doi • 10.5578/tt.20229810
Tuberk Toraks 2022;70(2):197-202
Received/Geliş Tarihi: 24.01.2022 • Accepted/Kabul Ediliş Tarihi: 30.03.2022

REVIEW
DERLEME

Unusual complications of non-invasive mechanical ventilation (NIV) and high-flow nasal cannula (HFNC): A systematic review

Biljana LAZOVIC[1] (ID)
Radmila DMITROVIC[1] (ID)
Isidora SIMONOVIC[1] (ID)
Antonio M. ESQUINAS[2] (ID)
Bushra MINA[3] (ID)
Sean ZACK[4] (ID)

[1] University Clinical Hospital Center Zemun, Belgrade Pulmonology Division, Belgrade, Serbia
[1] *Belgrad Klinik Hastane Merkezi, Pulmonoloji Kliniği, Belgrad, Sırbistan*
[2] Pulmonology Intensive Care Unit, Hospital Morales Meseguer, Murcia, Spain
[2] *Morales Meseguer Hastanesi, Pulmonoloji Yoğun Bakım Ünitesi,* Murcia*, İspanya*
[3] Zucker Medical School at Hofstra Northwell Section Chief, Pulmonary Medicine Lenox Hill Hospital, New York, USA
[3] *Lenox Hill Hastanesi, Hofsrta Üniversitesi Zucker Tıp Fakültesi, Göğüs Hastalıkları Kliniği,* New York*, Amerika Birleşik Devletleri*
[4] Pulmonary Critical Care Division Lenox Hill Hospital, New York, USA
[4] *Lenox Hill Hastanesi, Göğüs Hastalıkları Yoğun Bakım Bilim Dalı,* New York*, Amerika Birleşik Devletleri*

Cite this article as: *Lazovic B, Dmitrovic R, Simonovic I, Esquinas AM, Mina B, Zack S. Unusual complications of non-invasive mechanical ventilation (NIV) and high-flow nasal cannula (HFNC): A systematic review. Tuberk Toraks 2022;70(2):197-202.*

Address for Correspondence (Yazışma Adresi)
Dr. Biljana LAZOVIC
Clinic of Pulmonology,
Belgrade Clinical Hospital Center
BELGRADE - SERBIA
e-mail: lazovic.biljana@gmail.com

ABSTRACT

Unusual complications of non-invasive mechanical ventilation (NIV) and high-flow nasal cannula (HFNC): A systematic review

The first application of modern non-invasive mechanical ventilation (NIV) can be traced back to over 30 years ago when a patient suffering from Duchenne Muscular Dystrophy was successfully ventilated. Since then, the use of NIV has been on the rise throughout the world. Although a very modern and safe therapy, complications during its application are inevitable. In addition to some well-known complications, others have described more rare entities. In this article, we described such rare complications as pneumoperitoneum, pneumocephalus, parotitis, gastric perforation, and barotrauma. The purpose of this review was to describe unusual complications of NIV, their prevalence, and the mechanisms by which such complications arise. We performed a clinical review by searching PubMed, Embase, and Cochrane libraries with Mesh terms: 'non-invasive mechanical ventilation', 'high-flow nasal cannula', 'rare complication', 'unusual complication', and 'unexpected complication'. These terms were cross-referenced with other keywords: 'pneumoperitoneum', 'parotitis', 'pneumocephalus', 'gastric insufflation', and 'barotrauma'. We included 26 research papers. When applying mechanical ventilation, it is necessary to have a strong knowledge of the mechanics of the device as well as familiarity with the complications that may occur during its use, including less com-

mon ones. Prompt and effective treatment of such complications is required, as well as careful consideration of the potential causes of such events, during the application of NIV or HFNC.

Key words: *Non-invasive ventilation; high-flow nasal cannula; rare complication; unusual complication; unexpected complication*

ÖZ

Non-invaziv mekanik ventilasyon (NIV) ve yüksek akışlı nazal kanülün (HFNC) olağan dışı komplikasyonları: Sistematik bir derleme

"Modern" non-invaziv mekanik ventilasyonun (NIV) ilk uygulaması, Duchenne Musküler Distrofisi olan bir hastanın başarıyla ventile edildiği 30 yıl öncesine dayanmaktadır. O zamandan beri, özellikle Koronavirüs hastalığı 2019'un (COVID-19) ortaya çıkmasıyla birlikte, NIV kullanımı tüm dünyada artışa geçmiştir. Oldukça modern ve güvenli bir tedavi olmasına rağmen, uygulama sırasında komplikasyonlar gelişmesi kaçınılmazdır. Bazı iyi bilinen komplikasyonlara ek olarak, daha nadir görülen başka komplikasyonlar da tanımlanmıştır. Bu yazıda pnömoperitoneum, pnömosefali, parotit, gastrik perforasyon ve barotravma gibi nadir görülen komplikasyonları tanımladık. Bu derlemenin amacı, NIV'in olağandışı komplikasyonlarını, prevalansını ve bu tür komplikasyonların gelişme mekanizmalarını tanımlamaktır. PubMed, Embase ve Cochrane Library'de 'non-invaziv mekanik ventilasyon', 'yüksek akımlı nazal kanül', 'nadir komplikasyon', 'olağandışı komplikasyon' ve 'beklenmeyen komplikasyon' Mesh terimleriyle arama yaparak klinik bir derleme yaptık. Bu terimleri 'pnömoperitoneum', 'parotit', 'pnömosefali', 'gastrik insüflasyon' ve 'barotravma' gibi diğer anahtar kelimelerle eşleştirdik. Derlemeye yirmi sekiz araştırma makalesini dahil ettik. Mekanik ventilasyon uygularken, cihazın mekaniği hakkında yeterince bilgi sahibi olmak ve kullanımı sırasında nadir de olsa gelişebilecek komplikasyonlara aşina olmak gerekmektedir. Non-invaziv mekanik ventilasyonun veya YANK uygulaması sırasında bu tür olayların olası nedenlerinin dikkatli bir şekilde değerlendirmenin yanı sıra söz konusu komplikasyonları hızlı ve etkili bir şekilde tedavi etmek önemlidir.

Anahtar kelimeler: *Non-invaziv ventilasyon; yüksek akışlı nazal kanül; nadir komplikasyon; olağan dışı komplikasyon; beklenmeyen komplikasyon*

INTRODUCTION

Non-invasive mechanical ventilation (NIV) of the lung is defined as ventilatory support that is achieved via positive airway pressure, without the use of an endotracheal tube, laryngeal mask, or endotracheal cannula for airway securement (1). According to some authors, the history of NIV dates back more than 100 years, but the development of modern NIV is traced back to 1987 when Delaubier and Rideau successfully ventilated a patient with Duchenne Muscular Dystrophy (2). The prevalence of patients who use mechanical ventilation in home conditions is on the rise. Some Canadian authors reported that the prevalence of in-home mechanical ventilation prescriptions is increasing by 0.3/100.000 patients per year, with similar increases seen in some European countries (3). The use of NIV has been most prescribed by pulmonologists (52.9%), followed by intensivists or anesthesiologists (34.3%), and lastly by other specialists (12.6%) (4). The key indications for NIV are as follows: acute hypercapnic respiratory failure (AHRF, in 48% of cases), arguably its most significant and important one; acute exacerbation of chronic obstructive pulmonary disease (AECOPD); obesity hypoventilation syndrome; acute cardiogenic pulmonary edema (ACPE); neuromuscular disorders; and post-extubation ventilatory support (4,5). In patients with cancer, NIV has been recommended as palliative care to improve dyspnea. NIV is effective in treating exacerbations of chronic obstructive pulmonary disease and end-stage neuromuscular disease (6). While the emergence of high-flow nasal cannula (HFNC) is a relatively new treatment modality in adult respiratory failure, some research has found it to be not superior to NIV (7). Despite the development and application of newer systems for providing ventilatory support, complications are inevitable, both minor and major. Minor complications are seen as likely tolerable, without an associated increase in morbidity or mortality, while major complications lead to an increase in morbidity and are potentially life-threatening (8).

The objective of this manuscript is to provide a concise overview of the potential complications of NIV and HFNC, focusing on the more uncommon ones; the prevalence of such complications; and explanations for the potential mechanisms by which these complications arise.

MATERIALS and METHODS

We selected substantial studies from the databases of PubMed, Embase, and Cochrane libraries. The following Mesh terms were used: 'non-invasive ventilation', 'high-flow nasal cannula', 'complication', 'unusual complication', 'rare complication', and 'unexpected complication'. We analyzed papers published only in the English language, published between October 1980 and November 2019. The headline, abstracts, and full-text articles of the resulting studies were independently reviewed by three

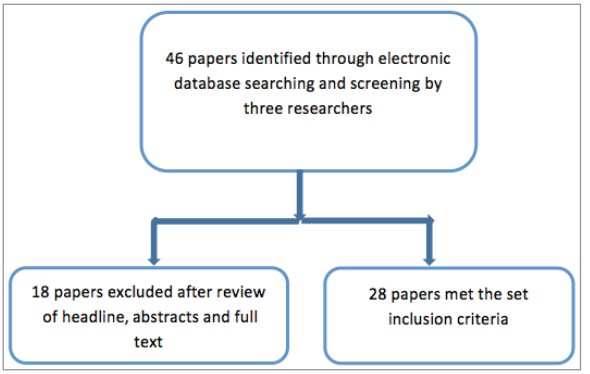

Figure 1. Schematic of research protocol.

Figure 2. Photo of a newborn submitted to NIV through a used but sterilized short binasal prong. Note: Consent to use the image was obtained from the newborn's caretaker. (Available from: https://www.researchgate.net/figure/Photo-of-a-newborn-submitted-to-NIV-through-a-used-but-sterilized-short-binasal-prong_fig1_34228519)

researchers. The reference lists of the articles were also reviewed, for potential inclusion in the study, so as to better detect articles not found by the electronic search. Given the above criteria, forty-five scientific research papers resulted, and this current article included twenty-six.

Most Common Complications of NIV and HFNC

The evaluation of the RCTs (NIV vs standard medical care) showed that the overall NIV failure occurred in 16.3% of patients and all-cause failure had a small but significant RR of 0.88. Our meta-analysis categorized NIV failure causes according to underlying disease states (5). According to data from various studies, the prevalence of continued hypoxemia despite NIV and their respective indications for NIV are combined hypercapnic/hypoxemic acute respiratory failure (ARF) (15-62%), hypoxemic ARF (7-52%), hypercapnic COPD ARF (5-40%), COPD (8-30%), post-extubation ventilatory support (16-25%), and pneumonia (up to 5.7%) (8,9). The most common minor complications include arm edema, CO_2 rebreathing, claustrophobia, discomfort, nasal skin lesions, patient-ventilator dyssynchrony, and noise (8). One study showed that HFNC is a safer form of oxygen delivery, as compared to other modalities in use in the intensive care unit setting. Reported adverse effects include nosocomial pneumonia, oxygen desaturation, more frequent visits to a general practitioner (GP) or primary care provider (PCP) for respiratory complications, pneumothorax, acute pseudo-obstruction, and cardiac dysrhythmia (10). The most common complications of NIV and HFNC are shown in Table 1.

Table 1. Some of the most common complications of NIV and HFNC described in the literature

NIV	HFNC
Discomfort	Aspiration
Claustrophobia	Abdominal distension
Nasal/oral dryness	
Aspiration pneumonia	

NIV: Non-invasive mechanical ventilation, HFNC: High-flow nasal canula.

Unusual Complications of NIV and HFNC

The following section will discuss the more unusual and uncommon complications of both NIV and HFNC use. They are also shown in Table 2 (11,17).

Pneumoperitoneum

Pneumoperitoneum is a very rare potential complication of mechanical ventilation, occurring in about 7% of patients undergoing NIV (11). By searching the appropriate databases, we found only three cases of pneumoperitoneum caused by NIV. The first described case was a 73-year-old patient hospitalized for gastrostomy tube (G-tube) placement. The patient suffered from amyotrophic lateral sclerosis (ALS), requiring the use of NIV at home. Vital signs were normal throughout the examination. Computed tomography (CT) showed free air in the abdominal cavity, which established the diagnosis of pneumoperitoneum.

Table 2. Unusual complications of NIV and HFNC

Citation	Complications	NIV	HFNC
Okamoto A, et al. 2014.	Pneumoperitoneum	Yes	No
Andreu-Ruiz A, et al. 2018.	Pneumocephalus	Yes	No
Martinez E, et al. 2017.	Parotitis	Yes	No
Gay PC. 2009.	Gastric perforation	Yes	No
Chauhan Z, et al. 2019.	Barotrauma	Yes	Yes

NIV: Non-invasive mechanical ventilation, HFNC: High-flow nasal canula.

Considering the overall stability of the patient, lack of hypoxemia, and the nature of the radiological findings, it was concluded that the pneumoperitoneum occurred as a complication of prolonged NIV administration (12). The second case was a 19-year-old patient with Duchenne disease, who required the use of NIV secondary to hypercapnic respiratory failure. As the patient was being administered NIV, the patient could not breathe spontaneously, and the abdomen subsequently became distended. On radiography, free sub-diaphragmatic air was found. There were otherwise no other clinical/radiological findings of an acute abdomen (13). Finally, the third case was a 37-year-old woman with acute respiratory distress, treated with NIV, and later developed abdominal distension. The diagnosis of pneumoperitoneum was confirmed on CT imaging (14). A possible explanation for the build-up of subphrenic air could be the presence of interstitial emphysema, created by the rise in intrathoracic pressure produced by NIV, allowing for the air to leak out of various diaphragmatic gaps into the abdomen (13).

Pneumocephalus

The presence of air within the intracranial cavity is a very rare complication of NIV, and the consequences of such a condition manifest with a decrease in consciousness, coma, or death (15). We found two articles on the presented topic meeting our search criteria. The patients presented within these articles were of varied ages, and diagnoses, and were the result of different mechanisms of occurrences.

In 1980, the 30-year-old patient was hospitalized after a motor vehicle accident. He was with limited mental status, with findings of bilateral miosis, otorrhagia, and a right clavicular fracture. Ventilatory support was provided by continuous positive airway pressure (CPAP) ventilation over several days. The patient then began to report diplopia and headache and exhibited profound rhinorrhea. Neurological imaging revealed free air within the left ventricle and between the cerebral cortexes. The authors did not propose a possible explanation for this case (16). On the other hand, others have postulated potential mechanisms of such pneumocephali in their patients. A middle-aged woman, with a history of obstructive hydrocephaly requiring ventriculoperitoneal shunt (VPS) placement, presented with acute respiratory distress and underwent NIPPV therapy. Several minutes later, she became acutely agitated and confused. NIPPV was immediately discontinued, and a head CT was performed, indicating pneumocephalus. As the patient had undergone a tooth extraction a few weeks prior, the authors believed the condition may have been caused by the passage of air into the retropharyngeal space, via the dental defect, following alongside the VPS, to evoke pneumocephalus as suggested by the presence of air in the neck beside the VPS (14).

Parotitis

Stones, bacterial and viral infections, medications, and obstruction of various etiologies are the most common causes of inflammation of the parotid glands. Parotitis caused by NIV is an extremely rare condition, with only a few references made in the literature. One case was reported in a 90-year-old woman who presented to the hospital with frequent diarrhea and severe abdominal pain. Computed tomography examination of the abdomen revealed occlusion of the mesenteric artery, requiring urgent surgical intervention. After the procedure, she was placed on bilevel positive airway pressure (BiPAP) ventilation due to hypoxemia. On postoperative day two, she developed erythema and edema along the right pre-auricular area, which was confirmed by an ultrasound examination indicating an enlarged parotid gland. Bilevel positive airway pressure was discontinued, and she was switched to HFNC. In the following days, her symptoms had ceased (17). Bilateral

parotitis during the use of CPAP has also been reported, as demonstrated in a case of a young woman who was admitted to the hospital for an exacerbation of her chronic obstructive lung disease, requiring CPAP ventilation. She developed bilateral edema of her parotid glands, confirmed via elevated amylase levels and an ultrasound exam. In this case, NIV was continued, and her symptoms regressed spontaneously within one week (18). During NIV, positive pressure is transmitted through the oral cavity, causing retrograde airflow and obstruction of the Stensen (parotid) ducts (18,19). Similarly, extrinsic compression of the Stensen ducts by an oronasal mask can also occur (20).

Gastric Perforation

During NIV therapy, aerophagia and gastric insufflation can occur in 30-40% of patients (21). According to some authors, gastric insufflation can cause vomiting and subsequent inhalation of gastric contents, leading to aspiration pneumonitis or pneumonia, abdominal compartment syndrome, stomach rupture, and possibly fatal outcomes (22,23). We found only one paper on this topic where a young man, with a history of congenital hypomyelination neuropathy, was admitted with severe abdominal pain. He had been using NIV at home for the past several months for his respiratory insufficiency. Computed tomography imaging revealed pneumoperitoneum and a collection of free fluid around the liver. During emergency laparotomy, perforation of the stomach was seen with a hematoma present on the inner wall of the stomach. The authors had theorized that high pressures during NIPPV administration could lead to gastric over-distension, forming hematomas, which could progress leading to gastric perforation and subsequent pneumoperitoneum (24). Some authors advise avoiding NIV pressures greater than 20-25 cm H_2O (22,23).

Barotrauma

Barotrauma is a common complication of NIV with the use of high positive pressures (namely BiPAP and CPAP). However, there is substantially less data on barotrauma as a potential complication of HFNC (25,26). One article described the case of a 78-year-old woman with chronic respiratory failure secondary to interstitial pulmonary fibrosis. Oxygen via HFNC was administered to the patient, at 60 Liters/min and 100% FiO_2, for persistent hypoxemia. After several days, the patient noted facial and neck swelling with dyspnea. On chest CT, extensive pneumomediastinum with subcutaneous emphysema was noted. Increasing flow rates will lead to subsequent increases in airway pressures, with positive end-expiratory pressures (PEEP) of 3-7cm H_2O recognized with HFNC. These pressures are usually negated with mouth opening, however, in certain clinical settings, barotrauma can occur with high oxygen flow rates (26).

CONCLUSION

The use of NIV has increased worldwide. Although exceedingly modern and safe, complications can still be expected to be seen. Pneumoperitoneum, pneumocephalus, parotitis, gastric perforation, and barotrauma (in HFNC) are rare occurrences but have nevertheless been described in clinical practice. The possibility of the development of the aforementioned complications should be considered before the application of such therapy, as well as the undertaking of certain treatment precautions to avoid potentially lethal outcomes in the case that such complications arise.

REFERENCES

1. *British Thoracic Society Standards for Care Committee. Non-invasive ventilation in acute respiratory failure. Thorax 2002; 57(Suppl 3): 192-21. https://doi.org/10.1136/thorax.57.3.192*
2. *Lobato SD, Alises SM. Modern Non-invasive mechanical ventilation turns 25. Arch Bronconeumol 2013; 49(Suppl 11): 475-9. https://doi.org/10.1016/j.arbr.2013.09.004*
3. *Povitz M, Rose L, Shariff SZ, Leonard S, Welk B, Jenkyn KB, et al. Home mechanical ventilation: A 12-year population-based retrospective cohort study. Respir Care 2018; 63(Suppl 4): 380-7. https://doi.org/10.4187/respcare.05689*
4. *Crimi C, Noto A, Princi P, Esquinas A, Nava S. A European survey of non-invasive ventilation practices. Eur Respir J 2010; 36(Suppl 2): 362-9. https://doi.org/10.1183/09031936.00123509*
5. *Esquinas AM, Oron Benhamoua M, Glossop AJ, Mina B. Non-invasive mechanical ventilation in acute ventilatory failure: Rationale and current applications. Sleep Med Clin 2017; 12(Suppl 4): 597-606. https://doi.org/10.1016/j.jsmc.2017.07.009*
6. *Diaz de Teran T, Barbagelata E, Cilloniz C, Nicolini A, Perazzo T, Perren A, et al. Non-invasive ventilation in palliative care: A systematic review. Minerva Med 2019; 110(Suppl 6): 555-63. https://doi.org/10.23736/S0026-4806.19.06273-6*

7. *Zhao H, Wang H, Sun F, Lyu S, An Y. High-flow nasal cannula oxygen therapy is superior to conventional oxygen therapy but not to noninvasive mechanical ventilation on intubation rate: A systematic review and meta-analysis. Crit Care 2017; 21(Suppl 1): 184. https://doi.org/10.1186/s13054-017-1760-8*

8. *Carron M, Freo U, BaHammam AS, Dellweg D, Guarracino F, Cosentini R, et al. Complications of non-invasive ventilation techniques: a comprehensive qualitative review of randomized trials. Br J Anaesth 2013; 110(Suppl 6): 896-914. https://doi.org/10.1093/bja/aet070*

9. *Moretti M, Cilione C, Tampieri A, Fracchia C, Marchioni A, Nava S. Incidence and causes of non-invasive mechanical ventilation failure after initial success. Thorax 2000; 55(Suppl 10): 819-25. https://doi.org/10.1136/thorax.55.10.819*

10. *Corley A, Rickard CM, Aitken LM, Johnston A, Barnett A, Fraser JF, et al. High-flow nasal cannulae for respiratory support in adult intensive care patients. Cochrane Database Syst Rev 2017; 30(Suppl 5): CD010172*

11. *Okamoto A, Nakao A, Matsuda K, Yamada T, Osako T, Sakata H, et al. Non-surgical pneumoperitoneum associated with mechanical ventilation. Acute Med Surg 2014; 1(Suppl 4): 254-5. https://doi.org/10.1002/ams2.52*

12. *Sánchez Garcia S, Sanz Díaz J, Rubio Solís D. Pneumoperitoneum as complication of noninvasive mechanical ventilation. Arch Bronconeumol 2017; 53(Suppl 10): 588-9. https://doi.org/10.1016/j.arbr.2017.08.002*

13. *Olgemöller U, Körber W, Criée C-P. Abdominal free air without signs of perforated abdominal viscus during non-invasive ventilation. Dtsch Med Wochenschr 2012; 137(Suppl 31-32): 1591-4. https://doi.org/10.1055/s-0032-1305183*

14. *Wolfromm A, Weis N, Espinoza S, Diehl JC, Fagon JY, Guerot E. Non-invasive positive pressure ventilation (NIPPV)-induced pneumocephalus and pneumoperitoneum in a patient with a one-way flow control ventriculoperitoneal shunt. Intensive Care Med 2011; 37(Suppl 5): 889-90. https://doi.org/10.1007/s00134-011-2191-7*

15. *Andreu-Ruiz A, Ros-Argente del Castillo T, Moya-Sanchez J, Garcia-Ortega AA. Tension pneumocephalus secondary to non-invasive mechanical ventilation in a patient with severe traumatic brain injury. Neurocirurgia (Astur) 2018; 29(Suppl 3): 157-60. https://doi.org/10.1016/j.neucir.2017.07.007*

16. *Klopfenstein CE, Forster A, Suter PM. Pneumocephalus. A complication of continuous positive airway pressure after trauma. Chest 1980; 78(Suppl 4): 656-7. https://doi.org/10.1378/chest.78.4.656*

17. *Martinez E, Dicpinigaitis PV. Development of acute parotitis after non-invasive ventilation. J Thorac Dis 2017; 9(Suppl 7): E605-E608. https://doi.org/10.21037/jtd.2017.06.86*

18. *Abdyullayev R, Saral FC, Kucukebe OB, Sayiner HS, Bayraktar C, Akgun S. Bilateral parotitis in a patient under continuous positive airway pressure treatment. Rev Bras Anestesiol 2016; 66(Suppl 6): 661-3. https://doi.org/10.1016/j.bjane.2014.05.008*

19. *Alaya S, Mofredj A, Tassaioust K, Bahloul H, Mrabet A. Acute parotitis as a complication of noninvasive ventilation. J Intensive Care Med 2016; 31(Suppl 8): 561-3. https://doi.org/10.1177/0885066616636021*

20. *Mottard N, Cour M, Chambonnet C, Friggeri A. Parotiditis secondary to NIV interface. Intensive Care Med 2014; 40(Suppl 7): 1023-4. https://doi.org/10.1007/s00134-014-3304-x*

21. *Gay PC. Complications of noninvasive ventilation in acute care. Respir Care 2009; 54 (Suppl 2): 246-57.*

22. *Mehta S, Hill NS. Noninvasive ventilation. Am J Respir Crit Care Med 2001; 163 (Suppl 2): 540-77. https://doi.org/10.1164/ajrccm.163.2.9906116*

23. *Luria O, Reshef L, Barnea O. Analysis of non-invasive ventilation effects on gastric inflation using a non-linear mathematical model. Resuscitation 2006; 71(Suppl 3): 358-64. https://doi.org/10.1016/j.resuscitation.2006.04.016*

24. *Nishimura T, Shirai K, Nakao A, Kotani J. Gastric perforation because of non-invasive positive-pressure ventilation: a review of complications. Surg Infect Case Rep 2016; 1(Suppl 1): 41-3. https://doi.org/10.1089/crsi.2016.29008.tn*

25. *Carron M, Gagliardi G, Michielan F, Freo U, Ori C. Occurrence of pneumothorax during noninvasive positive pressure ventilation through a helmet. J Clin Anesth 2007; 19(Suppl 8): 632-5. https://doi.org/10.1016/j.jclinane.2007.04.010*

26. *Chauhan Z, Deonarine U, Reyes Esteves A, Asif H, Hernandez F, Ferer G. Recognizing barotrauma as an unexpected complication of high flow nasal cannula. Chest 2019; 156(Suppl 4): A1875-A1876. https://doi.org/10.1016/j.chest.2019.08.1619*