ABSTRACTS

Assessment of asthma control: The SERENA study.

Corrado A, Renda T, Polese G, Rossi A; SERENA (Studio ossERvazionalE per il monitoraggio dell'asma non controllAto)/AIPO Study Group.

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Background: several studies suggest that many asthmatic subjects have uncontrolled asthma. The control of asthma is now considered the major goal of therapy.
Objectives: to ascertain the level of asthma control, by Asthma Control Test (ACT), in "real-life" clinical practice and the potential risk factors for uncontrolled disease in patients treated with inhaled corticosteroids (ICS) and long-acting beta-adrenergic agonists (LABA).
Methods: SERENA is a multi-centre, cross-sectional, 6-month observational, non-interventional study carried out in 16 Pulmonary Units in Italy. Asthmatic outpatients aged over 18, undergoing treatment with ICS at medium-high daily doses associated with LABA, were enrolled. The patients were divided in 3 subgroups according to the level of asthma control by ACT score (25:controlled; 20-24:partly controlled; <20: uncontrolled).
Results: Out of a total of 548 patients, 396 met the inclusion criteria. Only 9.1% of patients had asthma controlled, while partly controlled and uncontrolled asthma accounted for 39.6% and 51.3% respectively. The mean age was 54.5 ± 15.8 and the mean duration of asthma was 16.1 ± 14.1 years. There were more females than males (63% vs 37%) and females had highest prevalence of uncontrolled asthma (63.1%). The mean values of FEV1 % predicted were lower in the uncontrolled group ($p < 0.001$). The percentage of patients with at least 1 exacerbation, unscheduled visit and/or admissions was lower in controlled (22.2%, 8.3%, 8.3%) than in partly controlled (50%, 38.6%, 9.2%) and uncontrolled (83.2%, 66.2%, 27.8%) groups ($p < 0.0001$). The multivariate ordinal logistic regression analysis identified female sex, FEV_1 and exacerbations as the strongest independent factors associated with the uncontrolled disease.
Conclusion: This study highlights the importance in clinical practice of a periodic assessment by a validated asthma control instrument and exacerbations/health care contacts during previous year. Clinicians should be aware that a significant proportion of patients can have uncontrolled asthma, despite regular pharmacological treatment.

Programmatically selected multidrug-resistant strains drive the emergence of extensively drug-resistant tuberculosis in South Africa.

Müller B, Chihota VN, Pillay M, Klopper M, Streicher EM, Coetzee G, Trollip A,et al. PLoS One. 2013 Aug; 8(8):e 70919. doi: 10.13 71/journal.pone.0070919.

Background: South Africa shows one of the highest global burdens of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB). Since 2002, MDR-TB in South Africa has been treated by a standardized combination therapy, which until 2010 included ofloxacin, kanamycin, ethionamide, ethambutol and pyrazinamide. Since 2010, ethambutol has been replaced by cycloserine or terizidone. The effect of standardized treatment on the acquisition of XDR-TB is not currently known.
Methods: We genetically characterized a random sample of 4,667 patient isolates of drug-sensitive, MDR and XDR-TB cases collected from three South African provinces, namely, the Western Cape, Eastern Cape and KwaZulu-Natal. Drug resistance patterns of a subset of isolates were analyzed for the presence of commonly observed resistance mutations.
Results: Our analyses revealed a strong association between distinct strain genotypes and the emergence of XDR-TB in three neighbouring provinces of South Africa. Strains predominant in XDR-TB increased in proportion by more than 20-fold from drug-sensitive to XDR-TB and accounted for up to 95% of the XDR-TB cases. A high degree of clustering for drug resistance mutation patterns was detected. For example, the largest cluster of XDRTB associated strains in the Eastern Cape, affecting more than 40% of all MDR patients in this province, harboured identical mutations concurrently conferring resistance to isoniazid, rifamp icin, pyrazinamide, ethambutol, streptomycin, ethionamide, kanamycin, amikacin and capreomycin.
Conclusions: XDR-TB associated genotypes in South Africa probably were programmatically selected as a result of the standard treatment regimen being ineffective in preventing their transmission. Our findings call for an immediate adaptation of standard treatment regimens for M/XDR-TB in South Africa.

Smears and cultures for diagnosis of pulmonary tuberculosis in an asymptomatic immigrant population.

Assael R, Cervantes J, Barrera G.
Int J Gen Med. 2013 Sep 16;6:777-9

Background: The World Health Organization estimated in 2010 that 8.8 million new tuberculosis (TB) cases. About one-third of the world's population is infected and 10% will develop active TB disease. While cultures remain the international gold standard for diagnosing TB disease, in many other low-income countries, sputum smears remain the only and most accessible tool with which to diagnose active TB disease. As a consequence, in patients with TB who have negative smears, their TB remains undetected.
Aim: The objective of the study reported here was to demonstrate the proportion of smear-positive/culturepositive cases compared with smear-negative/culture-positive TB cases in Mexican immigrants bound for the USA.
Methods: A retrospective study was undertaken of the medical records of 122 active TB cases diagnosed at a clinic in Ciudad Juarez, Mexico, from 2009 to 2012. All cases were confirmed by culture, regardless of the sputum smear results.
Results: Of the cases, 80% (97 active TB cases) had negative sputum smears, while only 25 cases (20%) had at least one positive smear. All of the cultures were confirmed as positive for Mycobacterium tuberculosis complex.
Conclusion: The fact that 80% of the TB cases were smear negative and 20% smear positive shows that there is a clear gap between the actual state of active TB disease within patients under screening conditions, meaning that eight out of ten actual cases are being missed when sputum smear is the only diagnostic tool in asymptomatic patients with abnormal chest X-rays. Based on these results, it is highly recommended that countries that have not standardized culturing as the gold standard for the diagnosis of active TB do so, so that TB cases - which may endanger global public health - are not missed. It is also recommended that further studies be undertaken to determine the clinical background of the patients diagnosed by smear and culture to identify a direct relationship between clinical signs and symptoms and the smear result.

Evaluation of GenoType® MTBDRplus assay for rapid detection of drug susceptibility testing of multi-drug resistance tuberculosis in Northern India.

Maurya AK, Umrao J, Singh AK, Kant S, Kushwaha RA, Dhole TN.
Indian J Pathol Microbiol. 2013 Apr-Jun;56(2):139-43.

Background: The problem of multi-drug resistance tuberculosis (MDR-TB) is growing in several hotspots throughout the world. Rapid and accurate diagnosis of MDR-TB is crucial to facilitate early treatment and to reduce its spread in the community. The aim of the present study was to evaluate the new, novel GenoType® MTBDRplus assay for rapid detection of drug susceptibility testing (DST) of MDR-TB cases in Northern India.
Materials and Methods: A total of 550 specimens were collected from highly suspected drug resistant from pulmonary and extra-pulmonary TB cases. All the specimens were processed by Ziehl- Neelsen staining, culture, differentiation by the GenoType® CM assay, first line DST using BacT/ALERT 3D system and GenoType® MTBDRplus assay. The concordance of the GenoType® MTBDRplus assay was calculated in comparison with conventional DST results.
Results: Overall the sensitivity for detection of rifampicin, isoniazid and MDR-TB resistance by GenoType® MTBDRplus assay was 98.0%, 98.4% and 98.2% respectively. Out of 55 MDR-TB strains, 45 (81.8%), 52 (94.5%) and 17 (30.9%) strains showed mutation in rpoB, katG and inhA genes respectively ($P < 0.05$). The most prominent mutations in rpoB, katG and inhA genes were; 37 (67.3%) in S53 1L, 52 (94.5%) in S31 5T1 and 11 (20%) in C15T regions respectively ($P < 0.05$).
Conclusions: Our study demonstrated a high concordance between the GenoType® MTBDRplus assay resistance patterns and those were observed by conventional DST with good sensitivity, specificity with short turnaround times and to control new cases of MDR-TB in countries with a high prevalence of MDR-TB.

Chest Radiograph Findings and Time to Culture Conversion in Patients with Multidrug-Resistant Tuberculosis and HIV in Tugela Ferry, South Africa.

Brust JC, Berman AR, Zalta B, Haramati LB, Ning Y, Heo M, van der Merwe TL, Bamber S, Moll AP, Friedland GH, Shah NS, Gandhi NR.

PLoS One. 2013 Sep 6;8(9):e 73975. doi: 10.13 71/journal.pone.0073975.

Background: The majority of patients with multidrug-resistant tuberculosis (MDR-TB) in South Africa are co-infected with HIV, but the radiographic features of MDR-TB and their relationship with time to sputum culture conversion in the antiretroviral therapy era have not been described.
Methods: We reviewed baseline chest radiographs for 56 patients with MDR-TB from a rural area of South Africa. We analyzed the association of cavities, consolidation, pleural effusion and hilar lymphadenopathy with time to sputum culture conversion, adjusting for HIV status, baseline sputum smear and CD4 count.
Results: Of the 56 subjects, 49 (88%) were HIV-positive, with a median CD4 count of 136 cells/mm(3) (IQR 65-249). Thirty-two (57%) patients were sputum smear positive. Twenty-two (39%) patients had a cavity and 37 (66%) patients had consolidations. Cavitary disease and consolidations were each associated with longer time to culture conversion on bivariate analysis but not after adjusting for sputum smear status (aORs 1.79 [0.94-3.42] and 1.09 [0.67-1.78], respectively). Positive baseline sputum smear remained independently associated with longer time to conversion (aOR 3.45 [1 .39-8.59]). We found no association between pleural effusion or hilar lymphadenopathy and time to conversion. Seventy-nine percent of patients were cured at the end of treatment.
Conclusions: Despite high rates of HIV co-infection and advanced immunodeficiency, the majority of patients had severe pathology on baseline chest radiograph. Nevertheless, culture conversion rates were high and treatment outcomes were favorable. Cavitation and consolidation do not appear to have an independent association with time to culture conversion beyond that of baseline sputum smear status.

Longer storage duration of red blood cells is associated with an increased risk of acute lung injury in patients with sepsis.

Janz DR, Zhao Z, Koyama T, May AK, Bernard GR, Bastarache JA, et al.
Ann Intensive Care. 2013 Sep 24;3(1):33.

Background: The storage duration of red blood cells transfused to critically ill patients is associated with increased morbidity and mortality. Whether the association exists between storage duration of red blood cells transfused to patients with sep sis and the risk of developing ALI/ARDS is unknown. We aimed to determine the association of the storage duration of red blood cells transfused to patients with sepsis and risk of developing acute lung injury in the subsequent 96 hours, with comparator trauma and nonsepsis/nontrauma groups.
Methods: We conducted a retrospective observational study of 96 transfused, critically ill patients with sepsis, 176 transfused, critically ill patients with traumatic injury, and 125 transfused, critically ill nontrauma, nonsep sis patients. The primary outcome was the development of ALI/ARDS up to 96 hours after transfusion.
Results: In 96 patients with sepsis, 49 (51%) patients developed ALI/ARDS. The median storage duration of transfused blood in the ALI/ARDS group was greater (24.5 days, interquartile range (IQR) 20--3 1) compared with the patients who did not develop ALI/ARDS (21 days, IQR 15--27, p = 0.018). Longer median storage duration was independently associated with an increased risk of developing ALI/ARDS in the subsequent 4 days (odds ratio 1.8, p = 0.028). The same association was not seen in the trauma or nonsepsis, nontrauma patients.
Conclusions: Transfusion of blood with longer median storage duration to patients with sepsis is associated with a higher risk of developing ALI up to 4 days after transfusion. This same association is not seen in other critically ill patient populations.

Relationship between the Use of Inhaled Steroids for Chronic Respiratory Diseases and Early Outcomes in Community-Acquired Pneumonia.

Alm irall J, Bo líbar I, Serra-Prat M, Palom era E, Roig J, Hospital I, et al.

PLoS One. 2013 Sep 5;8(9):e73271. doi: 10.1371/journal.pone.0073271.

Background: The role of inhaled steroids in patients with chronic respiratory diseases is a matter of debate due to the potential effect on the development and prognosis of community-acquired pneumonia (CAP). We assessed whether treatment with inhaled steroids in patients with chronic bronchitis, COPD or asthma and CAP may affect early outcome of the acute pneumonic episode.

Methods: Over 1-year period, all population-based cases of CAP in patients with chronic bronchitis, COPD or asthma were registered. Use of inhaled steroids were registered and patients were followed up to 30 days after diagnosis to assess severity of CAP and clinical course (hospital admission, ICU admission and mortality).

Results: Of 473 patients who fulfilled the selection criteria, inhaled steroids were regularly used by 109 (23%). In the overall sample, inhaled steroids were associated with a higher risk of hospitalization (OR=1 .96, p = 0.002) in the bivariate analysis, but this effect disappeared after adjusting by other severity-related factors (adjusted OR=1.08, p=0.787). This effect on hospitalization also disappeared when considering only patients with asthma (OR= 1.38, p=0.542), with COPD alone (OR=4.68, p=0.194), but a protective effect was ob served in CB patients (OR=0.1 5, p=0.027). Inhaled steroids showed no association with ICU admission, days to clinical recovery and mortality in the overall sample and in any disease subgroup.

Conclusions: Treatment with inhaled steroids is not a prognostic factor in COPD and asthmatic patients with CAP, but could prevent hospitalization for CAP in patients with clinical criteria of chronic bronchitis.

Predictors for identifying the efficacy of systemic steroids on sustained exhaled nitric oxide elevation in severe asthma.

Matsunaga K, Hirano T, Akamatsu K, Minakata Y.
Allergol Int. 2013 Sep ;62 (3) :359-65. doi: 10.2332/allergolint.12-OA-0530.

Background: Some patients with asthma have high levels of exhaled nitric oxide fraction (FENO) despite inhaled corticosteroids (ICS) therapy. Early studies suggested that this might be explained by the presence of heterogeneous airway inflammation. We aimed to assess the predictors for identifying the efficacy of systemic corticosteroids on residual FENO elevations in severe asthma.

Methods: Twenty severe asthmatics with persistent FENO elevation (³40ppb) despite maintenance therapy including high-daily-dose ICS were enrolled. Asthma Control Questionnaire (ACQ), lung function, blood eosinophils, and FENO were assessed before and after 14 days treatment with 0.5mg/kg oral prednisolone/day.

Results: ACQ, blood eosinophils, FENO level, FVC, FEV_1, FEV_1/FVC ratio and the slope of the single nitrogen washout curve (N_2) were significantly improved by treatment with prednisolone. 70% of the subjects showed ³20% reductions in the FENO levels. The reduction in FENO levels was significantly correlated with the improvements in ACQ ($p < 0.0001$), FVC ($p < 0.01$), FEV_1 ($p < 0.0001$), and N_2 ($p < 0.05$). Among the measurements at baseline, the FENO levels and blood eosinophil numbers were identified as significant predictors of ³20% reductions in the FENO levels by systemic steroid therapy.

Conclusions: Systemic corticosteroids could suppress the residual FENO elevations in more than half of the patients with severe asthma and the reduction in FENO levels was associated with improvements in asthma control and airflow limitation. The FENO levels and blood eosinophil numbers were the predictors of improved residual airway inflammation by systemic steroid therapy in severe asthma.