5th INTERNATIONAL WORKSHOP ON LUNG HEALTH

Asthma & COPD - Personalised Medicine: From Myth to Real Life

BERLIN
18 – 20 January 2018

Presidents:
Francesco Blasi, Giorgio Walter Canonica

Chairmen:
Stefano Centanni, Johann Christian Virchow, Tobias Welte

Abstract Leaflet

Organizing Associations

AMR Allergies et Maladies Respiratoires

ILLH International League on Lung Health

International sessions of

AMPCM Association Monégasque pour le Perfectionnement des Connaissances des Médecins

Organizing Secretariat

Publi Créations

74 BD d'Italie, MONTE CARLO
MC, 98000 (MONACO)
PH: + 377 9797 3555
lunghealth@publicreations.com

P02. [19] Assessing inflammatory patterns in asthma endotypes: new diagnostic and therapeutic perspectives

Matteo Bradicich[1,2]; Ian Pavord[2]; Gareth Hynes[2]; Rahul Shrimanker[2]

[1]*Respiratory Pathophysiology and Rehabilitation Department, Cisanello University Hospital, University of Pisa, Pisa, Italy;* [2]*Respiratory Medicine Unit, Nuffield Department of Clinical Medicine, NDM Research Building, University of Oxford, Oxford, United Kingdom*

Background

Bronchial asthma is a chronic airway disease affecting more than three hundred million patients worldwide. Given the high prevalence of this disease and the social and economic burden resulting from under- or mistreatment, the optimal management of this condition represents therefore a key goal. In order to investigate the pathophysiological heterogeneity of this disease, a rather new trend in the Literature suggests categorising different asthmatic patient subpopulations on the basis of their specific molecular patterns, which are supposed to represent the key pathological determinant leading to one particular group of symptoms and signs – i.e. a phenotype – rather than another one. Therefore, asthma endotypes are the key for understanding and treating asthmatic patients with a precision medicine approach.

Overview

A clinical study led by Oxford (United Kingdom) and Pisa (Italy) Universities quantifies the differences in the expression levels of multiple sputum inflammatory molecules between different subpopulations of asthmatic patients, previously labelled on the basis of their sputum differential cell count as affected by eosinophilic, neutrophilic, mixed, or paucigranulocytic asthma.

Methods

37 asthmatic patients and 12 healthy controls were recruited. Assessment of symptom burden and medication usage as well as laboratory measures including blood and sputum cell count and cytokine levels in sputum supernatant – measured using MSD® and Luminex® – was performed. The asthmatic patients were subdivided in four subgroups (eosinophilic, neutrophilic, mixed, and paucigranulocytic) on the basis of their sputum differential cell count. A comparison of the sputum concentration of the inflammatory molecules taken into consideration (IL-2, IL-4, IL-5, IL-8, IL-13, IL-17, IL-25, IL-33, PGD2, LTE4, TNF-α) between the aforementioned subgroups was subsequently carried out.

Results

The study shows that sputum IL-8, IL-17 and TNF-α are leading molecules in the neutrophilic asthma endotype, whilst sputum IL-5 and IL-33 underlie eosinophilic asthma. The mixed endotype is defined by high levels of sputum IL-5, IL-8 and IL-33. There are no significant results regarding paucigranulocytic asthma.

Conclusions

These pathophysiologic differences might be used in a compact, multi-cytokine assessment test that defines univocally the specific patient's inflammatory pattern from a single sample of induced sputum. Such results shed light on the multifaceted inflammatory environment in bronchial asthma and might promote further research in order to define new targeted therapy strategies for those patients with difficult-to-treat asthma.

Table 1	Eosinophilic (n=15)	Neutrophilic (n=9)	Mixed (n=9)	Paucigranulocytic (n=4)	Healthy Controls (n=12)	p-value
Age (years) mean (SD)	56 (15)	61 (13)	58 (8)	62 (11)	45 (12)	0,107
Percentage female	54%	54%	86%	0%	57%	0,183
Age diagnosed (years) mean (SD)	52 (19)	42 (19)	41 (17)	38 (21)		0,597
Pre-bronch. FEV1 (L) median (IQR)	2,44 (1,25)	2,23 (0,92)	1,19 (0,89)	3,35 (1,02)	2,92 (1,04)	**<0,001**
% w/ Fixed Airway Obstruction	69%	69%	43%	67%		0,635
GP/A&E unscheduled visits mean (SD)	3,3 (3,6)	2,7 (1,4)	3,2 (2,7)	np		0,909
ICS dose (BDP equivalent, µg) median (IQR)	1000 (900)	1300 (1000)	1600 (1000)	400 (600)		0,113
Percentage on OCS	33%	0%	0%	0%		
OCS dose (median (IQR)) for those taking OCS (mg)	10,0 (8,75)	0	0	0		
FeNO (ppb)	80 (50-129)	25 (20-31)	32 (18-58)	30 (0.32-2852)	17 (12-23)	**<0,001**
Luminex IL-2 (pg/mL)	510 (285-920)	360 (160-840)	370 (250-540)	np	270 (48-1600)	0,660
Luminex IL-4 (pg/mL)	256 (161-408)	260 (140-490)	273 (140-532)	389 (0,08-2,0*10^6)	196 (106-364)	0,582
MSD IL-5 (pg/mL)	np	30,37 (15,65-58,93)	47,65 (7,91-287,0)	np	8,11 (1,95-33,77)	**0,049**
Luminex IL-8 (ng/mL)	3,73 (2,13-6,52)	15,89 (6,16-40,98)	11,55 (5,39-24,76)	np	10,96 (7,61-15,79)	**0,006**
Luminex IL-13 (pg/mL)	35,08 (18,63-66,06)	46,11 (25,24-84,24)	39,42 (19,46-79,84)	50,58 (92,10-277,74)	24,78 (13,74-44,70)	0,294
MSD IL-17 (pg/mL)	np	336,5 (165,4-684,5)	138,4 (81,85-234,2)	np	36,71 (13,59-99,14)	**<0,001**
Luminex IL-25 (pg/mL)	1300 (940-1900)	1000 (450-2300)	880 (260-3000)	800 (12-5,3*10^4)	530 (68-4200)	0,410
Luminex IL-33 (pg/mL)	93,07 (43,29-200,1)	42,14 (28,17-63,05)	76,69 (26,97-218,1)	np	87,45 (0,025-300016)	0,124
MSD LTE4 (pg/mL)	2394 (121-47546)	1229 (416-3632)	1474 (626-3473)	2457 (603-10015)	254,2 (145-446)	**0,030**
MSD PGD2 (pg/mL)	2050 (1400-3100)	3020 (845-10800)	1100 (260-4700)	3050 (92-10,1*10^5))	2500 (1200-5100)	0,645
MSD TNF-α (pg/mL)	np	594 (50,38-7003)	136,8 (58,54-319,6)	847,3 (0,016-4,6*10^5)	60,11 (15,03-240,5)	**0,032**
Blood eosinophils (x 10^9/L)	0,46 (0,34-0,61)	0,20 (0,13-0,30)	0,24 (0,13-0,43)	0,24 (0,04-1,30)	0,13 (0,7-,27)	**0,004**
Blood neutrophils (x 10^9/L)	4,0 (3,3-4,9)	4,2 (3,4-5,2)	4,0 (3,3-4,9)	3,6 (2,5-5,2)	2,9 (2,1-4,0)	0,220
Sputum eosinophils (%)	22,0 (12,0-40,3)	0,84 (0,36-2,0)	8,0 (4,9-13,0)	0,81 (0,037-17,9)	0,33 (0,14-0,78)	**<0,001**
Sputum neutrophils (%)	20,5 (12,3-34,1)	87,8 (83,2-92,6)	74,0 (67,2-81,6)	51,3 (16,1-163,1)	47,7 (29,0-78,6)	**<0,001**
Lost days (work/school) median (IQR)	16 (28)	10 (23)	15 (16)	np		0,948
% pts who lost days	13%	44%	22%	np		
AQLQ overall score median (IQR)	5,1 (2,8)	5,2 (1,3)	4,4 (2,8)	6,6 (0,78)		**0,089**
ACQ-5 final score median (IQR)	2,2 (2,7)	1,6 (1,6)	3,1 (1,5)	0,9 (1,4)		0,145

Table 1. Results given as stated. FeNO, sputum IL-2, IL-4, IL-5, IL-8, IL-13, IL-17, IL-25, IL-33, LTE4, PGD2, TNF-α, blood eosinophils, blood neutrophils, sputum eosinophils, and sputum neutrophils did not conform to a normal distribution, therefore for these values the geometric mean (confidence interval in brackets) is presented. P-values listed for Kruskal-Wallis test comparisons between the endotype groups and the control group. SD – standard deviation; FeNO – fractional exhaled nitric oxide; ppb – parts per billion; np – not performable. Fixed airway obstruction is defined as a post-bronchodilator FEV1 absolute change <200 mL or a post-bronchodilator FEV1 increase <12%.

Table 2	IL-8	IL-17	TNF-α	IL-5	IL-33
Neutrophilic	+	+	+	-	-
Eosinophilic	-	-	-	+	+
Mixed	+	-	-	+	+

Table 2. Summary of the different cytokine expression patterns, clustered on the basis of a higher or lower sputum concentration observed in each endotype subgroup of the study. "+" represents a particularly high sputum concentration, while "-" represents a not particularly high/particularly low sputum concentration. Both these cut-offs need to be more precisely defined by further investigation. TNF-α: Tumour Necrosis Factor-α.

P19. [79] Paraneoplastic manifestation of severe hyponatremia caused by Syndrome of inappropriate antidiuretic hormone secretion (SIADH) in small cell lung carcinoma

Daniela Buklioska Ilievska[1]

[1]*General Hospital ,,8-th September", Skopje, Macedonia*

Introduction

Paraneoplastic syndromes are a group of clinical disorders, associated with malignant diseases, not directly related to the localization of primary or metastatic tumors. These syndromes are described in lymphoma, thymoma, mesothelioma, Ewing's sarcoma, and a variety of carcinomas. Approximately 70% of malignancy-related cases are as result of small cell lung cancer (SCLC). Associated with lung cancer, include: neurologic, endocrine, dermatologic, rheumatologic, hematologic, ophthalmological syndromes, glomerulopathy and coagulopathy (Trousseau's syndrome). Small-cell lung carcinoma is an aggressive form of lung cancer, strongly associated with cigarette smoking, usually presents in central airways, infiltrating the submucosa. Common symptoms: cough, dyspnea, weight loss, fatigue. Over 70% of patients present with metastatic disease: liver, adrenals, bone, brain. Due to its neuroendocrine nature, small-cell carcinomas can produce ectopic hormones, adrenocorticotropic hormone and anti-diuretic hormone (ADH, also called vasopressin). Lambert-Eaton myasthenic syndrome is paraneoplastic condition linked to small-cell carcinoma. Published data suggest that the average incidence of clinically manifested SIADH in patients with newly diagnosed small cell lung cancer is only 4%. Syndrome of inappropriate anti-diuretic hormone secretion (SIADH) was first associated with malignancy when described in two patients with bronchogenic carcinoma in 1957.

Case Presentation

A 60 year old male, smoker for 30 years (48 pack-per-year smoking history), was hospitalized because of one month history of weakness, dry cough, chest pain, syncope. Physical examination - normotensive, afebrile, heart rate 100/min, weight 79 kg. Rhythmic heart action. Lung auscultation revealed diminished breath sound in right lung. Abdomen: bowel sounds present, with no organomegaly. Extremities: no edema, warm, pulses positive. Initial 12 lead ECG was normal. Laboratory results - hyponatremia 117mmol/L, with normal potassium, calcium, magnesium, phosphorus, urea, creatinin, uric acid, proteins in serum and urine, tumour markers (normal CEA, CA-19-9, AFP, PSA, Cyfra 21-1), mildly elevated NSE, reduced plasma osmolality 248,3mosm/kg and urine sodium below 40mEq/L/24 hours.

Chest X-ray presented parenchymal consolidation in right lung in communication with enlarged right hilus (Figure 1).

The patient undrewent bronchoscopy and biopsy. Bronchoscopy revealed paresis of right vocal cord, shortened main carina, left bronchial tree was normal. Right bronchial tree with edematous carina superior lat.dex., submucous infiltration with stenosis of anterior branch of upper lobe and intermediate bronchus (Figure 3, 4).

Patohystology morphologic features were consistent with small cell lung carcinoma (Figure 5).

Lung CT scan presented hypodense parenchimal change next to right hilus with compression of right bronchus and atelectasis, with mediastinal lymhadenopathy (Figure 2).

Also for staging abdominal ultrasound was performed, organs were normal, only enlarged adrenal glands were detected.

After hyponatremia was corrected, restricted fluid intake (maximum 1000ml/day), and health status improven, further treatment was continued at Institute of Oncology.

Discussion

Ectopic production of large amounts of ADH leads to syndrome of inappropriate antidiuretic hormone hypersecretion (SIADH), defined by hyponatremia, water retention, hypo-osmolality. ADH plays an important role in regulating the balance of fluids. It lowers the amount of urine the and increases the amount of water the kidneys take up. SIADH is characterized by neurological and psychiatric symptoms attributable to cerebral edema. Symptoms may be mild and vague at first, but tend to build. Severe cases may involve these symptoms: irritability and restlessness, loss of appetite, cramps, nausea and vomiting, muscle weakness, confusion, hallucination, personality changes, seizures, stupor, coma. The goal of treatment is very gradual coorrection of hyponatremia and fluid restriction. Hyponatremia inoncology practice, may be a negative prognostic factor in cancer patients based on a systematic analysis of published studies.

Keywords - small cell lung carcinoma, SIADH, hyponatremia, Lambert-Eaton myasthenic syndrome, paraneoplastic syndrome

FIGURE 1.

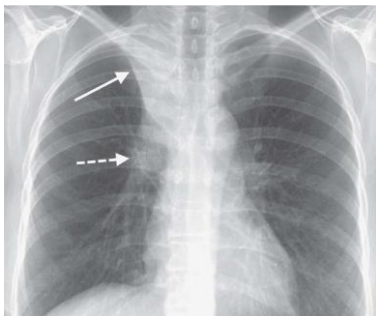


FIGURE 2.

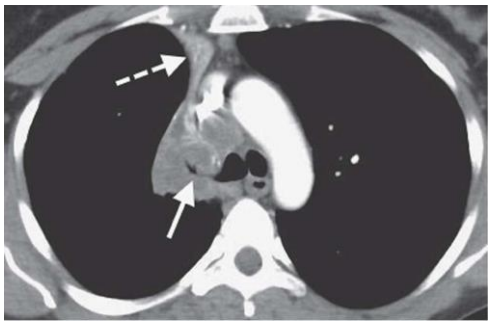


FIGURE 3.

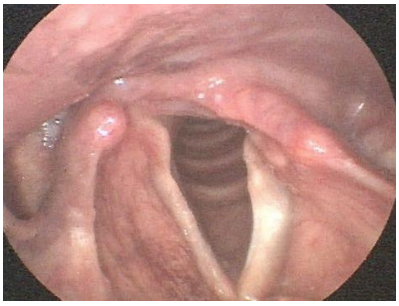


FIGURE 4.

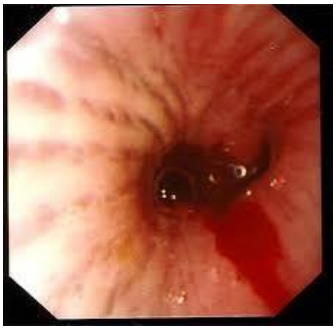
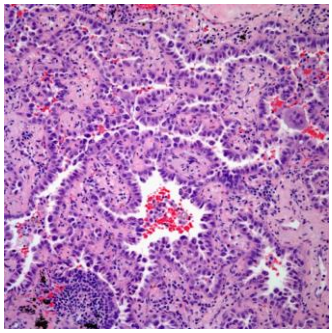


FIGURE 5.



P11. [33] Evaluation of Foreign Body Aspiration Cases: 5 Year Retrospective Study

Nejla Canbulat Sahiner[1]; Ayse Sonay Turkmen[1]; Dilara Sahin[1]; Meryem Kayhanlar[2]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Service Vocational School, Karaman, Turkey*

Aim:

This study was planned retrospectively for the evaluation of cases with foreign body aspiration of child emergency service.

Method:

During the last five years (2013-2017), a total of 51 cases were reached in the survey conducted by the archive review. The records of the cases were examined and evaluated in terms of age, gender, the year of application, the month of application, the time of application, the result of the application, and regions where foreign object is aspirated. The data were analyzed with descriptive statistics.

Results:

The mean age of the cases included in the study was 5.20 ± 3.65 (1-17 years). Male and female ratios were found to be very close to each other (51% male (n = 26), 49% female (n = 25)). It was determined that the applicants were mostly in February (n = 13) and June (n = 10). Children often (82.4%) were determined to insert foreign objects into the nostrils. The application time was usually between 24: 00 and 01: 00 (n = 15). 78.4% of the patients were discharged on the same day, 15.7% were referred to pediatric surgeon or ENT specialist and 5.9% were referred to a senior (3rd level) hospital.

Conclusion:

Foreign body aspiration is a condition that can cause bad results for children. Information about the subject should be given to the parents and necessary precautions should be taken.

Key words: child, emergency service, foreign body aspiration

P12. [34] Evaluation of Respiratory Distress Cases in Emergency Pediatric Service : Retrospective Study

Nejla Canbulat Sahiner[1]; Ayse Sonay Turkmen[1]; Meryem Kayhanlar[2]; Dilara Sahin[1]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Service Vocational School, Karaman, Turkey*

Aim:

This study was planned retrospectively for the demographic evaluation of cases with child respiratory distress in emergency service.

Method:

Archive records of the cases with respiratory complaints to the pediatric emergency department constituted the research data. The records of the children were examined for diagnosis age, gender, month of application and number of days of discharge. In addition, the demographic data were compared with the diagnosis obtained after the examination. Percentage, mean, ANOVA tests were performed in the evaluation of the data.

Results:

A total of 828 children were admitted in the last year with emergency respiratory symptoms. 33.3% of the children had croup, 24.6% had asthma, 19.6% had acute bronchitis, 14.5% had pneumonia and 8% had lower respiratory tract infection. The mean age of the children was 4.08 ± 3.9 and 64.9% were male (n = 538). Children usually referred to the hospital between 10: 00-12: 00 (n = 217). Maximum rate of application was in November and January (n = 315). 17.1% (n = 142) of the children were admitted to the hospital after the examination and had a mean of .86 ± 2.18 days in the hospital. There was a statistically significant difference ($p < 0.05$) between the diagnosis, age, sex, month of application and discharge days of the children.

Conclusion:

It was determined that respiratory system disturbances were more frequent in boys and that respiratory system disturbances were statistically different between age, gender, month of application and discharge days in children, the most common respiratory system complaints were croup, respiratory system disturbances were seen more frequently in boys.

Key words: child, emergency department, respiratory distress, acute bronchitis, asthma, lower respiratory tract infection, croup, pneumonia

P10. [32] Retrospective Investigation of Croup Cases Attending Pediatric Emergency Department

Nejla Canbulat Sahiner[1]; Ayse Sonay Turkmen[1]; Dilara Sahin[1]; Meryem Kayhanlar[2]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Service Vocational School, Karaman, Turkey*

Aim:

This study was planned retrospectively for demographic evaluation of croup cases.

Method:

Archive records of children who were diagnosed with croup by applying to the pediatric emergency department with respiratory complaints constituted research data. Records of children receiving croup recognition were examined in terms of age, sex, month of application and number of days of discharge. The data were analyzed with descriptive statistics.

Results:

A total of 276 children in the pediatric emergency department were identified as having a croup in the last year. The mean age of the children was 3.62 ± 2.65 and 69.2% were male (n = 191). Children usually referred to the hospital between 24: 00-05: 00 (n = 96). The most frequent applications were in October-February (n = 194). A total of 5 children were admitted to the hospital after the examination and stayed at the hospital for an average of 4 days.

Conclusion:

It has been determined that croup, which is a common respiratory disorder in children, is common in boys and usually occurs between October and February, application hours for croup were largely between 24: 00-05: 00 hours.

Key words: child, emergency department, croup

P17. **[65] COPD with Bronchiectasis : A more severe disease?**

Katerina Dimakou[1]; Adamantia Liapikou[5]; Kyriaki Tsikritsaki[1]; Anna Gousiou[2]; Maria Kaponi[1]; Nikoleta Rovina[4]; Loukas Thanos[3]; Michael Toumbis[5]

[1]5th Resp.Department,Sotiria Chest Hospital, Athens, Greece; [2]American College of Greece,Deere, Athens, Greece; [3]Radiological Department,Sotiria Chest Hospital, Athens, Greece; [4]1st Department of Pulmonary Medicine,Sotiria Chest HospitalMedical School; National and Kapodistrian University, Athens, Greece; [5]6th Resp.Department,Sotiria Chest Hospital, Athens, Greece

In order to estimate the presence of bronchiectasis in COPD and the relation with the clinical and functional parameters we studied 100 patients with COPD, stable state. The symptoms, their duration, the number of exacerbations/year, lung function and arterial blood gases were estimated. HRCT was performed in all patients *to look for* the presence and *extent* of bronchiectasis and the degree of emphysema. Two radiologists studied the CT scans separately without knowing the clinical and functional data of the patients. According to Smith scale for bronchiectasis (score: 0-24,) and Bankier, Parkf for emphysema (score:0-100)

The patients, 88men, mean age (±SD) 68 years (19,3), smoking history 74,4 PY (29,6). The main symptoms (mean duration in years (±SD) were : cough 11,7 (9,8), sputum:10,4 (9,7) and dyspnea: 6,9(6,0) MRC scale :2,4 (1,08). Bronchiectasis was diagnosed (score ≥3) in 70 patents (70%).

The results are shown in the following tables

Table 1.Radiographic and functional data

Patients	Score bronchiect.	Score emphysema	FVC (% perd)	FEV1 (% pred)	FEV_1/FVC	PaO_2	$PaCO_2$
Total (100)	4 (2,8)	17,9 (19,3)	78,5 (23,7)	49,9 (22,3)	48,6 (12,4)	68,3 (11,6)	B 38,7 (8,0)
COPD with bronchiectasis (70)	5,09 (2,4) *	19,25(21) *	72,9 (20) *	45,4(18,6) *	48 (12,7) *	65,9 (10) *	39,4 (8,4) *
COPD without bronchiectasis(30)	1,06 (0,9) *	14,3(13,6) *	88,5(21,6) *	55,9(18,9) *	52,5(12,4) *	74,8 (13) *	36,5(6,4)*

The values are expressed as mean (±SD). *p<0,001

Statistically significant difference was also found in the degree of dyspnoea between the groups with and without bronchiectasis and the number of exacerbations/year (p=0,001).

Table 2.Corellation of bronchiectasis score to:

	Score emphysema	MRC	Exacerbations /year	FVC(%pr)	FEV1(%pr)	FEV1/FVC	PaO2
p-value	0,024	0,001*	0,002*	0,001**	0,001**	0.015**	0,008**

* positive, **negative correlation

Our results indicate that evidence of bronchiectasis on HRCT is very common in COPD patients. The presence and extent of bronchiectasis are related to the clinical and functional severity of the disease.

P14. **[49] Tuberculosis infection during treatment with TNF-α antagonists. A report of three cases**

Valentina Dimitrova[1]; Diana Petkova[1]; Velin Stratev[1]; Tanya Dobreva[1]

[1]*University hospital, Varna, Bulgaria*

Introduction:

Treatment with new biological drugs is proved to be effective in the management of wide spectrum of systemic inflammatory diseases. The use of TNF-α antagonists increases the risk of infectious diseases including Mycobacterium tuberculosis infection.

Cases:

We describe three cases of severe tuberculosis infection: haematogenously disseminated and infiltrative pulmonary form occurring in the course of treatment of inflammatory bowel disease with infliximab and adalimumab. Two of the patients were males aged 21 and 31 years, diagnosed with Crohn's disease and were treated with adalimumab for 29 and 8 months resp. The third patient is 38 years old female, diagnosed with chronic ulcerative colitis and treated with infliximab for 6 months. All patients performed chest X-ray, tuberculin skin test and IGRA test for latent TB screening before starting the biological drugs. 3 to 4 months after onset of lung symptoms the diagnosis of active tuberculosis was confirmed on culture and histologically in one of the cases. When the diagnosis of TB was established all patients disrupted the biologicals and started treatment with the standard four drug regimen. During the treatment the female patient had progression of the disease – tuberculosis of soft tissues, which was managed surgically. In all patients the eradication of the bacilli occurred late after initiating anti-tuberculosis drugs and required extended treatment regimens.

Conclusion:

reatment with TNF-α antagonists puts the patients at risk of TB infection. Candidates for biological treatment should be carefully screened and monitored.

P03. **[22] A Survey of Aminophylline prescribing among Junior Doctors**

Naomi Drye[1]; Mansoor Ali[1]

[1]*Calderdale and huddersfield foundation trust, Halifax, United Kingdom*

Junior doctors are regularly asked to prescribe medications out of hours, which would normally be supervised by seniors or field experts. Aminophylline, a potentially toxic and dangerous drug, is one of these. For such medications local guidelines can vary, deviating from the BNF and causing potential problems for junior doctors on-call. Our aim was to assess their experience, knowledge and confidence in prescribing aminophylline as uncertainties and errors may result in patient harm. We performed an anonymous survey of 38 doctors (FY1-CT2 plus GP trainees) and asked; their knowledge of aminophylline; confidence and experience in prescribing; knowledge of guidance available (local and national) and their future needs with regards to prescribing. Results were analysed with excel. Most juniors knew the indications for using aminophylline. However, we found that greater than 50% of juniors were unaware of the potential side effects of the drug. Minimal had experienced teaching (14%). Fifty eight percent had no confidence in prescribing aminophylline with no participants being fully confident. Finally, 79% of doctors were unaware of local protocols. These results highlight potential compromises in patient safety and uncomfortable situations for junior doctors when protocols vary and are not easily accessible. Following this survey changes made included; making guidelines easily accessible, implementing teaching in prescribing aminophylline and including guidelines in induction handbooks. Finally, physicians were encouraged to ensure infusion finished within hours. Further auditing to access improvement is needed.

P18. [66] The 6-min walk work in patients with COPD

Ana Luísa Fernandes[1]; Graciete Luís[1]; Zita Camilo[1]; Joana Amado[1]; Paula Simão[1]; Ferreira Jorge[1]

[1]*Pulmonology Department, Hospital Pedro Hispano, Matosinhos, Portugal*

Introduction:

The 6-minute walk test (6MWT) is commonly used to assess exercise capacity in patients with COPD and the walking distance (6MWD) is considered the major outcome. Differences in body weight are known to influence exercise capacity. Therefore, the 6-min walk work (6MWW) (product of the 6MWD and body weight) may provide a better estimation of the work required to perform this test.

Objective:

To correlate clinical and functional variables with the 6MWD and the 6MWW.

Methods:

Retrospective study that included 95 COPD patients (GOLD criteria) that performed the 6MWT between July 2015 and July 2017. 6MWD, 6MWW, cardiorespiratory parameters (blood pressure (BP), heart rate (HR) and oxygen saturation), degree of dyspnea and lower limb fatigue (modified Borg scale) were recorded. Clinical and functional variables were obtained.

Results:

We included 82 males and 13 females with a mean age of 66,28,1±8,1 years (43-84 years), mean BMI of 25,46±4,77 kg/m2, mean FEV1 of 1,40±0,47 L, mean FVC of 2,66±0,67 L, mean RV of 4,51 ±1,19 L, mean TLC of 7,28 ±1,29 and mean DLCO of 43,73±17,58%. The mean mMRC was 1,53± 0,85 and mean packs per year was 68±33,03.

A negative and significant correlation was found between age and the 6MWD (-0,45; p<0,001) and also the 6MWW (r=-0,29;p=0,004). Correlations were observed between the 6MWD and other clinical and functional variables: height (r=0.6;p<0.01), mMRC (r=-0,24;p=0,022), FEV_1 (r=0,36;p<0,001), FVC (r=0,47;p<0,001), inspiratory capacity (r=0,24;p<0,022), SpO2 basal (r=0,26;p=0,11) and initial (r=0,31;p=0,002) and final (r=0,49;p<0,001) Borg dyspnea evaluation. The 6MWW was significantly correlated to height (r=0,31;p=0,002), FEV_1 (r=0,46;p<0,001), FVC (r=0,44;p<0,001), DLCO (r=0,38;p<0,001), inspiratory capacity (r=0,31;p=0,003) and final (r=0,28;p=0,006) Borg dyspnea evaluation.

According to the degree of spirometric obstruction (ERS/ATS criteria and GOLD criteria), there was no statistical significant difference between the mean values of 6MWD (p>0,05) and 6MWW (p>0,05).

Conclusion:

There are few studies in literature that evaluate de role of the 6MWW. Age, height, FEV_1, FVC, inspiratory capacity and final Borg dyspnea evaluation were the only parameters significantly correlated to the 6MWD and to the 6MWW. Both outcomes did not demonstrate a statistical difference with the degree of obstruction in COPD.

Key-words: COPD, 6-min walk work, 6-min walk distance

P20. [80] Neurogenic receptor signal pathway involved in airway inflammation in a mouse model of asthma following nanoparticles exposure

AN SOO JANG[1]; Byung-Kon Kim[1]; Sun- Hye Lee[1]; Pureun-Haneul Lee[1]

[1]*Soonchunhyang University Hospital, Bucheon, Korea,South*

Background:

The interaction between chronic inflammation and neural dysfunction points to an involvement linking the nervous and the immune system in the airways. In particular, environmental exposure to nanoparticles (defined as particulate matter having one dimension <100 nm), has been associated with an enhanced risk of childhood and adult asthma. But the impact of nanoparticles on neurogenic asthma remains to be determined.

Objective:

The aim of this study was to identify the impact of nanoparticles on nuro modulation such as transient receptor potential channel and purinergic receptor in a mouse model of allergic asthma.

Methods:

Using mice sensitized with ovalbumin (OVA) and OVA challenged (OVA sensitized/challenged mice) as well as mice treated with saline and challenged with air, and mice exposed to nanoparticles 200 ug/m^3 on days 21-23. The effect of nanoparticles on TRPV1, TRPV4, P2X4 and P2X7 was estimated using ELISA, immunoblotting, and immunohistochemical stain.

Results:

Nanoparticles exposure more increased in airway inflammation, and airway obstruction in OVA mice, and those were augumented in nanoparticles exposed mice. TRPV1, TRPV4, P2X4 and P2X7 protein increased in OVA and nanoparticles exposed mice lung tissue. Substance P, ATP, and CGRP increased in OVA mice lung, and augumented in nanoparticles exposed mice lung. Bradykinin, ATP, and CGRP were increased in nanoparticles exposed NHBE cells.

Conclusion:

These results indicate that neurogenic receptor might be involved in the pathogenesis of bronchial asthma, and nanoparticles can exacerbate asthma through neurogenic mechanism.

P05. [25] Demographic Evaluation of Acute Bronchitis Cases that Pediatric Emergency Service Applied

Meryem Kayhanlar[2]; Ayse Sonay Turkmen[1]; Nejla Canbulat Sahiner[1]; Dilara Sahin[1]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Service Vocational School, Karaman, Turkey*

Aim:

This study was planned retrospectively to evaluate the demographic characteristics of acute bronchitis.

Method:

Archive records of children who were diagnosed with acute bronchitis by applying to the pediatric emergency department with respiratory complaints constituted research data. The records of children diagnosed with acute bronchitis were examined in terms of age, sex, month of application and number of days of discharge. The data were analyzed with descriptive statistics.

Results:

A total of 162 children were diagnosed with acute bronchitis in the pediatric emergency department in the last year. The mean age of the children was 2.38 ± 3.23 and 72.8% were male (n = 118). Children usually referred to the hospital from 10:00 to 12:00 (n = 37) and from 19:00 to 22:00 (n = 44). Most applications were filed in December (n = 27) and January (n = 24). A total of 72 children were hospitalized after the examination and they had an average of 2.33 ± 2.99 days in the hospital.

Conclusion:

It has been observed that acute bronchitis, a common respiratory system disorder in children, occurs in boys, usually in winter months, and causes hospitalization.

Key words: child, emergency department, acute bronchitis

P06. **[28] Healthcare Spending and Utilization of Lung Cancer Patients Using 2002-2012 Nationwide Health Insurance Claims Data**

Poster Winner

Sun Jung Kim[1]; Park Eun-Cheol[2]; Nam Chung Mo[2]; Lee Sang Gyu[3]; Park Sohee[3]; Kim Tae Hyun[3]

[1]*Soonchunghyang University Department of Health Administration & Management, Asan, Korea,South;* [2]*Yonsei University College of Medicine, Department of Preventive Medicine, Seoul, Korea,South;* [3]*Yonsei University Graduate School of Public Health, Seoul, Korea,South*

Background:

Over the past decades, lung cancer has one of the highest fatality rates, and is the leading cause of cancer-related mortality and disease burden not only in South Korea but also worldwide. Studies focused on lung cancer are well documented, however, the factors that are associated with healthcare spending and utilization using long periods of large dataset is less researched in this country. The purpose of this study was to investigate how different individual and hospital factors are associated with total, inpatient, outpatient spending and utilizations measured by length of stays and outpatient days among nationwide dead or 5 years follow-up lung cancer patients using 2002-2012 health insurance claims data.

Materials and Methods:

We used nationwide lung cancer patients' health insurance claims during 2002-2012 which accounted for 1,417,380 (673,122 inpatients and 744,258 outpatients). We transposed the dataset into a retrospective cohort design study that the unit of analysis is information of each lung cancer patient. We included patients who newly diagnosed with lung cancer after 2005 and dead or follow-up of 60 months which eventually included patients diagnosed during 2005-2007. Furthermore, this study also excluded patients who had inpatient spending less than KRW 400,000 to minimize bias of real lung cancer patient selection. We then calculated various spending and utilization measures (total, inpatient, outpatient spending, length of stays and outpatient days). Finally we obtained total population for analysis of 53,451 lung cancer patients and matched 916 hospitals. Hospital data included characteristics of the hospital, such as hospital type, teaching status, number of beds, specialists, and nurses. In order to investigate individual and hospital factors associated with healthcare spending and utilization of lung cancer patients, multi-level linear mixed models that avoid problems created by possible nesting of patient level observations within hospital clusters and overestimation of significance were performed.

Results:

Our retrospective cohort design study using nationwide claim data of past decade showed that increase in new lung cancer cases during year 2005 to 2007 (16,654 in 2005, 18,149 in 2006, 18,648 in 2007 which are similar to actual number of patients reported by national cancer center), increased spending and utilization (total spending of KRW 22,883,645 to KRW 27,462,222; inpatient LOS of 51.4 days to 58.8 days; outpatient utilization of 25.4 days to 26.1 days for patient diagnosed in 2005 and 2007 respectively), and higher proportion of spending and utilization during very first periods after diagnosis and last periods before death or follow-up ends of lung cancer patients (about 70% over total), and higher spending and utilization trend among dead population (5-years survivors: total spending of KRW 24,486,381, inpatient LOS of 39.2 days, outpatient utilization of 40.9 days; Dead population: total spending of KRW 15,936,865~54,945,330, inpatient LOS of 44.4~107.8 days, Outpatient utilization of 9.0~66.0 days). Using the multi-level linear mixed analysis models, we found evidences of differences in the use of healthcare resources among individual and hospital factors

that individual with health insurance (2.9% higher in total spending, *P*<0.001; 23.8% higher in outpatient days, *P*<0.001), male (5.6% higher in total spending, *P*<0.001; 8.6% higher in outpatient days, *P*<0.001), 40-79 age group (28.0% to 61.0% higher in total spending, *P*<0.001; 24.8% to 34.0% in LOS, *P*<0.001; 38.9% to 65.8% higher in outpatient days, *P*<0.001) and hospital type with tertiary/large (27.6%, 12.7% higher in total spending), teaching (35.6% higher in total spending, *P*<0.001; 13.4% higher in LOS, *P*=0.001; 21.9% higher in outpatient days, *P*<0.001) had relatively higher spending and utilization among nationwide 5 year follow-up lung cancer patients.

Discussion & Conclusion:

This study might suggest that efficient manner of healthcare policy implementation for patients' spending and utilization in order to maintain financial viability of national health insurance program that the allocation of limited health-care resources demands an agreed rational allocation principle, and consequently priority setting is considerably importance. In addition, healthcare spending and utilization considered to be targeted to under-served population groups that will ensure efficient locus of healthcare service delivery to different sub-population groups. Results of this study might be useful to health policy makers not only in South Korea but also international readers that need to develop a national cancer management strategy that reduce differences in the use of healthcare resources and flexible healthcare benefits plan which might helpful to targeted sub population groups.

P21. **[94] Measuring the impact of COPD on daily communication; a clinimetric study**

Poster Winner

Jessie Lemmens[1]; Nicola Merkel[1]; Janina Muenstermann[1]; Tanja Vossen[2]

[1]*Zuyd University of Applied Sciences, Heerlen, Netherlands;* [2]*Proteion, Horn, Netherlands*

COPD is a highly prevalent disease that has a large impact on quality of life. To examine the symptoms that are related to communication, a questionnaire has been developed by a Dutch speech and language therapist (Vossen, 2008). It consist of 4 self-report scales concerning breathing, speech, voice & swallowing and a performance assessment in which a short text is read. Each item is rated on a 12 point (Borg) scale. The Dutch version proved to be a reliable and valid tool (Lenders et al, 2015; Marien et al, 2016) and thus was translated into German (Hille & Lemberg, 2015). In this study the internal consistency, test-retest reliability (self-report items), intra-observer reliability (performance assessment) and the discriminant validity according to GOLD stages of the German version were examined. 53 Germans suffering from COPD were recruited via sport lung groups, self-help groups, hospitals and general practitioners offices. 50 people, of which 26(52%) females, completed the questionnaire twice in a two week time period and 30 allowed the performance of reading a text to be recorded for analysis. The mean age was 66 (sd= 9.3), ranging between 41 and 83, and 33(66%) were retired. The majority 42(84%) did not smoke (anymore). Most prevalent (n=18/36%) was GOLD stage II and the other stages varied between 9 and 5 people. From 10 people the GOLD stage was not reported. According to the self-report items the main difficulties concerning communication were breathing while experiencing strain (100%) and voice production (64%). The least problems were reported in swallowing (26%). The internal consistency in both measurements was high (Cronbach alfa >0.8) for the total scale, the breathing scale and the reading scale, sufficient (Cronbach alfa = 0.7) for the voice scale and poor (Cronbach's alfa = resp.0.6/.44) for the swallow scale. The correlation calculated via resp. weighed kappa and ICC between the first and second measurements of the self-report items ranged between >0.8 and 0.93 for all subscales and total scores. The intra-observer analysis showed a weighed kappa of 0.96. There were significant differences ($p<0.05$) in scores between GOLD I and GOLD II & IV. The sample size of GOLD III was only 5 people, which was most likely too small for ANOVA testing. While several other health questionnaires focus on consequences of COPD, so far no reliable instrument concentrated on communication difficulties caused by COPD. This questionnaire is reliable and can be used to record communication problems in a German population with COPD. Even though further validity testing is recommend, the results of this study may help raise awareness that the impact on communication is larger than expected. The role of speech therapy in COPD treatment within the German Health Care system should be further investigated.

P01. [18] Comparison of osteoporisis in male smokers with or without chronic obstructive pulmonary disease

Sheikh Abul Hasanat Mohammad Mesbahul Islam[1]

[1]*Sylhet Mag Osmani Medical College, Sylhet, Bangladesh*

Background:

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide. It is identified as risk factors for osteoporosis. The occurrence of fractures as a consequence of osteoporosis can contribute to the disability and mortality of patients with COPD and add to the economic burden associated with the disease. It is established that smoking contributes to the pathogenesis of both COPD and osteoporosis. Osteoporosis is less common in male. We intended to investigate whether smoking and COPD is the independent risk factor of osteoporosis in male smoker in our population.

Aims and Objectives:

To see the frequency of osteoporosis in male smokers with and without chronic obstructive pulmonary disease.

Materials and Methods:

This cross sectional comparative study was carried out in the Department of Medicine Sylhet M.A.G. Osmani Medical College Hospital, Sylhet during 1st July 2013 to 30th June 2015. Seventy four male smokers with COPD and 66 age-matched male smokers without COPD (having normal lung function) were consecutively enrolled. All individuals were underwent Bone Mass Densitometry (BMD) by Dual-Energy X-Ray Absorptiometry (DEXA).

Results:

The age (62.57±8.02 years versus 60.65±7.12 years; p=0.139) and smoking pack-years (37.50 ± 16.77 versus 33.39 ± 13.82; p=0.118) did not differ significantly between COPD and non-COPD groups. T-score (-2.31 ± 0.92 versus -1.65 ± 0.93; p<0.001) and BMD (0.77 ± 0.11 gm/Cm2 versus 0.86 ± 0.12 gm/Cm2; p<0.001) of the neck of femur were significantly lower in COPD group than that of control group (0.77 ± 0.11 gm/Cm2 versus 0.86 ± 0.12 gm/Cm2; p<0.001). Similarly T-score (-3.01 ± 1.26 in COPD versus -1.92 ± 1.13; p<0.001) and BMD of the lumbar spine (0.86 ± 0.16 gm/Cm2 versus 0.97 ± 0.13 gm/Cm2; p<0.001) were significantly lower in COPD group than that of control group. Osteoporosis of the femoral neck was present in 36 (48.6%) COPD patients and 11 (16.7%) control subjects (p<0.001). Similarly osteoporosis in lumbar spine was 51 (68.9%) in COPD patients and 25 (37.9%) in control subjects (p<0.01). Multivariate analysis showed that presence of COPD significantly predicts osteoporosis (OR=3.508; 95% CI 1.511-8.142; p=0.003). But age, smoking-pack years and BMI did not have significant association with osteoporosis.

Conclusions:

The prevalence of osteoporosis in patients with COPD was higher than the age-matched control subjects without COPD. A lower FEV1 further increases the risk of osteoporosis in patients with COPD. COPD is risk factors for osteoporosis. Therefore, prevention of osteoporosis should be a part of medical care for COPD patients.

P22. [95] BODE index and CAT-test in the evaluation of pulmonary rehabilitation in chronic obstructive pulmonary disease patients with obesity

Poster Winner

Olga Nesterovska[1]; Ganna Stupnytska[2]

[1]*Bukovinian State Medical University, Chernivtsi, Ukraine;* [2]*Bukovinian State Medical University, Chernivtsi, Ukraine*

Pulmonary rehabilitation (PR) is considered to be one of the main methods of treatment and many studies have demonstrated its effectiveness in reducing dyspnea, increasing exercise capacity and improving quality of life. In order to evaluate the effectiveness of PR, integral indices, in particular the BODE index, are suggested to be used.

Objective:

to determine the effectiveness of PR in COPD patients with obesity using the BODE index and the CAT-test.

Material and methods:

pulmonary rehabilitation involved 48 patients with COPD and obesity. The BODE index (body mass index, forced expiratory volume in one second, dyspnoea and 6-min walk distance) and the CAT-test were evaluated before and after 6-month PR program. In addition to the PR, patients with COPD and obesity were prescribed a diet and physical aerobic exercise to reduce body weight.

Results:

The initial level of the BODE index and the CAT test in COPD patients with obesity was 4.96 ± 0.56 and 18.72 ± 1.71, respectively. After 6 months of PR the BODE decreased reliably by 22.4%. The CAT test in COPD patients with obesity also decreased reliably by 32.4%. In the structure of the BODE index, dyspnea and exercise capacity had the best dynamics (the number of points on the mMRC scale decreased by 23.3% and an increase in the distance traveled by patients in a 6-minute walk test from 232.04 ± 19.19 to 261, 84 ± 21.37). The body mass index decreased by 10.4%. FEV1 after the PR decreased slightly (by 9.4%).

Conclusions.

This study shows that COPD patients with obesity need a complex of physical exercises and a diet that contribute to lowering the body mass index and dyspnea, improving exercise capacity and COPD symptoms to be added to the PR.

P09. [31] A case of nontuberculosis mycobacterial lung disease in a patient with chronic eosinophilic colitis and malabsorption syndrome

Diana Petkova[1]; Donka Stefanova[2]; Iskren Kotzev[3]; Velin Stratev[1]; Boyan Balev[4]; Petar Genev[5]; Dimitar Kostadinov[2]; Valentina Dimitrova[1]; Tanya Dobreva[1]

[1]*Clinic of pulmonary diseases,UMHAT "St. Marina", Varna, Bulgaria;* [2]*University hospital of pulmonary diseases "St. Sofia", Sofia, Bulgaria;* [3]*Clinic of gastroenterology, UMHAT "St. Marina", Varna, Bulgaria;* [4]*Clinic of image diagnostics, UMHAT "St. Marina", Varna, Bulgaria;* [5]*Clinic of pathology, UMHAT "St. Marina", Varna, Bulgaria*

Introduction:

NTM have non-specific clinical presentation in immunocompetent patients and are difficult to diagnose in the presence of other chronic inflammatory conditions.

Case report:

A 67 years old female presented in the pulmonary clinic with occasional non-productive cough, fever and loss of weight. After a period of food intolerance and detected blood eosinophilia (12%) she was performed colonoscopy showing lymphoplasmocytic and eosinophilic infiltrates in the mucosa. PET CT demonstrated focal ventrally located opacity in the left lung with honey-combing structure and slight uptake of the FDG. On a subsequent HRCT this opacity was larger and there was additional finding of granuloma adjacent to the pleura and two nodules with 6-16 mm size in the left lung. The suspected diagnosis was eosinophilic granulomas. T-SPOT TB and HIV tests were negative. In the pulmonary clinic we performed true cut biopsy of the lesions with results displaying non-caseous granulomas, small areas of necrosis, possible sarcoidosis. A subsequent bronchoscopy with BAL showed cytology consistent with allergic alveolitis or Churg-Strauss syndrome. Though, c-ANCA and p-ANCA were negative. Microbiology of BAL showed positive cultures on MGIT and Lowenstein-Jensen media. Molecular testing for Mycobacterium tuberculosis complex was negative and for Mycobacterium avium complex – positive. This was confirmed by lung biopsy with histological result: infectious-type granulomatous disease; morphologic picture is most consistent with mycobacterial infection. Treatment with clarithromycin, rifampicin and ethambutol was started with general improvement of the patient condition.

P04. [23] Demographic Investigation of Children with Lower Respiratory Tract Infection in Pediatric Emergency Service

Dilara Sahin[1]; Nejla Canbulat Sahiner[1]; Ayse Sonay Turkmen[1]; Meryem Kayhanlar[2]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoğlu Mehmetbey University Health Service Vacational School, Karaman, Turkey*

Aim:

This study was planned retrospectively to evaluate the demographic characteristics of lower respiratory tract infections.

Method:

Archive records of children who were admitted to pediatric emergency department with respiratory complaints and diagnosed with lower respiratory tract infections constituted research data. Records of children diagnosed with lower respiratory tract infection were examined in terms of age, sex, month of application and number of days of discharge. The data were analyzed with descriptive statistics.

Results:

A total of 66 children were diagnosed with lower respiratory tract infections in the pediatric emergency department in the last year. The mean age of the children was 3.74 ± 4.21 and 54.5% were male (n = 36). Children usually referred to the hospital from 10:00 to 12:00 (n=18) and from 20:00 to 22:00 (n=13). Most applications were made in January (n = 11) and September (n = 11). A total of 2 children were admitted to the hospital after the examination and stayed in the hospital for 6 days.

Conclusion:

It has been determined that lower respiratory tract infections, which are common respiratory system disorders in children, occur in girls and boys alike and usually occur in January or September, and do not cause hospitalization in large numbers.

Key words: child, emergency department, lower respiratory tract infection

P23. [96] Synergistic Activity Of Colistin In Combination With N-Acetylcysteine Against Colistin-Resistant Acinetobacter Baumannii Grown In Biofilms

Francesco Sergio[1]; Lucia Pallecchi[2]; Francesco Blasi[3]; Stefano Aliberti[3]; Gian Maria Rossolini[4]

[1]*Global Respiratory Medical Affairs, Zambon S.p.A, Milan, Italy;* [2]*Dipartimento di Biotecnologie Mediche, Università di Siena, Ospedale Universitario Santa Maria alle Scotte, Siena, Italy;* [3]*University of Milan, Milan, Italy;* [4]*Florence Careggi University Hospital, Florence, Italy*

Rationale.

Acinetobacter baumannii is a major respiratory pathogen, representing a leading cause of hospital-acquired pneumonia and being associated with higher morbidity and mortality rates, especially in critically ill patients. *A. baumannii* infections are often recalcitrant to antibiotic treatment, as a consequence of the propensity of this pathogen to grow in biofilms, and of the increasing dissemination of strains expressing extensively drug resistance (XDR) phenotypes. Colistin is a last-resort agent for the treatment of infections caused by XDR *A. baumannii*, and nebulized colistin (alone or in conjunction of intravenous colistin) has been increasingly used for the treatment of respiratory tract infections caused by those strains. In this perspective, great concerns arise from the rising trend of resistance to colistin observed in this pathogen over the last recent years. In a previous study, we reported that high N-acetylcysteine (NAC) concentrations (achievable by topical administration) were able to potentiate colistin activity against a collection of colistin-resistant *A. baumannii* strains grown in planktonic phase. Here we demonstrate that such synergism exerts also a relevant antibiofilm effect.

Methods.

Two XDR *A. baumannii* clinical isolates expressing a colistin resistance phenotype were investigated (i.e. *A. baumannii* Z165 and *A. baumannii* Z167). Biofilm susceptibility testing was performed using the Nunc-TSP lid system. Biofilms were grown in cation-adjusted Mueller Hinton broth for 7 days, and successively exposed to NAC/colistin combinations. Three NAC concentrations (i.e. 1.6, 3.2 and 8 mg/ml) and three colistin concentrations (i.e. 2, 8 and 32 mcg/ml) were tested alone and in combination. Biofilm mass was determined by biofilm disruption and viable cell count (i.e. enumeration of colony forming units - CFUs) at time 0 (i.e. before exposure to NAC/colistin combinations) and after 24 hours of exposure.

Results.

Under the experimental conditions adopted, biofilms were formed by an average of 6.08 ± 0.49 and 5.89 ± 1.06 log CFU/ml, for *A. baumannii* Z165 and *A. baumannii* Z167, respectively. Antibiofilm activity was not observed with NAC alone, or colistin ≤ 8 mcg/ml alone. Colistin at 32 mcg/ml eradicated both biofilms. A relevant antibiofilm activity of NAC/colistin combinations was demonstrated for both tested strains. NAC potentiated colistin activity in a concentration-dependent way, but a relevant antibiofilm activity was already observed with colistin 8 mcg/ml plus NAC 1.6 mg/ml (i.e. reduction of >3 log CFU/ml compared to controls).

Conclusion.

Nebulized NAC/colistin combinations might represent a valid treatment option for biofilm-associated infections caused by colistin-resistant *A. baumannii* strains.

P13. [37] Biomarkers in Adult Asthma: Identifying the Role of the Peripheral Serotonergic System in Asthma Severity

Katherina Bernadette Sreter[1]; Sanja Popovic-Grle[2,3]; Dubravka Svob Strac[4]; Marina Lampalo[2]; Irena Jukic[5,6]; Nela Pivac[4]

[1]*Department of Clinical Immunology, Pulmonology and Rheumatology, University Hospital Centre "Sestre Milosrdnice", Zagreb, Croatia;* [2]*Clinic for Respiratory Diseases "Jordanovac", University Hospital Centre Zagreb, Zagreb, Croatia;* [3]*School of Medicine, University of Zagreb, Zagreb, Croatia;* [4]*Division of Molecular Medicine, Laboratory for Molecular Neuropsychiatry, "Ruđer Bošković" Institute, Zagreb, Croatia;* [5]*Quality Management, Croatian Institute for Transfusion Medicine, Zagreb, Croatia;* [6]*Faculty of Medicine, University of Osijek, Osijek, Croatia*

Background/Aims:

Asthma is a major worldwide healthcare problem. This common chronic inflammatory lung disease has an unclear pathophysiology. Previous research has linked the serotonergic system with asthma. Various studies to date have focused on the association of asthma with serum/plasma serotonin (5-HT) levels; however, the data are inconclusive. The aim of this study was to determine the concentrations of platelet 5-HT in adult asthmatic patients and evaluate their association with asthma severity.

Methods:

This prospective case-control study included 93 asthmatics and 49 healthy individuals (29 females, 20 males). Depression was a major exclusion criterion. Asthma severity was determined according to the Global Initiative for Asthma (GINA) criteria. Blood (8 mL) was drawn from a cubital vein into a yellow top Vacutainer tube containing 2 mL of acid-citrate-dextrose (ACD) anticoagulant solution. Blood samples were initially processed to obtain platelet-rich plasma. The platelet 5-HT concentrations were determined using the spectrofluorometric method. Total platelet protein concentrations were determined by the method of Lowry.

Results:

The median age of the asthmatic patients was 60 (range 18-88 years) versus healthy subjects 41 (range 25-63 years). There were 45 cases of intermittent/mild-to-moderate persistent (GINA I-III, 29 females, 16 males) and 48 cases of severe persistent (GINA IV, 27 females, 21 males) asthma. All groups exhibited similar gender distribution, with females predominating ($p=0.718$, Chi-square test). Age varied significantly among the groups ($p<0.0001$, ANOVA); younger individuals were present in the control group than in both groups of asthmatic patients. There were fewer smokers than non-smokers (never-smokers and former-smokers) in all groups. A greater percentage ($p<0.0001$, Chi-square test) of smokers was noted in the control group (63%) than in the asthmatic groups (7% in GINA I-III, 12% in GINA IV). There was a significant difference ($p<0.0001$, Kruskal-Wallis test) in platelet 5-HT concentrations between all groups (GINA I-III vs control ($p<0.0001$, Dunn's test), GINA IV vs control ($p=0.004$, Dunn's test), and GINA I-III vs GINA IV ($p=0.023$, Dunn's test). The lowest concentration of platelet 5-HT was found in the GINA I-III group.

Conclusions:

These preliminary findings are in line with data suggesting a possible association of the serotonergic system with asthma. Rather intriguing, however, is the result that the severe asthmatics demonstrated higher concentrations of 5-HT than patients with milder asthma. Further studies are warranted to investigate the possible application of platelet 5-HT concentration as a potential biomarker of asthma severity in adults.

P08. [30] Evaluation of Cases Pneumonia Attending Pediatric Emergency Department

Ayse Sonay Turkmen[1]; Nejla Canbulat Sahiner[1]; Dilara Sahin[1]; Meryem Kayhanlar[2]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Services Vocational School, Karaman, Turkey*

Aim:

This study was planned retrospectively to evaluate the demographic characteristics of pneumonia cases.

Method:

Archive records of children who were diagnosed with pneumonia in the pediatric emergency department with respiratory complaints were the research data. Records of children receiving pneumonia recognition were examined in terms of age, sex, month of application and number of days of discharge. The data were analyzed with descriptive statistics.

Results:

A total of 120 children were diagnosed with pneumonia in the pediatric emergency department in the last year. The mean age of the children was 3.00 ± 3.02 and 54.1% were male (n = 65). Children usually referred to the hospital between 10: 00-12: 00 (n = 42). The most frequent application was between November-December (n = 39). 48.3% of the children were admitted to the hospital after the examination and they stayed in the hospital for a mean of 4.6 days.

Conclusion:

It has been observed that pneumonia, a common respiratory system disorder in children, occurs in boys, usually in November-December, and causes hospitalization in large proportions.

Key words: child, emergency department, pneumonia

P07. [29] Retrospective Investigation of Asthma Cases Attending Pediatric Emergency Department

Ayse Sonay Turkmen[1]; Nejla Canbulat Sahiner[1]; Meryem Kayhanlar[2]; Dilara Sahin[1]

[1]*Karamanoglu Mehmetbey University Health Science Faculty, Karaman, Turkey;* [2]*Karamanoglu Mehmetbey University Health Service Vocational School, Karaman, Turkey*

Aim:

This study was retrospectively planned for the demographic evaluation of asthma cases.

Method:

Archive records of children who were diagnosed with asthma by applying to the pediatric emergency department with respiratory complaints constituted research data. Records of children receiving asthma diagnosis were examined in terms of age, sex, month of application and number of days of discharge. The data were analyzed with descriptive statistics.

Results:

A total of 204 children were diagnosed with asthma in the pediatric emergency department in the last year. The mean age of the children was 6.78 ± 4.73 and 62.7% were male (n = 128). Children usually referred to the hospital between 10: 00-16: 00 (n = 145). Most applications were made in March-May (n = 91). A total of 5 children were admitted to the hospital after the examination and stayed in the hospital for 2 days.

Conclusion:

It has been observed that asthma from children with respiratory system disorders, which is common in children, may occur in boys and usually on March-May, causing hospitalization.

Key words: child, emergency department, asthma

P16. [63] Rate of all-cause hospitalization at year 2 between treatment groups following diagnosis of nontuberculous mycobacterial lung disease in the US

Roald van der Laan[1]; Theodore Marras[2]; Mehdi Mirsaedi[3]; Gina Eagle[1]; Engles Chou[1]; Raymond Zhang[4]; Ping Wang[1]; Marko Obradovic[1]; Quanwu Zhang[1]

[1]*Insmed Inc., Bridgewater, NJ, USA;* [2]*University of Toronto, Toronto, ON, Canada;* [3]*University of Miami, Miami, FL, USA;* [4]*Orbis Data Solutions, Woburn MA, USA*

Background:

The study compared rates of hospitalization between treatment groups in patients with nontuberculous mycobacterial lung disease (NTMLD) in a US national managed care claims database.

Methods:

Patient (N=1039) pharmacy claims at year 1 following NTMLD diagnosis were classified into 3 treatment groups including ATS/IDSA guidelines based therapy (macrolide + ethambutol + rifamycin ± other drugs) (GBT), other antibiotics used by physicians for NTMLD (Other), and no treatment (Untreated). Hospitalization rates at year 2 were compared between treatment groups using mixed effects logistic regression to adjust for patient characteristics and comorbidities measured by Charlson Comorbidity Index (CCI) during the 12 months prior to NTMLD diagnosis (baseline).

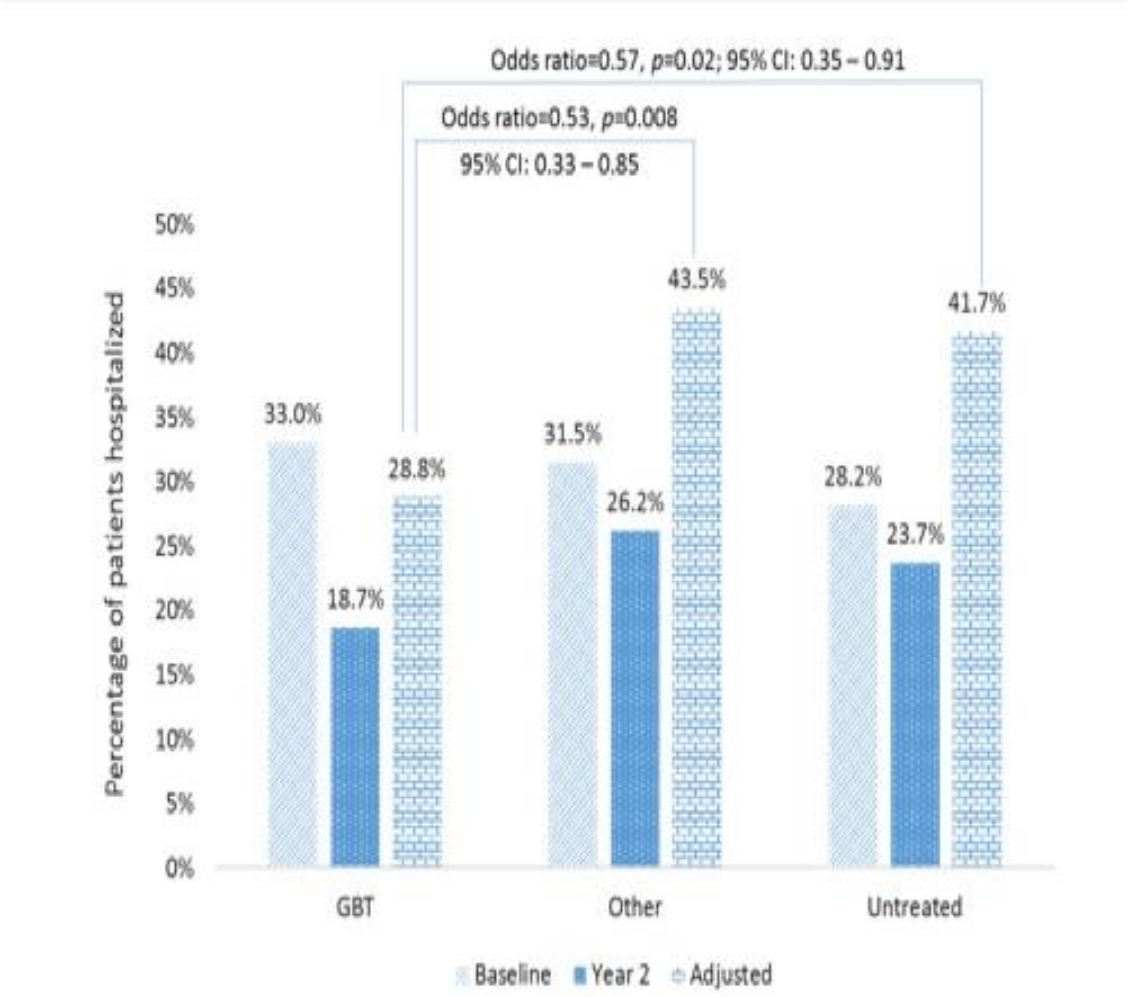
Results:

Mean age was 65, 64 and 71 years with 67%, 69% and 68% women in GBT (n=294), Other (n=298) and Untreated (n=447) respectively. At baseline, there was no difference on CCI (CCI≈2) between treatment groups. However, comorbidity distribution differed prominently in asthma (21.4%, 29.5% and 14.1%), arrhythmia (18.7%, 18.8% and 25.3%), cystic fibrosis (1.0%, 5.0% and 0.7%), immune deficiency (7.5%, 9.1% and 4.7%), pneumonia (50.3%, 43.0% and 34.9%), and tuberculosis (8.8%, 9.4% and 6.0%), and in immunosuppressant use (563.6%, 61.7% and 39.1%). Baseline hospitalization was 33.0% in GBT, 31.5% in Other, and 28.2% in Untreated. At year 2, unadjusted hospitalization rates were 18.7%, 26.2% vs 23.7%, and adjusted rates were 28.8%, 543.5% and 41.7% in 3 treatment groups respectively (Figure). GBT had a significantly lower risk of hospitalization after adjustment (compared to Other (odds ratio (OR)=0.53, 95% CI: 0.33-0.85, *p*=0.008), and compared to Untreated (OR=0.57, 0.35-0.91, p=0.02). Age ≥65 years (OR=1.56, p=0.01), baseline hospital admission (OR=1.69, p=0.002), and cystic fibrosis (OR=5.76, p<0.01) were associated with an increased risk of hospitalization at year 2 after NTMLD diagnosis. By removing patients with CF, the rate of hospitalization was further reduced with GBT in comparison to Other (OR=0.49, 0.30-0.81, p=0.005) or Untreated group (OR=0.57, 0.35-0.93, p=0.02).

Conclusions:

We observed a lower hospitalization rate in NTMLD patients receiving antibiotics that were concordant with first line ATS/IDSA guidelines recommendations in comparison with those who used other antibiotic regimens.

Figure. Percent of patients hospitalized at Year 2 between treatment groups following diagnosis of NTMLD



P15. [62] Relative Risk of All-Cause Mortality in Patients With Nontuberculous Mycobacterial Lung Disease in US Managed Care

Roald van der Laan[1]; Theodore Marras[2]; Vinnard Christopher[3]; Hamilton Keith[4]; Gina Eagle[1]; Engles Chou[1]; Raymond Zhang[5]; Marko Obradovic[1]; Quanwu Zhang[1]

[1]*Insmed Inc., Bridgewater, NJ, USA;* [2]*University Health Network, Toronto, ON, Canada;* [3]*New Jersey Medical School, Rutgers,The State University of New Jersey, Newark, NJ, USA;* [4]*University of Pennsylvania, Philadelphia, PA, USA;* [5]*Orbis Data Solutions LLC, Woburn MA, USA*

Purpose:

A health insurance claims database study was conducted to evaluate the relative risk of all-cause mortality and risk factors between patients diagnosed with nontuberculous mycobacterial lung disease (NTMLD) and an age-sex–insurance coverage matched control group.

Methods:

Patients from a national managed care insurance plan with physician claims for NTMLD on ≥2 separate occasions ≥30 days apart (n=2005) were identified between 2007 and 2016. A control group without NTMLD (n=6014) was matched 3:1 to the NTMLD sample according to age, sex and insurance coverage period. The date of first NTMLD diagnosis was assigned to the matched controls as an index date. All individuals in the analysis had ≥12 months of healthcare coverage before the index date. Mortality data originated from the Social Security Death Master File. The number of mortality records after 2011 was reduced about 30% owing to local reporting decisions. A Cox regression was used to compare survival between NTMLD patients and controls, adjusting for demographic factors and baseline health indicators.

Results:

Mean age was 67 years, and 66% were female. Mean follow-up time to death or to data cutoff date was 3.4 years for NTMLD and 3.65 years for controls. Mean Charlson comorbidity index score was 2.2 in NTMLD patients vs 0.5 in controls. Selected baseline health conditions in NTMLD vs controls included 36.5% vs 0.1% bronchiectasis, 52.0% vs 5.9% COPD, 44.5% vs 1.7% pneumonia, 23% vs 3.5% asthma, 2.1% vs 0% cystic fibrosis, 15.4% vs 12.4% diabetes, 3.8% vs 4.0% obesity, 9.9% vs 3.8% depression, 6.1% vs 0.6% lung cancer, 55.1% vs 14.6% use of immunosuppressive drugs, 23.0% vs 4.0% tobacco use, 2% vs 0.1% HIV infection, and 1.6% vs 0.1% organ transplant. The rate of all-cause mortality from the index date was 20.7 in NTMLD patients vs 5.6 in controls per 1000 person-years (rate ratio=3.73; 95% CI: 2.93-4.75). Multivariable adjusted Cox regression showed a doubling risk of all-cause mortality (hazard ratio [HR]=2.11; CI: 1.56-2.85; *P*<.001) in the NTMLD vs control group. The Cox model also showed that mortality more than doubled (HR=2.35) with each additional 20 years of age (*P*<.001) and increased 48% with male sex, 540% with moderate or severe liver disease (*P*<.001), 87% with lung cancer (*P*=.01), 65% with a psychiatric disorder (*P*=.002), 100% with an immune deficiency (*P*=.006), and 44% with use of an inhaled corticosteroid agent (*P*=.02). Obesity (HR=.31; *P*=0.02) and atherosclerosis (HR=.57; *P*=.035) were associated with a decreased risk of all-cause mortality.

Conclusions:

All-cause mortality more than doubled with NTMLD compared with an age-sex–insurance coverage matched control group in a large US national managed care insurance plan, even after adjustment for other risk factors. The incremental risk of all-cause mortality in NTMLD compared to controls represents a critical unmet medical need and requires effective management of the disease.

Rising Star winners

[17] Assessing inflammatory patterns in asthma endotypes: new diagnostic and therapeutic perspectives

Matteo Bradicich[1,2]; Ian Pavord[2]; Gareth Hynes[2]; Rahul Shrimanker[2]

[1]*Respiratory Pathophysiology and Rehabilitation Department, Cisanello University Hospital, University of Pisa, Pisa, Italy;* [2]*Respiratory Medicine Unit, Nuffield Department of Clinical Medicine, NDM Research Building, University of Oxford, Oxford, United Kingdom*

Background

Bronchial asthma is a chronic airway disease affecting more than three hundred million patients worldwide. Given the high prevalence of this disease and the social and economic burden resulting from under- or mistreatment, the optimal management of this condition represents therefore a key goal. In order to investigate the pathophysiological heterogeneity of this disease, a rather new trend in the Literature suggests categorising different asthmatic patient subpopulations on the basis of their specific molecular patterns, which are supposed to represent the key pathological determinant leading to one particular group of symptoms and signs – i.e. a phenotype – rather than another one. Therefore, asthma endotypes are the key for understanding and treating asthmatic patients with a precision medicine approach.

Overview

A clinical study led by Oxford (United Kingdom) and Pisa (Italy) Universities quantifies the differences in the expression levels of multiple sputum inflammatory molecules between different subpopulations of asthmatic patients, previously labelled on the basis of their sputum differential cell count as affected by eosinophilic, neutrophilic, mixed, or paucigranulocytic asthma.

Methods

37 asthmatic patients and 12 healthy controls were recruited. Assessment of symptom burden and medication usage as well as laboratory measures including blood and sputum cell count and cytokine levels in sputum supernatant – measured using MSD® and Luminex® – was performed. The asthmatic patients were subdivided in four subgroups (eosinophilic, neutrophilic, mixed, and paucigranulocytic) on the basis of their sputum differential cell count. A comparison of the sputum concentration of the inflammatory molecules taken into consideration (IL-2, IL-4, IL-5, IL-8, IL-13, IL-17, IL-25, IL-33, PGD2, LTE4, TNF-α) between the aforementioned subgroups was subsequently carried out.

Results

The study shows that sputum IL-8, IL-17 and TNF-α are leading molecules in the neutrophilic asthma endotype, whilst sputum IL-5 and IL-33 underlie eosinophilic asthma. The mixed endotype is defined by high levels of sputum IL-5, IL-8 and IL-33. There are no significant results regarding paucigranulocytic asthma.

Conclusions

These pathophysiologic differences might be used in a compact, multi-cytokine assessment test that defines univocally the specific patient's inflammatory pattern from a single sample of induced sputum. Such results shed light on the multifaceted inflammatory environment in bronchial asthma and might promote further research in order to define new targeted therapy strategies for those patients with difficult-to-treat asthma.

Table 1	Eosinophilic (n=15)	Neutrophilic (n=9)	Mixed (n=9)	Paucigranulocytic (n=4)	Healthy Controls (n=12)	p-value
Age (years) mean (SD)	56 (15)	61 (13)	58 (8)	62 (11)	45 (12)	0,107
Percentage female	54%	54%	86%	0%	57%	0,183
Age diagnosed (years) mean (SD)	52 (19)	42 (19)	41 (17)	38 (21)		0,597
Pre-bronch. FEV1 (L) median (IQR)	2,44 (1,25)	2,23 (0,92)	1,19 (0,89)	3,35 (1,02)	2,92 (1,04)	**<0,001**
% w/ Fixed Airway Obstruction	69%	69%	43%	67%		0,635
GP/A&E unscheduled visits mean (SD)	3,3 (3,6)	2,7 (1,4)	3,2 (2,7)	np		0,909
ICS dose (BDP equivalent, µg) median (IQR)	1000 (900)	1300 (1000)	1600 (1000)	400 (600)		0,113
Percentage on OCS	33%	0%	0%	0%		
OCS dose (median (IQR)) for those taking OCS (mg)	10,0 (8,75)	0	0	0		
FeNO (ppb)	80 (50-129)	25 (20-31)	32 (18-58)	30 (0.32-2852)	17 (12-23)	**<0,001**
Luminex IL-2 (pg/mL)	510 (285-920)	360 (160-840)	370 (250-540)	np	270 (48-1600)	0,660
Luminex IL-4 (pg/mL)	256 (161-408)	260 (140-490)	273 (140-532)	389 (0,08-2,0*10^6)	196 (106-364)	0,582
MSD IL-5 (pg/mL)	np	30,37 (15,65-58,93)	47,65 (7,91-287,0)	np	8,11 (1,95-33,77)	**0,049**
Luminex IL-8 (ng/mL)	3,73 (2,13-6,52)	15,89 (6,16-40,98)	11,55 (5,39-24,76)	np	10,96 (7,61-15,79)	**0,006**
Luminex IL-13 (pg/mL)	35,08 (18,63-66,06)	46,11 (25,24-84,24)	39,42 (19,46-79,84)	50,58 (92,10-277,74)	24,78 (13,74-44,70)	0,294
MSD IL-17 (pg/mL)	np	336,5 (165,4-684,5)	138,4 (81,85-234,2)	np	36,71 (13,59-99,14)	**<0,001**
Luminex IL-25 (pg/mL)	1300 (940-1900)	1000 (450-2300)	880 (260-3000)	800 (12-5,3*10^4)	530 (68-4200)	0,410
Luminex IL-33 (pg/mL)	93,07 (43,29-200,1)	42,14 (28,17-63,05)	76,69 (26,97-218,1)	np	87,45 (0,025-300016)	0,124
MSD LTE4 (pg/mL)	2394 (121-47546)	1229 (416-3632)	1474 (626-3473)	2457 (603-10015)	254,2 (145-446)	**0,030**
MSD PGD2 (pg/mL)	2050 (1400-3100)	3020 (845-10800)	1100 (260-4700)	3050 (92-10,1*10^5))	2500 (1200-5100)	0,645
MSD TNF-α (pg/mL)	np	594 (50,38-7003)	136,8 (58,54-319,6)	847,3 (0,016-4,6*10^5)	60,11 (15,03-240,5)	**0,032**
Blood eosinophils (x 10^9/L)	0,46 (0,34-0,61)	0,20 (0,13-0,30)	0,24 (0,13-0,43)	0,24 (0,04-1,30)	0,13 (0,7-,27)	**0,004**
Blood neutrophils (x 10^9/L)	4,0 (3,3-4,9)	4,2 (3,4-5,2)	4,0 (3,3-4,9)	3,6 (2,5-5,2)	2,9 (2,1-4,0)	0,220
Sputum eosinophils (%)	22,0 (12,0-40,3)	0,84 (0,36-2,0)	8,0 (4,9-13,0)	0,81 (0,037-17,9)	0,33 (0,14-0,78)	**<0,001**
Sputum neutrophils (%)	20,5 (12,3-34,1)	87,8 (83,2-92,6)	74,0 (67,2-81,6)	51,3 (16,1-163,1)	47,7 (29,0-78,6)	**<0,001**
Lost days (work/school) median (IQR)	16 (28)	10 (23)	15 (16)	np		0,948
% pts who lost days	13%	44%	22%	np		
AQLQ overall score median (IQR)	5,1 (2,8)	5,2 (1,3)	4,4 (2,8)	6,6 (0,78)		**0,089**
ACQ-5 final score median (IQR)	2,2 (2,7)	1,6 (1,6)	3,1 (1,5)	0,9 (1,4)		0,145

Table 1. Results given as stated. FeNO, sputum IL-2, IL-4, IL-5, IL-8, IL-13, IL-17, IL-25, IL-33, LTE4, PGD2, TNF-α, blood eosinophils, blood neutrophils, sputum eosinophils, and sputum neutrophils did not conform to a normal distribution, therefore for these values the geometric mean (confidence interval in brackets) is presented. P-values listed for Kruskal-Wallis test comparisons between the endotype groups and the control group. SD – standard deviation; FeNO – fractional exhaled nitric oxide; ppb – parts per billion; np – not performable. Fixed airway obstruction is defined as a post-bronchodilator FEV1 absolute change <200 mL or a post-bronchodilator FEV1 increase <12%.

Table 2	IL-8	IL-17	TNF-α	IL-5	IL-33
Neutrophilic	+	+	+	-	-
Eosinophilic	-	-	-	+	+
Mixed	+	-	-	+	+

Table 2. Summary of the different cytokine expression patterns, clustered on the basis of a higher or lower sputum concentration observed in each endotype subgroup of the study. "+" represents a particularly high sputum concentration, while "-" represents a not particularly high/particularly low sputum concentration. Both these cut-offs need to be more precisely defined by further investigation. TNF-α: Tumour Necrosis Factor-α.

[54] Circulating MDSC modulate IPF progression by orchestrating immunosuppressive and pro-fibrotic networks

Isis E. Fernandez[1]; Flavia Greiffo[1]; Marion Frankenberger[1]; Jurgen Behr[2,3]; Alistair Forrest[4]; Oliver Eickelberg[1,5]

[1]*Comprehensive Pneumology Center, Helmholtz Zentrum Munchen; Member of the German Center for Lung Research, Munich, Germany;* [2]*Asklepios Fachkliniken Munchen-Gauting, Munich, Germany;* [3]*Comprehensive Pneumology Center, Medizinische Klinik und Poliklinik V, Klinikum der Ludwig-Maximilians- Universität, Munich, Germany;* [4]*Harry Perkins Institute of Medical Research, QEII Medical Centre and Centre for Medical Research, the University of Western Australia, Perth, Australia;* [5]*Division of Respiratory Sciences and Critical Care Medicine, Department of Medicine, University of Colorado, Denver, USA*

Rationale:

Idiopathic pulmonary fibrosis (IPF) is a fibroproliferative lung disease with irreversible loss of lung function. Myeloid-derived suppressor cells (MDSC) are pathologically activated immature myeloid cells, which suppress immune responses in cancer, autoimmunity, and other inflammatory conditions. Recent literature supports that aberrant immune responses contribute to IPF pathogenesis. We reported, for the first time, that MDSC are increased in numbers, functionally active, and reflect disease status in IPF, in cross-sectional and longitudinal analysis serving as potent biomarker for IPF progression. Monocytic MDSC are the predominant subtype in IPF, and yet, differences between mature monocytes and monocytic MDSC, and their interaction in IPF have not been explored. Here we hypothesize that MDSC creates an immunosuppressive and pro-fibrotic environment in IPF, perpetuating disease.

Methods and results:

We included 170 patients, including patients with IPF (n=69), non-IPF ILD (n=56), COPD (n=23), and healthy controls (n=22). We detected increased circulating MDSC in IPF compared to controls (30.99±15.61 vs 18.96±8.17**%,** *p*=<0.005), and a positive correlation between MDSC and FoxP3+ Tregs (r=0.35, p=0.04). In IPF, circulating MDSC inversely correlated with VCmax % predicted (r=-0.48, *p*=<0.0001). Correlation analysis of ΔVCmax with ΔMDSC, from visit 1 and 2, showed a strong correlation for longitudinally assessed IPF patients (r=-0.6052). The mRNA levels of the costimulatory signals during T cell activation (CD28, ICOS, ITK, and LCK) were significantly downregulated in PBMC, of IPF patient with high circulating MDSC. Next, using label-free quantitative MS-analysis, monocytes and MDSC isolated from human blood of 10 IPF patients were analyzed (MACS and FACS sorted, respectively). In total, we identified and quantified more than 7000 proteins. Principal component analysis unequivocally discriminated both cell types, showing that proteome differences between them are larger than the biological variations between the donors. Comparing the sets of proteins identified in the two cell types we found 502 MDSC enriched and 1224 monocyte enriched proteins (2 to >30 log10-transformed LFQ intensity ratios). Next, we examined the potential for these two cell types to communicate with each other, by identification of the receptors and ligands expressed by each, and considering known receptor-ligand interactions, compiled from published datasets. In the combined dataset 200 ligands and 153 receptors were detected. From the cell-to-cell communication analysis we identified both autocrine signaling edges from monocyte to monocyte (339), MDSC to MDSC (290), and paracrine signaling edges from monocyte to MDSC (311) and MDSC to monocyte (316). Specific ligands predicted to signal from monocyte to MDSC included: ANXA1, CCL18, CXCL2, HSP90AA1, ICAM1, TGFB2, amongst others. While ligands from MDSC to monocyte included: COL1A1, FN1, HLA-C, HSPG2, MMP1,

S100A8-9, TGFB1, amongst others. Finally, FACS staining confirmed the surface expression of the cognate expressed receptors in both populations.

Conclusions:

In summary, this study explores for the first time the MDSC proteome in fibrosis. We detected an increase in MDSC in peripheral blood from IPF patients. We further detected a correlation between MDSC and FoxP3+ T cells, and a decrease in the transcript levels of CD28, ICOS, ITK, and LCK in PBMC of IPF patients, suggesting that elevated MDSC might cause a blunted immune response. MDSC inversely correlate with lung function, as such MDSC may serve as potent biomarker for IPF progression. Using network analysis, our proteome data shows an autocrine and paracrine signals from and between monocytes and MDSC. MDSC signals include strong pro-fibrotic molecules, supporting a pro-fibrotic modulation. Furthermore, confirmation by flow cytometry of exclusively expressed surface receptors, might lead to identification of novel proteins useful for therapeutic targeting of MDSC and monocytes in IPF.

BERLIN

18 – 20 January 2018

5th INTERNATIONAL WORKSHOP ON LUNG HEALTH

Asthma & COPD - Personalised Medicine: From Myth to Real Life

Organizing Secretariat

Publi Créations

74 BD d'Italie, MONTE CARLO
MC, 98000 (MONACO)
PH: + 377 9797 3555
lunghealth@publicreations.com