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Review

A Novel Approach to High-flow Nasal Oxygen Delivery: Physiological and Clinical Perspectives on Asymmetrical Cannulas

Begüm Ergan[1], Bişar Ergün[2]

[1]Department of Pulmonary and Critical Care, Dokuz Eylül University Faculty of Medicine, İzmir, Türkiye
[2]Clinic of Internal Medicine and Critical Care, Dr. İsmail Fehmi Cumalıoğlu City Hospital, Tekirdağ, Türkiye

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Abstract

High-flow nasal cannula (HFNC) therapy has become an essential therapeutic modality across a broad spectrum of indications, and it is currently regarded as the optimal initial therapeutic option for patients presenting with acute hypoxemic respiratory failure. A novel HFNC interface with an asymmetrical cannula has recently been introduced to optimize the physiological benefits of HFNC. It features prongs, one with a smaller diameter and another with a larger diameter, to enhance positive end-expiratory pressure and carbon dioxide washout. This is achieved by modulating the prong-to-nare area ratio to maintain a balance between airway pressure and dead space clearance. Recent studies have indicated that the use of an asymmetrical design may result in enhanced upper airway pressure and dead space washout. Asymmetrical cannulas may enhance patient comfort, reduce work of breathing, and lower minute ventilation. However, they do not significantly differ from standard cannulas in terms of gas exchange, oxygenation, diaphragm activity, lung compliance, dorsal fraction of ventilation, or lung impedance. Further research is needed to determine whether asymmetrical cannulas offer clinical advantages in specific patient populations, to identify optimal sizing parameters, and to assess their long-term safety and efficacy in diverse clinical settings.

KEYWORDS: Acute respiratory failure, asymmetrical cannula, dead space washout, high-flow nasal cannula, positive end-expiratory pressure

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INTRODUCTION

The high-flow nasal cannula (HFNC) delivers a mixture of warmed, humidified air and oxygen at a specified concentration and temperature through a nasal interface at high-flow rates.[1] An air-oxygen mixer allows for precise adjustment of the fraction of inspired oxygen (FiO_2) from 21 to 100%, regardless of the flow rate.[1] HFNC is considered to be the optimal first-line option for patients with acute hypoxemic respiratory failure.[2] Moreover, there is a wide range of potential indications for HFNC, and they vary depending on the clinical situation. Such indications include, postoperative patients, non-surgical patients with a low risk of extubation failure, patients with acute pulmonary edema, and patients with chronic obstructive pulmonary disease (COPD).[2-5]

The physiological effects of HFNC treatment have been demonstrated in numerous studies. HFNC improves mucus hydration and mucociliary function through effective inspired gas humidification, aiding expectoration, mucus clearance, and preventing airway dryness and injury.[6] The main factors influencing alveolar oxygen delivery include the FiO_2, the flow rate of supplemental oxygen, and inspiratory demand.[7] In cases of respiratory distress or acute hypoxemic respiratory failure, patients may require high-flow rates that exceed those of conventional oxygen delivery systems.[8] This can result in the inhalation of more ambient air, which contains 21% oxygen, further reducing the overall oxygen concentration of the inspired air.[1,8] The HFNC system delivers oxygen through the nasal prongs at a rate that generally exceeds the patient's flow rate. This ensures that very little room air is entrained, resulting in a more

Corresponding author: Bişar Ergün MD, e-mail: dr.bisarergun@hotmail.com

reliable delivered oxygen concentration.[9] Increasing the flow rate improves the respiratory pattern by increasing the tidal volume and decreasing the respiratory rate, thereby reducing the inspiratory effort.[10-12] The nasopharyngeal airway pressure increases in correlation with the flow rates produced by HFNC, reaching a peak at the end of expiration.[13,14] This positive end-expiratory pressure (PEEP) effect may increase end-expiratory lung volumes compared to low-flow devices.[11] The PEEP effect of HFNC is reduced during open mouth breathing.[15] Other factors affecting PEEP include body type, resistance to flow, patient position, and lung disease distribution.[1,16] HFNC therapy can reduce dead space rebreathing by facilitating the rapid clearance of carbon dioxide from the nasal cavity.[17] The nasopharyngeal dead space functions as a reservoir for fresh gas under HFNC treatment, thereby ensuring that during the initial phase of inspiration, the inhaled oxygen volume is maximized while carbon dioxide is efficiently washed out. This results in more efficient ventilation and gas exchange.[18] Moreover, decreasing dead space ventilation could lead to a reduction in the work of breathing.[12]

The impact and intensity of these physiological effects may vary depending on the set flow rate and the patient's specific characteristics.[12] In combination, the physiological effects result in a reduction in excessive respiratory drive, minute ventilation, and inspiratory effort.[12] As a result, the most obvious effects are increased patient comfort and oxygenation.[10-12] Additionally, HFNC may lower the risk of self-inflicted lung injury by decreasing the driving transpulmonary pressure.[12]

It is expected that these physiological effects and clinical benefits will enhance clinically meaningful outcomes, such as length of hospital stay, intubation rates, and, most importantly, mortality. Nevertheless, studies have not demonstrated a decline in either the rate of intubation or mortality.[19] In addition, the failure rate of HFNC support remains considerable.[20] Failure of the HFNC may result in admission to the intensive care unit (ICU).[21] The major concern is that the use of HFNC may delay necessary intubation and worsen outcomes in patients with acute respiratory failure.[22] Delayed intubation in patients who have failed HFNC is associated with an increased risk of adverse outcomes and mortality.[22,23]

Several strategies have been proposed to enhance the effectiveness of HFNC therapy in preventing failure and ICU admission.[24-27] To achieve this goal, studies have focused on a number of variables, including the HFNC interface, flow selection, prone positioning, and respiratory rate.[24-27] Nevertheless, the implementation of these strategies did not yield the anticipated substantial outcomes.[25,26]

A novel HFNC interface with an asymmetrical cannula design [Optiflow® Duet system (Fisher & Paykel, Healthcare, Auckland, New Zealand)] has been approved for clinical use to improve the efficacy of HFNC therapy. The objective of this narrative review is to provide an updated synthesis of the physiological mechanisms and clinical effects of HFNC therapy, with a specific emphasis on prong geometry and the potential advantages of the recently introduced asymmetrical cannula design.

The Role of Prong Size and Cannula Type on PEEP Effect and Wash-out Effect

The primary mechanisms of HFNC are believed to be the PEEP effects and washout effects.[28] Studies investigating cannula prongs have primarily focused their effects on these two main effects.[27-30]

The Relationship Between Prong Size and Airway Pressure

The nasal cannulas are constructed with a relaxed fit to enable the removal of expired gases from the anatomical dead space through the annular space between a person's nostrils and the outer prong walls of the cannula.[17,27,30] Airway pressure results from flow and resistance.[17,27] Variations in cannula prong sizes can lead to different levels of resistance at varying flow rates, resulting in varying airway pressures.[17,27] It is hypothesized that by constricting the oxygen flow to a smaller area, the velocity increases, thereby enabling the flow to enter with greater kinetic energy, which can subsequently be transformed into pressure further downstream.[30,31] On the other hand, other studies suggested that an increase in the airway pressure can be identified with the use of large cannulas, which help to reduce leakage around the prongs.[31,32] In assessing the impact of cannula size on the efficacy of HFNC, it is essential to consider not only prong size, but also the prong-to-nare area ratio or the relationship between prong and nare.[27,29,30] Zhao et al.[31] investigated the factors influencing nasal airway pressure during HFNC in a cohort of 35 healthy adults, comprising 16 males and 19 females. Upon reaching a flow rate of 30 L/min, the end-expiratory pressure generated by the larger cannulas began to exceed that of the smaller cannulas, with the discrepancy becoming increasingly pronounced as the flow rate increased.[31] The effect of the nasal cannula on end-inspiratory pressure was not as significant as on end-expiratory pressure.[31] They suggested that increasing the cannula size may reduce the HFNC jet flow and result in increased end-expiratory pressure due to a greater decrease in gas leakage, although they did not measure the occlusion ratio. They also found that women had higher end-expiratory pressure than men, possibly due to their smaller body size, resulting in lower nasal volume and a reduced air leakage at the same flow rate and cannula size.[31]

The Relationship Between Prong Size and Wash-out Effect

The influence of nasal prong size on dead-space clearance remains a topic of incomplete understanding. The results of animal experimental studies have indicated, that the clearance of extra thoracic dead space is dependent upon the presence of a less occlusive prong.[30,33] In a randomized controlled trial involving stable hypercapnic COPD patients, researchers investigated the impact of different levels of air leakage on PCO_2. They investigated the impact of different flow rates and levels of leakage. The leakage level was achieved by inserting a cannula through one or both nasal orifices. The results showed a significant correlation between increased leakage and decreased capillary PCO_2 levels.[34] In their investigation of the three-dimensional geometry of the human airway, Miller et al.[35] reached similar findings as previous studies. However, they found that the gas clearance of the extra thoracic dead space is more closely linked to the kinetic force of the airflow, generated by the higher velocity from the narrower prong nozzle, rather than to the reduced blockage of the nostrils.

Mechanism of Action of the Asymmetric Cannula and an Overview of Relevant Studies

Mechanism of Action of the Asymmetric Cannula Design

An optimal nasal cannula is expected to impact both airway pressure and dead space clearance. In order to achieve the maximum possible increase in upper airway pressure, the velocity of the flow can be increased both in the cannula and in the nostrils by the use of narrow-inner-diameter, thick-walled cannula prongs.[30] Although the use of this cannula model may result in an elevation of tracheal pressure, it could lead to prolonged clearance times due to augmented nasal occlusion.[30] Additionally, in patients with a high prong/nare area ratio, closing the mouth may increase airway pressure depending on the flow rate, which may limit the ability to breathe through the nose.[28] Caution is warranted when selecting the cannula size for certain vulnerable patients receiving HFNC, as pulmonary barotrauma — caused by increased transalveolar pressure and subsequent alveolar rupture — may lead to serious complications such as pneumothorax and subcutaneous emphysema.[36,37] A 14-year-old girl who underwent allogeneic hematopoietic cell transplantation for high-risk acute myeloid leukemia developed severe chronic graft-versus-host disease and was treated for presumed bronchiolitis obliterans syndrome. Despite cautiously administered nasal high-flow therapy (14-20 L/min) for refractory dyspnea, she experienced progressive respiratory failure; autopsy revealed pulmonary barotrauma with alveolar overdistension and septal destruction, without histopathological evidence of bronchiolitis obliterans.[36] Another case report described a 2-month-old infant who developed massive right lung overinflation with mediastinal shift and left lung atelectasis while receiving HFNC therapy (2 L/kg/min, FiO_2 0.6), which occurred despite appropriate device settings, highlighting a potential association between HFNC and barotrauma in infants.[37]

Design of the Asymmetrical Nasal Cannula

A novel asymmetrical nasal cannula interface has recently been approved for clinical use (Figure 1).[28] The asymmetrical cannula is designed with one prong featuring a smaller and the other a larger one.[28] This results in an increase in the total cross-sectional area of both prongs by approximately 30% to 40%.[28] The higher prong-to-nare area ratio resulting from the larger cannula may enhance the pressure experienced by higher occlusion. In comparison, the ratio of prongs to nares is reduced in the nasal cavity compared to the other side. Consequently, leakage around the cannula is maintained, and dead-space washout is enhanced (Table 1).[28]

Bench Studies

A bench study compared an asymmetrical large-size nasal cannula with a standard medium-size cannula. The asymmetrical large-sized nasal cannula demonstrated a higher end-expiratory nasopharyngeal pressure than the standard medium-sized cannula. Furthermore, the asymmetrical large-size nasal cannula exhibited more efficient CO_2 clearance in the upper airways than the standard medium-size cannula by reducing the volume of CO_2 rebreathing from the upper airways.[38]

In another bench study, Tatkov et al.[28] compared the standard nasal cannula with an asymmetrical nasal cannula on an upper-airway model. The study utilized three cannula interfaces: a large standard for the augmentation of nasal occlusion, a control standard, and an asymmetrical cannula. The occlusion areas of the large standard and asymmetrical cannulas were similar. The larger symmetrical cannula did not enhance dead space clearance. At higher respiratory rates, the device reduced clearance, compared to the symmetrical control cannula. At a respiratory rate of 15/min and a flow of 60 L/min, dead space clearance was similar between large standard nasal cannula and asymmetrical nasal cannula. However, at a respiratory rate of 35/min, the large standard nasal cannula clearance decreased, while the asymmetrical nasal cannula clearance increased significantly. The study highlighted that the asymmetrical interface led to notable improvements in performance when the breathing pattern exhibited reduced clearance time, due to increased frequency or expiratory flow limitation.

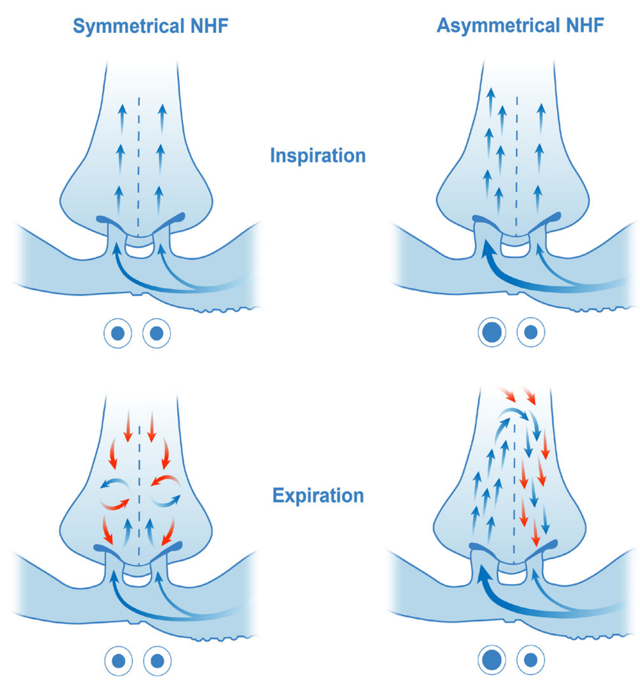
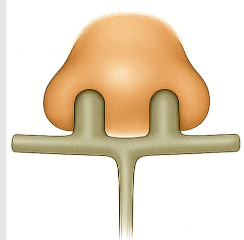
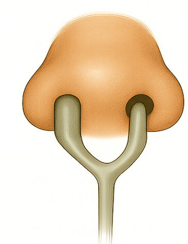


Figure 1. Flow dynamics in symmetrical and asymmetrical nasal cannula interfaces. Adapted from Tatkov et al.[28] (2023)

Schematic representation of the flow direction in cannulae and the upper airways during inspiration (top) and expiration (bottom) in a symmetrical interface (SI) (left) and an asymmetrical interface (AI) (right). Blue arrows indicate nasal high flow (NHF), which is equally split between the prongs in the SI. In the AI, NHF is biased toward the larger prong due to its lower resistance and the streamline of gas velocity within the cannula. Expired gas flow is indicated by red arrows. During expiration, the SI leads to equal mixing and purging via both nares. In the AI, the nare occluded by the smaller prong creates a lower resistance path for the expired gas to be cleared from the nasal cavity. The biased flow from the larger prong is also directed to the contralateral nasal cavity via the choanae, forming the reverse flow that peaks at the end of expiration.

Table 1. Effects of cannula type and nostril fit on PEEP and dead space washout

	 Small prong	 Large prong	 Asymmetrical cannula
PEEP effect	Since the oxygen flows through a narrower prong, its velocity and kinetic energy increase, which may then be converted into pressure downstream.[30,31]	Increasing the cannula size may reduce the HFNC jet flow but result in increased end-expiratory pressure due to a greater decrease in gas leakage.[31] Closing the mouth may increase airway pressure, depending on the flow rate, and limit the ability to breathe through the nose.[28]	A higher prong-to-nare area ratio from a larger cannula may enhance pressure generation due to increased occlusion.[28]
Wash-out effect	The clearance of extrathoracic dead space may depend on the use of less occlusive prongs, which facilitate washout through increased leakage.[34] Gas clearance of the extrathoracic dead space may be more closely linked to the kinetic force of the airflow — generated by the higher velocity from the narrower prong nozzle — rather than to the reduced blockage of the nostrils.[35]	When occlusive prongs are used, gas washout may be less effective due to minimal leakage.[34]	By contrast, a lower prong-to-nare ratio in the opposite nasal cavity preserves leakage and facilitates dead space clearance.[28]

PEEP: positive end-expiratory pressure, HFNC: high-flow nasal cannula

Clinical Studies

In a study conducted by Slobody et al.,[39] ten spontaneously breathing patients with acute respiratory failure, presenting within the prior seven days and exhibiting a PaO_2/FiO_2 ratio of less than 300 mmHg, were assessed using a conventional HFNC interface and an asymmetrical cannula interface. The objective was to examine the influence of the asymmetrical cannula on minute ventilation, work of breathing, and the underlying physiological mechanisms using esophageal manometry and electrical impedance tomography. The implementation of an asymmetrical interface resulted in a reduction in minute ventilation and work of breathing at both flow rates, 40 and 60 L/min. However, using the asymmetrical cannula did not affect oxygenation levels, regional or global dynamic lung compliance, the dorsal fraction of ventilation, or end-expiratory lung impedance.

Boscolo et al.[40] conducted a pilot physiological crossover randomized controlled study involving 20 adult patients who had received invasive mechanical ventilation for at least 24 hours and experienced acute hypoxemic respiratory failure after extubation. Patients were randomly assigned to receive asymmetrical or standard nasal cannulas. An asymmetrical cannula improved patient comfort compared to a standard cannula However, there were no significant differences between the two nasal cannula interfaces regarding lung aeration, diaphragm activity, ventilatory efficiency, dyspnea, and gas exchange.

CONCLUSION

The asymmetrical HFNC interface may represent a promising advancement in the delivery of high-flow nasal oxygen therapy. It offers a more individualized approach to achieving effective airway pressure and dead space clearance. Its unique design allows for the optimization of PEEP and carbon dioxide clearance by varying the prong-to-nare area ratio. While improvements have been observed in certain areas, the evidence is primarily based on studies with limited sample sizes. Further research is needed to determine whether asymmetrical cannulas offer clinical advantages in specific patient populations, optimal sizing parameters, and their long-term safety and efficacy in diverse clinical settings.

Ethics

Footnotes

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: All authors contributed equally to all contribution sections.

Conflict of Interest: One author of this article, Begüm Ergan, is member of the Editorial Board of the Thoracic Research and Practice. However, she was not involved in any stage of the editorial decision of the manuscript. The editors who evaluated this manuscript are from different institutions. Begüm Ergan reports educational grants from Fisher and Paykel outside the submitted work.

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