

^aSee results section for details of HHFNOx effects on patient course, e.g., serving as a “step-up” or “step-down” device.

BiPAP, bilevel positive airway pressure; CPAP, continuous positive airway pressure.

TABLE 2. CODE STATUS AND PATIENT OUTCOME

Code status	Patient outcome	Patient no. (%)
DNR pre-HHFNOx	Died in hospital	22 (100)
	Home	16 (73)
	Home hospice	2 (9)
	Home with home services	1 (4.5)
	Hospice	2 (9)
DNR post-HHFNOx	Hospice	1 (4.5)
	Died in hospital	79 (100)
	Home	63 (80)
	Home hospice	2 (2.5)
	Home with home services	4 (5)
	Hospice	2 (2.5)
	Rehabilitation facility	7 (9)
Full code status	Rehabilitation facility	1 (1)
	Acute rehabilitation	82 (100)
	Died in hospital	2 (2.4)
	Home	2 (2.4)
	Home with home services	55 (67)
	Outside hospital (ICU)	12 (14.7)
	Rehabilitation facility	1 (1.2)
	Subacute rehabilitation facility	9 (11)
TOTAL		1 (1.2)
		183

DNR, do not resuscitate; ICU, intensive care unit.

MSKCC. The median time on HHFNOx was 3 days (range: 1–27) and for those who died at MSKCC, the median time from HHFNOx order to death was 9 days (range: 0–296).

The majority of patients who had a DNR order either pre- (12%) or post-HHFNOx (43%) died at MSKCC (78%). Of note, there were 20 patients who received HHFNOx and then were later made DNR (median: 2 days later [range 0–20]). Only 7 of these 20 were admitted to the ICU, with 13 remaining relatively stable on HHFNOx while on the hospital ward. An ICU consult to assess respiratory insufficiency and provide management support to the staff was provided in 9 of 13. “Full code” status patients (82) tended to be discharged home (82%) or to an outside rehabilitation facility (11%) (Table 2).

Discussion

At MSKCC, patients with various malignancies and clinical trajectories have been treated with HHFNOx over the past 2 years, and the device generally seems well tolerated. Additionally, HHFNOx was effective in the stabilization or improvement of respiratory difficulties in the majority of treated patients, often obviating the need for ICU admission or for invasive ventilatory treatments such as mechanical ventilation. Strengths of our analysis include that this sizable cohort serves, to our knowledge, as the only clinical description of an HHFNOx device exclusively in the cancer population. Additionally, we used carefully preselected patient characteristics to best describe the details of HHFNOx use. Nonetheless, there are limitations of our retrospective study: Without predefined prospective endpoints, the results generated from

the manual chart abstractions are subject to bias. Although HHFNOx outcome patterns and associations seem to be present (that patients were usually stable or improved on the device, and that device escalation such as to endotracheal intubation was not commonly employed), the lack of a no-HHFNOx study arm precludes definitive conclusions or attributions. This heterogeneous population, including patients being treated both with curative and palliative goals, precludes sound observations on the effects of HHFNOx in specific populations. Given the retrospective design, as well as the clinical evolution of complex cases, the distinction between treatment intents is not fully possible in this study. Further prospective study should focus on this area. Additionally, we did not collect information on home oxygen support devices after discharge, limiting conclusions about the role of HHFNOx in discharge planning. Finally, reporting and scoring of dyspnea were not available for abstracting, thereby limiting the degree to which our results can be compared with those of studies examining dyspnea and other symptoms.

HHFNOx is currently only prescribed and administered in specialized clinical environments, and is not available to patients upon discharge to home or hospice (with the emergence of new technology, HHFNOx equipment will now become available in the home or hospice). These restrictions relate to the need for high oxygen delivery. To generate flows at rates up to 50 to 60 L/min, advanced air compression systems, which are feasible only in institutional settings, are required. HHFNOx therefore cannot be applied to home settings, and is not used in other institutional settings without such physical plant resources. The device is, however, safe and well tolerated, with no potential risks beyond those associated with traditional oxygenation strategies (e.g., flammability).

Among patients and health care providers (physicians, nurses, and respiratory therapists), the most common anecdotal benefit of HHFNOx compared with devices allowing equivalent amounts of oxygen delivery is that users are still able to eat and talk unencumbered. Additionally, patients report preference of HHFNOx over mask oxygen devices as the latter can result in a wet and/or cold sensation on the face, and can generally feel confining. To clearly document these benefits, and moreover, measure differences in outcomes including overall quality of life, oxygenation, hospital stay characteristics, code status, and mortality, devices such as HHFNOx would be best studied prospectively. Such an analysis could also assess the relative health care costs associated with HHFNOx approaches compared with those in which HHFNOx were not used. Capital expenses for the HHFNOx device utilized at MSKCC include the heated humidifier (\$900) and an air/oxygen blender, oxygen analyzer, and flow meter (\$925). Consumables per single patient use (tubing, nasal cannula, and adaptor) cost approximately \$30. Comparatively, the capital cost range for continuous positive airway pressure (CPAP) devices, which alternatively deliver low oxygen concentrations at set pressures, is \$2000 to \$4000. Bilevel positive airway pressure (BiPAP) devices able to deliver HHFNOx-level airway pressures are associated with costs exceeding \$10,000. Disposable nasal cannulas, Venturi face masks, and nonrebreather masks each cost \$2 to \$5.

Although HHFNOx is more expensive than older oxygen delivery methods, the prevention of escalated and more invasive oxygenation such as mechanical ventilation in ICUs

could make HHFNOx more cost effective. Moreover, the relatively small number admitted to the ICU after being given HHFNOx on the hospital ward may indicate a role for its use in preventing unnecessary ICU admissions in hypoxic patients who are perhaps more suited for palliation. Recent studies in the acute respiratory failure¹⁹ and postextubation²⁰ settings would support this notion. Given the lack of benefit documented thus far in the literature on palliative oxygen compared with room air administration,⁶⁻⁹ however, the true utility of HHFNOx in specific oncology populations should ideally be studied prospectively before its use is widely accepted. This analysis contributes to the understanding of currently available supportive oxygen therapies in the treatment of patients with cancer.

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