481. Lung injury, respiratory muscles and mechanical ventilation

P4634
Effect of imatinib and nilotinib on lipopolysaccharide-induced acute lung injury during neutropenia recovery in a mouse model
Sook Young Lee, Chin Kook Rhee. *Internal Medicine, Catholic University of Korea, Seoul, Republic of Korea*

Objective: Neutropenia recovery is associated with deterioration in oxygenation and exacerbation of pre-existing pulmonary disease. We aimed to evaluate effect of imatinib and nilotinib on lipopolysaccharide (LPS) - induced acute lung injury (ALI) during neutropenia recovery in a mouse model.
Method: We developed a mouse model of ALI during neutropenia recovery. Cyclophosphamide was administrated to induce neutropenia. During neutropenia recovery, ALI was induced by intratracheal instillation of LPS. Imatinib or nilotinib was administrated during neutropenia recovery.
Result: The numbers of inflammatory cells and neutrophil in bronchoalveolar lavage fluid in imatinib or nilotinib group were significatly lower than LPS group. Imatinib or nilotinib administration significantly reduced wet/dry ratio and ALI score. The level of myeloperoxidase and tumor necrosis factor-α in imatinib or nilotinib group were significantly lower than LPS group. Attenuation of ALI by imatinib or nilotinib was associated with PDGFRβ and C-kit pathway.
Consult: Imatinib or nilotinib effectively attenuated LPS-induced ALI during neutropenia recovery.

P4635
Effect of curcumin on LPS-induced neutrophil activation and acute lung injury
Hyejin Jeong[1], Chihyeong Yun[2]. *[1]Department of Anesthesiology and Pain Medicine, Chonnam National University Medical School, Gwangju, Korea; [2]Department of Cardiothoracic Surgery, Chonnam National University Medical School, Gwangju, Korea*

Curcumin has antioxidant, antitumor, and anti-inflammatory properties. Neutrophils play an important role in the development of organ dysfunction associated with severe infection. This study was performed to evaluate the effects of curcumin on lipopolysaccharide (LPS) - induced neutrophil activation and acute lung injury. To assess the anti-inflammatory effect of curcumin on LPS induced neutrophil activation, neutrophils from human blood were incubated with various concentrations of curcumin (0, 1, 10, 50 and 100 nM) and LPS (100 ng/ml). The protein levels for interleukin (IL)-6, 8 and tumor necrosis factor (TNF)-α were measured using ELISA 4 hr after incubation period. To elucidate the intracellular signaling pathway, We measured the levels of phosphorylation of p38 mitogen activated protein kinases (p38), extracelluar signal-regulated kinase (ERK)1/2 and c-Jun amino-terminal kinases (JNK) with western blot analysis and nuclear levels of nuclear factor (NF)-κB with electrophoretic mobility shift assays 0.5 hr after incubation period. We also examined the effect of curcumin (60mg/kg, IP) on acute lung injury and mortality of mouse treated with LPS(20 mg/kg, IP) to determine whether these effects of curcumin also have in vivo significance.
Curcumin attenuated LPS - induced neutrophils activation including expression of p38, JNK, NF-κB, IL-6, 8 and TNF-α. Mouse treated by Curcumin were protected from LPS-induced lung injury, as determined by wet/dry weight ratio, lung injury score and IL-6, 8 and TNF-α in bronchoalveolar lavage fluid (BALF) levels and mortality.Curcumin can attenuate LPS - induced acute lung injury and mortality via the attenuation of neutrophil activation caused by LPS.

P4636
Hydrogen gas inhalation ameliorates direct lung injury and indirect contralateral lung injury in a murine aspiration pneumonia model
Yuki Nishikawa[1], Kenichi Kokubo[1,2], Ryuji Hataishi[3], Toshihiro Shinbo[2], Minoru Hirose[1,2], Noriyuki Masuda[2,3], Hirosuke Kobayashi[1,2]. *[1]Graduate School of Medical Sciences, Kitasato University, Sagamihara, Kanagawa, Japan; [2]School of Allied Health Sciences, Kitasato University, Sagamihara, Kanagawa, Japan; [3]School of Medicine, Kitasato University, Sagamihara, Kanagawa, Japan*

Aim: Accumulated leukocytes in the lungs produce several inflammatory cytokines and reactive oxygen and nitrogen species (ROS and RNS), which will induce ALI/ARDS. It has been reported that hydrogen (H_2) gas has potential as

eliminating highly reactive ROS and RNS. The aim of the present study was to clarify the effect of H_2 gas inhalation on direct lung injury and indirect contralateral lung injury.
Methods: Anesthetized C57BL/6J male mice were intubated, and 5 μl of 0.1N HCl was administered to the left lung. Mice were randomly grouped to saline treatment instead of HCl (Sham), HCl-treatment (HCl), and 2% H_2 gas inhalation with the HCl-treatment (HCl-H_2) groups. Extra-vascular wet to dry ratio, myeloperoxidase (MPO) activity in the treated left lung and untreated right lung, and serum IL-6 level were evaluated 4 hrs after the treatment.
Results: This aspiration pneumonia model induced direct lung injury and contralateral lung injury. The extra-vascular wet to dry ratios of the left and right lungs were significantly larger in the HCl group compared to the Sham and the HCl-H_2 group (n=10, $P<0.01$), suggesting that H_2 gas was effective not only in the direct injured lung but also in contralateral lung. MPO activity of the left lung was also significantly larger in the HCl group compared to those in the Sham and HCl-H_2 groups (n=3, $P<0.05$). IL-6 was increased in the HCl group, but it did not statistically differ to the level in the HCl-H_2 group, suggesting H_2 gas did not interfere in the cytokine production.
Conclusion: H_2 gas inhalation ameliorated direct lung injury and indirect contralateral lung injury in a murine aspiration pneumonia model.

P4637

WITHDRAWN

P4638

Resistive breathing induces matrix metalloproteinases-9 and -12 expression in the lung

Dimitrios Toumpanakis[1], Olga Noussia[1], Ioanna Sigala[1], Tatianna Michailidou[1], Vasso Karavana[1], Charalampos Roussos[1], Stamatios Theocharis[2], Theodoros Vassilakopoulos[1]. *[1]1st Pulmonary Services and Critical Care Department, University of Athens, Greece; [2]1st Department of Pathology, University of Athens, Greece*

Resistive breathing (RB), encountered in obstructive airway diseases, is associated with large negative intrathoracic pressures and has been recently shown to induce acute lung injury and inflammation. Matrix metalloproteinases (MMP)-9 and -12, implicated in the pathogenesis of both asthma and COPD, are upregulated by inflammation and by mechanical stress per se. We hypothesized that RB induces MMP9 and -12 expression and activity in the lung.
Anesthetized, tracheostomised rats were breathing through a 2-way valve. The inspiratory line was connected to a resistance setting peak tracheal pressure at 50% of maximum (RB). Quietly breathing animals served as controls. After 3 and 6hrs of RB, bronchoalveolar lavage (BAL) was performed to measure cell count and cytokine levels by ELISA. Lung injury was evaluated by histology. MMP9 lung levels were measured by zymography and immunohistochemistry (IHC). MMP12 was detected by IHC. Alveolar macrophages from normal rats were incubated with BAL fluid from rats that underwent RB. MMP9 activity was measured in cell supernatants by zymography.
After 3 and 6hrs of RB, lung injury was detected by histology. Increased numbers of alveolar macrophages and neutrophils ($p<0.05$) and increased levels of IL1b and IL6 ($p<0.01$) were measured in the BAL following 6hrs of RB. MMP9 activity raised by 2-fold after 6hrs of RB ($p<0.001$). MMP9 was detected in alveolar macrophages and epithelial cells. After 3 and 6hrs of RB, increased levels of MMP12 were detected in alveolar macrophages. BAL fluid from animals that underwent 6hrs of RB, induced MMP9 in supernatants by 7.5-fold ($p<0.001$).
In previously healthy rats, RB resulted in increased MMP9 and -12 expression in the lung.

P4639

Study of cardiac and hemodynamic changes with airway pressure release ventilation and pressure control ventilation in children with acute respiratory distress syndrome

Hamdy Hamed Abo-Hagar, Rania Gaber, Gehan H. Abo El-Magd. *Pediatric, Faculty of Medicine, Tanta University, Tanta, Gharbia, Egypt Cardiology, Faculty of Medicine, Tanta University, Tanta, Gharbia, Egypt Chest, Faculty of Medicine, Tanta University, Tanta, Gharbia, Egypt*

Background: Acute respiratory distress syndrome (ARDS) is associated with high morbidity and mortality. Airway pressure release ventilation (APRV) was suggested to be a suitable mode for ventilating such patients with less liability of lung injury.
Aim: To compare the effect of APRV and pressure control ventilation (PCV) on cardiac and hemodynamic functions in children with ARDS.
Patients and Methods: Twenty children aged 1-14 years fulfilling ARDS criteria were included. The following parameters were recorded after ventilating the patients on PCV and APRV: ventilation parameters [peak inspiratory pressure (PIP) and mean airway pressure (MAP)], oxygenation parameters PaO_2/FiO_2 ratio and oxygen delivery, hemodynamic parameters and urine output.
Results: PIP significantly decreased from 29±7 with PCV to 24±4 cmH_2O with APRV, while MAP was significantly higher during APRV(17±5) than during PCV (13±3(cmH_2O. PaO_2/FiO_2 ratio increased significantly from 265±25 during PCV to 295±33 during APRV. Oxygen delivery increased significantly from 865±98 during PCV to 1196±127 ml/min during APRV. Cardiac index increased significantly from 3.2±0.2 during PCV to 4.1±0.3 l/min/m^2 during APRV. Urine output increased significantly from 0.78±0.1 during PCV to 0.97±0.2 ml/kg/h during APRV. The use of sedatives and inotropics were decreased significantly during APRV compared to PCV.
Conclusions: APRV may be a suitable mode for ventilating ARDS patients providing better lung recruitment and oxygenation, avoiding more lung injury and cardiac compromise compared with pressure control ventilation.

P4640

Protease-antiprotease imbalance in airway secretions in subjects with acute respiratory failure

Jennifer Acevedo, Maria Srinivasan, Mario Ponce, Samuel Rosero, Adriana Amelinckx, Philip Whitney, Michael Campos, Michael Campos. *Medicine, Univeristy of Miami, FL, United States*

Studies have shown that in the acute respiratory distress syndrome (ARDS) there is protease-antiprotease imbalance, reflected as an increase in the ratio of Human Neutrophil Elastase (HNE) to several protease inhibitors in BAL and plasma. This imbalance can be related to the pathophysiology of ARDS and may correlate with clinical outcomes. The purpose of the study was to determine if similar protease-antiprotease imbalance could be detected in airway secretions in subjects at risk of developing ARDS.
Free HNE activity (HNEA) and levels of the protease inhibitors alpha-1 antitrypsin (AAT) and secretory leukocyte protease inhibitor (SLPI) were measured in

samples of endotracheal aspirates samples collected serially in subjects intubated because of acute respiratory failure in a medical ICU (n=42 subjects, 10 eventually developed ARDS).
Contrary to reports studying BAL, we observed that free elastase activity is reduced in airway secretions of subjects that develop ARDS compared to subjects that did not. No differences were noted in AAT and SLPI concentrations in airway secretions among these groups. HNEA/AAT and HNEA/SLPI ratios were reduced in 19 subjects. In ARDS subjects, levels of HNEA returned to normal the first day after the onset of ARDS. There were no differences in survival between subjects who had detectable free HNEA compared with those that did not.
Analysis of protease-antiprotease balance in airway secretions of subjects with acute respiratory failure is not useful to discriminate subjects who develop ARDS and does not correlate with survival.

P4641

Is lactate a prognostic factor in acute cardiogenic pulmonary edema (ACPE)?

Caterina Bonino[1], Valentina Rosti[2], Chiara Travierso[2], Federico Piffer[2], Stefano Aliberti[3], Giovanna Guiotto[4], Giuseppina Petrelli[5], Antonio Voza[6], Antonio Villa[7], Roberta Marenzi[8], Anna Maria Brambilla[1], Roberto Cosentini[1]. *[1]Emergency Department, Fondazione IRCCS Ospedale Maggiore Policlinico, Milano, Italy; [2]Respiratory Medicine Department, University of Milan, Fondazione IRCCS Ospedale Maggiore Policlinico, Milano, Italy; [3]Respiratory Medicine Department, San Gerardo Hospital, Monza, Milano, Italy; [4]Emergency Department, San Paolo, Napoli, Italy; [5]Emergency Department, San Benedetto del Tronto Hospital, San Benedetto del Tronto, Italy; [6]Emergency Department, Humanitas Hospital, Milano, Italy; [7]Emergency Department, Fatebenefratelli e Oftalmico Hospital, Milano, Italy; [8]Emergency Department, San Carlo Hospital, Paderno Dugnano, Milano, Italy*

ACPE is a common cause of admission to Emergency Dpt(ED).
Lactate levels are a key factor in critical patients.
Aim: To investigate in ACPE patients relationship between high lactate levels (HLL) on admission (T0) and clinical failure and lactate clearance (LC) calculated in first hours(T1)and clinical failure.
Methods: Prospective, observational, multicentric, web-based study on ACPE patients admitted to18 EDs. HLL: ≥2mmol/L. LC: (LactateT0–LactateT1)/Lactate T0. Clinical failure: in-hospital mortality, ACPE mortality and IOT.
Results: From May2009 to June2011, 475 patients were enrolled. 46patients were clinical failure. Table1 shows data on admission. There was no significant difference in lactate level on admission. We calculated LC in 392patients. 42patients were clinical failure. There was a significant difference between LC in clinical success (0,31±0,66) and in clinical failure (0,08±0,59).

Table 1

Variables	Clinical success	Clinical failure	P
Sex M/F	234/195 (n=429)	24/22 (n=46)	Non significant
Age	79,02±10,3 (n=429)	84,17±9,38 (n=46)	< 0.05
RR (breaths/min)	32,49±7,19 (n=399)	33,69±7,81 (n=45)	Non significant
HR (bates/min)	107,19±23,24 (n=429)	104,24±25,37 (n=46)	Non significant
PAM (mmHg)	116,15±25,69 (n=429)	105,90±26,08 (n=46)	< 0.05
pH	7,29±0,12 (n=429)	7,29±0,11 (n=46)	Non significant
pCO2 (mmHg)	51,08±15,61 (n=428)	48,72±16,96 (n=46)	Non significant
HCO3 (mEq/L)	23,65±4,95 (n=424)	23,30±6,97 (n=46)	Non significant
Lactate T0 (mmol/L)	2,95±2,32 (n=429)	3,37±2,89 (n=46)	Non significant
Hb (gr/dl)	13,24±2,49 (n=419)	12,86±2,49 (n=46)	Non significant
Device O2 tp	90/426 (21%)	9/45 (20%)	Non significant
Device NIV	336/426 (79%)	36/45 (80%)	Non significant

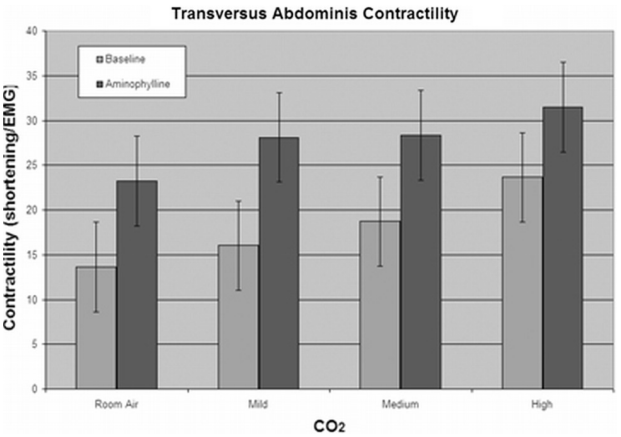
Conclusions: We observed that in ACPE patients HLL on admission are not predictive of clinical failure but reduction of lactate independently of baseline levels is associated with clinical success.

P4642

Aminophylline increases ventilation and abdominal muscle contractility in awake canines

Jenny Vannessa Jagers, Michael Ji, John Kortbeek, Paul A. Easton. *Critical Care, University of Calgary, AB, Canada*

Aminophylline (Amino) is still used in treatment of COPD. However, effects of Amino on ventilation and respiratory muscles are uncertain. Utilizing implants in awake canines, we examined the effects of Amino on costal diaphragm (Jagers et al. Resp Phys, 2009). Here we study the effect of Amino on abdominal muscles of expiration, by measurement of the transversus abdominis (TA).
Sonomicrometry transducers and EMG electrodes were implanted in the left TA. After recovery, the animals were studied awake, breathing through a mask. Airflow, $ETCO_2$, heart rate, muscle length, and moving average EMG were recorded during room air, and CO_2 stimulation, before and after Amino. Output included breath-by-breath breathing pattern, muscle shortening, peak EMG, $PaCO_2$ and heart rate. Results are shown at room air and 3 levels of CO_2.
For N=6 dogs (mean wgt 29.8 kg) studied after 25 days, minute ventilation, tidal volume, and respiratory frequency increased significantly with Amino, during resting breathing and all levels of CO_2. Mean aminophylline was 72 umol/L (therapeutic range 55-110 umol/L). TA shortening increased significantly with Amino while TA EMG activity remained unchanged, consistent with increased contractility of the TA with Amino.



In awake, intact, canines, after Amino, TA contractility is increased, as shown by greater muscle shortening per EMG. This enhanced action of expiratory muscles occurs at therapeutic levels of Amino.

P4643

Severity of ventilator induced lung injury does not contribute to ventilator induced diaphragmatic dysfunction

Christian Bruells[1], Kathy Reiss[3], Ashley Smuder[2], Matthew Hudson[2], Bradley Nelson[2], Stefan Uhlig[3], Scott Powers[2]. *[1]Department of Anesthesiology, Aachen University Clinic of the RWTH Aachen, Aachen, Germany; [2]Inst of Applied Physiology and Kinesiology, College of Human Health and Performance, University of Florida, Gainesville, FL, United States; [3]Inst. of Pharmacology and Toxicology, RWTH Aachen, Aachen, Germany*

Mechanical ventilation (MV) is a life-saving intervention for patients with respiratory failure. Even 12h of MV can promote diaphragmatic contractile dysfunction and atrophy (referred to as ventilator-induced diaphragmatic dysfunction, VIDD).The pathophysiology remains unclear but could be linked to inactivity, the physiological impact of positive pressure ventilation (PPV) on the diaphragm and/or ventilator-induced lung injury (VILI).
We tested the hypothesis, if negative pressure ventilation (NPV) compared to PPV will diminish VIDD.
The concomitant influence of VILI on VIDD was also examined.
Rats were ventilated with either PPV or NPV or breathed spontaneously (control) for 12h.
We measured diaphragmatic contractile properties, fiber size and markers of oxidative damage. Lungs were histologically examined and cytokine levels were assayed in bronchoalveolar lavage for evidence of VILI.
Compared to control, both PPV and NPV resulted in significant oxidative damage to the diaphragm along with fiber atrophy and contractile dysfunction. No significant differences existed in these measures between PPV and NPV groups. Both the PPV and NPV groups experienced VILI, graded by histologic scores or cytokines. Note, that the severity of VILI varied between animals within both the PPV and NPV groups. Nonetheless, the severity of VILI was not significantly correlated with the degree of VIDD.
Both PPV and NPV promote VIDD and VILI. The magnitude of VILI is not correlated with the degree of VIDD. Although these findings do not eliminate the possibility that VILI may play a role in VIDD, our results are consistent with the concept that diaphragmatic inactivation as major contributor to VIDD.

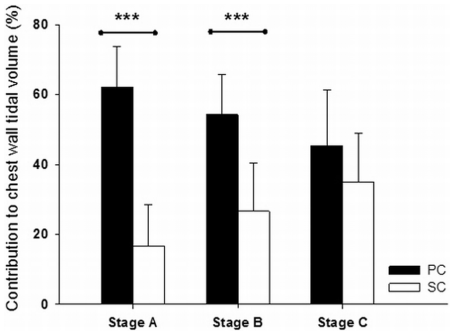
P4644

Contributions of rib cage (RC) and abdomen (AB) to tidal volume are useful indicators for the assessment of difficult-to-wean patients

Rita Priori[1,2], Biswajit Chakrabarti[3], Robert Angus[3], Nick Duffy[3], Robert Parker[3], John O'Reilly[3], Verity Ford[3], Helen Ashcroft[3], Karen Ward[3], Peter M.A. Calverley[2], Andrea Aliverti[1]. *[1]Dipartimento di Bioingegneria, Politecnico di Milano, Milano, Italy; [2]Clinical Sciences Centre, Aintree University Hospital, University of Liverpool, United Kingdom; [3]Weaning and Long Term Ventilation Service, Aintree Chest Centre, Aintree University Hospitals NHS Foundation Trust, Liverpool, United Kingdom*

Respiratory muscles impairment is an important determinant of the need for mechanical ventilation (MV) in difficult-to-wean patients. We investigated whether the relative contribution of rib cage (RC) and abdomen (AB) to tidal volume was a useful indicator of successful weaning from MV.
The contribution of RC and AB volume changes to tidal volume (Vt) were measured by opto-electronic plethysmography in 7 difficult-to-wean patients, during 20' of MV and 20' of spontaneous breathing (SB) after disconnection from MV.

Recordings were repeated at 3 weaning stages: A) tracheostomy and invasive ventilation; B) tracheostomy and non-invasive ventilation (NIV); C) decannulation and NIV. The compartment with the highest % contribution to Vt at the start of weaning (stage A) was defined as predominant compartment (PC), the other as secondary compartment (SC). PC was the rib cage in 5 patients and AB in 2. During SB, the contributions of PC and SC became progressively similar from stage A to C, with no significant differences at stage C (see figure).



Our results show that in difficult-to-wean patients the contribution to tidal volume of RC and AB becomes progressively more homogeneous as MV dependency decreases during weaning. Accurate monitoring of RC and AB contributions to Vt provides therefore useful indications for weaning assessment.

P4645

Abdominal muscle action during sustained hypoxia

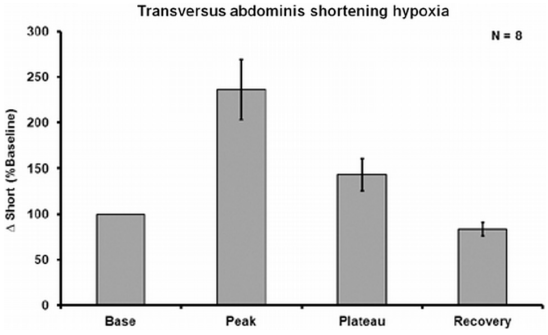
Michael Ji[1], Masato Katagiri[2], Teresa Kieser[1], Paul Easton[1]. *[1]Department of Critical Care Medicine, University of Calgary, AB, Canada; [2]Respiratory Medicine, Kitasato University, Sagamihara, Kanagawa, Japan*

Introduction: Classical studies suggest that expiratory neuronal activity is inhibited by hypoxia, and action of expiratory muscles during hypoxia is controversial. Isocapnic hypoxia sustained 20-60 minutes elicits a biphasic ventilatory response (roll-off), with initial peak followed by decline to a plateau. We demonstrated during sustained hypoxia, parasternal muscle activity rolls off with ventilation (ERJ 2011;38.S55).

Aim: To study ventilation and action of the abdominal expiratory muscle, Transversus Abdominis (TA), during sustained hypoxia in awake canines.

Methods: After implantation of sonomicrometry transducers and EMG electrodes in TA, and full recovery, we measured airflow, SpO2, ETCO2, mavg EMG and shortening (SHORT) of TA, during room air breathing (BASE) followed by 25 minutes of isocapnic hypoxia (mean 79.9% SpO2). The canines were awake, breathing through a mask. We report results 2-3 min after reaching SpO2 80% (PEAK) and final 5 min (PLATEAU) of sustained hypoxia, then room air breathing (RECOVERY).

Results: For N=9 (mean 28.7 kg, 27 days post implant), minute ventilation and tidal volume increased significantly from BASE to PEAK, then decreased to PLATEAU ($p<0.01$). Concurrently, mean EMG and SHORT of TA increased significantly from BASE to PEAK, then attenuated to PLATEAU ($p<0.01$).



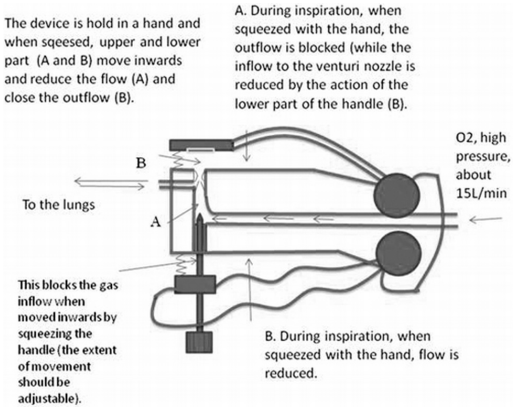
Conclusion: During sustained isocapnic hypoxia, the abdominal expiratory muscle, TA, is markedly activated during initial hypoxia, then attenuated with prolonged hypoxia.

P4646

Transtracheal lung ventilation with a manual respiratory valve with a variable flow

Dragan Pavlovic, Wolfgang Fischer. *Anesthesiology, Universitetsmedizin, Greifswald, Germany*

In cannot-intubate, cannot-ventilate situations, a lung ventilation through a thin transtracheal cannula may be attempted. However, it may be impossible to achieve sufficient ventilation if the lungs are spontaneously emptying and dangers of barotrauma may occur. Here we present a valve [1] as a bi-directional manual respiratory pump which low flow during inspiration (by reducing gas supply to the valve) and increased flow during expiration, by increasing gas supply to the valve, permitted more effective venturi effect and efficient expiration, with low gas consumption.



The effectiveness of the valve was tested in vitro. The valve permitted to shorten the expiratory time and achieve higher minute volumes (i.e. volumes of 7L/min of gas or higher), as compared with the ventilation with the similar transtracheal cannula without variable flows (volumes achieved were about 4L/min). Variable flow provided shortening of the inspiratory time and efficient expiratory aid, and permitted I:E ratios of 1:1, or even the inverse ratio ventilation. Satisfactory lung ventilation can be assured with transtracheal ventilation with a bidirectional manual respiration valve with variable gas flow.

Reference:

[1] Konrad Meissner, et al., Successful Transtracheal Lung Ventilation using a Manual Respiration Valve-an in vitro and in vivo Study, Anesthesiology. 2008 Aug;109(2):251-9.

P4647

Effects of anesthesia, muscle paralysis and controlled ventilation on gas exchanges evaluated by DLCO and pulmonary surfactant protein B: Preliminary results

Fabiano Di Marco[1], Daniele Bonacina[2], Emanuele Vassena[2], Elena Pitino[2], Piergiuseppe Agostoni[3], Stefano Centanni[1], Roberto Fumagalli[4]. *[1]Toraco Polmonare e Cardiocircolatorio, Univerità degli Studi di Milano, Italy; [2]Anestesia Rianimazione, Azienda Ospedaliera San Gerardo, Università Milano-Bicocca, Monza, Italy; [3]Scienze Cardiovascolari, Università di Milano, Italy; [4]Anestesia e Rianimazione Ospedale di Niguarda, Università Milano-Bicocca, Milano, Italy*

A recent study demonstrated that patients with no evident pulmonary disease, after at least 24 hours of mechanical ventilation, show a significant worsening of pulmonary gas exchange evaluated through DLCO (diffusing capacity of the lung for carbon monoxide). This worsening may be caused by an early alteration of alveolar-capillary membrane caused by mechanical ventilation itself, as previously demonstrated on animal models. We evaluated, in patients with no pulmonary diseases undergoing elective surgery, the effect of anesthesia, muscle paralysis and invasive controlled ventilation on DLCO, and the plasmatic levels of pulmonary surfactant protein B (SPB), an alveolar-capillary membrane anatomical damage marker. To date we enrolled 11 patients. In comparison to pre-surgery data, we found, just after anesthesia and paralysis, a significant reduction of DLCO (from 15.6±4.8 to 8.2±2.1 mLmm Hg-1min-1, $p<0.001$), due to a reduction of both lung volume (end-expiratory lung volume, EELV, from 2.8±1.3 to 1.5±.6 L, $p<0.001$), and the coefficient of diffusion (KCO, from 4.5±.8 to 3.7±.7 mLmm Hg-1min-1L-1, $p=0.032$). After this point DLCO, EELV, and KCO did not change significantly at 1 and 3 hours of surgery. Our preliminary results show that anesthesia and paralysis themselves can impair gas exchange, through an alteration not only limited to lung derecruitment. The precocity of this phenomenon, however, does not support the hypothesis of a biological effect" on the alveolar-capillary membrane, but a physical effect", with no modification after 3 hours of invasive controlled ventilation. The SPB analysis is still ongoing.

P4648

Prognostic factors of COPD patients admitted in ICU for acute exacerbation requiring invasive ventilation

Sabrina Lenel, Julien Monconduit, Vincent Jounieaux, Claire Andrejak. *Respiratory Diseases, Teaching Hospital, Amiens, France*

Background: For patients with chronic obstructive pulmonary disease (COPD), the first acute exacerbation requiring mechanical ventilation is a breaking point in the disease.

Methods: We conducted a retrospective study to estimate the cumulative survival

of COPD patients after their first intubation and the prognostic factors of these patients.

Results: Between January 2000 and December 2010, 110 patients (50.9% stage III and 30.6% stage IV according to GOLD) were admitted in intensive care unit (ICU) for acute exacerbation of their COPD. The main aetiologies of the acute respiratory failure were pneumonia (n=40) and acute cardiac failure (n=30). ICU mortality was 22% and the median survival time was 68 months. In cox multivariate analysis, three independent prognostic factors were found: admission in ICU for proved infectious exacerbation (HR=1.83; 95%CI [1.01-3.34], p=0.047), GOLD Stage III and IV (HR= 3.78; CI 95% [1.44-9.92], p=0.007) and acute renal failure (HR=5.79; CI95% [3.01-11.20], p<0.0001).

Conclusion: Cumulative survival of COPD patients were with acute respiratory failure depends mainly on severity of COPD, exacerbation aetiology and associated acute renal failure.