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Prevention of Postoperative Acute Lung Injury (ALI) - The Anaesthetist Role

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Abstract

Postoperative pulmonary complications such as Pneumonia, Acute Lung Injury (ALI), Acute Respiratory Distress Syndrome (ARDS) substantially increases the risk of morbidity, mortality, length of hospitalisation and financial burden. Risk factors can be broadly categorized into patient related, procedure related, anaesthesia related and post procedural care related. The prevention of postoperative ALI requires a comprehensive approach that includes preoperative risk stratification and optimizations, intra-operative lung protective strategies that includes lung protective ventilation, regional analgesia technique, avoiding excessive fluid, minimising blood and blood product transfusion, control oxygen therapy. Postoperative part is equally important and required multidisciplinary multi-model approach that includes- fast tracking protocol for enhanced recovery, good analgesia using multi-model therapy to minimised systemic opioid, vigilance monitoring, physiotherapy and lung expansion manoeuvres including use of non-invasive ventilation in selected patients and other supportive care such as nutritional support, glycemic control, selective naso-gastric drainage, thrombo- prophylaxis and early empirical antibiotic therapy in suspected infection and sepsis.

Keywords

Postoperative, Pulmonary complications, Acute lung injury, Lung protection, Fast tracking, Multi-model

Introduction

Anaesthesiologists are well versed with changes in respiratory mechanics with anaesthesia and surgery and play a great role in the management of both normal and injured lung in the perioperative setting. The role of anaesthesiologist in the peri-operative setting is to identify and optimised existing lung pathology and prevention of further lung injury while protecting the normal lungs from various potential injurious factors such as fluid, ventilation, unnecessary blood transfusion. Varieties of pulmonary injury or complication may developed in postoperative period ranging from simple atelectasis to frank pneumonia with severe Acute Lung Injury (ALI) or Acute Respiratory Distress Syndrome (ARDS) accounting for up to 7% in thoracic surgery [1]. Postoperative pulmonary complication not only leads to increased hospital stay, it accounts for substantial increase in morbidity and mortality in relation to anaesthesia and surgical outcome [2-5].

Proper preoperative optimization of the clinical conditions and satisfactory employment of intra operative proposed strategies have considerably reduced the post operative lung injuries.

In the immediate post operative period primary form of ALI strictly depends upon the systemic inflammatory response induced by the surgical and anesthetic events which should be distinguished from a secondary ALI, usually delayed and showing an onset from 3 to 12 days after surgery. The secondary ALI is triggered by several postoperative complications including sepsis, pulmonary embolism, gastric content aspiration, and pneumonia [6]. It is essential to understand that although ALI is a diffuse & heterogeneous process, and not all lung units are affected equally: normal and diseased tissue may exist side-by-side. The patho-physiology of postoperative ALI/ARDS involves alveolar-capillary endothelial injury or dysfunction with alteration in innate immune system, generation of reactive oxygen radicals, activation of coagulation etc. [7,8] resulting in fluid flooding into alveoli impairing gas exchange leading to hypoxaemia and respiratory failure. Postoperative ALI/ARDS has high mortality rate exceeding 45% in certain surgical populations [4,5]. Importantly patient co-existing pathology, surgical injury, medications and various perioperative health care delivery factors such as ventilator strategy, fluid-balance, physiotherapy, transfusion therapy might play crucial rule in many form of postoperative ALI [8,9]. The preventive aspect of ALI has been largely neglected or not emphasised in literatures, rather focused on cause and treatment of ALI. This might be because studies on ALI are typically performed in the critical care setting with already established lung injury and are beyond the potential preventive strategy. The peri-operative period is an important and attractive period where many clinical and therapeutic strategy can be applied as preventive approach for postoperative ALI. Early diagnosis

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and adequate postoperative treatment of the patients, who develop hypoxaemia or signs of increased work of breathing, by any possible intervention that can decrease the incidence of ALI, or help patients to better cope with the condition once it happens is mandatory to reduce the lung injury and the postoperative mortality. Despite the severity of the postoperative ALI, some cases of ALI are self-limiting where further investigations on the patho-physiological mechanisms involved are needed. The unexpected spontaneous resolution of ALI suggests the implication of a sort of endogenous modulating system that is actually still unknown. In this contest the role of the adenosine has been recently evaluated. Some studies have reported the possible positive effects of the adenosine in protecting the lung from the results of MV [10,11].

Aim of this review article is to highlight the importance of predicting adult patient at risk of postoperative pulmonary complications and anaesthetist interventions that might prevent major complications like postoperative ALI/ARDS. This article is mainly focus on the patients undergoing thoraco-abdominal procedures excluding paediatric patients.

General Anaesthesia and Pulmonary Physiology

General anaesthesia causes loss of muscle tone-resulting in loss of diaphragmatic and intercostal muscle power, this promote the reduction in lung volume and onset of atelectasis leading to ventilation-perfusion abnormality. More than 90% patients under general anaesthesia developed some form of atelectasis [12,13]. The mechanism responsible for atelectasis are broadly divided as compression atelectasis, absorption atelectasis and loss of surfactant atelectasis [14,15]. Compression atelectasis is caused by change in chest wall mechanics induced by anaesthesia such as reduction in lung volume, change with patient position, effects of BMI, surgical retraction and compression by other means. Absorption atelectasis is cause by administration of high inspire oxygen which displaces the nitrogen in the alveoli, if the alveolar unit gets obstruction proximally, the oxygen gets absorbed easily leaving behind collapse alveoli [12,16]. General Anaesthesia impaired the production of surfactant resulting in loss of surface tension in alveolar lining fluid promoting alveolar collapse [17].

The development of atelectasis is a significant factor in the pathogenesis of postoperative pulmonary complications such as hypoxaemia, pulmonary infection, postoperative ALI or ARDS [18]. The atelectasis induced by general anaesthesia may persist beyond 24 hrs in more than 50% of normal subjects and can persist up to one week [19]. Postoperative atelectasis can be asymptomatic or it may manifest as increased work of breathing and hypoxaemia.

The physiological effects of general anaesthesia are more evident in patients undergoing thoracic or upper abdominal surgery which causes reduction in vital capacity by 50% and FRC by 30%. these effects are caused by compression atelectasis due to diaphragmatic dysfunction, pain and splinting [20]. Following upper abdominal and thoracic surgery, the respiratory mechanics changes, patients tend to breathe small tidal volume with rapid rate to maintain the adequate minute ventilation (rapid shallow breathing) and poor coughing effort due to dynamic pain. This altered breathing patterns in addition to the residual effects of anaesthesia, impair muco-cilliary clearance and coughing contribute to the retention of secretion and postoperative pneumonia. These effects are complicated by patient co-existing general debility or pulmonary illness or conditions such as smoking and acute physiological alteration in fluid electrolyte balance. Numerous studies and systemic review have been conducted to quantify the different patient and procedure related factors for predicting the postoperative pulmonary complications [11,21-26]. Most commonly associated risk factors can be divided into patient related factors, surgical procedure related; anaesthesia related and post procedural care.

Patient Related Factors

Among the patient related factors some are modifiable or optimizeble. The important patient related factors are as follows

Age

Elderly patients have multiple associated co-morbid conditions, decreased overall organ reserve, altered physiology of cardio-respiratory system, general disabilities etc. Many authors don't consider age as a predictor of increased postoperative pulmonary complications. Few studies has shown age as an independent predictor of postoperative pulmonary complication [21,27].

Obesity

Obesity is known to have many pulmonary issues such as sleep apnoea, atelectasis, hypo-ventilation syndrome, severe associated with pulmonary hypertension, cor-pulmonale and hypercapnic respiratory failure. Many studies suggest obesity as risk factors for pulmonary complications [28-30], but some studies failed to show correlation between obesity and postoperative pulmonary complications [31-33]. Recent studies in cardiac surgery have shown that Body Mass Index (BMI) more than 35 were associated with higher pulmonary complication but not in patients with BMI less than 35 [34,35]. Patients with BMI of more than 40 have 30% chances of developing postoperative atelectasis and pneumonia after abdominal surgery [36].

Obstructive Sleep Apnoea (OSA)

Patients with OSA are associated with increased rate of postoperative pulmonary complications notably desaturation, atelectasis, respiratory failure, ALI/ARDS [37,38]. Rate of postoperative pulmonary complications are relatively low irrespective of severity of OSA when it is diagnosed pre-operatively. This implies that with proper preventive strategies postoperative pulmonary complications can be reduced in severe OSA also [37]. Recent survey by Auckley and Bolden has shown that large number of surgical patients (24-41%) are at risk of undiagnosed OSA during perioperative period [39]. Patients with sleep apnoea are at risk of development respiratory impairment leading to hypoxaemia, hypercapnia, negative pressure pulmonary oedema etc. These patients are also at risk for aspiration pneumonia and ARDS [39].

Personal habit: Smoking and alcohol

Current smoking is an independent risk factor (more than 2 fold) for development of postoperative ALI even without the evidence of chronic obstructive pulmonary disease and this risk remain elevated up to 1 year after smoking cessation [21,40]. Smoking have multiple effects on different organs and its main effects on pulmonary system are influenced by level of carbo-monoxide, nicotine, decreased mucocilliary clearance, increased mucous production and other elements capable of inducing inflammation and oxidative stress. (30) Patient with alcoholism are prone for variety of postoperative pulmonary complications including ALI, ARDS [3,41].

General health and immunity

General condition and overall health status also predict pulmonary risk. Poor functional status, general debilitated state, low albumin, significant weight loss are also some of the independent risk factors for postoperative complications. Patients with immune compromised state because of drugs any disease process are at risk for postoperative pneumonia and respiratory failure [21].

Obstructive lung diseases

Patients with Chronic Obstructive Pulmonary Disease (COPD) and Bronchial Asthma are associated increased risk of bronchospasm, hypoxaemia, hypercapnia, inadequate cough, atelectasis, pneumonia and ALI/ARDS in perioperative period [42-44]. For COPD there is no absolute prohibitive value of pulmonary function test that is absolute contraindication for surgery. Patients who are symptomatic, have poor cough or exercise capacity or have acute exacerbation should be optimised before taking as elective surgery. Well control Bronchial Asthma does not appear to have increased risk but sub-optimal control of asthma does pose a risk for pulmonary complications [45].

Other pulmonary diseases

Pulmonary hypertension has been recognised as independent predictor of perioperative complications after cardiac surgery [46,47]. Although it is not included as independent risk factor in non-cardiac surgery, presence of pulmonary hypertension is associated increased perioperative cardiac and pulmonary complications such as congestive heart failure, haemodynamic instability, pulmonary oedema, sepsis; respiratory failure, ALI/ARDS [48,49].

Interstitial Lung disease also poses increased risk for postoperative pulmonary complication. There is an increased risk of exacerbation of fibrosis following thoracic surgery. Low forced vital capacity, low diffusing capacity, ongoing exacerbation at the time of surgery and larger extent of resection have all been associated with postoperative exacerbation [50].

Recent or ongoing respiratory tract infection including bronchitis, pneumonia do increased the risk of postoperative pulmonary infection, atelectasis, ALI/ARDS. Patient with ongoing or recent attack of respiratory tract infection, it is recommended to treat the underlying infection before proceeding with an elective surgery [51].

Surgical Procedure Related Risk Factors

Surgical Lung Injury Prediction 2 (SLIP-2) model was used to predict the pulmonary complication (ARDS) in high risk patients in a multi-centric cohort analysis found that SLIP-2 model can help in predicting postoperative ARDS in high risk surgical patients [52]. Nine independent predictors of ARDS were identified; sepsis, high-risk aortic vascular surgery, high-risk cardiac surgery, emergency surgery, cirrhosis, admission location other than home, increased respiratory rate, FiO2 greater than 35% and SpO2 less than 95%.

Surgical site and duration of surgery

The distance of surgical incision site from the diaphragm is inversely related to the postoperative pulmonary complications. Incidences of pulmonary complication are highest in aortic aneurysm repair, followed by cardio-thoracic and upper abdominal surgeries, whereas, the lower abdominal and peripheral surgeries were associated with low incidence of pulmonary complications [21]. Regarding the duration, surgery lasting longer than 3-4 hrs are associated with higher incidence of pulmonary complication (40%) compared to surgery lasting less than 2 hrs (8%) [21].

Invasiveness of surgical procedure

Minimally invasive surgery or laparoscopic techniques are associated with less postoperative pain, early ambulation and less chances of postoperative complications [53-55].

Thoracic surgeries

Major thoracic surgery are associated with local trauma and or systemic inflammation such as in cardiopulmonary bypass [55,56]. Postoperative pulmonary injury depends not only on the direct parenteral damage due to manipulation or resection, but also on the pulmonary manifestation of systemic inflammatory response. Systemic inflammatory mediators cause damage to both capillary and alveolar endothelial disrupting the alveolar-capillary barrier, impairing gas exchange and causing extra-vascular fluid accumulation [6]. This extra-vascular water accumulation is the hallmark of ALI [57]. The main predictors of postoperative ALI in cardio-thoracic surgeries are pneumonectomy, fluid overload, single lung ventilation, cardiac surgery involving cardiopulmonary bypass (CPB) [6,10,58-61].

Anaesthesia Related Risk Factors

Anaesthetist has a great role in protection of injured lung or prevention of normal lung injury during the perioperative period. Despite the advancement in surgical and anaesthetic techniques, the incidences of postoperative ALI is remarkable. Proper Anaesthetic management can prevent, cause or exacerbate or ameliorate most of these injuries.

Preoperative preparation strategy

Smoking cessation: Smoking is a risk factor for postoperative pulmonary complications. Abrupt cessation of smoking can inhibit coughing and retention of secretion which leads to small airway obstruction. Ideally smoking should be stopped 8 week prior to undergoing surgery, less than 8 week abstinence may be associated with higher incidence of pulmonary complication than those who continued to smoke as evident from Warner et al study [62]. However, not all study support the observation of Warner et al. A systemic review by Theadom and Cropley who included 12 studies including the study of Warner et al concluded that smoking cessation should be pursued in most patients even very close to time of surgery. Although, longer the abstinence period, the greater reduction in risk of pulmonary complications [62]. Patients should be encouraged to abstain from smoking regardless of the time remaining before surgery [63]. Use of nicotine replacement therapy, bupropion and varenicline may be helpful to keep patients abstain from smoking and should be used.

Obstructive airway disease: Patients with obstructive airway disease should be aggressively treated to achieve the best possible baseline function. As preoperative strategy, smoking cessation, bronchodilator and steroid, hydration, antibiotic and chest physiotherapy may help to optimised the underlying condition. Use of steroid in perioperative period in patients with COPD is debatable, some studies have shown a definitely better outcome [64], and whereas some other studies the outcome was doubtful [65]. Use of steroid therapy should be individualised based on patient current medical status and planned operative procedure. For patients with bronchial asthma and having persisting symptoms with peak flow rate and FEV1 less than 80% of predicted, perioperative use of steroid is recommended [66].

Pulmonary training and patient education: Inspiratory muscle training for 2-4 week prior to surgery for high-risk operations such as abdominal aortic aneurysm repair, CABG, have shown a benefit in the form of decreased of atelectasis and other pulmonary complications [67,68]. Few studies have demonstrated that intense inpatient pulmonary rehabilitation program significantly improved exercise tolerance and operability (lung resection) in comparison to their baseline status [69-71]. Patient education and counselling explaining the benefit of lung expansion, deep breathing, coughing and incentive spirometry have a great role for prevention and reduction of lung atelactasis and other pulmonary complications.

Anaesthetic technique

There are inconsistent data regarding pulmonary complication with spinal/epidural anaesthesia in comparison to general anaesthesia, while some reporting no difference [72] whereas, other studies found high rate of pulmonary complication in the form of postoperative respiratory failure in patients undergoing general anaesthesia compared with spinal or epidural anaesthesia [73,74] patients who received general anaesthesia combined with neuraxial block for postoperative analgesia, found to have lower incidences of postoperative pneumonia and respiratory failure in comparison to those patients who receive parenteral opioid for postoperative pain [75,76]. These results suggest that addition of neuraxial anaesthesia rather than avoidance of general anaesthesia may be the key to reducing pulmonary complications.

Type of anaesthetic drugs

Though volatile anaesthetic inhibits hypoxic pulmonary vasoconstriction that might leads to intra-operative ventilation-perfusion mismatch resulting in arterial hypoxaemia. The hypoxic effects of volatile anaesthetic is more likely through impairment in haemodynamic due to myocardial depressant and vasodilatation resulting in hypotension, low cardiac output, tachycardia [77]. There is little evidence in clinical practice regarding the effects of inhaled or intravenous anaesthetic on pulmonary function or lung injury and type of anaesthetics use does not significantly impact intra-operative

oxygenation [6]. Long acting agent neuromuscular blocking drugs like pancuronium, there might be residual effects in postoperative period which may promote atelectasis or chances of pulmonary aspirations. Short or intermediate acting muscle relaxant should be preferred over long acting ones.

Mechanical ventilation

The role of mechanical ventilation in the development on postoperative ALI has been debated for years. The goal of mechanical ventilation is to provide adequate oxygenation and elimination of carbon-di-oxide with minimal pulmonary complication (atelactasis, barotrauma, oxidative damage). Conventional ventilation involved high tidal volume (10-12 ml/kg) which might show to have better gas exchange and intra-operative mechanics [78]. Recent focus has been shifted to protective lung ventilation in the form of low tidal volume with high PEEP, recruitment manoeuvres, pressure control ventilation, lowest possible FiO2 to provide the desire goal of mechanical ventilation. Aggressive mechanical ventilation has been recognised as one of the important risk factors for postoperative ALI [6,10,59]. Use of small tidal volume (6-8ml/kg) might protect the lung from mechanical insult of ventilation, reducing extra-vascular water accumulation and provides adequate arterial oxygenation [59]. Alveolar hyperinflation with cyclic stretching in prolonged mechanical ventilation may trigger lung injury [6,79] which is complicated by high inspired oxygen which promotes the production of free oxygen radical and other inflammatory bio-markers that ultimately causes disruption of alveolar-capillary barrier, a protein rich fluid then accumulates in the interstitial space, worsening the respiratory parameters due to gas-exchange disturbance [10,59].

Gajic et al. conducted a study in ICU set up with normal lung who were ventilated with conventional mode of mechanical ventilation, reported 24% incidence of ALI within 48 hrs of initiation of ventilation [80]. The main risk factors for ALI were use of large tidal volume, restrictive lung disease and blood product transfusion. Use of low tidal volume seems to be protective in those patients without pre-existing lung injury and required long term ventilator support [81,82].

The IMPROVE trial, which was conducted on 400 patients with intermediate to high risk factors for pulmonary complications undergoing major abdominal surgery to evaluate the effects of Intra-operative Protective Ventilation (IMPROVE) in the form of low tidal volumes, PEEP and recruitment manoeuvres on the pulmonary and extra-pulmonary outcome in comparison to standard practice of non-protective ventilations. As compared with a practice of non-protective mechanical ventilation, the use of a lung-protective ventilation strategy in intermediate risk and high-risk patients undergoing major abdominal surgery was associated with improved clinical outcome and reduced health care utilization [83]. However, the use of short term low tidal volume lung protective strategy for low risk patients has any benefit or not is not yet been proved through randomized control study [84]. Although some studies do suggest beneficial effects of low tidal volume lung-protective strategy even for short duration procedure for normal lungs [85-87].

A meta-analysis of 20 studies (n=2822) by Neto et al. on the use of low tidal volume ventilator strategy either for short or long term in critical care or operative setting in patients who do not have ARDS found that protective ventilation with low tidal volume was associated with better clinical outcome irrespective of duration of mechanical ventilation [88].

A recent meta analysis on the intra-operative lung protective ventilation in patient with normal lung was done by Tao et al. They included 4 high quality studies. The main finding in that meta-analysis was that lung protective ventilator strategies initiated at the onset of ventilation can reduce the incidence of atelectasis and pulmonary infection in surgical patients. However such protective ventilator strategies did not reduce the incidence of ALI, all-cause mortality or length of hospital or ICU stay [89].

The role of protective lung ventilation as evidenced from literatures is more useful in setting of Trauma, Sepsis, high risk surgery, multiple surgeries. There is no evidence of any harm in study with low tidal ventilator strategy in normal healthy lungs. Infect the protective lung ventilator with low tidal volume (4-8 ml/Kg) and ideally 6ml/Kg predicted body weight and it is more physiologically normal for healthy person. However, patients with obstructive disease the ventilator strategy should be modified to prevent dynamic hyperinflation.

One lung ventilation: Postoperative ALI after one lung ventilation in thoracic surgery is a distinctive entity, four independent factor for primary ALI, high intra-operative ventilation pressure, excessive intravenous fluid replacement, pneumonectomy and preoperative alcohol abuse are associated with postoperative ALI after thoracic surgery [6,90]. The incidences ranges from 2-4% after pneumonectomy with onset 1-3 days post surgery with mortality 25-50%, although ALI occur after lobectomy or segmentectomy, it has lower incidence and much lower mortality and it tends to affect the non-operative i.e. ventilated lung [91].

Transfusion Related Acute Lung Injury (TRALI)

Transfusion Related Acute Lung Injury (TRALI) is a recognised entity and cases has been occurring in the perioperative period [92,93]. Anaesthesiologists are routinely involved in Perioperative blood or blood product transfusion. It is also known by pulmonary hypersensitivity reaction, allergic pulmonary oedema, noncardiogenic pulmonary oedema and leukoagglutin reaction. The diagnosis of TRALI is basically a diagnosis of exclusion, Bilateral ALI associated within 6 hrs of blood or blood product transfusion after excluding the other possible causes of ALI [94]. The patho-physiology of TRALI is not yet clearly been understood, most accepted model being immunogenic injury where leucoagglutinating antibodies in the transfused plasma binding to recipient neutrophils which become activated and are subsequently sequestered in the lung activating complement and release of other inflammatory mediators resulting in endothelial damage, capillary leakage and ALI. The second postulated mechanism is that some biologically active mediator is blanked blood interact with lung tissue [95-98]. A delayed form of TRALI has been recognised that developed 6-72 hr after transfusion and is more apparent in critically ill or multiple trauma patient and is associated with high mortality rate [99]. Recently, antibodies directed against human Leukocyte Antigen (HLA) and Human Neutrophil Antigen-3a are implicated in majority of TRALI [100,101].

TRALI can occur with any blood component therapy, highest being the larger plasma containing component such as Fresh Frozen Plasma (FFP) and Platelet [98,102] occurrence of TRALI can be prevented by using single-donor plasma and or pooled human plasma inactivated by solvent detergent method [103]. TRALI can be largely prevented by applying preventive measure that reduces the HLA and HNA antibodies in blood component. Male donor or nulli-parous female donor has lower anti HLA and HNA antibodies. These measures include proper donor selection, increased haemovigilance system effectiveness, technique to reduce plasma component in cellular blood component (PRBC) and restrictive transfusion strategy, screening for anti HLBA and HNA antibodies in high risk donor [100,104,105].

By applying these preventive measures, keeping the appropriate transfusion strategy and early recognition of the clinical symptoms and to undertake therapeutic measure are the key to reduce the morbidity and mortality from the TRALI.

Perioperative fluid and ALI

Anaesthesia and surgery are associated with alterations in haemodynamic, metabolic, endocrine and immunological functions, which has considerable effects in normal fluid balance and distribution. These changes alter the capillary permeability and promote transfer of intra-vascular fluid to interstitium. Based on this theory, anaesthesiologist tends to infused large volume of intravenous

fluids during the perioperative period. However, recent emerging data show that not only the amount of intravenous fluid, the type of fluid and timing may also affect the postoperative outcome. Among the different organs, the effects of excessive fluid are more evident in the lungs, which may present in the form of pulmonary oedema compromising gas exchange and making the patient more susceptible to infections leading into pneumonia, ARDS [105]. There is no universal or accepted definition of optimal fluid. There are varied regimens of fluid replacement without a uniform definition of what is restrictive or liberal fluid during the perioperative period [106-108]. There is still no clear agreement on the perioperative fluid therapy. Rather a third category apart from liberal Vs Restricted has emerged as Goal directed therapy and is becoming more popular. The idea of goal directed therapy is to individualise the fluid therapy based on feedback of clinical observation and haemodynamic parameters change in response to fluid loading [106].

Direct association between perioperative liberal fluid administration and development of postoperative acute lung injury (ALI/ARDS) has been shown by many studies [6,109,110]. Alam et al has demonstrated a significant association between increased fluid administration and perioperative primary lung injury with Odd Ratio (OR 1.2 (1-1.4), P=0.02) for every 500 ml excess fluid administration [111]. several other studies were done on liberal Vs restrictive fluid strategy but many of these analysis were limited in that fluids were not directly assess against postoperative ALI/ARDS, rather were vague terminology such as respiratory or all major complication were used.

Most of the published data on liberal fluid therapy is associated with higher incidence of ALI/ARDS, but it is difficult to infer a direct cause effect relation, as the ALI/ARDS itself is a multi-factorial pathological process and liberal fluid therapy might be one of the several associated risk factors [108,109]. Evans et al. [109] has recommended a conservative strategy by administering intra-operative maintenance fluids at 1-2ml/kg/hr and positive fluid balance should not exceed more than 1.5 litre, to mitigate the risk of Postoperative ALI/ARDS in patients undergoing thoracic surgery. Hughes et al conducted a retrospective study to find relationship between development of postoperative ARDS and intra-operative fluid administration, intra-operative fluid administration in excess of 10ml/kg/hr was associated with development of postoperative ARDS while infusion in excess of 20 ml/kg/hr was associated with 3.8 times higher adjusted odd of developing ARDS [112]. In addition to the potential importance of the amount and timing of fluid administration, the type of fluid or choice of fluid may be equally play important role in clinical outcome [113]. The concept of perioperative fluid administration need to be revised and should not be continued simply because it is routine. Every patient should be evaluated properly and goal directed fluid therapy especially in high risk patients should be a key to ideal postoperative outcome with maximum fluid shift of no more 2 to 3 L.

Inhalation anaesthetics and lung protection

Considerable work has been done on the role of Volatile anaesthetic agent in prevention of ischaemic re-perfusion injury specially in cardiac and thoracic surgery as it help in pre and post-conditioning in ischaemia and re-perfusion. Recent studies has shown that volatile agent has immune modulating effects and protect lung by inhibiting the expression of pro-inflammatory mediator such as IL-8,Il-10, TNF etc. Lung protective effects have been documented in different studies by using isoflurane, sevoflurane, desflurane [114-117]. These exciting works indicates that volatile agents might have a significant role in attenuating the lung injury from host of insults, still need considerable work to define the extent on the role of volatile agent on lung protection.

Postoperative Strategy

Hyperoxia and post operative ALI

Contrary to popular belief of high oxygen supplementation in thoracic surgery to prevent postoperative hypoxia, recent concept is to provide minimal oxygen supplementation that can achieved a satisfactory peripheral arterial saturation. High inspired oxygen supplementation not only leads to oxidative damage but also causes absorption atelectasis [6,10,59]. Hypoxia and hyperoxia causes ischaemic re-perfusion type of injury where there will be production of superoxide radical and other inflammatory mediator that disrupt the glycocalyx barrier of endothelial protection which act as a microcilial layer lining the endothelium and behaving as a molecular shield [118,119]. Protecting this glycocalyx barrier in perioperative period may be one of the important duties of anaesthesiologist.

Uncontrolled prolonged exposer of high concentration of oxygen result in decreased mucocilliary function, atelectasis, pulmonary oedema and eventually pulmonary fibrosis similar to ARDS severe lung damage similar to that of ARDS, the pulmonary changes that occurred due to excess oxygen has been described as hyperoxic acute lung injury (HALI) [120-123]. The extent of lung injury in HALI depends on the duration and concentration of oxygen (above 50%), existing lung pathology, concomitant infection, mechanical stretching of positive pressure ventilation in mechanical ventilation lower the threshold for oxygen toxicity and enhanced the toxicity of oxygen [121]. Addition to generation of reacting oxygen species (ROS), hyperoxia may directly trigger the release of pro-inflammatory agents from pulmonary epithelial cells [124,125]. HALI is influenced by other factors such as hormones, drugs, morbid conditions, for example, fever, hypercarbia, insulin, adrenaline, noradrenaline enhanced toxicity. Whereas, hypothermia, barbiturates, antihistamines, sodium bicarbonate may ameliorate it [126]. With the newer lung protective strategy in the form of PEEP, low Tidal volume, minimal Fio2, the problem of HALI has been substantially reduced in recent times. However, the subset of patients who have already developed ALI or ARDS due to any other reason and requires prolonged hyperoxia may be at increased risk of HALI and the effects may be magnified with viral pneumonia as well as those in hyper-metabolic states such as in sepsis or poly trauma [121]. Recent work on oxygen therapy in disease lung has been stressed by many publications [127-129], unlike the normal healthy lung, the threshold for oxygen related harmful pulmonary effects may be lowered in injured or diseased lung. The precise range of arterial oxygenation in disease lung has not been defined yet. Targeting even normoxemia (SpO2>95%) by giving higher oxygen concentration may cause flaring up of lung inflammation in patients with existing ARDS [127]. A recent investigation suggests to maintain arterial oxygenation Pao2 in the range of (85to 110 mmHg) to improve the long term outcome of ARDS-survivors [128]. Martin and Grocott has stressed that more precise control of arterial oxygenation with better patient-defined targets of arterial PaO2 and SaO2, along with adaptation of a policy of permissive hypoxaemia for some patients may allow avoidance of both tissue hyperoxia and hypoxia [129,130]. The safe lower limit of arterial oxygen in critically ill patients remains to be established, evidences suggests that it may be well below the currently used oxygen target. It may be safer to allow some degree of hypoxaemia in order to avoid the toxic effects of oxygen [129].

Postoperative analgesia

Adequate postoperative analgesia not only provide pain relief to the patient but also help in reducing postoperative pulmonary complications by initiating early ambulation, reduces risk of deep venous thrombosis and help in performance of lung expansion manoeuvres. Regional anaesthesia and analgesia offered superior quality of analgesia over opioid based conventional analgesia. Recent developments in technical aspect in regional analgesia have the potential to provide prolonged analgesia across all age group without major side effect [131]. Use of neuraxial analgesia either as a sole anaesthetic technique [73,74] or as adjunct to general anaesthesia for postoperative analgesia [75,76] resulted in decreased incidences of postoperative pulmonary complications. Studies using epidural analgesia after thoraco-abdominal surgeries reported reduced postoperative complication than patients managed with conventional opioid analgesics [75,76,132,133]. In a meta-analysis on the use of epidural for thoraco-abdominal surgeries reported protective

effects against pneumonia and other pulmonary complications [134]. Patient controlled epidural analgesia (PCEA) was found to be superior to the intravenous patient-controlled analgesia with opioid in terms of analgesic efficacy and reduction in postoperative pulmonary complications [135,136]. Other regional techniques in thoraco-abdominal surgeries are para-vertebral, intercostal, intra-pleural analgesia. Para-vertebral analgesia are associated with similar analgesic efficacy with fewer pulmonary complications than epidural analgesia [137], however, few studies favour epidural analgesia [138,139]. With the advancement in knowledge and techniques of ultrasonography (USG) guided needle placement, varieties of truncal blocks such as para-vertebral, intercostal, transverse abdominis plane, rectus sheath and illio-inguinal/illiohypogastric can be easily and safely done. However there are limited studies comparing the USG guided truncal nerve block with established techniques [140].

Traditionally postoperative pain management was based on opioid analgesics, though opioid are effective but are associated with many side effects which substantially influence patient recovery and may delay discharge after surgery. The current concept of management of acute postoperative pain is to use multi-modal therapy in the form of combination of multiple drugs or techniques such as combining regional block with systemic analgesic to maximize pain relief with minimal side effects. In addition to regional analgesic, non-opioids, NSAIDs and adjuvants drugs complement with other analgesic and help in reducing side effects of a particular therapy [141-144], benefit of such approach may be more evident in elderly and compromised patients [145].

Fast tracking protocol/ enhanced recovery after surgery

The concept of fast tracking was proposed by Henry Khelet for colo-rectal surgeries, it is now widely accepted and practice for many different types of surgeries such bariatric, cardio-thoracic. It's a multi-modal multidisciplinary team effort. With the concept of fast tracking or enhanced recovery after surgery involving multi-modal analgesia (systemic analgesic non-opioid plus opioid with or without regional analgesia), early extubation, early mobilization and nutritional support resulted in improved outcome including socio-economic benefits and fewer postoperative pulmonary complications [146-149].

Naso-gastric tube

There are evidences that routine use of naso-gastric tube for decompressing the stomach is associated with increased risk of pulmonary micro-aspiration and higher rate of pneumonia and atelectasis, longer time to start oral intake relative to selective use of naso-gastric decompression. Naso-gastric tube should be introduced only in selective patient where patient developed symptomatic abdominal distension, unable to tolerate oral intake or excessive nausea-vomiting [133,150].

Other supportive care

Other important issues from the quality care aspect are prevention of thrombo-emboslism [151,152], good nutritional support [133], good glycemic control [153], early recognition and management of infection or sepsis, optimization of fluid and electrolytes and proper monitoring and identification of post-anaesthesia care unit events (desaturation, bradycardia, pain etc. [37] are some of the predictors of subsequent pulmonary complications.

Ultra-Lung-Protective Strategy

Some patients who have already developed ALI/ARDS often deteriorate despite on modern lung protective ventilation and present a clinical challenge for worsening hypoxaemia and hypercarbia. The concept of ultra-protective ventilation implies to these group of patients beyond the modern protective ventilation. Anaesthesiologist should be aware of the advanced therapies available, as these patients can present to the operating room. These therapies aim at increasing the oxygen status and provide support to the patient without inducing further injury to the lungs. Whether the improvement in oxygenation really correlates with improved outcome is doubtful [154]. Various ultra-protective strategies includes i) **Novalung iLA** membrane ventilator which is a form of plumeless extra corporeal membrane oxygenation (ECMO) driven by artero-venous pressure difference. Some case reports on its use are very encouraging [155,156]. ii) **Conventional ECMO** has been used successfully for severe ARDS. But compared to Novalung it is associated with more side effects, costly and less portability [157]. iii) **High frequency oscillation ventilation (HFOV)** has shown to improved temporarily oxygenation in ICU set up but the improvement in oxygenation has not been reflected in overall mortality [158,159]. Its role in operating room is doubtful, might help in patients with compromised lung undergoing major invasive procedure. iv. **Hydrogen sulphite**- inhaled hydrogen sulphite has been shown to and modulate extracellular matrix, activates anti-apoptotic and anti-inflammatory genes and down regulates genes that are involved in oxidative and other pro-inflammatory cell response and protecting against ventilator induced lung injury (VILI). It might have a role in activating or down regulating genes involved in vascular permeability too [160,161].

Summary

Varieties of pulmonary complications may develop in postoperative period ranging from simple atelectasis to ALI/ARDS in extreme which carries a higher mortality, some are predictive and preventable. Post-operative ALI may be primary or secondary to other patho-physiologic process outside lung such as sepsis. Anaesthesiologist has a great role to play in predicting and preventing postoperative ALI through identification and optimization of preoperative conditions, meticulous and lung protective strategies in the intra-operative and postoperative period emphasising on early detection and prompt interventions. Factor implicated for postoperative ALI are grossly divided into Patient related, procedure related, anaesthesia related and post procedural care.

Important patient related factors

Age, Obesity, Obstructive Sleep Apnoea, pre-existing lung pathology, Current Smoking and Drinking, immuno-comromised and general debilitated state.

Procedure related factors

Type of surgery- thoraco-abdominal procedure, invasiveness of procedure- laparoscopy vs Open, duration of procedure and associated fluid and blood loss.

Anaesthesia related factors

Anaesthesia technique- Regional Vs General, mechanical ventilation, perioperative fluid balance, blood and blood product use, hypoxia and hyperoxia.

Postoperative period that are important for prevention of pulmonary and other complications and speedy recovery of the patients are postoperative analgesia, early mobilization, lung re-expansion and physiotherapy, fluid balance and nutritional support, prevention of thrombo-embolism, glycemic control, selective use of nasogastric tube, following fast tracking protocol etc.

Conclusion

Postoperative ALI can be preventable to a large extent through multi-modal multidisciplinary approach. Anaesthesiologist play a crucial role in prevention of postoperative pulmonary complication through recognition and optimization of preoperative conditions, emphasising for less invasive surgical approach, lung protective anaesthetist strategies, applying fast tracking protocol and vigilance monitoring and active interventions in postoperative period.

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