and answer queries on asthma and doping, Royal Decree 641/2009 of the 17th of April, BOE 8/5/2009, that regulated doping control processes says, "All athletes with a license to participate in official state competitions may be selected at any time to undergo tests during competitions or outside competitions". No comments.

References

1. Drobnic F. La información desinformada: el asma en los deportistas de elite. De Maimónides a los Juegos Olímpicos. Arch Bronconeumol. 2001;37:364-5.
2. http://www.wada-ama.org/en/Science-Medicine/TUE/ (accessedd December 2009).
3. Naranjo Orellana J, Centeno Prada RA, Carranza Márquez MD. Use of beta2 agonists in sport: are the present criteria right?. Br J Sports Med. 2006;40:363-6.
4. Bergés R, Segura J, Ventura R, Fitch KD, Morton AR, Farré M, et al. Discrimination of prohibited oral use of salbutamol from authorized inhaled asthma treatment. Clin Chem. 2000;46:1365-75.
5. Roig M, Bergés R, Ventura R, Fitch KD, Morton AR, Segura J. Quantification of terbutaline in urine by enzyme-linked immunosorbent assay and capillary electrophoresis after oral and inhaled administrations. J Chromatogr B Analyt Technol Biomed Life Sci. 2002;768:315-24.
6. Drobnic F. Los agonistas adrenérgicos B2 y su influencia en el rendimiento físico. Archivos de Bronconeumología. 1997;33:136-42.

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Mortality in Lung Cancer and COPD

Mortalidad en cáncer de pulmón y en enfermedad pulmonar obstructiva crónica

To the Editor:

In the interesting article by Abal et al[1] entitled «Lung Cancer and COPD: a frequent association» a broad clinical cohort of 996 patients over a period of 5 years is assessed. The first conclusion is relevant and current: The association of both pathological conditions is frequent, and the most frequent histological diagnosis is squamous carcinoma; however, it is more difficult to take in its second and significant conclusion. The survival of patients with lung cancer and COPD is greater than that of patients with lung cancer without COPD. This second finding seems contrary to all that has been published so far with reference to comorbidities of both conditions, and we make reference to the excellent review in these same pages by Díez Herranz[2] in 2001 and other more recent sources.[3-5] It has even been reported that greater mortality has been seen in non-smokers with both conditions.[6] The authors themselves are surprised and theorize in the «Discussion» about a possible diagnostic bias and about the fact that patients with COPD may be diagnosed with lung cancer before patients without COPD. Probably, a repeat analysis of the data would make it possible to reconsider said conclusion, based on a view of the Kaplan-Meier survival curves (Fig. 1) and a significant difference of p = 0.016 obtained using the Mantel-Haenszel test (logarithmic ranges). Maybe due to the baseline differences between both groups (Table 4), it would be more appropriate to use an adjusted Cox regression model for the significant variables in the bivariate analysis, including sex, age, smoking and stage of lung cancer or other variables. The time in months/years between COPD diagnosis and cancer diagnosis could also be modelled. Finally, although in «Methods» section it is indicated that diagnosis and COPD classification were carried out according to GOLD directives, it would be interesting to repeat the same model eliminating those COPD cases diagnosed without spirometry.

Nevertheless, as Brody and Spira[3] state, most smokers never will develop either COPD or lung cancer, it is important to investigate this relationship in detail.

References

1. Abal Arca J, Parente Lamelas I, Almazán Ortega R, Blanco Pérez J, Toubes Navarro ME, Marcos Velázquez P. Cáncer de pulmón y EPOC: una asociación frecuente. Arch Bronconeumol. 2009;45:502-7.
2. Díez-Herranz J. Enfermedad pulmonar obstructiva crónica y cáncer de pulmón:implicaciones prácticas. Arch Bronconeumol. 2001;37:240-7.
3. Brody JS, Spira A. State of the art. Chronic obstructive pulmonary disease inflammation, and lung cancer. Proc Am Thorac Soc. 2006;3:535-7.
4. Kiri VA, Soriano JB, Visick G, Fabbri L. Recent trends in lung cancer and its association with COPD: an analysis using the UK GP Research Database. Prim Care Respir J 2009 Sep 15. pii: pcrj-2009-02-0021. doi:10.4104/pcrj.2009.00048. [Epub ahead of print].
5. Kiri VA, Fabbri LM, Davis KJ, Soriano JB. Inhaled corticosteroids and risk of lung cancer among COPD patients who quit smoking. Respir Med. 2009;103:85-90.
6. Turner MC, Chen Y, Krewski D, Calle EE, Thun MJ. Chronic obstructive pulmonary disease is associated with lung cancer mortality in a prospective study of never smokers. Am J Respir Crit Care Med. 2007;176:285-90.

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Response by the Authors

Respuesta de los autores

To the Editor:

We thank Joan B.Soriano for the interest shown in our recently published article.[1] We consider his comments are relevant and correct, and the suggestions undoubtedly improve on the original.

Following his advice, we have re-analysed the data eliminating the 16 COPD patients without spirometry. The Kaplan-Meier survival curves continue to be significantly different between patients with and without COPD, being greater in COPD patients (p = 0.006).

Indeed, as the author points out in his letter, and this is seen in the results, an adjusted Cox regression model was used for significant variables in the bivariate analysis, although only stage and treatment remained in the final model. COPD, on the contrary, was not statistically significant. In the discussion we commented on the

possibility of a diagnostic bias as a reason for the differences in survival due to the fact that COPD patients may be diagnosed in earlier stages, although maybe we should have placed greater emphasis on discussing the results of the multivariate analysis. Therefore, we must reconsider our conclusion and say that no significant differences in survival were seen between COPD patients and non COPD patients.

On the other hand, we think the idea of analysing the time between diagnosis of COPD and diagnosis of lung cancer is very interesting, as well as treatment with inhaled steroids and its influence on survival, studied by other authors.[2,3] Although collecting some of this data is difficult, since this is a retrospective study carried out using a lung cancer and not a COPD database.

References

1. Abal Arca J, Parente Lamelas I, Almazán Ortega R, Blanco Pérez J, Toubes Navarro ME, Marcos Velázquez P. Cáncer de pulmón y EPOC: una asociación frecuente. Arch Bronconeumol. 2009;45:502-7.
2. Kiri VA, Soriano JB, Visick G, Fabbri L. Recent trends in lung cancer and its association with COPD: an analysis using the UK GP Research Database. Prim Care Respir J. 2009. pii:pcrj-2009-02-0021. doi:10.4104/pcrj.2009.00048.
3. Kiri VA, Fabbri LM, Davis KJ, Soriano JB. Inhaled corticosteroids and risk of lung cancer among COPD patients who quit smoking. Respir Med. 2009;103: 85-90.

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Does Decapitated Parapneumonic Pleurity Exist?

¿Existe una pleuritis paraneumónica decapitada?

To the Editor:

"Decapitated meningitis or partially treated bacterial meningitis" is characterized by a being a condition in which clinical characteristics and cerebrospinal fluid parameters analysed are altered because the patient received antibiotics prior to spinal puncture.[1] However, this observation has not been described in other fluids secreted secondary to usual infections seen in daily practice, such as parapneumonic pleural effusion (PPPE). Subject experts and scientific societies define PPPE as any pleural effusion (PE) associated or secondary to bacterial pneumonia or a lung abscess,[2-4] including in some infections viral pneumonias[3] and, in other cases, PE associated with bronchoectasia.[4] According to these, pleural fluid (PF) in the PPPE is an exudates composed predominantly by polymorphonuclear (PMN) cells.[2-5] Therefore, although the condition is compatible with this entity, it is advisable to carry out other additional diagnostic tests as also a pleural biopsy, if the PF has a predominance of mononuclear cells (MN).[2,3,6] However, in our experience, it is not unusual to find patients who, in spite of complying with clinical criteria for PPPE, have a PE with a predominance of lymphocyte cells, and we have observed that previous antibiotic treatment may have some influence. A deep search in the medical literature revealed no clear evidence on this subject, this is why we decided to carry out a retrospective study of all the patients with PE and PPPE criteria that were assessed between January 2007 and September 2008 in our centre. A patient was considered to have PPPE when they had a clinical condition suggestive of respiratory infection, lung condensation, and PE with criteria for exudates and a favourable response to antibiotic treatment with or without pleural drainage. We excluded cases with nosocomial infections, with prior PE and those with specific diagnosis during the study or after a minimum 6-month follow-up. A multivariate study was performed of the influence of clinical and epidemiological variables (age, gender, previous diseases, time of evolution of the symptoms and the dosage, time and type of previous antibiotics) and radiological ones on the results of the analytical study of the pleural fluid. We included 61 patients, 20 of whom (33%) were women. Mean age was 58±17 years. Forty-four (72%) of the patients were on antibiotic treatment (for at least 24 hours) prior to thoracocentesis, and, in 2 patients, this was not known. The antibiotics used were: betalactamates (alone or combined), in 28 patients; fluoroquinolones in 9 patients, and macrolides in 7 patients. In 22 (36%) cases, the PE was loculated and, in 25 (41%), pleural drainage was indicated. In 12 (20%), PF culture was positive. Thirty-two (56.1%) had a predominance of PMN cells (>50%) and 25 (43.9%) of MN cells. In 4 cases, a differential cell count was not possible. In the multivariate analysis, previous treatment with antibiotics was the only independent predictor of a formula with a predominance of MN cells in the PF (OR=6.6; CI 95%=1.3–33.7; p=0.03). The mean percentage of PMN cells in the cases with prior treatment was 51±27% compared to 75±22% in those that had not received antibiotics (p=0.03). Antibiotic treatment also influenced other variables, such as pH values (7.34 versus 7.11; p=0.004), but other parameters such as glucose values, LDH, ADA or proteins were not affected. The value of ADA in patients with PF with a predominance of PMN cells was 48±38UI/mL whereas in those patients with a predominance of MN cells it was 21±7,6UI/mL, being <45UI/mL in all cases. In spite of good evolution, the physician responsible for the patient decided to indicate a blind pleural biopsy in 10 cases and a thoracoscopy in 3. All results were compatible with a non-specific acute inflammatory process.

The predominant cells in the PF is influenced by the aetiology of the PE and the moment of thoracocentesis, in relation to the beginning of the pleural condition,[2,3,5,6] so that acute cases such as PPPE, pulmonary embolism, or PE with a predominance of PMN cells and those conditions with a longer time of evolution, such as tuberculosis (with the exception of the early phase), neoplasias or the evolution over time of the above usually present with a predominance of lymphocytes.[5,6] For this reason, in cases of PE with a predominance of MN cells pleural biopsy is indicated.[2,4,6] In our opinion, the influence of external factors had not been analysed so far, such as prior antibiotic treatment, which could influence PF differential cell counts. The result of this observation leads us to theorize that, as in other infectious processes, such as bacterial meningitis, there could exist "decapitated parapneumonic pleuritis". This would mean that in a clinical and radiological context suggestive of PPPE, but in cases where PF has a predominance of lymphocyte cells with ADA values within normal ranges and the patient has received antibiotics previously, it might be appropriate to wait for a therapeutic response to antibiotic treatment, before carrying out other more invasive procedures. However, it seems likely that the results of this observation could also be explained, at least partially, by the low specificity of the definition of PPPE, since it is possible that some patients included in this study could have a PPPE secondary to a viral process, a non-specific inflammatory process or