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Review paper

The practical considerations of managing negative pressure pulmonary edema for anesthesiologists – literature review

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ABSTRACT

Introduction: Negative pressure pulmonary edema (NPPE) is an uncommon perioperative complication with a potentially fatal outcome. It is most predominant in young healthy men undergoing surgical procedures under general anesthesia. Due to its rare occurrence and uncharacteristic clinical presentation, it poses a potential diagnostic pitfall.

Aim: The purpose of this article is to present clinical characteristics and management of NPPE.

Material and methods: This paper is based on the available literature and the authors' experience.

Results and discussion: Clinical presentation of NPPE is uncharacteristic and includes i.e. agitation, tachypnea, tachycardia, cyanosis and pink frothy sputum. Postponed extubation after general anesthesia is believed to be optimal in order to prevent NPPE as it minimizes asynchrony of muscle function reversal and probability of laryngospasm. Differential diagnosis includes and is not limited to pulmonary edema, aspiration pneumonia, anaphylaxis, septic shock, pulmonary embolism or exacerbation of bronchial asthma. Management of NPPE is symptomatic and focuses on symptomatic treatment and maintaining an open airway passage. Endotracheal intubation with low tidal volume ventilation of 6 mL/kg of ideal body weight with a plateau pressure of less than 30 cm H_2O and high positive end-expiratory pressure (PEEP) may improve patients outcomes.

Conclusions: It is crucial for anesthesiologists to familiarize themselves with this phenomenon for early recognition and proper therapeutic decisions. It should be emphasized that under the highest risk of developing NPPE are young male patients and the most common cause is post-extubation laryngospasm.

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1. INTRODUCTION

Negative pressure pulmonary edema (NPPE) is a self-limiting, non-cardiogenic pulmonary edema, caused by high negative intrathoracic pressure generated mainly during forced inspiration against an obturated airway. This phenomenon was first described in an experiment with resistance in the inspiratory phase of respiration in dogs.[1,2] The incidence of NPPE is 0.05%–0.10% of all anesthesiologic procedures,[2] but, its non-specific clinical presentation and rare occurrence may cause diagnostic difficulties, which can consequently lead to an underestimation of its incidence.[3] Some researchers report that 12% of patients with acute upper airway obstruction develop NPPE.[3] Failed diagnosis and improper management of NPPE has a mortality rate of 40%.[4] The most predominant risk factors of developing NPPE are male gender, young age and increased muscle mass, all of which increase the probability of generating high negative intrathoracic pressure in the event of an airway obstruction.[3,5,6] The occurrence of NPPE is also associated with active smoker status, endotracheal intubation and prolonged operative time.[7] Head and neck surgery procedures significantly rise incidence of NPPE, as in some studies 63% of all NPPE cases developed post-operatively in such patients.[5]

2. AIM

The purpose of this article is to present characteristics of NPPE, with an emphasis on risk factors, clinical symptoms, prevention, differential diagnosis and management, as this phenomenon has been hitherto poorly described in Polish medical literature.

3. MATERIAL AND METHODS

This paper is based on the available literature and the authors' experience.

4. RESULTS AND DISCUSSION

4.1. Etiology and pathophysiology

The etiology of pulmonary edema is based on the disruption of pulmonary fluid homeostasis, which consists of four major components, such as rise of hydrostatic pressure (or decreased oncotic pressure) in the pulmonary capillaries, decline of the hydrostatic pressure in pulmonary interstitium, increased capillary permeability and impaired lymphatic drainage.[2] There are two mechanisms suggested for disturbing this homeostasis.[3] The first concept is a complex of cardiovascular phenomena induced by the increase in the negative intrathoracic pressure, generated in an attempt of inspiration during obstruction of the airway. Pressures as high as –50 cm H_2O to –100 cm H_2O (average intrathoracic pressure is set between –3 cm H_2O and 10 cm H_2O) directly causes both an increase in the venous return to the heart and decrease in the interstitial hydrostatic pressure. The heart is under stress caused by increased blood return, which causes cardiac output to fall because of very high preload. Impaired ventilation induces hypoxemia, leading to rise in the systemic vascular resistance, a consequence of catecholamine release in response to stress, and contraction of pulmonary blood vessels, all of which cause an increase in intrathoracic blood volume and hydrostatic pressure in the vessels, which promote transfer of fluid from the capillaries to the interstitium, and further to the alveoli.[2,3]

The second mechanism suggested is based on mechanical stress on the capillary wall caused by high-negative intrathoracic pressure, which causes higher permeability of the pulmonary blood vessels and thus, formation of pulmonary edema.[3]

NPPE is classified into two types, depending on etiology of the precipitating factor. Type I NPPE occurs shortly after the incidence of upper airway obstruction, whereas type II develops, when chronic airway obstruction is relieved.[2]

Type I NPPE is much more common and is responsible for the majority of the NPPE incidents related to anesthesiology. The most prominent causes of NPPE in anesthesiology procedures are laryngospasm following extubation, displacement, obstruction or biting of the airway management equipment. Furthermore, it has been suggested that an important aspect may be the return of muscle function after muscle relaxation with non-depolarizing drugs,[6] as the function of the respiratory muscles returns faster than that of the pharyngeal and laryngeal muscles, due to the latter being more sensitive to curarization.[8] Thus, if the tongue falls backward obstructing the airway, and the diaphragm contracts simultaneously, it leads to negative intrathoracic pressure. There are reports suggesting that obstruction of the upper airway may have been caused by Sugammadex.[9]

Other examples of type I NPPE causes include choking, epiglottitis and strangulation.

Type II NPPE is a possible complication of laryngological procedures such as tonsillectomy or upper airway tumor resection. In this instance, a different pathophysiological background is suggested. Patients who require such treatments have a chronic partial airway obstruction, which can cause positive end expiratory pressure (PEEP).[2] After removing causes of chronic obturation, the respiratory pressures instantly return to physiological values, thus creating a relatively high, negative intrathoracic pressure and initiate the pathomechanisms mentioned above.[3]

4.2. Clinical presentation

NPPE may present itself with agitation and restlessness, tachypnea, tachycardia, gradual oxygen desaturation and cyanosis. Other symptoms include cough, pink frothy sputum and accessory respiratory muscles involvement. Among clinical findings there are wheezing or crackles on auscultation. Bronchoscopy may reveal congestive plaques and mucosal bleeding.[10] Chest radiographs typically show bilateral diffused interstitial and alveolar infiltrates without pleural effusion.[2,11] In computed tomography (CT) centrally localized heterogenous non-segmental alveolar consolidations are present.[12]

4.3. Prevention and management

There are several precautions an anesthesiologist can take to prevent NPPE. It is reported that the most successful method of avoiding this complication is postponed extubation in order to ensure full reversal of the neuromuscular blockade.[13] Other measures include usage of laryngeal masks, which lower the risk of laryngospasm during emergence from anesthesia in adults,[7] as well as topical usage of local anesthetics on the larynx, throat packs, or careful oropharyngeal suction performed to minimize irritation of the laryngeal structures.[14]

Rapid onset of NPPE requires fast assessment of the situation by the physician. It is important to differentiate between cardiogenic and non-cardiogenic causes of pulmonary edema for proper treatment choice. One should also consider aspiration pneumonitis, anaphylaxis, septic shock, pulmonary embolism and exacerbation of bronchial asthma. During the COVID-19 pandemic, SARS-CoV-2 infection must be considered in differential diagnosis. In this instance, there is a difference of ground-glass opacities found in CT – COVID-19 associated abnormalities localize predominantly in basal and subpleural parts of the lung, whereas pulmonary edema opacities are present in the perihilar region.[15]

The management of NPPE is based on symptomatic treatment. However, this may vary depending on patient clinical presentation and arterial blood gas results. Proper airway maintenance is a crucial first step in rescue therapy in which endotracheal intubation with ventilation support may be necessary. Although NPPE management is yet to be precisely described, some authors suggest low tidal volume ventilation in order to protect the lungs, as a means to improve the patients' condition.[16] Studies have shown that lung protective ventilation protocol of low tidal volume of 6 mL/kg of ideal body weight with a plateau pressure of less than 30 cm H_2O and high positive end-expiratory pressure (PEEP) improve clinical outcomes of patients both with and without ARDS.[17,18] It is possible to improve patient's condition with a bronchodilator.[16] Although administration of diuretics is common,[5] their effectiveness in treating NPPE does not have a strong evidence basis, since the edema is caused by high-negative intrathoracic pressure resulting in interstitial fluid shifts, not by general fluid overload.[19] Implementation of rescue therapies, which include prone positioning and extracorporeal membrane oxygenation (ECMO), should be considered.[16] There are reports of successful use of ECMO in treating severe cases of NPPE.[20] This condition, if recognized early and with proper management implemented, tends to self-resolve within 12–24 h.

5. CONCLUSIONS

NPPE is a rare, serious and difficult to diagnose complication in anesthesia practice.

It should be emphasized that under the highest risk of developing NPPE are young male patients and the most common cause is post-extubation laryngospasm.

Management is based on symptomatic treatment which should include ventilation support with low tidal volume and plateau pressure and high PEEP.

Conflict of interest

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