Eur J Clin Pharmacol (2008) 64:715–722
DOI 10.1007/s00228-008-0473-y

PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Factors predicting hospital readmissions related to adverse drug reactions

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Received: 7 September 2007 / Accepted: 11 February 2008 / Published online: 3 April 2008

Abstract
Objective To analyse the contribution of adverse drug reactions (ADR) to hospital readmissions.
Methods This was a case–control study in which unscheduled admissions of patients who had been admitted to the hospital during the two previous months were assessed during a 21-month period. The patient was considered a case when the main diagnosis of readmission complied with the World Health Organisation's definition of an ADR. For each case, two controls were selected from those patients that had been admitted for ADR without readmission (n=177). Information on drugs and other risk factors was obtained from cases by interview and from controls by clinical record review.
Results There were 26,559 unscheduled admissions of which 81 were readmissions associated with ADR (4.5% of the unscheduled readmissions). There were no statistically significant correlations with sex, age or medical history, with the exception of arterial hypertension. The main drug products causing readmission were acenocoumarol (15, 18.5%), antihypertensive-diuretics (14, 17.3%), anticancer drugs (11, 13.6%) and digoxin (seven, 8.6%). In the multivariate logistic analysis, the variables predicting readmission were acenocoumarol [odds ratio (OR) 12.2, 95% confidence interval (CI) 3.8–38.3, P<0.0001], a record of diabetes mellitus (OR 2.6, 95% CI 1.3–5.5, P<0.01), the number of drugs taken at the moment of ADR (OR 1.2, 95% CI 1.1–1.4, P<0.001) and high blood pressure (OR 0.3, 95% CI 0.2–0.6, P<0.001) even though the latter was a negative predictor, preventing readmission. Of the 81 readmissions associated with ADR, 28 (34.6%) were preventable.
Conclusion A medical record of diabetes mellitus, polypharmacy and acenocoumarol treatment were risk factors predicting hospital readmission related to ADR.

Keywords Adverse drug reaction reporting systems · Case-control studies · Hospital readmissions

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Introduction

Hospital readmission after discharge is a common and very serious health problem that affects a large number of patients (5–30%) [1]. However, the majority of studies carried out to date have analysed readmission as an indicator of the quality of hospital clinical practice [1–4]; very few have described adverse drug reactions (ADR) as the cause of readmission, even though there is an abundance of literature on ADR as the causes of admission or prolongation of the stay [2–7]. As a consequence, any estimation of the contribution of ADR to hospital readmission using the information provided in these studies is extremely difficult. In addition, most analyses have concentrated on medication-related problems (MRP), which is a wider concept that not only includes

ADR but also adverse drug events and medication errors. The method of defining readmissions as well as the window period or the restriction of the study to a single service in which the readmission occurs (frequently internal medicine) also vary from one study to another [8]. Depending on this variability, ADR may be the cause of 2–35% of hospital readmissions [2–5].

A number of studies have found that a portion of the ADR-related readmissions, as can be said of all hospital admission in general, could have been prevented [9, 10]. As such, it is important to determine the factors associated with ADR-related hospital readmission (type of ADR, main medications involved and the profile of patients with a greater susceptibility to ADR-related readmission) as this knowledge would likely enable the implementation of preventative measures.

Readmission for ADR is considered to be a severe reaction in the European Union [11] (the severity criteria in the EU are: ADR that cause death, endanger life, require hospitalisation or prolongation of the hospital stay, cause permanent or significant disability or invalidity or constitute a congenital disorder or birth defect). Furthermore, within the hospital environment there is a tendency to under-report ADR, and this had increased the interest in developing new methods for detecting ADR in this area [12]. This search is facilitated by a study of he hospital discharge report, which requires that the diagnosis (main and secondary) motivating the admission be included. In addition, many countries use the International Classification of Diseases (ICD) of the American Hospital Association (AHA), which includes the E Code (Supplementary Classification of External Causes of Injury and Poisoning) for diseases resulting from ADR. The search for E Code diagnoses in the discharge report enables ADR to be detected in the cohort being studied.

This study was designed with the following endpoints:

1. to make a prospective determination of ADR-related hospital readmissions; that is, those cases where this was the primary diagnosis during the 60-day period following discharge (window period);
2. to estimate the percentage number of ADR related readmissions that could potentially be avoided;
3. to evaluate the usefulness of the codes assigned to the discharge report (ICD) as a retrospective method for detecting ADR-related readmissions.

Material and method

Selection and definition of cases (ADR-related readmissions) and controls

This study was designed as a case–control study. It was carried out in Galdakao Hospital, a tertiary hospital with 365 beds that provides all medical and surgical services except for obstetrics and paediatrics and which also houses the Basque Country Pharmacovigilance Unit. During a period of 21 months (July 2001 to April 2003), we analysed prospectively all non-scheduled patient admissions. The hospital computer system was used to obtain a daily list of readmitted patients (excluding scheduled readmissions, as it was considered unlikely that they would be ADR-related), and the clinical records of the current admissions were reviewed. The patient was considered a case when the diagnosis of the cause of readmission complied with the World Health Organisation's (WHO) definition of an adverse reaction: "any unexpected reaction that occurs when using a drug, at the usual dose for treatment, prevention, diagnosis or modification of a biological function" [11] and resulting in an admission to the same hospital within 60 days of discharge (window period). After having received informed consent from the selected patients (cases), sociodemographic–clinical information was obtained by asking the cases to complete a specially developed questionnaire that provided data on sex, age, medical history, diagnosis (es) on admission, service where admitted, drugs and adverse reactions. Information was also obtained on the previous admission, the service where admitted and medication on discharge.

Causality assessment of drug–ADR relation was made case by case. In each case, the first diagnosis was established by the doctor in charge of the patient, and his criteria were accepted by the research group. All patients initially categorised as having an ADR were assessed again by three of the authors (MG, CA and BR), who met every week in an evaluation session so as to reach a consensus decision, using a sole algorithm (method of Karch–Lassagna, the official in the Spanish Pharmacovigilance System). The concordance among different evaluators was therefore not analysed.

The control group comprised patients who had a hospital admission associated with an ADR during the same study interval without this being a cause for readmission. The calculation of the number of patients needed was made on the following assumptions: an odds ratio (OR)=4; exposure frequency between controls (according to the prevalence of ADR in non-scheduled admissions); P=5%; statistical power=80%; confidence level=95%; case:control ratio of 1:2. Based on these criteria, the case-control study consisted of 82 cases and, consequently, 164 controls. The Galdakao Hospital Research Committee approved the study.

Selection of variables

The data obtained on the questionnaire (cases) and by clinical record review (controls) were coded and entered into an EXCEL file. Four different age groups were

considered: ≤ 50, 51–65, 66–80 and >80 years. In the case group, the services where discharge took place were grouped as: cardiology, internal medicine, digestive medicine, neurology, nephrology, oncology and others (including surgical services). The following diagnoses were isolated from the review of all the clinical records: cerebrovascular accident (CVA), cardiac arrhythmia due to atrial fibrillation (CAAF), arterial hypertension, diabetes mellitus, human immunodeficiency virus (HIV) infection, ischemic cardiopathy, heart failure, neoplasia and impaired renal function. Each of the drugs or pharmacological groups considered as having a narrow therapeutic margin was considered to be a variable to be analysed, together with preventability, a variable obtained after application of the criteria proposed by Schumock and Thornton [13] (Table 1).

Study of the avoidability of ADR-related readmission and admission

The Schumock and Thornton criteria [13] were applied to all cases of ADR-related readmission and admission (where the ADR appeared as the principle diagnosis) in order to assess whether or not it was preventable.

Usefulness of the ICD as a method for detecting ADR

For each of the cases of readmission associated with a detected ADR, we retrospectively searched the hospital Documentation Service for the diagnosis code on the discharge report. This code verified whether the discharge report for the case had any E Code diagnosis that expressed an ADR according to the ICD and which would have, therefore, been predisposed to being detected retrospectively.

Table 1 Schumock and Thornton's [13] criteria for determining the preventability of an adverse drug reaction

Criteria determining the preventability of an ADR
Was the drug involved in the ADR not considered appropriate for the patient's clinical condition?
Was the dose, route and frequency of administration not appropriate for the patient's age, weight and disease state?
Was required therapeutic drug monitoring or other necessary laboratory test not performed?
Was there a history of allergy or previous reactions to the drug?
Was drug interaction involved in the reaction?
Was toxic serum drug level documented?
Was poor compliance involved in the reaction?

ADR, Adverse drug reaction

Statistical analysis

Calculations were made of the means, standard deviations and percentages for a descriptive analysis of the sample. The χ^2 test was used to measure the association between different previous clinical records (medical background) and readmissions or admissions. Student's *t* test was used for a comparison of the means for the number of drugs taken prior to readmission and admission. The readmission risk factors were determined by developing models of univariate logistic regression, considering the medical background, the drugs of narrow therapeutic margin, preventability and the number of drugs taken at the moment of readmission as explanatory variables. Finally, a multivariate logistic regression analysis with stepwise procedure was established to determine the variables contributing to readmission.

Statistical significance was assumed when the *P* value was less than 0.05. The calculations were made using the SAS System statistics package V8.02 (SAS Institute, Cary, NC) .

Results

During the study period there were 26,559 unscheduled admissions to Galdakao Hospital, of which 1802 (6.8%) were readmissions with a previous admission during the 60 previous days. Of these readmissions, 81 were associated with ADR (4.5% of all unscheduled readmissions); 47 (58%) were males and 34 (42%) were females. During the same period a random selection was made of 177 admissions for ADR that were not readmissions (controls). Table 2 presents the sociodemographic characteristics and medical background of the patients in the sample. The start of treatment with the index drug in the case group was: 35 cases (43.2%) previous to admission, 41 cases (50.6%) at discharge following admission and five cases (6.2%) after admission, but before readmission. In 39 cases, the readmission occurred in the interval of 1–15 days after discharge, in 18 cases in the interval of 16–30 days, in 16 cases in the interval of 31–45 days, and in eight cases it occurred in the interval of 46–60 days (Table 2). A comparison of sociodemographic variables and the disorders reported in both groups (cases and controls) revealed statistically significant differences only in the mean of number of drugs taken prior to admission or readmission (4.9 vs. 6.2, respectively). There were no differences in terms of sex or age of cases and controls, whether the analysis was carried out on two age groups (≤ or > 65 years) or on four age groups (≤50, 51–65, 66–80, >80 years), nor in any aspect of the medical history, with the exception of high blood pressure (which was present in

Table 2 Sociodemographic characteristics and medical background of the cases (readmissions) and controls (admissions)

Sociodemographic characteristics and medical background parameters	Readmissions, *n* (%)	Admissions *n*, (%)	Statistical significance (*P* value)[a]
Number of subjects	81	177	
Sex			0.69
Male	47 (58.0)	98 (55.4)	
Female	34 (42.0))	79 (44.6)	
Age (years)			0.80
≤65	28 (34.6)	64 (36.2)	
>65	53 (65.4)	113 (63.8)	
Age (years)			0.92
<50	13 (16.1)	25 (14.1)	
51–65	15 (18.5)	39 (22.0)	
66–80	35 (43.2)	74 (41.8)	
>80	18 (22.2)	39 (22.0)	
Number of drugs prior to ADR (mean)	6.2	4.9	0.001
Time to readmission (days)			–
1–15	39 (48.1)		
16–30	18 (22.2)		
31–45	16 (19.8)		
46–60	8 (9.9)		
Medical background:			
Cerebrovascular accident	10 (12.3)	12 (6.8)	0.14
Cardiac arrhythmia by AF[a]	25 (31.0)	46 (26.0)	0.41
Arterial hypertension	21 (25.9)	85 (48.0)	0.0008
Diabetes mellitus	20 (24.7)	27 (15.2)	0.07
HIV infection	9 (11.1)	12 (6.8)	0.24
Coronary heart disease	15 (18.5)	25 (14.1)	0.36
Heart failure	13 (16.1)	20 (11.3)	0.29
Cancer	20 (24.7)	30 (16.9)	0.14
Renal failure	12 (14.8)	22 (12.4)	0.60

[a] χ^2 test
[b] AF, Atrial fibrillation

25.9% of the readmissions in comparison to 48% of the admissions; P=0.0008).

The drug products causing readmission were mainly acenocoumarol (15 cases, 18.5%), antihypertensive-diuretics (14 cases, 17.3%), anticancer drugs (11 cases, 13.6%), digoxin (seven cases, 8.6%), glucocorticoids (six cases, 7.4%), antibiotics (six cases, 7.4%) and non-steroid anti-inflammatory drugs (NSAIDs)/non-narcotic analgesics (five cases, 6.2%). These seven pharmacological groups were responsible for 79% of all ADR-related readmissions. In the control group (admissions for ADR), the main groups of suspect drugs were the same, even though the only significant one (P<0.0001) was acenocoumarol (five cases, 2.8%). There were no statistically significant differences when the cases and controls were compared in terms of the group of drugs considered of narrow therapeutic margin. Detailed information is provided in Table 3.

The main services where the cases and controls were admitted were digestive medicine, internal medicine and cardiology. Full information is provided in Table 4. There was statistical significance in the differences in the service where the cases and controls were admitted (χ^2=20.25; P= 0.0025). In terms of causality, three of the 81 cases (5.7%) were considered to be conditional, 24 (29.6%) were considered possible, 48 (59.2%) were considered probable, and six (7.4%) were considered definite.

Multivariate logistic analysis revealed that the only variables predicting readmission were the intake of acenocoumarol [odds ratio (OR) 12.2, 95% (confidence interval) CI 3.8–38.3, P<0.0001)] a history of diabetes mellitus (OR 2.6, 95% CI 1.3–5.5, P<0.01), the number of drugs taken prior to ADR (OR 1.2, 95% CI 1.1–1.4, P<0.001) and high blood pressure (OR 0.3, 95% CI 0.2–0.6, P<0.001), even though the latter was a negative predictor, preventing readmission (Table 5).

Hospital readmissions and admissions caused by preventable ADR

Of the 81 readmissions due to ADR, 28 (34.6%) were considered preventable according to Schumock and Thornton's criteria [13]. Inadequate monitoring of acenocoumarol was the main cause of preventable readmission in ten cases (35.7%), followed by inadequate monitoring of digoxin in four cases (14.3%), alteration of the sodium and potassium levels brought about by diuretics in three cases

Table 3 Distribution of the drugs associated with readmission (cases) or admission (controls) due to adverse drug reactions, according to their narrow therapeutic margin and pharmacological class

	Readmissions, *n* (%)	Admissions, *n* (%)	Statistical significance (*P* value)[a]
Narrow therapeutic margin			0.22
Yes	24 (29.6)	40 (22.6)	
No	57 (70.4)	137 (77.4)	
Total	81 (100)	177 (100)	
Pharmacological class			
Acenocoumarol	15 (18.5)	5 (2.8)	0.0001
Antihypertensives and diuretics	14 (17.3)	50 (28.3)	0.06
Anticancer drugs	11 (13.6)	12 (6.8)	0.07
Digoxin	7 (8.6)	23 (13)	0.31
Glucocorticoids	6 (7.4)	5 (2.8)	0.09
Antibiotics	6 (7.4)	20 (11.3)	0.33
NSAIDs/non-narcotic analgesics	5 (6.2)	10 (5.6)	0.87
Other cardiovascular drugs	3 (3.7)	8 (4.5)	0.76
Opioids	3 (3.7)	1 (0.6)	0.06
Anti-HIV agents	3 (3.7)	8 (4.5)	0.76
Others	8 (9.9)	35 (19.8)	0.05
Total	81 (100)	177 (100)	

NSAID, Non-steroid anti-inflammatory drug; HIV, human immunodeficiency virus

[a] χ^2 test

(10.7%) and hypotension caused by antihypertensive agents in three cases (10.7%). The pharmacological groups mentioned (acenocoumarol, digoxin, and antihypertensive-diuretics) were responsible for 71.4% of all preventable readmissions. Table 6 presents a full description of preventable and non-preventable ADR causing readmission. Of the 177 admissions, 62 (35.0%) were considered to be preventable (acenocoumarol (5, 8.1%), antihypertensive-diuretics (22, 35.5%) and digoxin (24, 38.7%).

In terms of Hospital Services, the greatest number of preventable readmissions (10, 35.7%) were admitted to digestive medicine; all the haemorrhages caused by inadequate monitoring of acenocoumarol were attended to by this service. Digestive medicine, cardiology and neurology attended 64.3% of all preventable readmissions. There was statistical significance in the differences of preventability according to the service where the cases and controls were admitted (χ^2=22.5; P=0.0004). See Table 4 for details.

Usefulness of the ICD as a method for detecting ADR

Of all ADR-related readmissions, only 28 cases (34.6%) would have been detected using the ICD; 53 (65.4%) would not have been detected.

Discussion

The percentage of ADR-related readmissions compared to the total number of hospital admissions in this study (0.002%) is lower than that reported by Hewitt (0.4%) [4] and similar to that found by Jiménez-Bridge et al. (0.001%) [2]. However, in our study, ADR represented 6.8% of all unscheduled readmissions, whereas previous studies have reported 2%. [2], 4.5% [5], 5% [8] and 22.1% [4]. As already mentioned,, this wide difference in values is the result of the different methodology used (screening method and window period).

Table 4 Distribution of the cases (readmissions) and controls (admissions) according to the Service where admitted and preventability

Service	Readmissions, *n* (%)[a]	Preventable readmissions, *n* (%)[b]	Admissions, *n* (%)[a]	Preventable admissions, *n* (%)[b]
Digestive	23 (28.5)	10 (35.7)	23 (13)	6 (9.7)
Internal medicine	15 (18.5)	2 (7.1)	34 (19.2)	8 (12.9)
Oncology	10 (12.3)	–	10 (5.6)	–
Cardiology	9 (11.1)	4 (14.3)	47 (26.6)	23 (37.1)
Neurology	9 (11.1)	4 (14.3)	17 (9.6)	5 (8.1)
Nephrology	5 (6.2)	1 (3.6)	26 (14.7)	16 (25.8)
Others	10 (12.3)	7 (25.0)	20 (11.3)	4 (6.5)
Total	81 (100)	28 (100)	177 (100)	62 (100)

[a] Statistical significance of the comparison between cases and controls according to the service where admitted (χ^2 =20.25, P=0.0025)

[b] Statistical significance of the comparison of preventability between cases and controls according to the service where admitted (χ^2 =22.50, P =0.0004)

Table 5 Variables associated with readmission. Model for multivariate logistic regression

Model	Coefficients	
	OR (95% CI)[a]	*P* value
Intake of acenocoumarol	12.20 (3.88–38.34)	<0.0001
Diabetes mellitus	2.63 (1.26–5.48)	<0.01
Number of drugs prior to ADR (mean)	1.24 (1.10–1.39)	<0.001
Arterial hypertension	0.31 (0.16–0.60)	<0.001

[a] Odds ratio (95% confidence interval)

The percentage of patients readmitted for ADR in our study (6.8%) is comparable, despite the large number of variables involved, to the incidence of drug-related admissions (2.4–6.5%) [7, 14–17]. It would appear, therefore, that a previous hospital admission is not associated with a reduced risk of ADR-related readmission. However, it does appear that hospital readmission is associated with patients suffering from a larger number of complaints and receiving a greater number of drugs, and who, therefore, would be exposed to a higher risk of suffering ADR [18]. Alternatively, the use of a prospective follow-up of readmissions, i.e. intensive monitoring of ADR, would provide an explanation of why the number of cases is higher than when any other detection method is used [16], although the exclusion of scheduled readmissions could have underestimated this incidence rate.

This study has potential weaknesses: its prospective/retrospective design, a potential bias in the selection of the control group, clinical judgement being used to assess the admission or readmission as ADR-related and ignorance of the total number of admissions related to ADR.

Among the factors that have traditionally been seen to influence the risk of suffering an ADR are age and sex. The older the age, the greater the risk of suffering ADR [16–19]. In our study, the number of ADR was positively correlated with increasing age for both cases and controls (Table 2). To date, the data available on the influence of sex on the incidence of ADR have been contradictory. Whereas some authors have reported that females have a greater risk of suffering ADR [18–21], others have found no relationship whatsoever [17].

Of all the medical backgrounds evaluated in our study, high blood pressure was the only factor that differed significantly between the cases and controls. No similar relationship was found in other studies. In fact, multivariate logistic analysis of the variables contributing to readmission showed that hypertension was a protective factor. This result can not be easily explained. However, a comparison of the control group with the cases (readmissions) revealed that the former had a larger number of ADR-associated events with antihypertensive-diuretics drugs (28.3 vs. 17.3%). This trend was also seen for cardiology (26.5 vs. 11.1%) and nephrology (14.7 vs. 6.2%): both services admitted a larger number of patients for ADR. As a result, it could be considered that hypertensive patients who are admitted for an ADR, often caused by an antihyper-

Table 6 Preventable and non-preventable ADR related readmissions according to class of drug involved and problem detected

Class of drug involved and problem detected	Preventable readmissions, *n* (%)	Non-preventable readmissions, *n* (%)
Acenocoumarol		5 (9.4)
Inadequate monitoring	10 (35.7)	
Antihypertensives and diuretics		7 (13.2)
Hypotension due to antihypertensives	3 (10.7)	
Abnormal levels of K + or Na + due to diuretics	3 (10.7)	
Renal failure by interaction furosemide and captopril	1 (3.6)	
Anticancer drugs	–	11 (20.8)
Digoxin		3 (5.7)
Toxic levels	4 (14.3)	
Glucocorticoids		4 (7.5)
Hyperglycemia	2 (7.1)	
Antibiotics	–	6 (11.3)
NSAIDs/non-narcotic analgesics	–	5 (9.4)
Other cardiovascular drugs		2 (3.8)
Orthostatic hypotension due to nitroglycerin	1 (3.6)	
Opioids	–	3 (5.7)
Anti-HIV agents	–	3 (5.7)
Others		
Phenytoin: toxic levels	2 (7.1)	
Insulin: need decreased	2 (7.1)	
Gliclazide, risperidone, mianserin, gabapentin	–	4 (7.5)
Total	28 (100)	53 (100)

tensive-diuretic drug, receive subsequent treatment and follow-up after discharge that reduces the risk of another admission of the same type.

In terms of the drugs associated with readmissions, four drugs or drug groups (acenocoumarol, antihypertensive-diuretics, anticancer drugs and digoxin) were responsible for 58% of all ADR-related readmissions. This profile is comparable to that of the pharmacological groups that may cause hospital admission [7, 14, 17, 18] or readmission [4, 5]. A large number of readmissions in our study was brought about by acenocoumarol (15 cases, 18.5%); this is especially striking because acenocoumarol is a drug subject to exhaustive monitoring during and after hospitalisation. However, given the nature of the population that was readmitted, mainly the elderly with multiple complaints, it is probable that the monitoring of acenocoumarol in this population is more difficult than in other groups. This possibility does not, however, exclude possible deficiencies in the control of this drug after hospital discharge.

Our results with NSAIDs/non-narcotic analgesics related to readmissions are not surprising, since they are not drugs usually prescribed on discharge. However, the number of admissions related to NSAIDs/non-narcotic analgesics was low (n=10). Although a bias in selecting the controls cannot be completely excluded, a recent multicentre study on drug utilisation carried out in Spain reported a lower use of NSAIDs in Spain than in the USA or northern Europe [22] however, the use of gastroprotective agents together with NSAIDs in Spain is high (41.6%) [23]. Both sets of data, plus an ignorance of the total number of admissions related to ADR, and how many of these were associated with NSAIDs, could explain the result observed.

Of the ADR-related readmissions evaluated, 34.6% were considered preventable. These figures are similar to those published by Lagnaoui et al. [9] (25%), Goettler et al. [10] (30.7%) and Bannwarth et al. [18] (37.9%). Given the wide variability regarding the preventability criteria and the fact that these studies analysed hospital admission and not readmission, a direct comparison of our results with these data is difficult. It seems, therefore, that the prevention of ADR-related hospital admissions and, consequently, also that of hospital readmission are associated with a multitude of variables, many of which are inherent to the hospital where the study is performed. Multivariate logistic analysis revealed that the only variables predicting readmission were the intake of acenocoumarol, diabetes mellitus, number of drugs used prior to ADR and high blood pressure, even though the latter prevented readmission. These results differ from those published by Otero et al. [24] who reported that the use of drugs with a narrow therapeutic margin, age over 75 years and self-medication were predictive covariables; however, their study referred to admissions and not readmissions, and to adverse events, not ADR.

The final end-point of this type of studies is to establish measures aimed at preventing ADR-related hospital admission (readmission in this case). As Forster et al. [25] pointed out, improved communication between the hospital and primary healthcare, patient counselling, patient information leaflets, the reporting of possible changes in drug therapy and control studies as well as the planning of discharge by systematic procedures seem to be preventative measures yet to be studied. Applying these measures to groups with a greater risk of ADR-related admission could provide some indication of their viability. In our centre, the only routine procedure at hospital discharge when readmission was caused by ADR is written advice in the discharge report to avoid the drug responsible. Unfortunately, other procedures, such as follow-up by telephone or discharge through systematic procedures are not yet routine in Spain, except for a few hospitals.

In our study, the largest number of preventable readmissions (71.4%) occurred in elderly patients and treatments involving acenocoumarol, digoxin or antihypertensive-diuretics. This drug profile and the causes associated with preventable ADR-related admission or readmission is similar to those found in other studies [26–28]. The problem of oral anticoagulant agents (OAC) as the cause of hospital admission has also been shown in earlier studies [20, 24] which mention various difficulties in their monitoring process, even though haemorrhage brought about by OAC is a dose-dependent effect, inherent to the action mechanism of the drug. In this regard, the introduction on the market of new oral anticoagulants that do not require monitoring could improve the situation [29]; unfortunately, the first of these OAC marketed (ximelagatran) has been withdrawn due to hepatotoxicity. With respect to digoxin, a drug with a narrow therapeutic range, prescribers should ensure that patients are treated with the minimum effective dose. In the case of diuretics, more frequent monitoring of potassium or sodium serum levels could reduce the number of patients admitted with dehydration and/or renal failure. In the case of hypotension caused by antihypertensives, information to patients prior to changes of drugs or at the start of treatment could be a measure of easy application.

Of all ADR-associated readmissions, only 34.6% would have been detected using the ICD, a result similar to that found by Stowasser et al. [3]. Among the factors that could explain this limited efficiency could be its absolute dependence on the express mention of the ADR in the report written by the doctor as, logically, only written information is subject to coding by clinical documentation services. Coding is carried out by clerical employees who may have only a limited awareness of medical and pharmacological terminology and, in some cases, this may lead to incorrect coding. In spite of these limitations, the revision of ICD codes in hospital discharge reports could be an important source of

information for pharmacovigilance as, among other possibilities, it would overcome, at least partially, the considerable under-reporting that occurs in hospitals.

When resources are scarce, the number of preventable readmissions related to drugs could be reduced by focussing preventative actions on four groups of drugs—acenocoumarol, antihypertensive-diuretics, anticancer drugs and digoxin—especially acenocoumarol, and by paying special attention to medical records of diabetes mellitus and polypharmacy.

Acknowledgements This study was supported by the Galdakao Hospital Research Committee. C. Aguirre benefitted from partial leave from the Basque Foundation for Health Innovation and Research BIOEF (BIO04/LF/22).

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