Effect of heated humidified high-flow nasal cannula (HFNC) oxygen therapy in dyspnea patients with advanced cancer, a randomized controlled clinical trial

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Received: 30 September 2021 / Accepted: 11 August 2022 / Published online: 19 August 2022
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Abstract
Purpose Heated humidified high-flow nasal cannula (HFNC) oxygen therapy is one of the most important oxygen therapy methods, which are commonly applied to relieve dyspnea in advanced cancer patients. Our study aims to observe the efficacy and safety of HFNC oxygen therapy on dyspnea patients with advanced cancer and explore the clinical application.

Methods Sixty subjects with advanced cancer requiring oxygen therapy from a grade 3, class A hospital in China were recruited and randomized (1:1) to traditional nasal catheter oxygen therapy or HFNC. Primary outcomes were dyspnea, oral dryness, and sleep condition, which were recorded after 72-h treatment. Secondary outcomes were heart rate (HR), respiration rate (RR), \( \text{SpO}_2 \), \( \text{PaO}_2 \), and \( \text{PaCO}_2 \), which were recorded after 2, 6, 24, and 72 h treatment.

Results Seventy-two hours after treatment, there were significant improvements in all primary outcomes (\( P < 0.001 \)). \( \text{PaO}_2 \) and RR were statistically changed 2 h after HFNC treatment (\( P < 0.001 \)). \( \text{PaCO}_2 \) and HR were statistically changed 24 h after HFNC treatment (\( P < 0.001 \)).

Conclusion HFNC oxygen therapy has good effect, high safety, and is easy to be accepted by dyspnea patients with advanced cancer. It can be used as the first choice of oxygen therapy for these patients and has broad clinical prospects.

Trial registration. This work was retrospectively registered in the Chinese Clinical Trials Registry (ChiCTR2100049582) on August 4, 2021.

Keywords Neoplasms · Dyspnea · Oxygen inhalation therapy · Patient comfort · Randomized controlled trial

Introduction
Cancer ranks as a leading cause of death in the world [1]. There are many clinical complications in patients with advanced cancer, in which dyspnea is one of the most common symptoms [2]. Dyspnea is a debilitating symptom among advanced cancer patients [3], which can cause physical and psychological distress and severely affect patients’ quality of life (QOL) [4–6]. The high prevalence of dyspnea ranges from 21 to 70% of patients [7]. Unlike cancer-related pain, the standardized treatment of dyspnea has not been well promoted and popularized. Thus, in order to effectively alleviate the dyspnea of patients with advanced cancer, palliative care is needed [8], which is mainly to relieve symptoms, relieve pain, and improve the quality of life. Moreover, with the increase in the demand for improved quality of life and the failure of conventional treatment, such as radiotherapy and chemotherapy, some patients prefer palliative treatment [9].

A review reported that the interventions of cancer-related dyspnea include opioids, oxygen, psychotropic drugs, and nebulized furosemide [10]. Oxygen therapy, non-invasive ventilation, and invasive mechanical ventilation are typically the main respiratory support strategies...
[11] to relieve dyspnea. Among them, oxygen therapy is widely used because of its convenient use, simple operation, and low cost. Oxygen therapy can be divided into low-flow and high-flow oxygen therapy. The fraction of inspired oxygen \((F_\text{I}O_2)\) delivered by conventional nasal catheter oxygen inhalation is unstable and cannot be accurately regulated [12]. Moreover, some patients who use traditional oxygen therapy cannot effectively improve dyspnea, and still face pain and discomfort caused by dyspnea. Recently, high-flow nasal cannula (HFNC), also known as nasal high-flow (NHF) oxygen therapy, is a new type of respiratory support technology which can provide accurate oxygen concentration (21–100%) through air/oxygen blender [13], which is a promising novel oxygen delivery device, whose specific mechanisms offer some beneficial effects over conventional low-flow oxygen inhalation systems [14]. After heating and humidification, the highest gas temperature can reach 37 °C and the humidity can reach 100%. The gas flow rate provided is higher than the patient’s inspiratory peak flow [15, 16]. HFNC can provide positive end-expiratory pressure (PEEP) that may help to improve oxygenation and counteract the effects of intrinsic PEEP on work of breathing, which has been confirmed that can be used in the patients with acute hypoxic respiratory failure [17, 18], patients after surgery [19, 20], patients with respiratory failure without endotracheal intubation [21], immunosuppressive patients [14], and patients with obstructive sleep apnea [22]. However, few studies have assessed the effect of HFNC on advanced cancer patients with dyspnea [8].

Thus, the aim of this study was to explore the physiologic effects of HFNC on advanced cancer patients with dyspnea, which can only accept palliative treatment. The changes of \(S_\text{a}O_2, P_\text{a}O_2, P_\text{a}CO_2\), respiratory rate (RR), and heart rate (HR) were observed before and after 2, 6, 24, and 72 h treatment. The primary outcomes including dyspnea, dryness of mouth, and sleep quality were observed before and after 72-h treatment.

Methods

Study design

A randomized, controlled trial was performed in the department of oncology and in the First Hospital of Zibo City in China. The trial was approved by the First Hospital of Zibo City in China Ethics Committee (No.2019016) and registered in the Chinese Clinical Trials Registry (ChiCTR2100049582). All patients signed informed consent form prospectively.

Patients

Sixty patients with advanced cancer who can only receive palliative treatment from March 2019 to March 2020 in the oncology regular ward of the First Hospital of Zibo City in China were consecutively enrolled as the study participants by the research personnel. Inclusion criteria: (I) age between 18 and 80 years; (II) patients with advanced solid cancer: lung cancer patients or patients with lung metastases from other solid cancers; (III) meeting grade 4 of the mMRC; (IV) the curative treatment was not effective and palliative care was accepted; (V) respiratory rate > 30 times/min; (VI) ratio of arterial oxygen tension to inspired oxygen fraction \((P_\text{a}O_2/F_\text{I}O_2) < 250 \text{ mmH}_2\text{O}\); and (VII) signed informed consent form. Exclusion criteria: (I) intolerant, irritable, and uncooperative; (II) invasive assisted ventilation was needed for exacerbation of the disease; and (III) duration of hospital stay < 3 days. All enrolled subjects received training on oxygen therapy in order to gain the trust and cooperation of subjects and their caregivers. The trial was terminated when the patient experienced one of the following conditions: (I) did not tolerate oxygen therapy; (II) abandoned treatment for various reasons; and (III) died. All the patients who met the criteria were randomly divided into the intervention group (HFNC oxygen therapy, 30) and the control group (conventional nasal catheter oxygen inhalation therapy group, 30). Randomization was conducted using random number generated by SPSS version 22.0 random number generator.

Study outcomes

The primary outcomes were dyspnea, oral dryness, and sleep quality measured before and after 72 h. The secondary outcomes were HR, RR, \(S_\text{a}O_2, P_\text{a}O_2, P_\text{a}CO_2\). Baseline characteristics including age, gender, heart rate (beats per minute), respiratory rate (breaths per minute), \(S_\text{a}O_2, P_\text{a}O_2, P_\text{a}CO_2\), dryness of mouth score, VAS score, SRSS score, and drug types and doses were collected. Subjects’ comfort, including (I) dyspnea, was assessed by visual analog scale (VAS) dyspnea score. VAS [23] is a horizontal line, 100 mm in length, and anchored by word descriptors at each end, which uses “no shortness of breath at all” and “maximum shortness of breath.” The patients were asked to mark on the line the point that they feel represents their current state. The distance (mm) between the beginning of the horizontal line and this mark represents the degree of dyspnea perception; (II) the degree of oral dryness was evaluated from 0 to 10 points. The higher the value, the drier the oral cavity is; (III) the sleep quality was assessed by the sleep state self-rating scale.
(SRSS), which was designed to assess the sleep quality of hospitalized subjects. There are 10 items in total. Each item has a 5-point scale (1–5). The higher the total score, the worse the sleep. This scale has a minimum score of 10 (basically no sleep problems) and a maximum score of 50 (most severe). The changes of RR, HR, and blood oxygen saturation ($S_O2$) at each time point were monitored by cardiogram monitors. $P_{O2}$ and $P_{CO2}$ were recorded by blood gas analyzer.

**Study procedures**

All subjects received palliative treatments. Palliative treatments include (I) anti-infective treatment: antibiotics, such as cephalosporins; (II) anti-asthmatic drug treatment: aminophylline or dyphylline; (III) antitussive and expectorant treatment; (IV) correcting water electrolyte and acid–base imbalance; (V) nutritional support treatment; and (VI) pain control: morphine. Treating physician gave both groups equal medication according to the patient’s needs and the principles of treatment. The dosage of all medications was determined by the treating physician for every patient as usual. The intervention group was additionally treated with HFNC oxygen therapy, using the nasal high-flow heating and humidification oxygen therapy instrument (model: HUMIDIUM-BM, HiFent, Respircare). The appropriate size of nasal cannula was selected for every patient, and the temperature of humidification gas was set at 31–37 °C. The inhaled oxygen concentration ($F_{O2}$) was adjusted according to the patient’s $S_O2$, ranging from 21 to 100%. According to patient’s degree of dyspnea and tolerance, the flow rate was set between 30 and 50 L/min. In the control group, oxygen was inhaled by conventional nasal catheter for more than 24 h. The oxygen flow was set at 2–8 L/min according to the specific needs of patients. We set the oxygen flow from 2 L/min, and if it did not improve patient’s $SpO2$, we continued to increase the oxygen flow by 1 L/min at a time until a maximum of 8 L/min. If a greater benefit was observed for patients in the HFNC group, we would continue to administer HFNC to patients until they were discharged.

**Statistical analysis**

SPSS version 22.0 (SPSS Inc., Chicago, IL, USA) was used for data processing and analysis. The mean ± standard deviation was used for normally distributed data and the median (interquartile range) [M (P25, P75)] was used when the measurement data were non-normally distributed. Counting data was expressed by a numerical value, and the chi-square test was used for comparison between different groups. The independent sample $t$-test was used to compare the normal measurements between the two groups and the Mann–Whitney $U$ test was used to compare the non-normal measurements. Matched samples $t$-test was performed on data measured at multiple time points. $P < 0.05$ was statistically significant.

**Results**

**Patients**

A total of 60 subjects were eligible for inclusion and underwent randomization in the study from March 2019 to March 2020, with 30 in the control group (conventional nasal catheter oxygen therapy) and 30 in the intervention group (HFNC oxygen therapy). The participant flow diagram (Fig. 1) shows that all the subjects completed the whole treatment. Post hoc manifests 1-β can reach 0.86 (effect size $= 0$, $\alpha = 0.05$).

**Baseline characteristics**

Table 1 shows the baseline characteristics of all subjects. A total of 60 subjects were enrolled in this study. Before treatment, there were no significant differences between the two groups ($P > 0.05$). And in this trial, only five patients used morphine to control pain, two in the intervention group and three in the control group. All these five patients had
morphine dosages of 10–20 mg per day. Morphine use was balanced and comparable between the two groups. Meanwhile, in this trial, major subjects were lung cancer patients and a small percentage were patients with lung metastases from esophageal, gastric, or breast cancers. All patients had lung abnormalities.

**Primary outcome**

The dyspnea in the intervention group was improved after 72-h treatment ($P < 0.001$), while the dyspnea in the control group was not ($P = 0.415$). The degree of dryness of mouth after 72-h treatment was mildly increased without statistical significance in the intervention group ($P = 0.056$), while significantly increased in the control group ($P < 0.001$). The sleep quality in the intervention group was better than before ($P < 0.001$), while there is no improvement in the control group. The detailed data are shown in Table 2.

$P < 0.05$ indicates that there is a statistical difference in this index between groups and within each group.

**Secondary outcomes**

**The blood gas analysis ($P_aO_2$, $P_aCO_2$) and $S_aO_2$ at different time points**

$P_aO_2$ increased to varying degrees over time within the two groups. The difference of $P_aO_2$ between the two groups was statistically significant after 2, 6, 24, and 72 h ($P < 0.001$). $P_aCO_2$ in the intervention group was lower than that before treatment after 24- and 72-h treatment ($P < 0.001$) and was lower than that in the control group after 24- and 72-h treatment ($P < 0.001$). $S_aO_2$ began to increase after 2-h treatment in the intervention group and after 6-h treatment in the control group ($P < 0.001$). $S_aO_2$ in the intervention group increased statistically at each time point compared with the previous time point (Table 3).

$^a$ Indicates a statistically significant difference compared with the control group; $^b$ indicates that the comparison within the group was statistically significant compared with that before treatment ($P < 0.001$); $^b, c, d, e$ indicate that the comparison within the group was statistically significant compared with 2, 6, 24, and 72 after treatment ($P < 0.001$), respectively. $P < 0.05$ indicates that the comparison at different time points within each group was statistically different.

**Physiological indicators (RR, HR) at different time points**

RR and HR began to decrease after 2-h treatment in the intervention group, while after 6-h treatment in the control group ($P < 0.001$). After 6, 24, and 72 h, there were statistically significant differences in RR between the two groups ($P < 0.001$). After 24 and 72 h, there were statistically significant differences in HR between the two groups ($P < 0.001$) (Table 4).

$^a$ Indicates a statistically significant difference compared with the control group; $^b$ indicates that the comparison within the group was statistically significant compared with that before treatment ($P < 0.001$); $^b, c, d, e$ indicate that the comparison within the group was statistically significant compared with 2, 6, 24, and 72 after treatment ($P < 0.001$), respectively. $P < 0.05$ indicates that the comparison at different time points in the group was statistically different.

**Discussion**

To the best of our knowledge, this is the first randomized controlled trial using HFNC in advanced cancer patients. In this study, we found that HFNC can enhance patients’ comfort, which is reflected in the decrease of VAS score, dryness of mouth score, and SRSS score. The beneficial effects of HFNC in several objective parameters, such as RR, HR, $S_aO_2$, $P_aO_2$, and $P_aCO_2$, were also showed.

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Table 1  Baseline patient characteristics before treatment

| Baseline patient characteristics | Control group | Intervention group | $\chi^2$ | $P$ |
|--------------------------------|---------------|--------------------|---------|-----|
| Age ($\pm$)                     | 58.5 ± 10.84  | 59.2 ± 8.93        | -0.273  | 0.786 |
| Gender                         |               |                    | 0.067   | 0.795 |
| Male                           | 16 (53.33)    | 17 (56.67)         |         |      |
| Female                         | 14 (46.67)    | 13 (43.33)         |         |      |
| Heart rate (beats per minute)  | 107.07 ± 10.28| 107.8 ± 9.14       | -0.292  | 0.771 |
| Respiratory rate (breaths per minute) | 30.03 ± 2.94 | 30.17 ± 3.31       | -0.165  | 0.870 |
| $S_aO_2$                        | 89.30 ± 2.94  | 88.87 ± 2.97       | 0.568   | 0.572 |
| $P_aO_2$                        | 60.26 ± 6.5   | 60.76 ± 5.5        | -0.322  | 0.749 |
| $P_aCO_2$                       | 48.28 ± 5.13  | 47.08 ± 5.32       | 0.893   | 0.375 |
| Dryness of mouth score          | 6.50 ± 1.50   | 6.07 ± 1.55        | 1.099   | 0.276 |
| VAS score                       | 8.57 ± 1.10   | 8.23 ± 1.36        | 1.044   | 0.301 |
| SRSS score                      | 36.97 ± 2.04  | 36.27 ± 2.00       | 1.342   | 0.185 |

$^*\text{Indicates a statistically significant difference compared with the control group}$; $^a$ indicates that the comparison within the group was statistically significant compared with that before treatment ($P < 0.001$); $^b, c, d, e$ indicate that the comparison within the group was statistically significant compared with 2, 6, 24, and 72 after treatment ($P < 0.001$), respectively. $P < 0.05$ indicates that the comparison at different time points within each group was statistically different.

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There are several explanations for the improvement of dyspnea. First, HFNC can increase expiratory resistance of the nose because of the different sizes of the cannula and the jet-flow effect against exhaled gas [24]. The expiratory pressure will further prolong the duration of exhalation, so decreasing respiratory rate. The slower and deeper breathing can decrease the work of breathing [25–27] and increase tidal volume [24], which can decrease the proportion of dead space volume and then improve breathing efficiency [24]. Thus, patients can breathe more comfortably with less dyspnea. Compared with HFNC, the conventional nasal catheter oxygen inhalation provides oxygen at flow rates <15 L/min [28–30]. It lacks the ability to wash out the nasopharyngeal dead space and decrease work of breathing. Secondly, HFNC can decrease anatomical dead space in the upper airway, which is attributed to the high-flow effect [14, 24]. Nasopharyngeal dead space washout can reduce rebreathing of expired air and CO₂ and create a fresh oxygen reservoir within the upper airways [31, 32], thus improving breathing efficiency and reducing tachypnea [24, 33–35]. Thirdly, the high flow of delivered gas which exceed the patient’s demand can help overcome resistance during inspiratory period [36]. Meanwhile, the inspiratory airflow dynamics is improved with HFNC, as evidenced by the fact that the pressure remained above atmosphere for most of the inspiratory phase [24]. This increase would help subjects overcome resistance and raise the driving pressure for inspiration, thus decrease work of breathing and dyspnea. Fourthly, HFNC therapy delivers a low level of positive airway pressure in expiratory phase [37–39] which contributes to lung compliance increment, alveoli recruitment, and end-expiratory lung volume increment [40]. Thus, the oxygenation was improved and the dyspnea was lessened. Lack of humidification and secretions in the airways, such as sputum, become thicker and harder to expel, making it more likely that subjects with advanced cancer will experience dyspnea [41]. As is shown before, HFNC plays a vital role in heating inspired gas close to body temperature level (37 °C) and humidifying the respiratory system to saturation, especially in high flow rates, where conventional nasal catheter oxygen inhalation fail [36]. The mucociliary function and secretion elimination is facilitated [42]. Furthermore, the required metabolic cost of warming and humidifying of inspired gas is reduced, especially in subjects whose RR are increased with advanced cancer [33]. Thus, another reasonable explanation is the fully and effectively humidification of HFNC, which can help subjects clear airway more easily and relieve dyspnea. Owing to mechanism mentioned above, the effect of HFNC on dyspnea was better than that of conventional nasal catheter oxygen inhalation among patients with advanced cancer.

Dryness of the mouth can be caused by breathing dry or insufficiently humidified oxygen [43], which may frequently result in discomfort. AARC Clinical Practice Guideline
suggested that the humidification provided by the nasal mucosa becomes insufficient when administered at flow rates exceeding 4 L/min [11]. The consist of an active heated humidifier of HFNC system allows patients to be administered fully humidified high-flow oxygen [13], thus the HFNC system reduced discomfort related to symptoms of mouth dryness in patients with advanced cancer. Several investigators have reported that improving the humidification of the inspired gas ameliorates patient comfort, which is congruent with our study [43].

Owing to the less dyspnea and dryness of the mouth by using HFNC, sleep quality was significantly improved in the experimental group after intranasal high-flow oxygen inhalation, while there was no significant change in the control group. It should be mentioned that HFNC may generate some noise, which is unavoidable. However, our previous study [44] used the sound level meter (8922, AZ® Instrument Corp., Taiwan China) to measure noise and found that when the HFNC flow rate was 60 L/min, the maximum noise was 65.9 dB, which could be tolerated. And in this trial, the maximum flow rate was set to 50 L/min and we considered it can be tolerated by patients.

HR and RR were chosen to reflect the degree of improvement of vital signs before and after treatment. As is mentioned above, the high flow of HFNC can flush out the dead space in upper airway, improve gas exchange and lung volume, enhance the breath efficiency, and increase tidal volume, thus HNFC exert various effects in the respiratory system, especially lower respiratory rate and effort [18].

We speculate that owing to the comfort of patients which is attributed to lower work of breath and less dyspnea, HFNC can reduce anxiety in patients. Thus, with less anxiety, the patients are calmer, which helps the heart rate decreased.

Based on the observation about persistent improvement of $S_{pO_2}$ measured by pulse oximetry, we can conclude that HFNC is associated with greater overall oxygenation [17]. First, the conventional nasal catheter oxygen inhalation provides oxygen at flow rates that are lower than patients’ inspiratory demands. As a result, the room air is entrained and administered oxygen is diluted [36]. The final concentration of oxygen truly delivered to the patient is higher than the set $F_{O_2}$ initially ($F_{O_2SET}$). On the contrary, the HFNC which has the ability of generating high flow rates with HFNC can create of a great oxygen reservoir in nasopharyngeal area and increase tidal volume [31, 32]. Thus, the oxygenation was greater in the intervention group. Thirdly, there is an analysis demonstrating that higher pressures are obtained during expiration than inspiration, which are flow dependent [40]. It delivers a low level of positive airway pressure in the expiratory phase [37] which transmits to the alveoli, contributing to lung compliance increment, alveoli recruitment, and end-expiratory lung volume increment [40]. Also, we found that with the prolongation of time, the improvement of blood oxygen saturation was greater. It is possible that the

### Table 3  $S_{pO_2}$, $P_{O_2}$, and $P_{CO_2}$ at different time points

| Index   | Before       | After 2 h | After 6 h | After 24 h | After 72 h | $F$   | $P$  |
|---------|--------------|-----------|-----------|------------|------------|-------|------|
| Control group |              |           |           |            |            |       |      |
| $S_{pO_2}$ | 89.30 ± 2.94cde | 89.90 ± 2.82cde | 90.97 ± 2.19bde | 91.30 ± 2.22bde | 92.20 ± 2.38abcd | 26.058 | < 0.001 |
| $P_{O_2}$  | 60.26 ± 6.50fde | 61.13 ± 5.52bde | 60.67 ± 5.03bde | 77.46 ± 5.49bde | 78.85 ± 7.08abcd | 253.200 | < 0.001 |
| $P_{CO_2}$ | 48.28 ± 5.13   | 48.39 ± 5.47 | 48.09 ± 5.19 | 48.02 ± 3.76 | 47.91 ± 3.62 | 0.211 | 0.797 |
| Intervention group |             |           |           |            |            |       |      |
| $S_{pO_2}$ | 88.87 ± 2.97pode | 92.23 ± 2.32abde | 93.93 ± 1.80abde | 94.90 ± 2.26abde | 95.87 ± 1.80abcd* | 112.104 | < 0.001 |
| $P_{O_2}$  | 60.76 ± 5.4bode | 71.01 ± 6.42de* | 81.47 ± 4.9bde* | 83.03 ± 6.41bde* | 84.62 ± 6.33abcd* | 634.688 | < 0.001 |
| $P_{CO_2}$ | 47.08 ± 5.32fde | 46.89 ± 5.52de | 46.52 ± 5.23de | 43.86 ± 4.64abde* | 43.04 ± 4.53abcd* | 41.709 | < 0.001 |

### Table 4  RR and HR at different time points

| Index   | Before           | After 2 h       | After 6 h       | After 24 h      | After 72 h     | $F$   | $P$  |
|---------|------------------|-----------------|-----------------|----------------|----------------|-------|------|
| Control group |               |                 |                 |                |                |       |      |
| HR      | 107.07 ± 10.28cde | 107.77 ± 9.75cde | 102.27 ± 9.58bde | 101.50 ± 9.97bde | 99.17 ± 9.10abcd | 143.943 | < 0.001 |
| RR      | 30.03 ± 2.94cde  | 29.93 ± 2.46cde  | 29.37 ± 2.65abde | 28.40 ± 2.76abc | 27.80 ± 3.25abcd | 25.134 | < 0.001 |
| Intervention group |           |                 |                 |                |                |       |      |
| HR      | 107.8 ± 9.14pode | 104.8 ± 5.96cde  | 101.7 ± 8.25bde  | 96.87 ± 6.44abce* | 93.53 ± 6.96abcd* | 161.908 | < 0.001 |
| RR      | 30.17 ± 3.31pode | 28.9 ± 1.73cde  | 27.6 ± 3.48abce* | 26.57 ± 3.86abce* | 25.33 ± 3.26abcde* | 48.133 | < 0.001 |
HFNC can be a useful respiratory support strategy in sup-
porting advanced cancer patients to feel more comfortable.

This study has some important limitations. First, the sample size was small and the duration of this trial was short. The longest observation time of this study was only 72 h. Because we considered that comfort is of paramount importance for patients with advanced cancer requiring palliative care, we conducted this 72-h trial with the main outcome indicators being patient comfort indicators such as dyspnea. However, the short duration of this trial did not allow us to know if there was longer survival in patients with HFNC.

The long-term effect of HFNC, such as its impact on survival, needs to be further studied. Second, there are many subjective outcome measures, and more objective indicators are needed to verify the effect of HFNC. Third, we did not include patients with no lung abnormalities, and we only observed the effects of HFNC in advanced cancer patients with lung abnormalities. Therefore, our findings may have some implications for advanced cancer patients with lung abnormalities, but may not suitable for generalization to advanced cancer patients without lung abnormalities.

This study demonstrated that HFNC is a kind of promising oxygen therapy in advanced cancer patients with dyspnea undergoing palliative treatment. HFNC can significantly improve the symptoms of dyspnea, dryness of mouth, and sleep quality among patients with advanced cancer. Moreover, HFNC can effectively decrease RR, HR, and P_{a}CO_{2}, while increase S_{O}2 and P_{a}O_{2}. Consequently, HFNC can be a useful respiratory support strategy in supporting advanced cancer patients to feel more comfortable.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00520-022-07330-w.

Author contribution Conceptualization: ZX, PL; methodology: ZX, PL; formal analysis and investigation: ZX, PL, CZ; writing — original draft preparation: ZX, PL, CZ, DM; writing — review and editing: ZX, PL, CZ, DM; funding acquisition: DM; supervision: DM.

Funding This work was supported by Qilu Hospital of Shandong University [2018-6].

Availability of data and material All data can be available on https://www.chictr.org.cn/index.aspx.

Code availability SPSS version 22.0 (SPSS Inc., Chicago, IL, USA).

Declarations

Ethics approval All procedures performed in studies involving human participants were in accordance with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The trial was approved by the First Hospital of Zibo City in China Ethics Committee (No.2019016).

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent for publication Consent for publication was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

Additional declarations for articles in Life Science Journals that report the results of studies involving humans and/or animals Not applicable.

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