Influence of the adequacy of data collection, during two years, in the management of community-acquired pneumonia in emergency departments

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ABSTRACT

Objective. The aim of this study was to analyze whether structured data collection of patients with community-acquired pneumonia (CAP) in the Emergency Department (ED) improves compliance with clinical guidelines regarding inpatient and outpatient treatment and prescription of antibiotics at discharge.

Material and methods. We performed a quasi experimental, multicenter, pre/post-intervention study. The intervention consisted of basic training for the participating physicians and the incorporation of a data collection sheet in the clinical history chart, including the information necessary for adequate decision making regarding patient admission and treatment, in the case of discharge. We analyzed the adequacy of the final destination of patients classified as Fine I-II and antibiotic treatment in patients receiving outpatient treatment, with each participating physician including 8 consecutive patients (4 pre-intervention and 4 post-intervention).

Results. A total of 738 patients were included: 378 pre-intervention and 360 post-intervention. In the pre-intervention group, Fine V was more frequent and patients were older, had more ischemic heart disease, active neoplasms and fewer risk factors for atypical pneumonia. Of the patients with Fine I-II, 23.7% were inadequately admitted and 19.6% of those discharged received treatment not recommended by guidelines. No differences were observed in the target variables between the two groups.

Conclusion. The adequacy of the decision to admit patients with Fine I-II CAP and outpatient antibiotic treatment can be improved in the ED. Structured data collection does not improve patient outcome.

Key words: community-acquired pneumonia, emergency department, antibiotic treatment, adequacy of admission

INTRODUCTION

The incidence of community-acquired pneumonia (CAP) is around 2-5 cases/1,000 inhabitants per year, which may rise up to 15-35 during periods of viral epidemia. (1) The economic impact of CAP is high, (2) with an important difference in costs based on whether the patient is treated in the hospital or as an outpatient. (3) Therefore, two key aspects for the management of less severe CAP are to assess whether the patient really requires hospital admission and to correctly choose antibiotic treatment for patients who are discharged. Both decisions are often made by staff working in emergency departments (ED). With regard to the decision of hospital admission, prognostic scales, such as the FINE (4) or CURB65 (5), have long been used. According to current clinical guidelines, the combination of these scales, with relevant clinical aspects, defines the critieria of hospital admission. (6-9) On the other hand, these same guidelines indicate the antibiotics of choice for patients who are discharged with the aim of avoiding therapeutic failure and the appearance of bacterial resistance. (10)

Although some studies have reported the inadequacy of hospital admission and antibiotic treatment in CAP (11), and others have shown that compliance with protocols and clinical guidelines improves patient outcome, (12) no study has determined the effect of other interventions to minimize these dysfunctions. Thus, the present study evaluated the grade of compliance of ED physicians with the guidelines regarding hospital admission and outpatient treatment of patients with CAP, as well as the effects of a training intervention and the incorporation of a structured data collection sheet in improving this compliance. Our hypothesis was that providing emergency physicians with a notebook containing a structured data collection sheet that allocates the patient into a specific category and suggests antibiotic selection, would in turn improve the ratio of patients being managed according to guidelines.

MATERIALS AND METHODS

Study design

We performed a quasi experimental, multicenter pre/post intervention study in 49 EDs corresponding to 8 autonomous communities and including both tertiary university and county hospitals. The present study is a sub-study of the INSPIRA study (investigation of the adequacy of the management of patients with CAP

and acute descompensation of chronic obstructive pulmonary disease (COPD) in Spanish EDs) which was designed prior to its initiation. In the pre-intervention phase, a variable number of investigators was contacted from each center (1 – 4) to retrospectively collect data for the last 4 patients with CAP treated by these investigators. The intervention consisted of providing a data collection notebook which contains all the epidemiological, clinical and laboratoty variables necessary to retrieve all the clinical data necessary for adequate decision making. Among other data, this notebook also included all the items necessary to classify patients according to the Fine scale, as well as the antibiotics recommended at discharge from the ED. The participating physicians were the same in both phases of the study and they received specific training on completing the data collection sheet and were advised that the assessment of the adequacy of decision making regarding admission and antibiotic treatment prescribed would follow the prevailing guidelines. This training was of no longer than 60 minutes. It did not include specific training as to the content of the guidelines in order to isolate the intervention and considering the objective of analyzing the adequacy of the management of a highly frequent disease with widely disseminated and updated guidelines. During the post-intervention phase, 4 consecutive episodes of CAP treated by each of the participating physicians were collected. During the preintervention phase, data collection was done at the discretion of the emergency physicians, and during the post-intervention phase, data were entred into the notebook so all data necessary for FINE calculation was collected. Later, an external CRO (clinical research organization) transferred all data into a database, as well as the missing values, by accessing medical reports. After completing the database, researchers checked around 3% of data randomly, in order to ascertain the consistency and accuracy of the database. The inclusion criteria were: over 18 years of age and having signed informed consent. The protocol was approved by the Ethical Committee of each participating center. CAP was defined according to the criteria of the Infectious Diseases Society of America. (13)

The decision as to hospital admission from the ED was made by the attending ED physician. In doubtful cases, different specialists (respiratory physicians, internal medicine physicians...) were consulted for a consensus decision regarding discharge.

Study period

From January 2010 to April 2012.

Variables

The independent variables collected included epidemiologic (age, sex, place of residence, vaccinations, risk factors for atypical pneumonia), clinical (past history and history of the current episode in the ED), radiological, analytical and variables related to treatment. Suspecting CAP atypical bacteria, blood serology was conducted, including Legionella pneumophila urinary antigen detection (Binax Now L. Pneumophila Urinary Antigen Test; Trinity Biotech, Bray, Ireland). With these data the patients were classifed according to the Fine criteria. To evaluate the target variables of the study, only patients classified as Fine I or II were taken into account, given that these stages are of greatest concern when undertreating patients using the optional protocol. Two target variables were considered (dependent). The first was the percentage of inadequate admissions involving patients with CAP Fine I or II who were admitted to hospital, despite the absence of comorbidities, pleural effusion, respiratory insufficiency or added social problems. The second variable was the percentage of patients with CAP discharged directly from the ED with inadequate antibiotic treatment, according to the criteria of the guidelines of the Spanish Society of Medical Emergencies and Emergency Medicine (SEMES) prevailing at the time of the study. These guidelines recommend combinations of beta-lactamics and a macrolide or monotherapy with a fluoroquinolone. (9)

STATISTICAL ANALYSIS

The data were collected with an electronic notebook for data collection which had been specially designed for the study. The database included ranges and rules for internal coherence to guarantee quality of the data. The categorical variables are expressed as absolute and relative frequencies while continuous variables are expressed as mean, standard deviation, median, and minimum and maximum values. To compare the pre- and post-intervention groups, parametric tests (Student's t) or nonparametric tests (Mann-Whitney U) were used for the quantitative variables according to the characteristics of distribution of the study variables. For the qualitative variables, the Chi-square test was used or the Fisher's exact test if the values were less than 5. Statistical analyses were performed using the statistical package SAS version 9.1.3.

RESULTS

A total of 738 patients with CAP were included in the study, 378 in the pre-intervention phase and 360 in the post-intervention phase (2 and 20 patients, respectively were excluded from each period because of a lack of fundamental data in the data collection notebook). Table 1 shows the distribution of the patients in each group. The pre-intervention group was significantly older, had a greater percentage of patients with active neoplasm, ischemic heart disease or classified as Fine V, and the patients with the risk of having atypical pneumonia was lower compared with the post-intervention group.

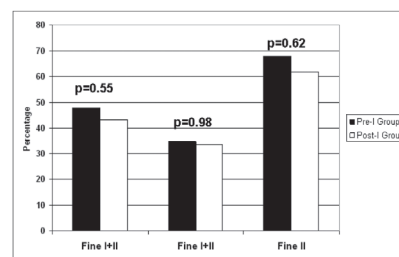Table 2 shows the classification of the pa-

Figure 1. Distribution of inadequate hospital admissions based on the Fine scale.
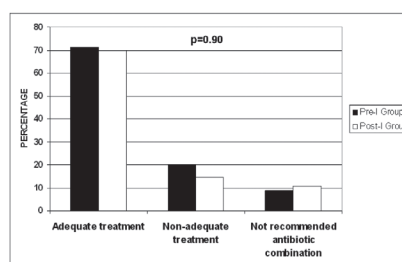

Figure 2. Distribution of the prescription of inadequate treatment at patient discharge in patients with community acquired neumonia (CAP) Fine I or II. Patients were deemed to receive adequate treatment with the prescription of an antibiotic schedule strictly adjusted to the recommendations of the prevailing guidelines. Inadequate treatment was considered as that with insufficient coverage, and non-recommended drug combinations were considered as those with an unnecessary antibiotic combination (fluoroquinolone + amoxicillin-clavulanic acid or fluoroquinolone + cefuroxime).

Table 1. Characteristics of patients included in the study.

	Pre-intervention Group N= 378	Post-intervention Group N =360	p
EPIDEMIOLOGIC HISTORY			
Age (years) (mean (SD))	65,7 (19.2)	62.5 (19.7)	0.025*
Sex (male) (n (%))	229 (60.5%)	205 (56.9%)	0.104
Active smoker (n (%))	195 (51.5%)	197 (54.7%)	0.410
Lives in a residence (n (%))	45 (11.9%)	22 (5.8%)	0.062
Anti-pneumoccocal vaccination (n (%))	36 (9.5%)	60 (15.9%)	0.207
Anti-influenza vaccination (n (%))	118 (31.2%)	167 (44.2%)	0.135
Risk of atypical pneumonia (n (%))	12 (3.1%)	41 (10.9%)	0.001*
PAST HISTORY			
Diabetes	97(25.6%)	71 (19.7%)	0.054
Chronic obstructive pulmonary disease	82(21.6%)	82(22.8%)	0.723
Ischemic heart disease	51(13.4%)	32(8.9%)	0.047*
Cardiac insufficiency	45(11.9%)	37(10.3%)	0.482
Cerebral vascular accident	39(10.3%)	29(7.7%)	0.288
Renal insufficiency	27(7.1%)	32(8.5%)	0.382
Active neoplasm	40(10.5%)	18(4.8%)	0.004*
Asthma	21(5.5%)	27(7.1%)	0.284
Diagnosis of pneumonia in the previous 12 months (n (%))	33(8.7)	31(8.6)	0.109
Hospitalization for pneumonia in the previous 12 months (n (%))	20(5.2)	20(5.6)	0.586
CURRENT EPISODE OF PNEUMONIA			
Vital signs			
Respiratory rate (rpm) (mean (SD))	22.3 (6.1)	21.6 (6.2)	0.218
Diastolic blood pressure (Mg.) (mean (SD))	128.1 (23.3)	129.4 (24.3)	0.539
Temperature (ºC) (mean (SD))	37.4 (1.1)	37.4 (1.1)	0.968
Heart rate (bpm) (mean (SD))	97.3 (18.3)	96.1 (18.5)	0.946
Basal oxygen saturation (%)(mean (SD))	90.8 (6.7)	91,5 (6.0)	0.224
Patients with GCS 15 points (n (%))	367(97.1%)	351(97.5%)	0.587
Chest X-ray findings			
Single infiltrate	296(78.3%)	292(81.1%)	0.260
Multiple infiltrates	77(20.4%)	62(17.2%)	0.287
Pleural effusion	41(10.9)	32(8.9%)	0.079
Analytical data			
Leucocytes (cells/mm3) (mean (SD))	13037 (6067)	12966 (6054)	0.917
C-reactive protein (mean (SD))	15.3 (18.5)	16.5 (19.5)	0.924
Sodium (mmol/l) (mean (SD))	137.0 (5.1)	137.1 (4.1)	0.840

bpm, beats per minute; GCS, Glascow coma score; n, number; rpm, respirations per minute; SD, standard deviation. * significant difference

tients according to the Fine scale. A total of 299 patients were classified as Fine I and II, with no statistically significant differences between the pre- and post-intervention phases. With regard to this classification, it is of note that the percentage of patients with CAP Fine V was greater in the pre-intervention group.

Among the 299 patients with Fine I and II, 71 (23.7%) were inappropriately admitted to hospital, 32 (23.9%) in the pre-intervention and 39 (29.1%) in the post-intervention groups. These differences were not statistically significant for either the global or individualized analysis of the Fine I and II patients (figure 1). The percentage of patients treated on an outpatient basis reduced with the increase in the Fine scale, although statistically significant differences were only observed in patients with CAP Fine IV who were more frequently treated as outpatients in the post-intervention group (table 2).

No differences were observed in empiric antibiotic treatment administered to patients treated as outpatients or among all patients treated (table 3) or in isolated less severe patients, according to the Fine classification (figure 2). Of patients classified as Fine I and II, 14 (20%) in the pre-interven-

tion group and 18 (19.4%) in the post-intervention group received inadequate treatment, being treated with monotherapy not recommended in the guidelines. Likewise, 6 patients (8.6%) in the pre-intervention and 10 (10.8%) in the post-intervention group were treated with drug combinations not recommended in the guidelines.

Table 2. Distribution of patients with community acquired neumonia (CAP) based on the Fine scale and the percentage of patients treated on an outpatient basis.

	Pre-intervention group N= 378 n (%)	Post-intervention group N =360 n (%)	p
Fine I	81 (21.6)	105 (29.6)	0.181
Fine II	53 (14.4)	60 (17.5)	0.355
Fine III	70 (18.7)	56 (15.8)	0.320
Fine IV	127 (33.9)	109 (30.7)	0.096
Fine V	46 (12.3)	30 (7.9)	0.029*
Patients treated as outpatients			
Fine I	53 (65.4)	70 (66.6)	0.330
Fine II	17 (32.0)	23 (38.3)	0.338
Fine III	4 (5.7)	9 (16.0)	0.257
Fine IV	2 (1.57)	5 (4.5)	0.018*
Fine V	1 (2.17)	0 (0)	1.00

* significant difference

Table 3. Distribution of antibiotics administered to outpatients (including all the Fine groups).

	Pre-intervention group N= 77 n (%)	Post-intervention group N =107 n (%)	p
Amoxicillin-clavulanic acid (monotherapy)	11 (14.2)	16 (14.9)	0.907
Cefuroxime (monotherapy)	1 (1.2)	2 (1.8)	0.171
Clarithromycin (monotherapy)	2 (2.5)	0 (0)	0.170
Levofloxacin 500 mg/day	26 (33.7)	42 (39.2)	0.058
Levofloxacin 1000 mg/day	4 (5.1)	4 (3.7)	0.152
Ciprofloxacin	0 (0)	1 (0.9)	1.00
Moxifloxacin	23 (29.8)	24 (22.4)	0.052
Beta-lactamics + macrolide	4 (5.1)	8 (7.4)	0.138
Unnecessary combinations	6 (7.7)	10 (9.3)	0.124

DISCUSSION

The present study demonstrates that the risk of patients with milder forms of CAP continues to be overestimated, with almost one out of every four patients with CAP Fine I-II (23.7 %) being admitted to hospital even when not fulfilling strict criteria for hospitalization, thereby increasing both the risk and economic costs. This is not surprising, but even when all medical participants were provided with a notebook containing guidelines, adherence was not 100% by all profesionals.

Since the publication of the Fine scale (4) or CURB65, (5) which includes the use of risk scales, many studies have shown that patient risk is overestimated in the deci-

sion making related to admission from the ED. (14) On the other hand, CAP is a very prevalent disease and the guidelines are regularly updated and widely available. If this is so, why does decision making in the ED not follow the recommendations of the guidelines? Many factors may influence decision making. Among others, the special working conditions in the ED, the high heterogeneity in their organization, greater or lesser access to the clinical history of the patient and the non-homogeneous training of ED professionals. (15-17) On the other hand, the availability of observation or short-stay areas may contribute to improving the adequacy of decision making, and these are not present in all EDs. (18,19)

The aim of the present study cannot be answered by studies involving an intervention which follows the recommendations of the guidelines, (20,21) that is, to determine whether the problem lies in data collection in the ED, which is an essential step in decision making. To answer this question we took into account the wide diffusion of clinical practice guidelines and the knowledge that these recommendations should be part of correct medical practice of ED professionals. For this reason, in our study, no recommendation was provided, but rather the professional was simply given the data collection notebook which should be considered, in some way, useful as a guide to collect all the information

for adequate decision making. It should be considered, that in the pre-intervention phase of the present study the physician calculated the Fine score retrospectively from the clinical history, that is, after the decision regarding in- or outpatient treatment had been made. We cannot be sure if this classification had been done or not when the attending physician decided whether to admit the patient. In contrast, in the post-intervention phase, there was no doubt as to whether all the patients had been assessed using the risk scale. Nonetheless, there continues to be a trend in overestimating the risk and unnecessarily admitting patients. Our study presents different results from similar studies, although the methdology used in them is different. Hinojosa et al (22) described a percentage of inadequate admissions of only 6 % in their study, also designed in two phases. Nonetheless, they included patients with CAP Fine III in a single center and thus, the patients were recruited by the same ED physicians working homogeneously and a modification in their behavior cannot be ruled out by the fact of being observed (Hawthorne effect) having influenced the final result. (23) In the study by Julian-Jiménez et al (12) the approach was different, with the intervention involving the application of clinical practice guidelines for the treatment of CAP. Improvements were obtained in the mortality and the remaining indicators of outcome and management. It is of note that in this latter study the authors used biomarkers in addition to the Fine scale.

On the other hand, outpatient treatment, which was mainly based on the antibiotic prescribed, was not recommended by the guidelines in almost one out of every five patients (19.6%), and this did not improve during the study which promoted the collection of all clinical data necessary for adequate decision making. With regard to antibiotic treatment, the reasons for not following the guidelines remain unknown. This is even more surprising in Spain where more antibiotics continue to be prescribed than the European mean, probably due to the fear of undertreating an infectious disease, (24) which is one of the main diagnoses at discharge in Spanish ED. (25) In the present case of CAP, this aspect is of note, taking into account that the recommendations are simple. The proportion of monotherapy with amoxicillin-clavulanic acid is particularly remarkable considering the availability of safer and more effective oral alternatives than one with a wide spectrum for atypical microorganisms. (26,27) On the other hand, both the choice of the antibiotic and the dose are key to ensure treatment efficacy and avoid resistance as in the case of oral levofloxacin, (28) with which doses lower than the recommended 1 g/day during the first 24-72 hours continue to be used.

Our study has several limitations. Firstly, despite being multicentric and performed in different autonomous communities and different level hospitals, participation was voluntary and thus, the sample may have been biased. It was not a randomized study because we wanted the researches to be the same in both phases. If we had randomized, some researches would have had a chance to use the case report form (or "the data collection sheet") while others would not. We belived that the study design in two phases eliminated the bias that the selction of researchers could cause.

On the other hand, the definition of inadequate hospital admission is always debatable considering that aspects such as the personal circumstances of the patients or their settings may influence the decision to admit the patient, overlooking more objective criteria. Finally, as mentioned above, the availability of observation or short-stay units which allow reassessment of the patient and thus, more adequate admission is not consistent in all the centers. Nonetheless, we believe that the information obtained on the management of CAP of low severity (Fine I and II) and the outpatient antibiotic treatment prescribed in Spanish EDs is significant and orientative in that there is an important margin for improvement on the one hand, and on the other, the reason for not following the guidelines does not seem to be related to structured collection of clinical data necessary for adequate decision making. The reasons underlying the systematically observed deviation from the protocols for CAP in the ED should be studied in future studies by health institutions in order to unify criteria and improve existing protocols, with the ultimate goal of offering top quality medical care.

REFERENCES

1. Menéndez R, Torres A, Aspa J, Capelastegui A, Prat C, Rodríguez de Castro F. neumonía adquirida en la comunidad. Nueva normative de la Sociedad Española de Neumología y Cirugía Torácica (SEPAR). Arch Bronconeumol 2010;46:543-58.
2. Sicras-Mainar A, Ibáñez-Nolla J, Cifuentes I, Guijarro P, Navarro-Artieda R, Aguilar L. Retrospective epidemiological study for the characterization of community-acquiered pneumonia and pneumococcal pneumonia in adults in a well-defined area of Badalona (Barcelona, Spain). BMC Infect Dis 2012;12:283. doi:10.1186/1471-2334-12-283.
3. Julián-Jiménez A, González del Castillo J, Candel González FJ. When, where and how should a patient with community acquired pneumonia be admitted? Rev Clín Esp 2013;213:99-107.
4. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. N Engl J Med 1997;336:243-50.
5. Lim WS, Van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. Thorax 2003;58:377-82.
6. Mandell LA, Wunderink Rg, Anzueto A, Bartlett JG, Campbell GD, Dean NC, et al. Infectious Diseases Society of America/American Thoracic Society consensos guidelines on the Management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S27-72.
7. Simonetti AF, Viasus D, Garcia-Vidal C, Carratalà. Management of community-acquired pneumonia in older adults. J Ther Adv Infect Dis 2014;2:3-16.
8. Mattila JT, Fine MJ, Limper AH, Murray PR, Chen BB, Lin PL. Pneumonia. Treatment and diagnosis. Ann Am Thorac Soc 2014;11(Suppl 4):S189-92.
9. Julián-Jiménez A, Candel FJ, Piñera P, González del Castillo J, Moya MS, Martínez M. Recomendaciones INFURG-SEMES: manejo de la infección respiratoria de vías respiratorias bajas en urgencias. Monografías de Emergencias 2009;3:1-21.
10. Sibila O, Restrepo MI, Anzueto A. What is the best antimicrobial treatment for severe community-acquired pneumonia (including

the role of steroids and statins and other immunomodulatory agents). Infect Dis Clin North Am 2013;27:133-47.

11. Potena A, Simoni M, Cellini M, Cartabellotta A, Ballerin L, Piattella M, et al. Management of community-acquired pneumonia by trained family general practitioners. Int J Tuberc Lung Dis 2008;12:19-25.

12. Julián-Jiménez A, Palomo de los Reyes MJ, Parejo Miguez R, Laín-Terés N, Cuena-Boy R, Lozano-Ancín A. Improved Management of community-acquired pneumonia in the emergency department. Arch Bronconeumol 2013;49:230-40.

13. Bartlett JG, Breiman RF, Mandell LA, File TM, JR. Community-acquiered pneumonia in adults: guidelines for management. The Infectious Diseases Society of America. Clin Infect Dis 1998;26:811-38.

14. Jo S, Kim K, Jung K, Rhee JE, Cho IS, Lee CC, Singer AJ. The effects of incorporating a pneumonia severity index into the admission protocol for Community-acquired pneumonia. J Emerg Med 2012;42:133-8.

15. Miró O, Escalada X, Gené E, Boqué C, Jiménez Fábrega FX, Netto C, et al. Estudio SUHCAT(2): mapa físico de los servicios de urgencias hospitalarios de Cataluña. Emergencias 2014;26:19-34.

16. Miró O, Escalada X, Gené E, Boqué C, Jiménez Fábrega FX, Netto C, et al. Estudio SUHCAT(2): mapa funcional de los servicios de urgencias hospitalarios de Cataluña. Emergencias 2014;26:35-46.

17. Miró O, Escalada X, Gené E, Boqué C, Jiménez Fábrega FX, Netto C, et al. Estudio SUHCAT(3): mapa docente e investigador de los servicios de urgencias hospitalarios de Cataluña. Emergencias 2014;26:47-56.

18. Llopis Roca F, Ferré Losa C, Juan Pastor A, Martín Sánchez FJ, Sempere Montes G, Llorens Soriano, et al. Proyecto REGICE. Gestión clínica de las unidades de corta estancia en España (REGICE-2). Emergencias 2014;26:359-62.

19. Llopis Roca F, Ferré Losa C, Juan Pastor A, Martín Sánchez FJ, Sempere Montes G, Llorens Soriano P, et al. Proyecto REGICE. Gestión clínica de las unidades de corta estancia en España (REGICE 2). Emergencias 2014;26:359-62.

20. Aujesky D, McCausland JB, Whittle J, Obrosky DS, Yealy DM, Fine MJ. Reasons why emergency department providers do not rely on the pneumonia severity index to determinate the initial site of treatment for patients with pneumonia. Clin Infect Dis 2009;15;49:100-8.

21. Tripp DG. Did an acute medical assessment unit improve the initial assessment and treatment of community acquired pneumonia-a retrospective audit. N Z Med J 2012;125:60-7.

22. Hinojosa Mena-Bernal J, Hinojosa Mena-Bernal C, González Sarmiento E, Almaráz Gómez A, Martín Santos S, Zapatero Gaviria A. Adecuacy of the admissions and care provided to the patients with community-acquired pneumonia. Rev Clin Esp 2011;211:179-86.

23. Cizza G, Piaggi P, Rother KI, Csako G; Sleep Extension Study Group. Hawthorne effect with transient behavioural and biochemical changes in a randomized controlled sleep extension trial of chronically short-sleeping obese adults: implications for the design and interpretation of clinical studies PLoS One. 2014. 9(8): e104176.

24. Llor C. Can the use of antibiotics be improved in outpatients in Spain. Enferm Infecc Microbiol Clin 2014;32:409-11.

25. Martínez Ortiz de Zárate M, González Del Castillo J, Julián Jiménez A, Piñera Salmerón P, Llopis Roca F, Guardiola Tey JM, et al. Estudio INFURG-SEMES: epidemiología de las infecciones atendidas en los servicios de urgencias hospitalarios y evolución durante la última década. Emergencias 2013;25:368-78.

26. Garau J, Fritsch A, Arvis P, Read RC.Clinical efficacy of moxifloxacin versus comparator therapies for community-acquired pneumonia caused by Legionella spp. J Chemother 2010;22:264-6.

27. Hess G, Hill JW, Raut MK, Fisher AC, Mody S, Schein JR. Comparative antibiotic failure rates in the treatment of community-acquired pneumonia: Results from a claims analysis. Adv Ther 2010;27:743-55.

28. Friedman H, Song X, Crespi S, Navaratnam P. comparative analysis of length of stay, total costs and treatment success between intravenous moxifloxacin 400mg and levofloxacin 750mg among hospitalized patients with community-acquired pneumonia. Value Health 2009;12:1135-43.