



Postoperative Negative Pressure Pulmonary Edema (NPPE)

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OBJECTIVE

The objective of this systematic review is to examine current published evidence regarding risk factors for, diagnosis of, and treatment recommendations for NPPE in the postoperative period.

INTRODUCTION

- NPPE often occurs during the emergence phase of anesthesia soon after the removal of the endotracheal tube or supraglottic airway
- Onset of NPPE frequently occurs within minutes of upper airway obstruction with rapid onset of hypoxemia and acute pulmonary edema
- While NPPE is a rare complication of anesthesia, it is a true post-anesthesia emergency and requires immediate identification and intervention by the anesthesia provider
- There are currently no sizeable recent clinical studies available in the literature characterizing risk factors, diagnosis, and treatment NPPE during the postoperative period
- No evidence-based clinical guidelines exist for diagnosis and treatment

METHODS

- Inclusion criteria
 - Studies from peer reviewed journal articles published from 2016-2020
 - NPPE after surgical procedure
- Exclusion criteria
 - Older than 5 years
 - Written in a foreign language
 - Pulmonary edema not in postoperative period
 - Nonhuman subjects
- Databases included: ScienceDirect, CINHAl, Ovid, MEDLINE, and PubMed
- Search terms: NPPE and anesthesia
- 220 articles screened; 11 articles reviewed after meeting inclusion criteria

REFERENCES

Available upon request

REVIEW OF LITERATURE

Source and Study Type	Patient characteristics & ASA	NPPE presentation	Treatment	Outcomes
Bhattacharya et al. (2016) Literature review with case presentation	Illustrative case presented of 25yo male taken to OR for repair of facial fractures. Preoperative evaluation normal. ASA I. No PMH.	Two episodes of biting ETT with total airway occlusion and negative inspiratory effort lasting several minutes with SpO2 85%. Immediate, copious frothy secretions in ETT. CXR BLL infiltrates. Persistent hypoxia.	Admitted to ICU with positive pressure ventilation and sedation.	Hypoxia resolved in 17h. Extubated POD1. DC home POD4.
Chen et al. (2018) Case report	22yo male, basketball player. ASA I. Percutaneous endoscopic interlaminar lumbar discectomy for back and leg pain with weakness. Otherwise normal PE and preoperative evaluation.	Extubation when conscious, spontaneously breathing, & purposeful movements. Sudden forceful respirations. HR 130, BP 155/90, RR 35, SpO2 from 98% to 65%. Production of pink, frothy sputum. Bilateral rales on PE. ABG pH 7.34, CO2 40, PaO2 71. CXR bilateral infiltrate and opacity. CT chest 2h after event with increased vascular diameter, mosaic pattern attenuation, bilateral pleural effusions.	60 min stabilization in OR. Airway kept unobstructed. FIO2 5L/min via mask ventilation. Dexamethasone, 20mg furosemide. Prophylactic cefazolin.	Patient transferred to orthopedic floor. Repeat ABG pH 7.37, CO2 48, PaO2 95. FIO2 requirements gradually decreased to room air by 24h. POD3 CXR and CT with complete resolution of infiltrate & DC home. FU 6 weeks with normal PE & CXR.
Guru, Agarwal, Pimentel, McLaughlin, & Bansal (2018) Case report	64yo male. PMH compensated liver cirrhosis, Hepatitis C, hepatocellular carcinoma, peripheral neuropathy. ASA III. Excision vocal cord papilloma.	Acute hypoxic RF immediately following extubation. PE with bilateral lung crepitus, normal heart sounds, pink frothy sputum. CXR bilateral alveolar shadows and patchy interstitial infiltrates mostly in perihilar area. ECG changes in lateral leads. Echocardiography mid-septal and anterior wall hypokinesis. Normal coronaries on angiography.	Reintubated in OR. IV furosemide. ICU – sedation. MCV, TV 6ml/kg, PEEP 7, FIO2 70%. Fluid restriction.	Respiratory status improved with resolution of pulmonary edema in 12h. Subsequent hospital course uneventful.
Hao, Basnet, Melnick, & Kim (2019) Case report	31yo male. ASA I. Smoker. No PMH or surgical history. Traumatic injury from automatic nail gun with nail lodged in distal humerus with nondisplaced linear fracture. PE and lab unremarkable.	In PACU, somnolent & required jaw lift for supraglottic airway obstruction. SpO2 70% improved to 90% with nasopharyngeal airway. At 6h – blood-tinged sputum. At 12h –persistent cough, 3 tablespoons of bloody sputum. CXR patchy bilateral infiltrates. CT chest 5 lobe ground-glass opacity with consolidation in posterior lobes. Hgb drop 14.2g/dL to 12.7g/dL. Dx with diffuse alveolar hemorrhage from NPPE.	Transferred to pulmonary critical care service. Exclusion of other differential diagnoses by extensive lab testing. Managed supportively. FIO2 requirements gradually decreased.	DC home POD2. CXR 2 week follow up with complete resolution of bilateral infiltrates.
Kuo, Duo, Su, & Huang (2020) Literature review and retrospective pilot study	Review of n=27,498 undergoing general anesthesia. 2 cases NPPE. Case 1- 46yo male ASA II, PMH asthma. Undergoing sinus surgery. Case 2- 29yo female, ASA I. Undergoing nasal surgery. Both cases with negative preoperative CXR.	Case 1 - laryngospasm after sugammadex and deep extubation. Difficult mask ventilation persisted several minutes after laryngospasm. Case 2 - patient bit ETT causing upper airway occlusion following sugammadex. NPPE defined as new onset pulmonary edema after extubation or removal of LMA.	No treatment information provided.	Cases admitted to ICU excluded from study. No outcome information provided.
Lee, Lee, Lee, Cho, & Park (2017) Case report	17 yo female. ASA I. Lateral node neck dissection. PMH papillary thyroid cancer removal 1year prior.	Extubation after adequate spontaneous respiration and confirmation of neuromuscular strength. Immediate sudden apnea and RF after extubation. SpO2 70%, lethargy. SpO2 improved with PPV. Then, copious pink frothy sputum and SpO2 90%. Coarse inspiratory rhonchi bilaterally. CXR perihilar opacities bilaterally. Emesis of pink frothy sputum x1 in PACU.	Positive pressure ventilation with venturi mask with FIO2 10L/min.	POD1 dyspnea improved, improved opacities improved on CXR. POD2 only mild right mid-lung haziness on CXR. POD6 complete resolution on CXR, DC.
Postaci, Sacan, Yilmaz, Ornek, Alay, & Gogus (2016) Case report	29yo male. ASA I. Right hand tendon repair. PE and laboratory data normal.	LMA removed without difficulty. Difficult inspiration, paradoxical chest movement, wheezing, cyanosis. SpO2 85%. 4-5min later SpO2 decreased again & hemoptysis. Bilateral rales. CXR bilateral, common interstitial infiltration.	Propofol and 100% FIO2 via face mask ventilation during acute laryngospasm. SpO2 <90% with face mask after NPPE, so non-invasive mechanical ventilation with continuous positive airway pressure initiated. Bronchodilators and furosemide 20mg IV given.	Positive pressure ventilation DC at 6h and transitioned to 2L/min FIO2 via nasal cannula. Comfortable on room air at 24h. DC home at 48h.
Raj, Quari, & Jha (2016) Case report	40yo female ASA I. Right percutaneous nephrolithotomy. PE and laboratory data normal.	Stridor after extubation with dyspnea and restlessness. SpO2 80-85%. PE – fine crepitations with occasional rhonchi. New tachycardia 120-130. ABG with hypoxia, hypercarbia, and acidosis. CXR with infiltrates.	Mask-ventilation during stridor. Morphine 6mg and furosemide 20mg IV. Head elevated. Fluid restriction. Continuous positive airway pressure x24h.	Repeat CXR 12h resolving pulmonary edema with resolution at 24h. DC POD7.
Silva, Guedes, Filho, Chaves, & Araujo, (2018). Case series	n=4 Case 1- 52yo male ASA II, for appendectomy. Case 2 – 23yo female, ASA 1, for breast reduction. Case 3- 44yo male, ASA 3 for laser nephrolithotripsy. Case 4- 7yo male, ASA 1 for reduction of humeral fracture.	Case 1 - laryngospasm post extubation with breathing against closed glottis x1min. Sudden drop Spo2 <69% after airway became patent. Pink, frothy sputum. PE- rales. BP normal. CXR normal. Case 2 - Mild upper airway obstruction post extubation. Breathed against closed glottis about 120 seconds. 1h nausea followed by dyspnea, tachypnea, psychomotor agitation, peripheral cyanosis, pink frothy oral secretions. PE rales/rhonchi Case 3 - upper airway obstruction after LMA removal. 20min later productive cough with pink, frothy sputum, hypertensive. Case 4 - laryngospasm after extubation reversed with positive pressure ventilation. 5min later with psychomotor agitation, productive cough, pink frothy discharge from mouth.	Case 1- Head elevated. 100% O2 via face mask. Case 2 – O2 via Hudson mask, head elevated. Hydrocortisone 1.5g IV, furosemide 40mg IV, 2L lactated ringers solution. Case 3- Head elevated, noninvasive ventilation with 100% O2 via face mask, IV furosemide 40mg, 25mg captopril. Case 4- reintubation with mechanical ventilation x2h then extubated.	Case 1- SpO2 92% on room air in 90min. DC POD2. Case 2- 3h in PACU then to regular floor. DC the next day. Case 3- ICU with DC in 24h. Case 4- DC at 48h.
Tsai et al. (2018) Retro-spective matched, case-control	Cases (n=16) Matched controls (n=131) without desaturation or clinical signs of pulmonary edema. ASA I-II (n=115) ASA III-IV (n=32)	NPPE defined as SpO2 <90% with witnessed signs of upper airway obstruction after removal of ETT or LMA in OR. In addition to abnormal CXR and/or cough with pink, frothy sputum.	N/A	N/A
Venkatesh, Gautam, Dutta, & Bala (2016) Case report	15yo. Asian male. ASA I. Eye and vitreoretinal exploratory surgery at outpatient surgery center. PE and labs normal.	Brief laryngospasm with paradoxical chest movements. SpO2 40%, dusky skin. Improved SpO2 followed by pink, frothy sputum. Bilateral crackles.	Suxamethonium chloride 50mg IV when unable to bag mask laryngospasm. Transferred to ICUat local hospital. Positive airway pressure. Furosemide 40mg IV & maintenance parenteral fluids.	Status returned to normal POD1.

DISCUSSION

- Patient characteristics
 - Mostly young, healthy, patients with normal preoperative examination
 - Twice as many males than females
 - Often after witnessed laryngospasm or another mechanical occlusion of the upper airway
 - A few cases occurred after sugammadex
- NPPE Presentation
 - Hypoxia; respiratory distress; adventitious lung sounds, mainly crackles and rales; production of pink, frothy sputum; and abnormal chest radiography including CXR and/or CT chest showing evidence of perihilar infiltrates and opacities. Psychomotor agitation. Two cases reported hemoptysis
- Treatments provided for NPPE varied greatly, but mostly focused on supportive care
 - Ensure airway patency usually with positive pressure ventilation via invasive or noninvasive mechanical ventilation
 - Amounts of FIO2 required and administered varied
 - Some cases reported treating with steroids, sedation, and/or elevation of head of bed
 - Some articles report diuresis and fluid restriction, while others administered IV fluids.
 - The use of bronchodilators was noted in a few of the studies but was reported as not supported by randomized trials
 - The use of steroids in NPPE was also reported as controversial and requires further research
 - Antibiotics were administered in some cases, although NPPE is not an infectious process

CONCLUSIONS

- Patient outcomes presented in the articles reviewed were largely positive
 - Data likely skewed as only one article reviewed included critically ill patients
- This review supports the need for prospective and/or randomized studies evaluating NPPE in order to develop evidence-based, standardized clinical guidelines for the diagnosis and treatment of NPPE

“The Spirit of God has made me; the breath of the Almighty gives me life”
(Job 33:4, NIV)