

High flow oxygen therapy in intensive care and anaesthesiology

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Abstract

Following the review of the current literature, the principles and practical effects of the application of high flow oxygen therapy (HFO₂T) among intensive care patients and those subjected to surgical procedures were presented. The results of HFO₂T usage go beyond achieving stable and controlled oxygen concentration in the inspiratory air. Additional effects are associated with obtaining positive pressure during exhalation, CO₂ wash-out and functional reduction of dead space, end-expiratory lung volume increase as a result of micro-atelectasis reduction and improved distribution of tidal volume. As a result of optimal humidification and heating of the inspiratory mixture, resistance of breathing and work of breathing are reduced. The described HFO₂T effects encourage attempts to use it not only as a passive oxygen therapy tool, but also as an alternative device for noninvasive ventilation or early intubation. The range of applications evaluated in the literature includes acute hypoxemic respiratory failure, initial phase of ARDS, COPD, perioperative period and applications during diagnostic processes (gastroscopy, bronchoscopy). A special form of HFO₂T, currently undergoing evaluation, is the adaptation of the method for patients with tracheostomy, which mainly improves the processes of moisturizing the breathing mixture. HFO₂T requires further evaluation in large, randomised trials, however, the effects of use to date are encouraging.

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Passive oxygen therapy (POT) is one of the basic interventions applied to improve oxygenation in cases of increasing symptoms of acute hypoxaemic respiratory failure. The concentration of oxygen in the inspiratory air of patients with maintained respiratory activity can be increased using various measures of passive oxygen therapy (nasal masks, nasofacial masks, nasal catheters, respiratory helmets, and others), which improve O₂ pressure in the arterial blood [1, 2]. However, the use of these devices in which the oxygen flow does not exceed 15 L min⁻¹ due to technical reasons ([e.g.] a reduction in pressure in the hospital grid being necessary) in cases of increasing symptoms of respiratory failure, usually associated with a significantly increased demands for the inspiratory flow within the range of 30–120 L min⁻¹, does not allow one to achieve higher and stable oxygen concentrations using the measures mentioned above [1, 3, 4]. Sim *et al.* [5] evaluated the effectiveness of selected POT devices in healthy volunteers at an O₂ flow of 12 L min⁻¹.

Standard oro-nasal masks enabled one to achieve an oxygen concentration in the respiratory mixture between 50 and 60%. Non-rebreather oxygen masks, causing marked discomfort in patients, allowed one to increase the oxygen concentration to a maximum of 70% oxygen at an O₂ flow of 15 L min⁻¹. Commonly used single nasal catheters also limit this concentration to 40–60% [1]. Nasal delivery was first used during the early years of the 20th century although the concept of therapeutic oxygen treatment dates back to the beginning of the 19th century (Thomas Beddoes, 1760–1808). Oxygen was delivered nasally to victims of mustard gas intoxications during the World War I and, in the 1920s, to paediatric patients using rubber catheters of small diameters (8–10 Fr). Attempts were made to limit the irritating effects of higher flows of oxygen on the nasal mucosa, separating the O₂ stream to each nostril using a rubber “Y”-type cannula. The originator of this solution was Alvan Barach (1895–1977) from Columbia University (USA).

A similar device was developed in Great Britain in 1925; the device was supplemented (in the mid-1930s) with metal rubber-reinforced catheter tips; additionally, with metal rubber-reinforced catheter tips; additionally, the means of their stable fixation were designed using special tapes and glasses frames (so-called “oxygen glasses”). Thanks to advances in plastic technology, a modern version of the plastic nasal cannula for oxygen delivery was developed in the 1940s [6]. Although some other passive oxygen therapy devices were in use, such nasal catheters won widespread popularity, allowing patients to more easily communicate with people around them and facilitating eating and drinking without the claustrophobic sensations associated with using masks. The advantages of using this method of oxygen delivery, which are still current, led to the use of nasal oxygen supply with devices generating high flows of humidified and warmed inspiratory air [2, 4, 6–8]. The development of nasal cannulas designed for this system of oxygen therapy were preceded by comprehensive constructive works based on the analysis of casts of the nasopharyngeal cavity obtained during pathomorphological examinations, visualisation with radioactive markers, analysis of pressures in the nasopharynx determined with Pitot tubes and laser Doppler flowmetry. Additionally, mathematical models have recently been developed that determine the distribution of high flow of the respiratory mixture based on 3D computed tomography. They have confirmed earlier experimental studies supplemented with acoustic rhinometry of the nasopharyngeal cavity [6]. Based on the above findings, high flow nasal cannulas (HFNCs) were designed which allow one to apply an oxygen flow of 60–70 L min⁻¹, ensuring special conditions in order to improve oxygenation and affect some other factors of gas exchange and biomechanics of the respiratory system [2–10]. The first special recipients of this method of oxygen therapy were newborns and infants [6]; in this population it became an effective alternative to continuous positive airway pressure (CPAP) [6, 11, 12].

PHYSIOLOGICAL ASPECTS OF HIGH FLOW OXYGEN DELIVERY

An increase in the flow velocity in the airway is a clear attempt to keep up with the increasing demands for inspiratory flow, while the use of high flow oxygen delivery enables the controlled and precise dilution of oxygen in the surrounding air without fluctuations in the oxygen stream and increases in the patient’s respiratory effort [7, 9, 10, 13]. Figure 1 illustrates this phenomenon, comparing the effect of oxygen dilution in the atmospheric air in patients using the conventional devices of passive oxygen therapy, which generates unstable and variable increases in O₂ concentration in the inspiratory air and, additionally, enables one to correct this condition by increasing the oxygen flow velocity in the respiratory mixture.

The management strategy described above, ensuring appropriate proportions of oxygen in breathable gases adapted to patient’s inspiratory flow demands and effectively and proportionally controlling the oxygen fraction (FiO₂) within the range of 0.21–1.0, is called high flow oxygen therapy (HFOT) [3, 9, 10, 13]. To achieve such effects, several options of increasing O₂ flow velocity can be applied [9]. These include:

1. The Venturi effect in a high oxygen pressure-powered valve. The resulting lowered pressure causes the phenomenon of mixing oxygen with respiratory air; FiO₂ is determined in a mixer (blender) and should not exceed a level of 0.3 as the functioning of the system is entirely dependent on the oxygen flow.
2. Two sources of high air and oxygen pressure. FiO₂ is determined according to the total amount of oxygen divided by the total flow stream delivered.
3. A high flow turbine, which enables the supply of warmed and humidified gases with a flow of 60–70 L min⁻¹. FiO₂ is determined by a O₂ blender integrated with the turbine; more often the turbine is equipped with an inlet of low pressure oxygen supplied from the outside using a calibrated flowmeter, which enables one to achieve FiO₂ — 0.21–1.0 and a flow of 60 L min⁻¹.
4. In the majority of modern ventilators, HFOT can be administered using the ventilator’s turbine and the system of high flow gases (air and oxygen), as in options 2 and 3. FiO₂ is determined by the ventilator blender [6, 9, 10, 13–15].

The use of high flow oxygen delivery was meticulously evaluated under experimental and clinical conditions in the early nineties of the 1990s yet only at the beginning of the 20st century was a device accelerating the oxygen stream selected that enables one to achieve high oxygen flows in the clinical setting [3, 6, 7, 14]. For this purpose, a small turbine was used generating a substantial flow (option 3 described above) connected with a calibrated mixer of oxygen and atmospheric air, which allowed one to precisely control FiO₂ in the range of 0.21–1.0; additionally, an efficient warming and humidifying system with a single connecting cable and the nasal cannula adjusted to the size of nostril (described above) was applied. This system can also be connected with a special adaptor enabling the administration of HFOT to the tracheostomy tube of spontaneously breathing patients [3, 6, 8, 10, 15]. A humidifying system ensuring warming and humidification of the respiratory mixture stream is an essential factor for the effective and stable functioning of the device within a wide range of flows. Nowadays, the MR850 humidifier with an MR290 water chamber (Fisher & Paykel, Auckland, New Zealand) is most commonly used. The water cavity produced by the same manufacturer in the AIRVO™ 2 device is even more effective and larger (Fig. 2). At their maximum flow, the above devices allow one to achieve an

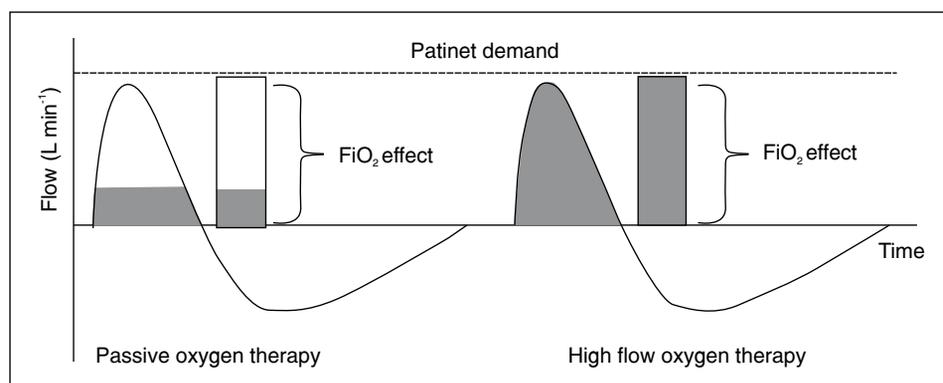


Figure 2. The FiO_2 change in the inspiratory air depending on the flow velocity of the inspiratory mixture during passive and high flow oxygen therapy. The concentration O_2 is obtained according to the total amount of oxygen delivered divided by the total stream of inspiratory air. For instance, if the patient demand for inspiratory flow during respiratory failure is 60 L min^{-1} , while traditional nasal cannula delivers $10 \text{ L min}^{-1} \text{ O}_2$ ($\text{FiO}_2 = 1.0$), the aspiration of additional 50 L of air ($\text{FiO}_2 = 0.21$) will cause that at the total patient flow demand of 60 L min^{-1} the air will contain 20 l O_2 , which is going to ensure the FiO_2 "effect" of 0.33 ($20/60$) in inspiratory air. A precise increase in oxygen fraction in inspiratory air (e.g. to $\text{FiO}_2 = 1.0$) is achievable by adjusting the velocity of respiratory mixture flow to patient demands

absolute humidity of $44 \text{ mgH}_2\text{O L}^{-1}$ and 100% relative humidity, as well as a temperature of 37°C (so-called conditioned respiratory air) [3, 6]. Such conditions during the inspiratory flow facilitate the maintenance of the respiratory epithelium function associated with mucociliary clearance, hydration of the epithelial sol, maintenance of the ciliary transport (up to 20 mm min^{-1}) and significantly decrease airway flow resistances [5, 6, 9]. It has been suggested that conditioned inspiratory air may be the major factor of successful HFOT, which additionally allows the safe long-term administration of this kind of therapy [9,10]. Considering the above, attention should be paid to some other humidifiers, including popular "bubbling" devices, which enable one to provide conventional oxygen flow of $10\text{--}12 \text{ L min}^{-1}$, absolute humidity of $5\text{--}30 \text{ mg L}^{-1}$ (also during non-invasive ventilation [NIV]) that cause all adverse bronchial effects [5, 8]. Mauri *et al.* [16], analysing the comfort of breathing, subjectively assessed by patients undergoing HFOT, have found that a temperature of 31°C was better accepted by patients, as compared with 37°C ($P < 0.0001$); however, at increased flow and O_2 demands, conditioned air was well tolerated. The fact that is often unrealised is the importance of effective humidification for the energy balance of the body. This phenomenon is relevant as the warming and humidification of each litre of air in the nasopharyngeal cavity (from an average room temperature of 21°C and 50% relative humidity), requires approximately 26 kcal per each breath, which translates into $156 \text{ kcal min}^{-1}$ (at 12 breaths per min). The acceleration of breathing characteristic of increasing respiratory failure, as well as some other features of enhanced metabolism in systemic diseases (shock, trauma), result in additional significant increases in the energy costs of maintaining optimal respiratory conditions [17].

An clear improvement in the effectiveness of HFOT, were observed under clinical and experimental conditions,

facilitating the decisions concerning additional examinations and drawing attention to special properties of gases during high flows, which exceed the effective increase in FiO_2 . Extremely important observations have recently been made, focusing on a variety of biomechanical changes accompanying mainly the nasal supply of oxygen and increasing the clinical efficacy of HFOT. They include:

1. The effect of CO_2 washing-out, which, according to the majority of study findings, is the one of the major factors of the additional, indirect effectiveness of HFOTs. This effect results from the fact that a quick stream of the inspiratory gas mixture removes part of the CO_2 from the expiratory air retained in the nasopharyngeal cavity and provides this area with oxygen, which increases the amount of O_2 in the next portion of inspiratory air at a reduced amount of CO_2 . Moreover, the above effect leads to the functional decrease in the volume of anatomical dead space, which is particularly visible in patients with COPD [13, 14, 18, 19]. It is not clear whether an open or closed mouth affects the changes observed; however, animal studies have demonstrated that reduced leak in the nasopharyngeal cavity by closing the animal's mouth improves the effectiveness of CO_2 washing-out. Chanques *et al.* [20] have not reported such differences. Möller *et al.* [21] in their randomised study on 10 volunteers with the use of volume capnography and Krypton scintigraphy (81 mKr) have found a correlation between HFOT and CO_2 washing-out from the upper airway. The direct measurement of CO_2 and O_2 in the trachea has confirmed limited reversible breathing.
2. A reduction in inspiratory nasopharyngeal resistance that limits the flow during intensified inspiration due to nasopharyngeal collapse, and which is particularly pronounced in patients with obstructive sleep apnoea.

Upper airway collapse is one of the main factors of this pathology. HFNCs have been demonstrated to reduce epiglottic resistance: indirectly, due to generating the stream of inspiratory flow; and directly, through mechanical splinting of the airways and the nasal muscles, in particular. The above phenomena, resulting in a total decrease in airway resistances, facilitate the inspiratory flow and reduce the total work of breathing [3, 6, 13, 14]. According to Vargas *et al.* [14], assessing the inspiratory flow of gases, as well as elastic and non-elastic breathing resistances, the pressure-time product (PTP) which well illustrates this condition during HFNC decreased significantly from 204.2 cm H₂O s⁻¹ observed during passive oxygen therapy to 156.0 cm H₂O s⁻¹ (on average), which was accompanied by a reduced respiration rate ($P < 0.01$). The above findings additionally indicate the facilitated inspiratory flow of gases and reduced intrinsic positive end-expiratory pressure (PEEP). Similar results were reported by Di Musi *et al.* [22]. In the small non-randomised population of COPD patients, POT was compared with HFNC by measuring the electrical activity of the diaphragm and recording pressure-time product demonstrating significantly reduced values of both parameters. It can thus be concluded that HFNC substantially and significantly decreases the respiratory drive and work of breathing, which confirms the total effect of HFOT [22].

3. The effect of airway positive pressure is directly proportional to the vector of high flow and to its value [10, 13]. In the group of healthy volunteers at the flow velocity of 60 L min⁻¹ and with a closed mouth, the median of positive pressure was 7.4 cm H₂O. Under similar conditions, a flow reduction to 35 L min⁻¹ enables one to achieve a pressure of 2.7 cm H₂O [23]. The positive pressure effect decreases within the range of 0.6–2

cm H₂O, yet does not subside when the patient's open mouth is open [20]. It should be stressed that the phenomenon described here is also somewhat affected by the nasal cannula size. A cannula size exceeding 2/3 of the nostril diameter, along with excessive sealing, results in an obvious increase of positive pressure in the expiratory phase. This can be dangerous when HFNC is used in neonates whenever lung-damaging pressure values are reached [3, 7, 23, 24]. Okuda *et al.* [25] have indirectly confirmed an increase in oesophageal pressure proportional to the change in the flow value by measuring oesophageal pressure and using impedance tomography, as well as the forced oscillation technique (FOT), which corresponded to HFNC-generated positive pressures during expiration, elevating end-respiratory lung volume (EELV). Positive pressure during HFOT is generated in the open system and is affected by reactions to the increased flow of the respiratory mixture; moreover, the pressure value can be individually and gradually tailored (open/closed mouth). Therefore, this technique is neither a form of CPAP, as the nasal cannula does not tightly fit the nostrils [9, 13, 14], nor a ventilation option in NIV in which continuous positive airway pressures are used. Furthermore, there is a significant difference between the technique discussed and PEEP during invasive ventilation (although in some literature reports, the positive pressures during HFOT are incorrectly defined as PEEP [6, 10, 19, 20]).

4. The limitation of physiological micro-atelectasis of the lungs is associated with the above-described phenomena of decreasing inspiratory resistances and provision of changeable yet positive expiratory pressures. An increasing respiratory lung area is an additional factor that improves oxygenation in HFOT. Evaluation of the clinical effects of HFNC using electrical impedance tomography

Table 1. Physiological effects of high-flow oxygen therapy and their possible clinical sequels

Physiological effects HFOT	Clinical sequels
Improved availability and stability of oxygen concentrations	Use of real and assumed oxygen concentrations in inspiratory air
Reduced respiratory resistances	Lower work and costs of oxygen breathing
Better bronchial mucociliary clearance	Lower risks of infective complications and accumulation of secretions in the bronchial tree
Maintained relative and absolute humidity of the respiratory mixture	Efficient mucociliary transport, hydration of the ciliary sol
Maintained temperature of the respiratory mixture irrespective of the flow size	Improved energy balance
Decreased dead space and CO ₂ washing-out	Improved elimination of CO ₂
Generation of positive airway pressure	Limited micro-atelectasis, better distribution of tidal volume, reduced i-PEEP
Possible recruitment of alveoli	Increased respiratory area and FRC

HFOT: high flow oxygen therapy; i-PEEP: intrinsic PEEP

Table 2. Selected indications for HFOT using HFNC or a tracheostomy tube

Indications for HFOT	Comments
Acute and increasing respiratory failure	Stability of oxygen supply in the range of FiO ₂ 0.21–1.0 under optimal humidification and warming of the respiratory mixture
Mild ARDS (according to the Berlin definition) PaO ₂ /FiO ₂ >200 < 300	May concern patients with lack of tolerance to NIV or those that were not administered NIV
No effectiveness or tolerance to conventional passive oxygen therapy	Low clinical and gasometric efficacy of the oxygen therapy option administered
Lack of tolerance or effects of the non-invasive option of ventilation used	Lack of adjustment of NIV interface to patient demands, wrong mode of ventilation
Chronic obstructive pulmonary disease	Effective elimination of CO ₂ under conditions of controlled supply of O ₂ maintenance of respiratory drive
Sleep apnoea syndrome	Initial therapy or use of “splinting effect” of the nasopharynx in cases of intolerance of other instrumental ways of treatment
Respiratory distress in the group of immunosuppressed patients	Low risk of additional of superinfection and possible improvement of oxygenation
Preparation to undergo difficult intubation	Improved oxygenation potential in cases of anticipated additional intubation manoeuvres
Post-operative hypoxaemic respiratory failure	Fighting the effect of postoperative atelectasis and residual effects of anaesthetics on respiration
Cardiogenic lung oedema	Influence on left ventricular contractility and preload, controlled increases in FiO ₂
Diagnostic examinations of the airway in patients with their own breathing preserved	Bronchoscopy, other forms of larynx and trachea visualisation in patients of limited respiratory effectiveness
Palliative end-of-life care, do-not-intubate status	Patients with contraindications for intubation
Long-term oxygen therapy, in the home setting as well	Patients with neurological diseases or those with COPD requiring effective home oxygen therapy using HFNC or tracheostomy adapters

ARDS: acute respiratory distress syndrome; NIV: non-invasive ventilation; COPD: chronic obstructive pulmonary disease; HFNC: high nasal flow cannula

enables one to find a significant correlation between the size of flow versus end-expiratory impedance of the lungs and increased air pressure. As a result, the oxygen pressure increases and the respiration rate slows down [25, 26]. Mauri *et al.* [19] have found likely sequels of reduced micro-atelectasis also in the form of better distribution of the tidal volume in the lungs. An indirect marker of improved lung aeration is also increasing EELV, as mentioned above, which is a sum of several HFOT effects followed by a decrease in expiratory flow velocity and tidal volume [3, 6, 8, 10, 13, 14, 20, 25] (Table 1).

PRACTICAL POSSIBILITIES OF USING HIGH FLOW OXYGEN THERAPY

INDICATIONS AND CONTRAINDICATIONS

The basic and real indication for HFOT is the lack of possibilities to obtain a stable and controlled concentration of O₂ during classical passive oxygen therapy in acute hypoxaemic respiratory failure. In many other clinical situations, HFOT is an alternative to non-invasive ventilation or intubation and the implementation of active oxygen therapy. As the number of HFOT applications is increasingly high, it is difficult to list all the fields of clinical medicine in which this treatment has been used [2, 3, 7, 9, 15, 18]. Table 2 contains the major and clinically confirmed examples

of the use of HFOT. On the other hand, the contraindications are limited and are obviously neglected in numerous, even large assessment studies. However, in analysing the attempts to use HFOT, some reservations may be found. These include:

- nasal cannula intolerance or anatomical incompatibility of the cannula size,
- relevant expiratory disorders and excessive increases in expiratory work,
- no clinical effects of the use of HFNC or HFOT via tracheostomy,
- haemodynamic disturbances associated with high oxygen flow.

HIGH FLOW OXYGEN THERAPY IN INTENSIVE CARE UNITS

The most abundant group of patients undergoing HFOT in intensive care units (ICUs) is that with increasing hypoxaemic respiratory failure in various systemic diseases. In such cases, according to the rule described above, HFOT is an alternative to PT or NIV. Xu *et al.* [27] analysed randomised studies in electronic databases (Pubmed, EMBASE, Scopus and Web of Science), comparing HFNC, PT and NIV in a group of 4,231 adult ICU patients. Although HFNCs significantly reduced the risk of oxygen therapy failure ($P = 0.04$), it did not affect the prevention of intubation, as compared with

passive oxygen therapy. Its use after the removal of the endotracheal tube significantly reduced the incidence of endotracheal re-intubations ($P < 0.00001$). Moreover, compared to NIV, HFNC also reduced the incidence of intubations ($P = 0.02$) when administered after NIV. In such cases, the evaluation of oxygenation and gasometry improvement are the overriding factors for the continuation of treatment using HFOT. In addition, HFOT is sometimes used as an alternative to early endotracheal intubation or NIV. Having analysed 12 randomised studies, Lee *et al.* [28] have observed better comfort and tolerance of ICU patients to HFNC with low respiratory work and higher oxygenation values, as compared with NIV or conventional POT methods. Moreover, the POT methods showed higher 90-minute mortality in patients in comparison with HFOT. Huang *et al.* [29] having analysed 2,781 ICU patients, have pointed out that the use of HFNC after long-term intubation is associated with a similar risk of re-intubations, as compared with NIV and conventional POT options. Moreover, in cases of removal of the endotracheal tube in critically-ill patients, HFNC resulted in significantly better results than the remaining methods ($P = 0.0007$) and was associated with less complications severe complications, improved tolerance and better comfort for patients. Additionally, using HFNC, attempts can be made to use initial respiratory treatment in mild and moderate cases of acute respiratory distress syndrome (ARDS) ($\text{PaO}_2/\text{FiO}_2 < 300$). The management protocol assuming the possibility of applying non-invasive ventilation at this stage of treatment can be replaced by HFNC in some patients. In several reports available, the authors simply insist on using HFOT according to the Berlin ARDS definition [30]. A large study by Frata *et al.* [31], carried out in 23 French and Belgium ICUs and involving comparative randomised observations of NIV, PT and HFNC has demonstrated that none of the options of oxygen therapy affected later incidences of endotracheal intubation ($P = 0.18$); HFNC, however, resulted in the lowest intubation rate during a 28-day observation ($P = 0.009$) in a subgroup of patients with $\text{PaO}_2/\text{FiO}_2 \leq 200$ mmHg. In total, the authors have also observed lower mortality ($P = 0.047$) in the HFNC group (also during a 90-day observation) and increased numbers of mechanical ventilation-free days ($P = 0.02$). The above findings led to numerous reports; among them the study by Ni *et al.* [32] is worth noticing, in which 3,881 patients with $\text{PaO}_2/\text{FiO}_2 < 300$ mmHg were evaluated. The authors have observed that this index improves after HFNC. However, the therapy has no effect on PaCO_2 , pH and the duration of ICU treatment. A prospective study in a markedly smaller group of patients with ARDS ($n = 45$) was conducted by Messika *et al.* [33]. Pneumonia was the cause of 82% of ARDS while the intubation rate in those patients was 40%; however, they initially presented with worse

clinical conditions assessed according the simplified acute physiology score II (SAPS II). Over half of patients requiring non-invasive ventilation were successfully treated with HFNC. Thus, the authors concluded that HFNC can be the first-line treatment in patients with developing ARDS. Another group of patients frequently hospitalised in multi-profile ICUs are those with an exacerbation of COPD. The basic HFOT effects reducing the dead space and concentration of CO_2 were discussed earlier. Although, Osadnik *et al.* [34] and Yeung *et al.* [35], having analysed high-quality randomised studies, demonstrated that it is rather NIV, as a first-line intervention in standard ICU management, that decreases the probability of death and endotracheal intubation in patients with exacerbated hypercapnic respiratory failure. Nevertheless, the search for an alternative to such management based on HFOT gives satisfactory outcomes, due to HFNC-induced increases in the ventilation dead space, as opposed to NIV. In their single-centre small study, Di Musi *et al.* [22] have observed that HFNC after the removal of the endotracheal tube substantially reduces the respiratory drive and lowers the work of respiration, as compared with patients treated with conventional oxygen therapy. In their retrospective study, Braunlich and Wirtz [36] have drawn attention to the fact that HFNC applied during exacerbations not only increases PaO_2 but also statistically significantly decreases the pressure of CO_2 . This is of great importance given that, despite the arguments regarding the usefulness of NIV in the treatment of COPD which were pointed out earlier, more than 30% of patients with COPD show bad tolerance to this kind of therapy. This is especially true during exacerbations in which HFNC can be the treatment of choice preventing endotracheal intubation. Similar observations were reported by Kim *et al.* [37]; in a group of 33 patients with a sudden exacerbation of COPD, they found a significant reduction in CO_2 pressure by 4.2 ± 5.5 mmHg ($P = 0.006$) already during the first hour of treatment, as compared with conventional POT. In the majority of studies, the authors have emphasised the clinical effectiveness of the mechanisms reducing dead space and CO_2 washing-out at the most commonly applied flows of about 40–45 L min^{-1} which, under optimal conditions for humidifying and warming the respiratory mixture, results in the satisfactory effects of CO_2 elimination and full control over an increasing PaO_2 proportional to the size of flow applied. It should be noted that the findings presented, although encouraging, were, in the majority of cases, reported in single-centre, often retrospective studies. In the nearest future, the use of HFNC should become increasingly common and objectivise the number of reports regarding the efficacy of HFNC based on prospective large-scale studies, an aspect which is exemplified by a study demonstrating the usefulness of HFNC among patients

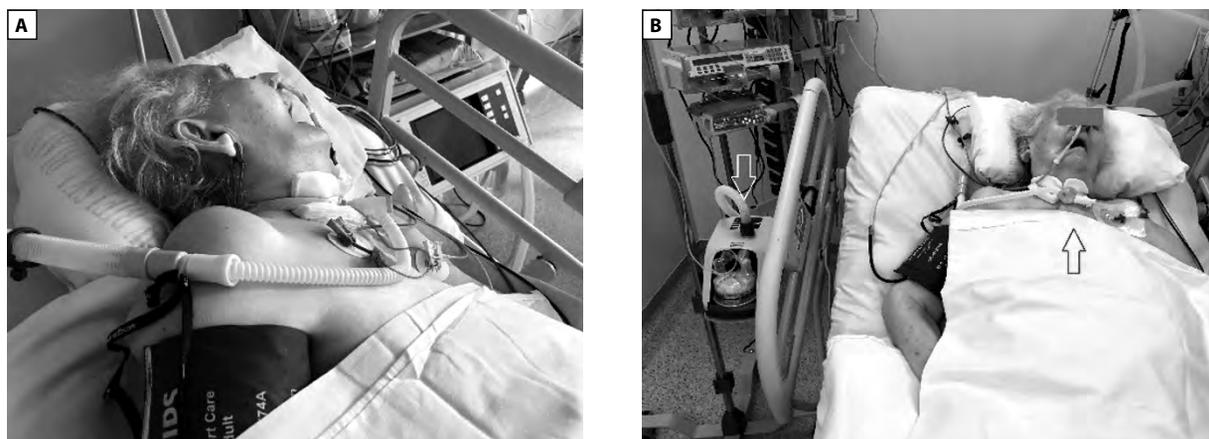


Figure 2. Use of HFOT through tracheostomy; **A** — OPT870 Optiflow™ adaptor (Fisher & Paykel, Auckland, New Zealand) for AIRVO®2 (the same producer); **B** — in HFOT through a tracheostomy tube (author's material)

with COPD undergoing home oxygen therapy. Storgaard *et al.* [38] used HFNC in 200 patients, as an intermittent measure to improve respiration efficiency and analysed the incidence of COPD exacerbations, distances of a six-minute walk test, FEV_{1,0}, PaCO₂ and some other parameters. The six-hour use of HFNC daily over 248 days, on average, substantially improved the patients' general condition and reduced the number of COPD exacerbations (3.12 vs. 4.95 episodes patient per year; $P = 0.001$), simultaneously increasing FEV_{1,0}. Moreover, the incidence of required hospitalisations dropped and the walking distance was prolonged. All the positive changes observed did not affect mortality, however. In cases of chronic respiratory failure, it should also be considered that in a proportion of patients (12%) endotracheal intubation has to be replaced with tracheostomy. With their own respiration rhythm maintained, these patients use oxygen therapy through catheters and special connectors providing the inflow of humidified oxygen to the airways. Unfortunately, even the use of artificial noses humidifying the respiratory mixture does not prevent severe complications resulting from ciliary epithelium dysfunction. In such cases, HFOT with the special Optiflow™ system (Fisher & Paykel®, Auckland, New Zealand [Fig. 2]) and the delivery of conditioned inspiratory air results in significantly better oxygenation outcomes in patients with tracheostomy. Stripoliet *et al.* [39], in assessing this mode of oxygen therapy in the group of 40 patients, have demonstrated no improvement in the biomechanical properties of the respiratory system, a lack of reduced work of respiration and the respiration rate, or improved gas exchange. It seems, however, that searching for HFOT effects in the above study was inappropriate as the main biomechanical benefits of HFOT are achieved in the naso-pharyngeal cavity. In cases of tracheotomy, however, the basic effect is optimal conditioning of the respiratory mixture under stable and controlled FIO₂ condi-

tions and the moderate influence of the high flow stream on the mechanics of ventilation. A casuistic presentation by Mitaki *et al.* [40], describing only 2 patients, has confirmed the flow-proportional generation of positive pressures (maximum 1.76–2.01 cm H₂O with a flow of 60 L min⁻¹) in the airway, reduced respiratory effort and increased tidal volume. The use of HFOT in patients with tracheostomy described in the literature and observed by the author of the present review (Fig. 2) may be an important alternative in patients requiring the long-term artificial respiratory route. Nevertheless, since the number of reports is scarce, drawing explicit conclusions regarding this issue is impossible.

HIGH FLOW OXYGEN THERAPY IN ANAESTHESIOLOGY AND PERIOPERATIVE MANAGEMENT

Patients with limited oxygen reserve and a high surgery-related risk often require perioperative oxygen therapy, usually after surgery due to general conditions but also in the period of direct preparation to undergo general anaesthesia and endotracheal intubation. The risk of critical reduction in arterial blood saturation with oxygen is a rational indication for optimal oxygen therapy and the consideration of HFNC as a preoxygenation tool. Such a management strategy can limit unfavourable sensations connected with the use of non-rebreather oxygen masks or even the best selected NIV interfaces. Moreover, the effective supply of O₂ during HFNC creates a reserve also during apnoea associated with the period of endotracheal intubation, more so that O₂ delivery can be continued during intubation manoeuvres (apnoeic oxygenation). The observed decreases in CO₂ resulting from the action of HFNC itself are obvious, even in patients morbidly obese or with difficult intubation conditions [7, 9]. In most cases, the duration of HFNC prior to intubation is relatively short — 5–7 minutes at most [9]. The shorter preparation time

used by Raineri *et al.* [41] has been found sufficient, even in cases of difficult intubations of patients undergoing abdominal surgical procedures — 4-minute use of HFNC with the oxygen flow of 60 L min^{-1} prevented significant desaturation. HFNC applied postoperatively reduces the demands for mechanical ventilation even after long-term procedures, which have been concluded by the authors assessing the use of HFNC in patients anaesthetised for cardiac surgeries; in a group of 495 HFNC patients undergoing surgery, ventilatory support was required substantially less frequently in those administered HFNC ($P < 0.001$), as compared with individuals receiving passive oxygen therapy; however, there were no differences in the incidences of re-intubations and ICU treatment time [42]. Such effects result from the counteraction of inevitable changes in the respiratory system during HFOT occurring during general anaesthesia and being enhanced during ongoing HFNC, which increase the respiratory area and limit atelectasis, especially the normalisation of work of respiration. Moreover, they reduce the number of re-intubations, estimated at about 20% [7]. Admittedly, while the well-planned OPERA study has not confirmed the superiority of HFNC over POT, the evaluated population of patients undergoing abdominal surgical procedures was small [43]. Hernandez *et al.* [44], analysing a group of 529 patients, have found that the risk of postoperative intubation was substantially lower among patients administered HFNC, as compared with those with conventional oxygen therapy (4.9% vs. 12.2%). While attempting to interpret numerous report findings regarding HFNC in the perioperative period, irrespective of their quality, it should be noticed that the physiological elements of HFOT effects described above meet the potentially adverse changes in the respiratory system occurring in the postoperative period. Thus, it is possible to imagine that a group at increased surgical risk or anticipated intubation-related difficulties will use HFNC throughout the perioperative period. Additionally, HFNC may be used in patients with increased risk undergoing surgeries with central blocks. In such cases, particularly in the forced position (e.g. lithotomy position), the foci of atelectasis and ventilation disorders are likely to develop, which may be theoretically prevented by HFNC.

HIGH FLOW OXYGEN DELIVERY IN OTHER CLINICAL SITUATIONS

The use of HFOT may concern groups of patients presenting small oxygen reserves (COPD, morbid obesity, structural abnormalities of the bony thorax, fibrosing pneumonia, late periods of pregnancy, etc.) qualified for diagnostic procedures. A special example is bronchoscopy or gastroscopy in such patients. Besides effective oxygenation, the biomechanical assets of HFOT described above reduce the risk of

respiratory complications [3, 7, 45]. Lucangelo *et al.* [46], who used HFNC during bronchoscopy have demonstrated markedly better perioperative values of PaO_2 and $\text{PaO}_2/\text{FiO}_2$ at flows of 60 L min^{-1} than in patients administered POT through the Venturi mask the authors successfully applied POT through the trach tube during urgent gastroscopy in an ICU patient, finding stable values of saturation of arterial blood at a flow of 50 L min^{-1} and FiO_2 0.5. Another specific group of patients in whom POT should be considered are patients with immune deficiency disorders in the course of systemic diseases presenting the symptoms of impaired oxygenation. In such cases, the avoidance of endotracheal intubation is a relevant factor limiting the risk of additional infective complications. The reasons in favour of HFNC in such indications are unclear [3, 7, 9, 47, 48]. It is believed that HFNC is a good solution for patients in the immediate period after organ transplantations. However, among patients with chronic multi-organ immunosuppression, a randomised controlled study conducted by Lemiale *et al.* [47] has not demonstrated differences in the incidences of intubations and mortality comparing HFNC, NIV and POT patients. According to the post-hoc analysis, patients treated with HFNC were characterised by a decreased incidence of intubations (31% HFNC, 43% TB, 65% NIV; $P = 0.04$). Similar results were observed in a retrospective cohort of 115 patients; in this study, however, the mortality during POT was significantly lower, as compared with NIV (20% vs. 40%, $P = 0.02$). The above observations have not been confirmed in the randomised HIGH trial involving 776 adult patients with deficient immunity immune deficiency disorders treated in 32 French ICUs [48]. The study patients presented features of respiratory failure ($\text{PaO}_2 < 60 \text{ mm Hg}$ or $\text{SpO}_2 < 90\%$, respiration rate $> 30 \text{ min}^{-1}$), which spoke in favour of HFNC or POT. However, HFOT in this group did not present reduced mortality recorded on day 28, as compared with the POT group. Although Helvitz and Einav [7] summarising the issues of HFOT among patients with immune deficiency disorders have noticed inconsistent study findings, they stressed the heterogeneity of data obtained during frequently critical conditions of patients. The continuation of these considerations are attempts to use HFNC in the group of palliative patients with a clear prognosis in whom intubation, active respiration support and resuscitation are contraindicated. The provision of comfort of such patients is still the ethical responsibility of physicians and, in this case, HFNC fulfils its role [7, 10, 13].

SUMMARY

The clinical data regarding the use of high flow oxygen therapy suggest the usefulness of this method of O_2 delivery in everyday ICU practice, in anaesthesiology and perioperative medicine. It is worth noticing that in the majority of

studies, despite the use of HFNC as a form of POT in various diseases, no explicit effects of this method on a reduction in mortality have been noted. Moreover, an unequivocal answer to the question whether HFOT really reduces the incidence of endotracheal intubations is being sought [2, 3, 8, 9, 28, 29, 32]. Undoubtedly, this option of management is an alternative to non-invasive ventilation in some cases, although clearer evidence is needed. Besides extremely optimistic reports in which large populations of patients were evaluated showing very positive features of HFNC, there are more cautious studies demonstrating a relatively low quality of up-to-date studies suggesting further well-planned randomised research [49–51]. It should be noted that analyses of HFNC are not confined only to experimental or clinical observations but also with regard to economic conditions. In 2018, Eaton Turner *et al.* [52] evaluated the financial aspects of the use of HFNC in British ICUs. They have found out that early administration of HFNC using Optiflow™ ensures an estimated reduction in treatment costs by £469 (i.e. 2,330.93 PLN according to the exchange rate of 4.97 PLN: 1 GBP) per ICU patient, as compared with standard passive oxygen therapy at £611 (3,036.97 PLN), as compared with the use of NIV. An additional factor in the positive economic assessment of HFNC is likely to be a difficult-to-estimate reduction in the number of endotracheal intubations and their consequences.

The analysis of possible uses of high flow oxygen therapy presented against theoretical assumptions raises hopes for a well-functioning and effective treatment tool in some forms of respiratory failure, one which can be an alternative to and supplement the methods of management already used in many fields of medicine.

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