

Peri-operative adverse respiratory events and post-operative noninvasive ventilation

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Abstract: Postoperative respiratory adverse respiratory events (AREs) are a common phenomenon. Multiple causes contribute to peri-operative impairment of respiration and the development of postoperative AREs. AREs have been associated with poor patient outcomes and impose an unplanned burden on the medical system. The treatment of perioperative AREs should be tailored to treat the injurious processes that predominate in the case at hand. Specific characteristics of non-invasive ventilation techniques may make them particularly relevant to specific types of post-operative AREs. Future research needs to focus on identification of patients at risk for perioperative AREs and on matching of ventilation techniques to specific causes of ARE.

Keywords: Noninvasive ventilation; respiration; surgical procedures; operative; postoperative complications

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Introduction

The perioperative setting provides ample opportunity for the occurrence of postoperative respiratory adverse respiratory events (AREs). Postoperative respiratory AREs are therefore a common phenomenon. However, the post-operative setting also offers a unique platform for prevention and expert treatment of AREs. In this review the epidemiology and causes of post-operative AREs are discussed. The implications of AREs to both the patient and the medical state are presented. Examples are provided for some of the characteristics of different non-invasive ventilation techniques and their relevance to specific postoperative AREs, and future research directions on this topic are proposed.

Post-operative AREs: the extent of the problem

Post-operative hypoxemia was first identified shortly after the introduction of pulse oximetry to the peri-operative setting. An early study (n=173 patients) noted that after discontinuation of oxygen, arterial oxygen saturation levels (SpO₂) were lower postoperatively than they had been preoperatively. Hypoxemic episodes (SpO₂ ≤90% for ≥15 s) were found to occur commonly (in 41% of the patients), quite a while after discontinuation of supplemental oxygen (median 15, range, 1–100 minutes) and most were moderate to severe (SpO₂ ≥90% for ≤2 min or SpO₂ ≤85%) (1). Later studies show only slightly lower rates of postoperative hypoxemia. A prospective observational study of all adults admitted consecutively

to a single post anesthesia care unit (PACU) after elective surgery (n=340) identified AREs in 19.7% of the patients (2). Another prospective observational study of patients after minimally-invasive colorectal surgery (n=85) identified prolonged cumulative hypoxemic times in the first postoperative day; 36% of the patients had an SpO₂ of 90% or lower for >1 hour (4.2% of the day) (3). These studies relied on nursing records. Monitor records suggest the extent of the problem may be much greater. In a two-center study conducted on patients >45 years old after noncardiac surgery (n=833), analysis of 48 hour continuous (1-minute interval) pulse oximetry recordings showed that more than a third of the patients (37%) had at least one hypoxemic episode (smoothed SpO₂ <90%) lasting ≥ 1 hour and about one in ten (11%) had at least one hypoxemic episode lasting \geq 6 hours. An SpO₂ <90% was observed in one of every five patients (21%) for an average 10 minutes per hour, and in one of twelve patients (8%) for an average 20 minutes per hour. Strikingly, nursing records captured only 5% of these episodes with 90% of the episodes with SpO₂ <90% for ≥ 1 hour being missed (4).

Causes and risk factors for postoperative hypoxemia and AREs

Impairment of oxygenation may occur secondary to an increase in the proportion of either the pulmonary circulation shunted via airways uninvolved in gas exchange (shunting) or the tidal volume ventilating airways with poor or no pulmonary circulation (dead space). Impaired oxygenation in the peri-operative period is probably mostly caused by an increase in shunting; airway closure occurs due to multiple causes in the perioperative period. Alveolar collapse occurs during prolonged apneas (5), which may occur during either induction (6) or emergence from anesthesia. Cephalad displacement of the diaphragm, particularly in dependent lung areas, occurs during supine and Trendelenburg positioning (7-9), often resulting in atelectasis. Diaphragmatic displacement may be exacerbated by surgical retraction of the upper abdomen, rib-cage or even lung during specific types of surgery (10). Intraabdominal gas insufflation also adversely affects respiratory system compliance, pulmonary blood flow and gas exchange (11-14).

The occurrence of postoperative hypoxemic episodes is also strongly related to the use of specific medications. Although some recent literature suggests that the severity of atelectasis does not differ between relatively healthy

Journal of Emergency and Critical Care Medicine, 2019

patients ventilated with an FiO₂ of 0.3 or an FiO₂ of 1.0 intraoperatively (15), absorption atelectasis may become clinically meaningful in the presence of a preexisting significant ventilation-perfusion (V/Q) mismatch (16). Early studies tied the occurrence of peri-operative hypoxemia to a high American Society of Anesthesiologists (ASA) physical status class; prolonged surgery and preoperative mean SaO₂ values $\leq 95\%$ (1). High ASA physical status and low preoperative SpO₂ values probably reflect the presence of cardiac and/or respiratory comorbidities which increase V/Q mismatch. Furthermore, a systematic review and metanalysis of the literature suggests that intraoperative inspired oxygen fraction (FiO₂) is related to postoperative gas exchange in patients undergoing general anesthesia. In patients ventilated with a high intraoperative FiO₂, the postoperative PaO₂ was lower (mean difference -4.97 mmHg, 95% CI: -8.21 to -1.72, P=0.003), the alveolar-arterial oxygen gradient was higher and there was more atelectasis (17).

The use of muscle relaxants (2,18-21) and opiates (22,23) has also drawn attention with regards to their association with pulmonary complications. Nine papers have studied the relationship between residual neuromuscular blockade and pulmonary complications in the PACU. The most significant association was found between neuromuscular blockade and an increased incidence of hypoxaemia. However, the threshold for defining residual neuromuscular blockade differed between the studies (24). Finally, low core temperatures and an overall decreased level of consciousness have also been associated with increased rates of post-operative pulmonary complications (25).

Adverse post-operative respiratory events are related to post-operative outcomes and costs

One fourth to one half of the adverse events occurring in the PACU are related to respiratory/airway issues (26,27). Post-operative adverse events may occur in both high and low risk patients. A retrospective study of 701 AREs occurring in 364 patients in the PACU noted that more than half of the patients had an ASA physical status of I or II (26). Half of the patients with a post-operative adverse event receive a higher level of postoperative care than initially planned (26).

Prolonged episodes of hypoxemia and hypopneic episodes after surgery have been tied to postoperative increases in troponin, tachycardia and cardiac ischemia (3,28). A retrospective, matched-cohort study of 253 AREs occurring in 156 patients in the PACU, showed that indeed most such events involve hypoxia (55.73%) and respiratory depression (27.67%) (29).

AREs have also been shown to prolong PACU length of stay (LOS) (81.65±54.79 vs. 38.89±26.09 min) and PACU costs (\$31.99±17.80 vs. \$18.72±8.39). In one study, even after matching, the odds of prolonged PACU LOS after an ARE was 17.58 (95% CI: 4.11-75.10; P<0.001) (29). In another retrospective study, continuous SpO₂ monitoring data from the PACU stay of 125,740 patients was used to evaluate the relation of postoperative episodic hypoxemia with intubation within three days of surgery and hospital resource utilization. The models were adjusted to patient conditions, procedural, and anesthesia risk factors. O₂Sat values lower than 89% occurred in 14.3% of the patients. O₂Sat <89% (P<0.001) and oxygen therapy for >60 min in the PACU (P<0.001) were both associated with doubling of the odds of intubation. Propensity matched patients (n=37,354) were used to study the relationship between postoperative oxygen requirements and postoperative resource utilization, showing a significant increase in hospital charges (day of surgery, respiratory charges and total charges), hospital LOS and the rates of reintubation and use of invasive or non-invasive ventilatory support (30).

Non-invasive support techniques

The high flow nasal cannula (HFNC) is an open gas delivery system which enables delivery of oxygen at flow rates up to 40 (Vapotherm[®]) or 60 (OptiflowTM) liters per minute. The gas is delivered heated to 33–37 °C and humidified up to 100% in order to improve patient comfort. The user interface for adult patients is relatively simple; clinical settings include only the percent of oxygen delivered and required flow rates. Animal models show that use of the HFNC generates a mild increase in nasopharyngeal and tracheal pressures (31,32). Experiments in healthy adults demonstrate generation of pharyngeal pressures ranging between 0.3 to 9.7 cm H₂O, dependent on subject sex, opening *vs.* closure of the mouth and the amount of flow administered (33). Thus limited positive end expiratory pressure is to be expected with this mode of support.

The HFNC has no safety features; neither device has alarms for patient disconnection or apnea. While the simple user-device interface encourages use of the HFNC in less monitored environments, this generates major concerns for patient safety as long as tools to identify post-operative high-risk patients are lacking.

Continuous positive airway pressure (CPAP) ventilation and non-invasive positive pressure ventilation (which combines CPAP with inspiratory positive airway pressure) are time-tried, semi-closed methods of ventilatory support. Devices that provide CPAP or NIPPV are capable of generating positive end expiratory pressures according to the settings determined by the user, thereby preventing alveolar collapse throughout the respiratory cycle (34). Specific maneuvers may also be used to recruit atelectatic lung, although gas flow may inadvertently be directed to lung zones with greater compliance that are already open (35). The use of semi-closed ventilation devices requires a greater understanding of respiratory physiology and specific ventilation skills for selecting the ideal patientdevice interface and for determining device settings. It therefore remains questionable whether the success rate observed with the use of such devices in randomized clinical trials performed in expert centers can be extrapolated to other settings.

Non-invasive respiratory support in the perioperative period

Non-invasive respiratory support may be provided either preventively or therapeutically in the perioperative period. Most studies of non-invasive respiratory support in this setting have been performed on patients with some impairment of oxygenation (i.e., therapeutically). Pulse oximetry monitoring is traditionally employed to allow early diagnosis of hypoxemia in the PACU. Pulse oximetry was thought to enable timely oxygen administration, thereby preventing the occurrence of AREs. However, a systematic review of the literature published by the Cochrane group identified only five RCTs comparing pulse oximetry to no pulse oximetry in the perioperative period (n=22,992). The studies identified were of poor quality. They showed that the incidence of hypoxemia in the PACU is indeed lower with pulse oximetry (X1.5-3.0 less). However, the only study that also assessed the associated rate of postoperative complications, showed no difference in cardiovascular, respiratory, neurological or infectious complications, hospital LOS, transfers to an ICU or in-hospital deaths with or without pulse oximetry monitoring (36).

The paucity of literature showing benefit from monitoring probably stems from an inherent unease towards studying the value of "blinded" versus "unblinded" treatment. However, monitoring does not ensure adequate treatment; signals may remain unrecognized and even when recognized, may remain suboptimally treated. This may well be the case with oxygen delivery in the PACU. Traditionally, conventional oxygen therapy (i.e., face mask with an oxygen flow of \leq 15 liters per minute) is the first line of treatment for most post-operative cases. However, the degree to which various methods of oxygen delivery are capable of improving perioperative hypoxemia may depend on the degree of predominance of the various causes of hypoxemia.

Following upper abdominal surgery, the relative contribution of the abdominal compartment to the respiratory effort decreases by almost 50% (37). The surgical incision site plays an important role in determining the severity of diaphragmatic inhibition (38). It is therefore unsurprising that following abdominal surgery, NIPPV and helmet CPAP are more effective than conventional oxygen therapy in preventing the development of secondary infections and reintubation and in decreasing ICU LOS (39,40). This also explains why use of the HFNC in this population yields similar outcomes to conventional oxygen therapy (41). As noted above the HFNC generates relatively low positive end expiratory pressures. This mode of support is therefore not likely to prevent alveolar collapse or recruit derecruited lung areas. Yet there is often need to counteract lung derecruitment with positive end expiratory pressures after extubation in the presence of increased intraabdominal pressures in obese patients (42) or a need to recruit atelectatic lung after laparoscopic (43,44) and gastric bypass (45) surgery. With regards to frail elderly patients; those undergoing general surgery may gain no benefit at all from any non-invasive respiratory support unless they undergo preoperative respiratory muscle training (46).

Coronary artery bypass surgery patients are typically prone to ischemic complications. Two single center studies (47,48) and one multicenter study (49) compared the outcomes of patients after cardiac surgery using two non-invasive respiratory support techniques. One single center study compared CPAP to conventional oxygen therapy (47), another compared CPAP to NIPPV (48) and the multicenter study compared CPAP to HFNC (49). It would seem that any type of respiratory support is better than conventional oxygen therapy for improving oxygenation (48) and overall comfort (47) but CPAP and HFNC yield similar rates of intubation and mortality (49). Interpreting these results is difficult given that these studies have all focused on respiratory outcomes and none reported cardiac complications.

Pulmonary hypertension and right ventricular failure

remain major concerns following lung resection. Hypoxemia and hypercarbia are common in these patients, many of which may also have had abnormal partial arterial pressures of oxygen and carbon dioxide prior to surgery. Ongoing hypoxia may exacerbate pulmonary hypertension. The only study that compared CPAP to conventional oxygen therapy in this population showed a much greater increase in PaO₂ with CPAP (from 72±23 to 122±61 mmHg) than with conventional oxygen therapy (from 68±14 to 93±37 mmHg) and was terminated early when higher rates of endotracheal intubation and death were observed with conventional oxygen therapy (50). Also, animal models of one lung ventilation show a decrease in pulmonary blood flow and in V/Q mismatch with increased PEEP (51). Both mechanisms support preferring CPAP to conventional oxygen therapy for treatment of post-operative hypoxemia in patients after lung resection. In the only existing study on the topic, the number of patients was small (n=48) and no information was provided regarding the effect of ventilatory support on either pulmonary artery pressures or the V/Q ratio.

Post-operative administration of both excessive and insufficient amounts of oxygen may be damaging. An ongoing trial (registered NCT02546830) intends to address whether automated administration of O_2 is better than conventional administration of O_2 after major abdominal or thoracic surgery for preventing complications (52).

Summary

Postoperative AREs may arise from multiple processes that impair lung function. Such complications have been associated with poor patient outcomes and impose a significant unplanned burden on the medical system. Ideally treatment of perioperative respiratory deterioration should be tailored to treat the injurious processes that predominate in the case at hand. For example, respiratory muscle weakness should be overcome with intense bedside training, lung derecruitment will respond to noninvasive ventilation techniques that can reverse alveolar collapse and maintain a positive airway pressure through the ventilatory cycle, and the response of the pulmonary vasculature to an increase in intrathoracic pressure and to blood gas composition should be taken into consideration when treating extreme ventilation perfusion mismatch. Additional studies on the effects of non-invasive ventilation techniques on lung volumes, recruitment and perfusion and on the cardiovascular system after specific types of surgery would greatly enhance our ability to tailor post-operative

Journal of Emergency and Critical Care Medicine, 2019

non-invasive ventilation to the post-operative needs of our patients.

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Footnote

Conflicts of Interest: Sharon Einav - Patents with Medtechnica, consulting for MSD and Medtechnica, travel cost reimbursements from Zoll, Medtechnica and Diasorin, lecture for Fisher & Paykel with no travel cost reimbursements or financial renumeration, participation in multicentre trials run by Artisanpharma, Eisai and Astra Zeneca. Marc Leone - Lectures for MSD, Pfizer, Octopharma, Aspen, Orion, 3M. Consulting for Amomed, Aguettant, travel support from LFB.

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Journal of Emergency and Critical Care Medicine, 2019

Page 6 of 7

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Journal of Emergency and Critical Care Medicine, 2019

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