Negative Results Associated With Medication in the Emergency Department of a Hospital

V. García,[a] I. Marquina,[b] A. Olabarri,[c] G. Miranda,[d] G. Rubiera,[e] and M.I. Baena[f]

[a]Servicio de Farmacia, Hospital Valle del Nalón, Langreo, Asturias, Spain
[b]Servicio de Farmacia, Clínica Vicente San Sebastián, Bilbao, Vizcaya, Spain
[c]Servicio de Farmacia, Clínica Quirón Zaragoza, Zaragoza, Spain
[d]Servicio de Farmacia, Hospital Universitario Central de Asturias, Oviedo, Asturias, Spain
[e]Servicio de Medicina Preventiva, Hospital de Cabueñes, Gijón, Asturias, Spain
[f]Grupo de Investigación de Atención Farmacéutica, Universidad de Granada, Granada, Spain

Abstract

Objective: To find out the prevalence of negative results associated with medication (herein referred to as NRM) in patients attending the emergency department. To classify the results by severity, avoidability, and cost, as well as to establish the factors associated with their appearance.

Method: Observational, descriptive, and cross-sectional study carried out in the emergency department of a tertiary hospital. Patient surveys and emergency department records were used as sources of information. The Dader Method and guidelines from the Third Consensus of Granada were used. Pearson χ^2 test was used to find the association between age, gender, and number of drugs and showing signs of NRM. Avoidability was measured using Baena et al's criteria and severity was assessed according to whether or not the patient had been admitted into an observation stall or on to a hospital ward.

Results: Twenty-four point per cent of patients visited the emergency department because of NRM. 16.1% needed to be hospitalised to solve their health issue. 83.9% of all patients with NRM and 77.3% of those hospitalised due to NRM could have been avoided. Statistically, there was a higher prevalence of NRM in patients taking 5 or more different drugs. An estimated €14 666 178 was spent on treating avoidable NRM cases in 2003.

Conclusions: The prevalence of NRM in those who attended the emergency department, the high percentage of avoidability and the cost imposed on the health service seem to sufficiently argue a case for the consideration that NRM as a problem which requires the implementation of prevention programmes based on drug-treatment monitoring.

Key words: Negative results associated with medication. Drug-related problems. Avoidability. Severity. Age. Gender. Poly-medication.

Resultados negativos asociados con la medicación en un servicio de urgencias hospitalario

Objetivo: Conocer la prevalencia de los resultados negativos asociados con la medicación (RNM) entre los usuarios del servicio de urgencias. Caracterizarlos por su gravedad, evitabilidad y coste, así como encontrar factores asociados con su aparición.

Método: Estudio observacional, descriptivo y transversal en el servicio de urgencias de un hospital de tercer nivel. Como fuentes de información se emplearon la entrevista a los pacientes y la historia de urgencias. Se trabajó según el método Dáder y las directrices del Tercer Consenso de Granada. Se empleó el test de la χ^2 de Pearson para buscar la asociación entre edad, sexo o número de medicamentos y presentar los RNM. La evitabilidad se estableció según el criterio de Baena et al y la gravedad por el ingreso o no del paciente en boxes de observación o planta de hospitalización.

Resultados: El 24,4% de los pacientes acudió a urgencias a causa de un RNM. El 16,1% necesitó hospitalización para resolver el problema de salud. El 83,9% de todos los RNM y el 77,3% de los ingresos causados por RNM fueron evitables. Se encontró estadísticamente más prevalencia de RNM entre los pacientes que tomaban 5 o más medicamentos. Se estimó un gasto de 14.666.178 € en el tratamiento de los RNM evitables del año 2003.

Conclusiones: La prevalencia de RNM en la población atendida, su elevado porcentaje de evitabilidad y el coste que suponen para el

servicio de salud parecen argumentos suficientes para considerar los RNM como un problema para el cual es necesario establecer programas de prevención basados en el seguimiento farmacoterapéutico.

Palabras clave: Resultados negativos asociados con la medicación. Problemas relacionados con los medicamentos. Evitabilidad. Gravedad. Edad. Sexo. Polimedicación.

INTRODUCTION

Nowadays, iatrogenicity produced by drug therapy is a matter of concern to the healthcare sector and to governments, as a consequence of the literature published on drug treatment-related morbidity and mortality. Data published by Ernst and Grizzle, updating the model for estimating the costs associated with drug-related morbidity and mortality regarding the medications designed by Jonson and Bootman, represent a classic in this respect. They estimate that drug-related morbidity and mortality cost 177.4 billion dollars in year 2000. The average cost per treatment failure was 977 dollars, and that this cost rose to 1488 dollars when inappropriate treatment and the appearance of new medical problems took place. Hospital admissions generated 70% of the costs (121.5 billion dollars), followed by admissions to long-stay centres, which accounted for 18% of the costs (32.8 billion dollars).[1,2]

A more recent study evaluated and classified patients attending the emergency department attributed to unintentional injury caused by using drugs based on data obtained in 63 hospitals in the United States that participated in the National Electronic Injury Surveillance System-All Injury Program. They estimated that 27 753 656 people visit the emergency department every year, and that 1 754 210 are admitted for negative effects deriving from the use of drugs.[3]

Many studies have evaluated and classified the iatrogenicity associated with drug treatments. Sometimes the authors measure adverse reactions,[4,5] other times admissions,[6-8] or look for an association with certain factors, such as compliance or the relationship with healthcare personnel, etc.[9,10] In other types of articles, numerous types of event caused by the use of medications are described[11-14] and, as well as describing them, the cost of hospital stays or expenses is estimated.[15]

If we carry out a bibliographical search in the Internet, we find that many terms are used to describe the unwanted effects of the use of drug treatments, such as *drug-related problems, drug misadventures, drug-related illness, medication-related problems,* and many more. Henceforth we shall adopt the terminology used by the Third Granada Consensus.[16] As well as variations in the names given to the concepts, the scenarios for evaluating the presence of negative results associated with the medication (NRM) can vary according to the interest shown in detecting them in the outpatient or hospital setting. In our work, we studied NRM in patients attending the hospital emergency department, gathering information in both the outpatient and hospital settings and covering the population of an extensive geographical area. Lastly, there are also many ways of classifying the NRM. We used the system

developed by the Pharmaceutical Care Research Group at the University of Granada, which is, in our opinion, a universal, unequivocal tool for the detection and classification of NRM, and the factors associated with their presence.

It is important for us to continue to use this same work methodology, thus ensuring our conclusions are applicable to the population and can determine especially vulnerable groups of the population and take measures aimed at preventing the appearance of NRM.

The purpose of our study was to ascertain the prevalence of NRM among patients attending the emergency department that need a consultation, and to classify them according to the Third Granada Consensus.[16] Another aim is to discover whether age, sex and/or polymedication are factors associated with the appearance of NRM, and characterise them according to their severity, preventability and cost.

METHOD

Observational, descriptive, and cross-sectional study carried out in the emergency department of a tertiary hospital. The size of the sample was assigned according to the number of visits to this department during the year 2001. The sample design consisted of conglomerates with sub-sampling and equal probabilities, without replacement during the first stage. During the second stage, there was systematic sampling, where the conglomerates were days and a systematic sample of patients seen by the emergency department was selected on each day. The maximum permissible error was 0.01, with a 95% of confidence interval. In accordance with these criteria, and to obtain a representative sample of the population attending the emergency department, 7 non-consecutive days in the year 2003 were chosen during the months of March, April, and May, and 1 in 3 patients attending the emergency department was interviewed during the 24 hours of each of those days.

Patients presenting symptoms of voluntary drug intoxication, those not waiting for the medical consultation, those referred to other hospitals and patients of the Mother-Child Centre were excluded. Those who attended the emergency department more than once with the same NRM were accounted for only once.

The information was gathered by interviewing the patients using a previously validated questionnaire.[17] When the data collection stage was complete, the information on the questionnaires and the emergency department records was analysed, using the Dader method as the work system. The NRM were classified using the Third Granada Consensus classification[16] (Table 1). This differentiates between NRM (unsatisfactory health results of patients because of the drug treatment and associated with the use or failure of the medicines used) from causes that originate them or PRM (problems related to medication: failure to comply with the therapy, dispensing error, duplication, etc). The International Classification of Diseases (ICD-9) was used to classify the diagnoses and health problems described in the medical

Table 1. Classification of Negative Results Associated With Medication. Third Granada Consensus, 2007

Need

Untreated health problem. The patient has an associated health problem for which he is not receiving the medication required

Effect of unnecessary medication. The patient has a health problem associated to taking a medication he does not need

Effectiveness

Non-quantitative inefficacy. The patient has a health problem associated to the non-quantitative inefficacy of the medication

Quantitative inefficacy. The patient has a health problem associated to the quantitative inefficacy of the medication

Safety

Non quantified lack of safety. The patient has health problems associated to the non-quantitative lack of safety of a medication

Quantitative lack of safety. The patient has a health problem associated to the quantitative lack of safety of a medication

histories in the emergency department records. A slight NRM was considered to exist when the patient concerned was released after the medical consultation; moderate NRM when the patient was kept under observation prior to release, and severe NRM when the patient needed to be admitted to hospital to solve the health problem. Preventability was evaluated according to the Baena[18] criteria. Medical literature commonly defines patients as polymedicated when five or more medications are prescribed,[11,12] which is the criteria we have used in this study.

Each case was evaluated twice. The first analysis was done with pairs of pharmacists who first suggested the presence or absence of NRM on the basis of the information elicited during the interview and from emergency department records. Later, an emergency doctor and pharmacist who had not participated in the initial analysis finally determined whether there was an NRM or not.

All the data obtained was analysed using the SPSS® computer programme version 12.0. The statistical test used to find out

the factors associated to the presence of NRM was the χ^2 Pearson test, and the Student t test was used to compare the averages.

The cost associated with the NRM was calculated based on the average cost per non-admitted emergency visit and the Diagnosis Related Groups (DRG) provided by the hospital Accounts Department for the emergencies leading to admissions.

RESULTS

Description of the Sample

Of the 639 patients selected for interview, 5 were excluded because they did not comply with the criteria for inclusion. Of the 634 remaining, 562 were evaluable, those were the cases included in the study (88.6%). Thirty-five patients did not supply all the information, while 37 did not collaborate.

The characteristics with regard to sex were: 264 women (47%) and 298 men (53%). The average age was 51.0 years (95% confidence interval [CI], 49.3-52.9). The average was 51.0 and the interval spanned from 1 year to 99 years. Table 2 contains these and other characteristics of the studied population.

Prevalence of Negative Results Associated With Medication

Of the 562 patients who have been evaluated, 137 (24.4%) presented primary NRM, ie, the reason why they visited the emergency department was a PRM.

Secondary NRM was also found, based on the interview conducted with the patients and the information obtained from the emergency report. NRM came out due to a health problem of the patient, but it was not the reason for the visit. Precisely 37 patients (6.6%) presented a secondary NRM. Within this group of 37 people, 14 also had a primary NRM.

If we take into account that in the year 2003, when the study was conducted, a total of 131 359 patients were seen, we can

Table 2. Characteristics of the Sample[a]

Sex	Female		Male	
	47.0%		53.0%	
Age	Average	Between 15 and 65 years of age		≥65 years
	51.0	60.3%		35.4%
No. of medications	Without medication	Between 0 and 4 types of drugs	≥	≥5 drugs
	28.3%	49.6%		22.1%
Chronic disease	AHT	Diabetes		COPD
	11.8%	5.7%		6.2%
Smoking	Non-smoker	Between 1 and 20 cigarettes/day	≥	≥20 cigarettes/day
	67.0%	26.0%		7.0%

[a]AHT indicates arterial hypertension; COPD, chronic obstructive pulmonary disease.

Table 3. Classification of the Negative Results Related With Medication Found in the Sample According to the Third Granada Consensus

Type NRM	Count by Type	Count by Dimension
Untreated health problem	49 (35.8%)	Need
Effect of unnecessary drug	3 (2.2%)	52 (38.0%)
Non-quantitative inefficacy	38 (27.7%)	Efficacy
Quantitative inefficacy	28 (20.4%)	66 (48.1%)
Non-quantitative lack of safety	12 (8.8%)	Safety
Quantitative lack of safety	7 (5.1%)	19 (13.9%)

estimate there were 32 051 emergencies with an NRM which was the reason for the visit during this period.

The primary NRM found in our sample was mainly efficacy, followed by necessity. They are set out in detail in Table 3.

Preventability and Severity of the Main Negative Results Associated With the Medication

On 115 (83.9%) occasions of the 137 on which the patient attended the emergency department because of an NRM, the visit could have been avoided if the patient's drug treatment had been correctly followed up. Statistically significant differences were seen in the preventability results among the different types of NRM, with a $\chi^2=28.8$ and a value of $P<.0002$. The majority of avoidable types of NRM were untreated health problems, the effects of unnecessary mediation and quantitative inefficacy.

Hundred seven (78.1%) of the patients were released after the diagnosis. On 8 occasions (5.8%) patients were kept under observation for 24 hours and in 22 (16.1%) the patients had to be kept in. It was considered that 17 (77.3%) of these hospitalisations and that 83.9% of all NRM could have been avoided.

The main factors associated with the presence of NRM were age, sex, and polymedication.

Thirty-one point five percent of the patients ≥65 years presented an NRM, but younger patients were 20.6%. The frequency of presenting NRM of the subjects ≥65 years was 1.8 times greater than the younger subjects (95% CI, 1.20-2.63).

Fifty-six point nine percent of the patients with NRM were female. The figures tell us that women present NRM with a frequency of 1.70 times greater than men (95% CI, 2.51-1.15).

The average number of drugs taken by the patients with NRM was 3.0, and 2.4 in those not presenting NRM. The student t test showed there was a statistically significant difference between both values ($P=.02$). A total of 9.4% of the patients not taking medication presented a main NRM, in comparison to 33.3% of those taking up to four drugs and 23.4% of those taking 5, or more. The differences were statistically significant ($P<.001$). With regard to the polymedication and NRM association, we

obtained a value of $\chi^2=0.08$ and $P=.77$, which indicates a lack of any statistically significant association between the condition of being a polymedicated patient and presenting a primary NRM. However, in the case of patients taking 6 or more medications, we do obtain an association among these variables, showing that these individuals are 1.75 times more likely to experience an NRM (95% CI, 1.072-2.882).

We carried out a multivariate analysis with the primary NRM dependent variable, and independent variables of age, sex, and amount of drugs. The only factor associated with the presence of primary NMR was polymedication.

Cost of the Main Negative Results Associated With Avoidable Medication

The cost of the patients attending the emergency department for avoidable NRM during the seven days of the study was estimated at €18 384 for those who were not admitted, and €45 411 for those who were admitted. According to this data, the average cost per avoidable NRM for a patient who is not admitted was €191 and for a patient who requires admission it is €2671. The average cost per NRM needing to be admitted (avoidable or not) was €2730. Based on the number of emergency visits during 2003, we calculate that the minor emergencies or those not admitted who presented an avoidable NRM could amount to €4 165 553 and €10 500 625 for the serious cases or cases requiring the patient to be admitted.

DISCUSSION

The percentage of patients that did not collaborate (5.8%) can be considered small if we take into account the setting in which the patient or companion is being asked to participate by answering the questions on the questionnaire. The same might be said of the cases where it was not possible to complete all the information (5.0%). It is for this reason that we emphasise that these losses in no way detract from the significance of the results obtained.

The literature consulted to compare the prevalence and types of NRM adopt the terminology used by the First[19] or the Second[20] Granada Consensus, according to which the negative health results associated with the use of drug therapy are called problems related to medication (PRM). In the Second Consensus, these are classified in 6 categories, which correspond to those set out in Table 1. In the Third Granada Consensus,[16] the process of using the medications is separated from the results associated with the medications. The first are called PRM and the second NRM (negative results associated with medication). Thus, the term PRM used in articles published to date is replaced by the term NRM.

Tuneu[11] observed that 19.5% of patients visited the emergency department because of NRM, while according to Baena[13] the figure was 33.2% while Cubero-Caballero[14] observed that 27.2% of the patients were admitted in emergency boxes.

Table 4. Classification of Negative Results Associated With Medication (NRM) According to the Third Granada Consensus. Data From Several Authors

Type of NRM	Own, %	Baena, %	Tuneu, %
Untreated health problem	35.8	28.5	30.5
Effect of unnecessary drug	2.2	3.2	2.5
Non-quantitative inefficacy	27.7	27.5	5.0
Quantitative inefficacy	20.4	32.1	7.5
Non-Quantitative lack of safety	8.8	7.4	54.5
Quantitative lack of safety	5.1	1.3	

In Table 4 we show the classification of the NRM found by different authors according to the Third Granada Congress. There is a noticeable difference in comparison to the Tuneu[11] classification, especially with regard to the percentage of safety NRM. Perhaps the reason for the differences is partly due to the fact that his article follows the classification of NRM from the First Granada Consensus,[19] which meant it needed to be adapted to the Third.[16] On the other hand, it confirms that the majority of the side effects detected, safety NRM, were mild, and in our study they could be neglected in the search for more important NRM. With Baena[13] we observed a very similar distribution of NRM, which certainly is attributable to the same work system used in both studies.

Preventability and Seriousness of the Negative Results Associated With Medication

With regards to preventability, this is where the results were most uniform, finding in the literature consulted percentages which were always in excess of 60%,[6,7,8,13] data which concurs with ours.

The percentage of patients admitted because of an NRM varied between 38% and 6.5% of patients with NRM.[11,13,21,22] The Spanish data references varied between 6.5% and 13.0%, very close to those obtained in this study.[11,13,21]

The high preventability rates and the high cost of NRM support the idea of the importance of establishing policies designed for their prevention. To do this, pharmaceutical follow up and health education plans are needed to prevent these as much as possible.

Associated Factors

In the search for an association between NRM and age, some authors did find a statistically greater incidence of NRM in older patients,[11,13] while others, although they follow the same trend, are not statistically significant.[7,8]

In terms of gender, scientific literature often reports that there are more NRM in women, sometimes statistically important and in others this is not specified or is not statistically significant.[6,9,13,23] No study has been found showing that men present more NRM than women statistically.

In the relationship between NRM and the number of drugs, once again, our results concurred with those of other authors[7,11,13,23] who have looked for NRM in patients visiting the emergency department. However, this relationship has not always been found in the scientific literature, as occurred in the studies by Martin[6] and Tafreshi,[22] although an association is found in the majority of studies. It should come as no surprise that the bivariate statistical analysis did not show more NRM in polymedicated patients, since considering a patient as polymedicated or not depended on a certain definition in which 5 was established as the cut-off point. As we saw in our sample, when 6 was taken as the number of drugs to be polymedicated, the numbers did reach statistical significance. The most important factor is that the patients with NRM were taking, on average, more medicines than those not presenting NRM.

Obviously, when the influence of several variables is studied, a multivariate statistical analysis is required. The fact that elderly people presented more NRM could be due to the fact that they take more medications, and this is the factor causing the greater prevalence of NRM in this group, rather than their advanced age per se. Similarly, the fact that women present more NRM could also be because, on average, they take more medications. It would appear that this reasoning is confirmed by the combined analysis of the 3 variables: age, gender, and number of medications, as only the latter was shown to be a risk factor for presenting an NRM as a reason to visit the emergency department. The fact of taking 5 or more drugs was a statistically significant risk factor for presenting an NRM, with an OR=2.27, with respect to those not taking drugs. The fact of taking 1 to 4 drugs was also a risk factor, although this did not reach statistical significance (OR=1.37).

Cost of the Main Negative Results Associated With Medication

The best work to use for comparing results is that done by Baena,[13] as it is the closest in time and uses a similar methodology. The average cost per serious NRM, ie, those patients needing to be admitted, was €2871, very close to the €2730 obtained in this work. A cost of almost 12 million euros was calculated for the avoidable NRM during the year 2001, a figure which in this study has risen to 14.5 million in 2003. Once again, these values are very similar, which supports the validity of the results obtained and draws attention to the enormous healthcare cost of avoidable NRM.

This work has shown the high number of visits to the emergency department as a result of NRM and the high proportion of these that would have been avoided with correct pharmaceutical follow up. The next step could be to carry out a comparative study, to look at the relative frequency of NRM with and without pharmaceutical follow up to quantify the impact of this activity on patient's health.

References

1. Jonson JA, Bootman JL. Drug-related morbidity and mortality. A cost of illness model. Arch Intern Med. 1995;155:1949-56.

2. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. J Am Pharm Assoc. 2001;41:192-9.
3. Budnitz D, Pollock D, Weidenbach N, Mendelsohn A, Schroeder T, Annest J. National Surveillance of Emergency Department Visits for Outpatient Adverse Drug Events. JAMA. 2006;296:1858-66.
4. Sánchez Cuervo M, Delgado Téllez de Cepeda L, Delgado Silveira E, Prieto Moix S, Bermejo Vicedo S. Detección y análisis de reacciones adversas a medicamentos en el servicio de urgencias de un hospital general. Farm Hosp. 2006;30:78-84.
5. Bond CA, Raehl CL. Adverse drug Reactions in United States Hospitals. Pharmacotherapy. 2006;26:601-8.
6. Martín MT, Codina C, Tuset M, Carné X, Nogué S, Ribas J. Problemas relacionados con la medicación como causa de ingreso hospitalario. Med Clin (Barc). 2002;118:205-10.
7. Climente Martí M, Quintana Vargas I, Martínez Romero G, Atienza García A, Jiménez Torres NV. Prevalencia y características de la morbilidad relacionada con los medicamentos como causa de ingreso hospitalario. Aten Farm. 2001;3:9-22.
8. Koh Y, Fatimah BM, Li SC. Therapy related hospital admission in patients on polypharmacy in Singapore: a pilot study. Pharm World Sci. 2003;25:135-7.
9. O'Neil CK, Poirer TI. Impact of patient knowledge, patient-pharmacist relationship, and drug perceptions on adverse drug therapy outcomes. Pharmacotherapy. 1998;18:333-40.
10. Baena MI, Fajardo P, Martínez-Olmos J, Martínez-Martínez F, Moreno P, Calleja MA, et al, en representación del Grupo de Investigación en Atención Farmacéutica. Universidad de Granada. CTS-131. Cumplimiento, conocimiento y automedicación como factores asociados a los resultados clínicos negativos de la farmacoterapia. Ars Pharm. 2005;46:365-81.
11. Tuneu Valls L, García-Peláez M, López Sánchez S, Serra Soler G, Albana Aranda G, de Irala Indart C, et al. Problemas relacionados con los medicamentos en pacientes que visitan un servicio de urgencias. Pharm Care Esp. 2000;2:177-92.
12. Blix HS, Viktil KK, Moger TA, Reikvam A. Characteristics of drug-related problems discussed by hospital pharmacists in multidisciplinary teams. Pharm World Sci. 2006;28:152-8.
13. Baena Parejo MI. Problemas Relacionados con los Medicamentos como causa de Consulta en el Servicio de Urgencias del Hospital Universitario Virgen de las Nieves de Granada. Tesis doctoral. Universidad de Granada. Facultad de Farmacia; 2003.
14. Cubero-Caballero S, Torres-Murillo JM, Campos-Pérez MA, Gómez del Río S, Calleja-Hernández MA. Problemas relacionados con los medicamentos en el área de observación de urgencias de un hospital de tercer nivel. Farm Hosp. 2006;30:187-92.
15. Rodríguez-Monguió R, Otero MJ, Rovira J. Assesing the economic impact of adverse drug effects. Pharmacoeconomics. 2003;21:623-50.
16. Grupo de Investigación en Atención Farmacéutica. Universidad de Granada. Grupo de Investigación en Farmacología. Universidad de Granada. Fundación Pharmaceutical Care España. Sociedad Española de Farmacia Comunitaria. Tercer Consenso de Granada sobre Problemas Relacionados con Medicamentos (PRM) y Resultados Negativos asociados a la Medicación (RNM). Ars Pharm. 2007;48:5-17.
17. Baena MI, Calleja MA, Romero JM, Vargas J, Zarzuelo A, Jiménez-Martín J, et al. Validación de un cuestionario para la identificación de problemas relacionados con los medicamentos en usuarios de un servicio de urgencias hospitalario. Ars Pharmaceutica. 2001;42:147-71.
18. Baena MI, Marín R, Martínez Olmos J, Fajardo P, Vargas J, Faus MJ. Nuevos criterios para determinar la evitabilidad de los problemas relacionados con los medicamentos. Una revisión actualizada a partir de la experiencia con 2.558 personas. Pharm Care Esp. 2002;4: 393-96.
19. Panel de consenso ad hoc. Consenso de Granada sobre Problemas Relacionados con Medicamentos. Pharm Care Esp. 1999;1:107-12.
20. Grupo de Investigación en Atención Farmacéutica (CTS-131). Universidad de Granada. (España). Grupo de Investigación en Farmacología Aplicada y Farmacoterapia (CTS-259). Universidad de Sevilla. (España). Grupo de Investigación en Farmacología (CTS-164). Universidad de Granada. (España). Segundo Consenso de Granada sobre Problemas Relacionados con Medicamentos. Ars Pharmaceutica. 2002;43:179-87.
21. Otero López MJ, Alonso Hernández P, Maderuelo Fernández JA, Ceruelo Bermejo J, Domínguez-Gil Hurlé A, Sánchez Rodríguez A. Prevalencia y factores asociados a los acontecimientos adversos prevenibles por medicamentos que causan ingreso hospitalario. Farm Hosp. 2006;30:161-70.
22. Tafreshi MJ, Melby MJ, Kaback KR, Nord TC. Medication-related visits to the emergency department: a prospective study. Ann Pharmacother. 1999;33:1252-7.
23. Courtman BJ, Stallings SB. Characterization of Drug-Related Problems in Elderly Patients on Admission to a Medical Ward. Can J Hosp Pharm. 1995;48:161-6.