Analysis of the Errors Associated With the Prescription, Preparation, and Administration of Cytostatic Drugs

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Abstract

Objective: To analyse errors relating to the process of prescription, validation, preparation, dispensing, and administration of cytostatic drugs, set out in the risk management programme regarding cytostatic drugs at our hospital.

Methods: Prospective, descriptive and cross-sectional study, of 3-year duration (2003-2005) on the total number of errors reported in the chemotherapy risk management programme.The dosing of cytostatic drugs is centralised in the Pharmacy Department, which prepared an average of 12966 cytostatic preparations per annum during the study period. The prescription validation procedure for chemotherapy is therefore centralised at the Pharmacy Department and is the responsibility of the area pharmacist who detects the majority of prescription errors and keeps a record of all the errors detected in the circuit. Most chemotherapy dosing errors are detected when the preparations are checked prior to dispensing. Pharmaceutical validation errors are detected in the clinical units after the checking of the prescription by the nursing staff and administration errors are gathered through voluntary communication by nursing staff or, occasionally, by the patients themselves. The classification used for errors "by error type" is in accordance with the Spanish adaptation of the National Coordinating Causal for Medication Error Reporting and Prevention prepared by Otero. The qualitative variables analysed were measured as rates and/or percentages.

Results: During the study period (between 2003 and 2005), 268 errors were reported, 87.91% of which were detected in the medical day hospital. An increase in errors was seen in 2005, affecting 13.91% of the patients as opposed to 6.69% and 4.81% in the years 2003 and 2004. The largest number of errors was reported by the nursing staff (54.08%) followed by the pharmacist with 39.55% and the doctor 4.47%. Prescription errors (45.14%) were the most frequent, followed by validation (33.58%) and preparation (16.41%) errors. Among the prescription errors, the greatest percentages correspond to underdosing (32.32%), overdosing (16.16%), and dose reversal (11.11%). A total of 11.94% (32) of these reached the patient and 88.06% were prevented.

Conclusions: The assessment of care practices and the critical, constructive analysis of the errors detected therein can be used as a tool that will enable the continuous improvement of procedures and the increased clinical safety of the patients. The collaboration of all the personnel involved in the circuits with known and shared objectives can enable a more exact dimension to be obtained of our current care situation in aspects for the clinical safety of patients.

Key words: Prevention of medication errors. Chemotherapy.

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Errores asociados con la prescripción, validación, preparación y administración de medicamentos citostáticos

Objetivo: Analizar los errores relacionados con el proceso de prescripción, validación, preparación, dispensación y administración de medicamentos citostáticos, recogidos en el programa de gestión de riesgos con medicamentos citostaticos en nuestro hospital.

Métodos: Estudio prospectivo, descriptivo y transversal, de 3 años de duración (2003-2005), sobre la totalidad de los errores comunicados en el programa de gestión de riesgos asociados con quimioterapia. La dosificación de medicamentos citostáticos está centralizada en el servicio de farmacia, que elaboró una media anual de 12.966 mezclas citostáticas en este período de estudio. El procedimiento de validación de la prescripción de quimioterapia está, asimismo, centralizado en el servicio de farmacia y es responsabilidad del farmacéutico del área, que detecta mayoritariamente errores de prescripción y asume a su vez el registro de todos los errores detectados en el circuito. La detección de errores de dosificación de la quimioterapia proviene en su mayoría de la revisión de las mezclas elaboradas, pre-

via a la dispensación. Los de validación farmacéutica se detectan en las unidades clínicas tras la revisión de la prescripción por parte del personal de enfermería, y los de administración se recogen a partir de la comunicación voluntaria por parte del personal de enfermería o, en ocasiones, del propio paciente. La clasificación utilizada para los errores «por tipo de error» sigue la adaptación española de la clasificación Nacional Coordinating Causal for Medication Error Reporting and Prevention realizada por Otero. Las variables cualitativas analizadas se midieron como tasas y/o porcentajes.

Resultados: En el período de estudio 2003-2005 los errores registrados fueron 268, el 87,91% de los cuales se detectó en hospital de día médico. Se observa un incremento de los errores en 2005, que afectan a un 13,91% de los pacientes atendidos frente a un 6,69 y un 4,81% de los años 2003 y 2004. El mayor número de errores fue comunicado por el personal de enfermería (54,08%), seguido del farmacéutico con un 39,55% y el médico en un 4,47%. El error de prescripción, con 45 casos (14%) fue el más frecuente, seguido de la validación (33,58%) y la elaboración (16,41%). Entre los errores de prescripción, los mayores porcentajes corresponden a infradosis (32,32%), extradosis (16,16%) e inversión de dosis (11,11%). Un 11,94% (32) de éstos llegaron al paciente y el restante 88,06% se previno.

Conclusiones: La evaluación de la práctica asistencial y el análisis crítico y constructivo de los defectos que en ella confluyen pueden ser una herramienta que permita la mejora continua de los procedimientos y el incremento de la seguridad clínica de los pacientes. La colaboración de todo el personal implicado en los circuitos con objetivos conocidos y compartidos permite obtener una dimensión más exacta de nuestra realidad asistencial en los aspectos de la seguridad clínica de los pacientes.

Palabras clave: Prevención de errores de medicación. Quimioterapia.

INTRODUCTION

The interest shown by healthcare professionals and healthcare services in quality of care has evolved since the 1970s from the scientific-technological standpoint to the efficient use of healthcare resources and moving towards user satisfaction. Nowadays we are faced with a dimension of quality, which is essentially aimed at elevating the patients' clinical safety.

Different international studies have shown that the incidence of adverse events (AE) in hospitalised patients oscillates between 4% and 16.6%, approximately 50% of which are considered avoidable.[1-3]

The initiatives proposed by WHO and OPS[4] and the European Health Committee[5] all recommend that different governments make patient safety the focal point of all healthcare policies.

The Spanish National Health System shares this concern, and has established a number of actions in this respect, including the study of adverse effects,[6] the consensus document[7] and the translation of the British National Health Service on the 7 steps for patient safety,[8] among others. With regard to drug safety, the so-called "high risk" drugs are those which, if used incorrectly, are very likely to cause serious harm or even the death of patients[9] and cytostatic drugs, both oral and parenteral, are included in this group.[10] The GEDEFO[11] group consensus document represents an important initiative in terms of patient safety and the prevention of errors with this type of drugs.

The errors associated with the prescription-preparation process and the administration of cytostatic drugs may have fatal consequences for patients because of the narrow therapeutic margin of such drugs. Often, the dose finally administered may be determined by the limiting toxicity of the doses or accumulated toxicity where small increases can have fatal consequences.[12]

Among the causes of errors occurring in the chemotherapy setting may be: *a)* causes inherent to this type of drugs such as the optimum dose of the cytostatic, associated with anthropometric parameters and clinical variables among patients, or even within the same patient, variations between cycles caused by the toxicity of earlier cycles; similarly, there are variations within the same diagnosis and for the same association of cytostatics according to the frequency of administration (weekly, 3-weekly, monthly, etc), and finally variations in doses of the same drugs, when these form part of different chemotherapy protocols for different diagnoses; *b)* the coexistence of research protocols with dosing scales, the coexistence of different protocols in terms of dose intensity and the compassionate use of drugs and associations that are not clearly established; *c)* the lack of alert systems; *d)* the learning curves experienced by residents at clinical hospitals and the learning curves of high turn-over auxiliary staff; and *e)* the increasing pressure on healthcare systems.[13] Nowadays it has been estimated that 162 000 cases of cancer are diagnosed in Spain every year.[14]

Incidents or near misses are important because, although they may not cause harm if they are detected before they reach the patient, there are enough of them to be analysed. These reiterated prescription errors, whether they involve the dose per patient or any other aspect regarding stability, distribution or cytostatic drug delivery must be the subject of rigorous examination.

Since 2003, our hospital has been running a Programme for the Management of Risks Associated with Chemotherapy (PGRQ, *Programa de Gestión de Riesgos Asociados a la Quimioterapia*) that includes, among other factors, on-going training for nursing and auxiliary staff involved in these processes, the explicit, documented tutelage of critical points in the prescription and validation processes of the chemotherapy, at the beginning of the learning curve of oncology, haematology and hospital pharmacy, and the communication circuit for reporting errors associated with chemotherapy.

With this study we intend to make a qualitative and quantitative analysis of the errors related to the prescription, dispensation and delivery of cytostatic drugs, set out in the PGRQ with cytostatic drugs in our hospital.

METHOD

The communication circuit for errors associated with chemotherapy forms part of the PGRQ and is based on the fact that anybody (doctor, pharmacist, nurse, auxiliary, etc) related to the prescription, validation, dispensation and administration process and even the distribution of chemotherapy mixtures, is capable of detecting potential or real errors in this circuit.

A prospective descriptive transversal cross-sectional study was conducted of the total errors communicated in the PGRQ of outpatients and in patients with impact on their chemotherapy treatment, during January 2003 and December 2005 period.

The dosing of cytostatic medications is centralised in the pharmacy department, which prepared an average of 12 966 cytostatic mixtures per annum during the study period. The prescription validation procedure for chemotherapy is therefore centralised at the pharmacy department and is the responsibility of the area pharmacist who keeps a register of all the errors detected in the circuit. The majority of the errors in the medical chemotherapy prescription process are detected during the systematic pharmaceutical validation of all prescriptions, while the dosing errors are mainly detected during the check made before dispensing to the patient, that is carried out at our hospital by a nurse in the pharmacy department, when they are checked against the individualised document created for each patient that has been issued by the Oncofam® chemotherapy management programme and certified by a pharmacist to be correct: number of cytostatics prepared for the patient, each cytostatic, each diluent, the packaging (glass, 24-hour, 48-hour, 5-day infuser, etc), the appearance and colour are correct, the special packaging (needles, bags, etc, are correct), the light label (label and photoprotective bag), the cold label and if the complementary medication is correct in terms of quantity and quality. Pharmaceutical validation errors are usually detected in clinical units after the nurse responsible for the patient checks that all the items listed in the medical prescription for chemotherapy agree with those on the label of each mixture provided by the pharmacy service. A systematic check is made of the patient's name and surnames, the medical history number, the clinical unit and bed (if any), drug substance and dose, type of diluent and volume, final mixture volume, infusion time in minutes and speed in millilitres/hour and drops/minute, route of administration, date of administration expiry date and time, storage instructions (cold and light) and in some cases the complementary information regarding the appropriate fungible, etc. The errors occurring during the chemotherapy administration stage are basically gathered when they are voluntarily notified by the persons involved, who are usually nursing staff, and occasionally the patients themselves.

The pharmacist enters each incident or error notified via this system onto a database designed for the purpose. This includes the date, the patient's medical history, the medical unit, type of error or incident, a brief description of the incident, person reporting this and whether or not it reached the patient and/or had consequences.

To classify the errors, the Spanish adaptation of the NCCHERP (National Coordinating Causal for Medical Error Reporting and Prevention) was used.[15]

The sample for the study was all the errors detected and registered in this period.

The qualitative variables analysed are measured as rates and/or percentages.

RESULTS

Since 2004, when the PGRQ became operational, 268 errors have been registered.

An important increase in the number of errors was seen in 2005, affecting 13.91% of patients seen as opposed to 6.69% and 4.81% in the years 2003 and 2004 respectively. Table 1 shows the distribution of the data about the errors found, in absolute values and the error rate, in terms of the number of patients seen, stays and mixes made, as well as the distribution of errors by clinical units, with 87.31% of the patients at the oncohaematology day hospital.

Table 2 shows the errors distributed by error type, in absolute and percentage terms, with reference to the same concepts, the most frequent (45.14%) being prescription, followed by pharmaceutical validation with 33.58%.

Among the healthcare professionals involved in detecting errors, the nursing staff detected 145 errors (54.08%), of which 79 (29.47%) were nurses at the day hospital, 44 (16.41%) were nurses from the pharmacy service and 22 (8.20%) to hospitalisation nurses; the pharmacist detected 106 errors (39.55%), the doctor (oncologist or haematologist) 12 (4.47%), the patient 1 (0.37%), and other professionals 4 (1.49%).

Table 3 shows the prescription errors detected and prevented by the pharmaceutical validation of the chemotherapy prescription in absolute and percentage values, in total 99 (93.3% of 106 errors detected by the pharmacist and 81.81% of all the prescription errors). Of these, the majority subtype was underdose with 32 (32.32%), followed by overdose with 16 (16.16%). The sum of dose-related errors (underdose, overdose, dose inversion, missing doses) represent, as accumulated data 66.66% of the total number of errors detected by pharmaceutical validation.

The overall number of errors in the circuit corresponding to overdose and underdose was the largest given that they also occurred during the validation (7 from underdose and 9 from overdose), preparation (1 overdose), and administration (1 overdose). To summarise, there were a total of 84 dosing errors (31.65% of the total), of which 66 (78.57%) occurred during the prescription and the remainder in the rest of the circuit. Of all the errors in the circuit, those involving doses were: 39 (47.61%) underdose, 27 (30.95%) overdose, 11 (13.09%) dose reversion, and 7 (8.33%) absence of dose.

In terms of the type of cytostatic involved in all the errors reported, 48 (17.9%) errors were considered to involve the complete cycle, while in the rest of the cytostatics most frequently

Table 1. Distribution of Errors by Clinical Units and Annual Distribution, and Error Rate Based on Mixtures Prepared, Patients, and Stays

Years	Errors Detected	Number of Mixtures	Rate of Errors × 1000 Cytostatic Mixtures	No. of Patients	Rate of Errors × 1000 Patients	Number of Visits	Rate of Errors × 1000 Visits for Administering Chemotherapy
2003	53	11 710	4.5	792	66.9	8795	6.0
2004	49	13 234	3.7	1018	48.1	8505	5.7
2005	166	13 954	11.9	1193	139.1	8916	18.6
3 years	268	38 898	6.8	3003	89.2	26 216	10.2
Errors by Clinical Units							
Patients hospitalised in medullar transplant: 2							
Patients hospitalised in oncohaematology: 32							
Patients in oncohaematology day hospital: 234 (87.31% of total errors)							

Note: We use the term "visit for delivering chemotherapy," defined in our SELENE® computer system, as each day a patient (hospitalised or out-patient) comes in to receive, or receives intravenous chemotherapy while hospitalised.

Table 2. Classification of the Errors per Type Based on Mixtures Prepared, Patients, and Visits

Type of Error	Number (% of the Total)	% of Mixtures Associated to Error Type (3-Year Period)	% of Patients Affected by Each Type of Error (3-Year Period)	% of Visits During Which Each Type of Error Occur (3-Year Period)
Prescription	121 (45.14)	0.311	4.029	0.461
Validation	90 (33.58)	0.231	2.997	0.343
Preparation	44 (16.41)	0.113	1.465	0.167
Administration	11 (4.10)	0.28	0.366	0.041
Others	2 (0.74)	0.005	0.066	0.007
Total	268 (100)	0.688	8.924	1.022

Table 3. Sub-classification of the Errors Detected by the Pharmacist by Pharmaceutical Validation of the Medical Prescription for Chemotherapy

Error Type (Total)	Sub-classification	No. (%)	Description
Prescription (99)	Underdose	32 (32.32)	6 in infusion; 3 with oral or intravenous etoposide; 4 due to lack of zeros; 2 in the protocol for weekly 5-fluorouracil; 4 in the cycle with could be weekly or 3-weekly, such as tratuzumab or carboplatin or paclitaxel; 13 other cases
	Overdose	16 (16.16)	4 with etoposide, 3 with the andriamycin cycle with ifosfamide, 2 infusor 2 prednisone, 5 other cycles
	Dose reversion	11 (11.11)	7 FEC cycle (5-fluorouracil, epirubicin, and ciclofosfamide); 2 cisplatin and gemcitabin; and 2 for 5-fluorouracil with folinic acid
	Administrative	7 (7.07)	4 labelling, 3 clinical history
	Missing date	8 (8.08)	
	Stability defect	8 (8.08)	2 Docetaxel, 2 etoposid, 2 carmustin, 1 Gemcitabin and 1 Rituximab
	Lack of dose	7 (7.07)	2 mesna, 3 carboplatin, 2 gemcitabin
	Wrong guideline	4 (4.04)	2 cycles of citarabin prescribed each 24h which it should have been each 12; 2 others
	Wrong protocol	2 (2.02)	
	Wrong cycle	2 (2.02)	
	Missing cytostatic	2 (2.02)	2 in CHOP protocol
Total		99 errors	

involved were: 5-fluorouracil in 21 cases (7.8%), docetaxel in 16 (5.97%), etoposide in 15 (5.59%), cyclophosphamide in 14 (5.22%), gemcitabin and paclitaxel in 12 (4.47%) each, and cysplatin in 10 cases (3.73%).

Of all the errors detected in the period, 32 (11.94%) reached the patient and were subsequently detected, as shown in Table 4.

In the analysis of the qualitative aspects of the errors detected and their frequency, it was possible to establish as clinical points for special control (especially the initial phases of the learning curve of the residents of the hospital pharmacy and oncohaematology) the prescriptions for chemotherapy with infusers, etoposide cycles alternating with intravenous and oral routes, and the weekly or 3-weekly administration regimes, such as those for carboplatin paclitaxel and trastuzumab.

DISCUSSION

With regard to the methodology used, creating systems for registering and notifying safety problems is an essential strategy for learning from mistakes and avoiding its recurrence in the context of continuous improvement.[16,17] They focus on incidents (where no harm has been caused) or on errors that have produced minimal damage. The main purpose is to identify areas or vulnerable elements of the system before the patient is harmed and to continuously train healthcare professionals by analysing large numbers of cases.[18,19]

In our opinion, the data obtained represents to a certain degree, the real situation of care practices, somewhat biased by the lack of the required safety culture, due, on the one hand, to fear of possible repercussions and, on the other, to the shame of exposing someone else's error, and especially one's own. In this context it is far simpler to detect errors in the medical order for chemotherapy (prescription) which is an explicit, written document registered in the patient's clinical history, than during the pharmaceutical validation, which may not have a specific document, or the preparation, because it is impossible to establish systems for measuring the doses of the drug doses, and even in administration, where an error in speed or frequency of administration can easily go unnoticed, or where on occasions it is difficult to follow the record of administration and cases in which only a patient with a good knowledge of his treatment can contribute to prevent an error.

Based on our results, we consider that the largest number of errors detected between 2003 and 2005 can be attributed to an increase in the clinical safety culture among the people involved in the process rather than any deterioration or relaxation of our safety practices.

Table 4. Sub-classification of the Errors Reaching the Patient

Error Type (Total)	Sub-classification	Number	Description
Prescription (15)	Dose	4	2 in infusions prescribed as daily doses per total dose, and 2 calculation errors when multiplying by body surface
	Administrative	3	Wrong identifying label of a pre-printed chemotherapy protocol for a certain patient
	Stability defect	4	3 docetaxel, 1 rituximab
	Total or partial protocol	4	An entire protocol, or part of it, is prescribed on the wrong date
Pharmacist Validation (6)	Overdose	2	Reading error
	Underdose	1	Reading error
	Missing cytostatic	1	Cytostatic missing in the protocol which was not detected
	Administrative	2	There was a more up-to-date prescription which was not in the pharmacy
Preparing the Mixture (1)	Extra dose	1	A 2-day infusion was prepared instead of a seven day infusion
Administration (10)	Patient error	2	A patient is administered a cytostatic mixture which was not prescribed for him
	Stability error	1	Cytostatic administered past its expiry date
	Infusion speed	1	Intrathecal intravenous preparation administration
	Form of administration	1	The cytostatic prescribed was not administered
	Dose and protocol	5	2 doses scheduled 12 h apart are adminstered together

Most of the errors seen in outpatients as opposed to hospitalised patients are attributed to the differing burdens placed on healthcare personnel working at the oncohaematological medical day hospital as opposed to the medullar transplant unit or the hospital beds in oncohaematology, drawing attention to the difference between admissions for chemotherapy in different clinical units.

On the same grounds, it must be said that the registration of pharmaceutical validation errors has been rigorous and that the collaboration of nursing staff has partly reduced the bias caused by the lack of a specific document for this purpose.

With reference to prescription errors, numerous cases of overdose with serious documented toxicity and even patient death[20,21] are described in the scientific literature, and also underdosing and defective techniques that may or may not include oral administration[22] or the failure to administer protective drugs, such as mesna in ifosfamide or cyclofosfamide cycles, for example, which can have serious repercussions, as well as another set of circumstances that can eventually reduce the efficacy of the treatments, which is even more difficult to document, but has the same seriousness.

Different authors have reported errors detected in the drug prescription, validation, and preparation and administration circuit. In the different studies taken into account that analyse the subject of errors with cytostatic medications, there are factors such as the varied methodology and the lack of uniformity, which hinder the evaluation of the results. Goyache Goñi[23] found that the accumulated dose-related errors in chemotherapy prescriptions increased to 64.6%, which was similar to the data of 66.66% we detected, while there are differences with regard to the distribution of the subtypes found by this author with 35.5% overdose, 24% underdose, 3.1% of dose omissions, and 3% of extra doses in the cycle. The same occurs in the mistaken protocol prescription error where this author found 1% and we found 4.04%. Other authors found a lower percentage of error in the doses of chemotherapy prescribed, these being 38.5%,[24] 38%,[25] and 47.79%.[26] Our results differ slightly from those described, perhaps because of the analytical method that adds to the dosing errors, as well as those corresponding to prescription that did not occur during the pharmaceutical validation, preparation and administration that are not evaluated by other authors.

Some authors, such as Aguirrezábal et al, suggest that chemotherapy prescriptions should be restricted to doctors with the necessary experience, and that established protocols should be available as a measure for decreasing the frequency of errors. In this study we have not analysed if the frequency of errors is higher in the first part of the learning curve of hospital pharmacy and oncohaematology residents, but we do have some tools for preventing these such as: *a)* established protocols; *b)* explicit restrictions regarding the validation of chemotherapy prescriptions by first-year hospital pharmacy residents; *c)* explicit definition of the most frequent critical points in the pharmaceutical validation for the safe performance of our usual practices; *d)* collaboration with experts and nursing personnel in the pharmacy department and oncohaematology day hospital to develop multidisciplinary clinical sessions related to clinical safety for oncohaematology patients.

The main bias or difficulty of the study with regard to the process of validating the data derived, specifically, from the complexity of the process subject to analysis (prescription-cytostatic drug administration circuit) and the lack of a safety culture in the Spanish National Health System that sometimes hinders these initiatives for the error made or identified to be reported, which are really properly understood and do not get the collaboration they deserve, which means that not all the errors or incidents occurring are reported.

Although there may be a clear bias towards detecting medical prescription errors rather than pharmaceutical validation or the preparation and administration of cytostatic medications by nursing staff, the spread of clinical safety will allow a more reliable portrait of our assistance reality.

The evaluation of healthcare practices and the critical constructive analysis of the errors detected here can be used as a tool to enable the continuous improvement of procedures and more clinical safety for the patients.

References

1. Brennan TA, Leape LL, Laird N, Hebert L, Localio AR, Lawthers AG, et al. Incidence of adverse events and negligence in hospitalised patients: results of the Harvard Medical Practice Study. N Eng J Med. 1991;324:370-6.
2. Wilson RM, Runciman WB, Gibberd RW, Harrisson BT, Newby L, Hamilton JD. The Quality in Australian Health-Care Study. Med J Aust. 1995;163:458-71.
3. Aranaz JM, Aibar C, Gea MT, León MT. Los efectos adversos en la asistencia hospitalaria. Una revisión crítica. Med Clin (Barc). 2004;123: 21-5.
4. Organización Panamericana de la Salud. Por la seguridad del paciente [accessed February 15, 2005]. Available from: http://www.paho.org/Spanish/DD/PIN/ahora03_nov04.htm
5. La prevención de efectos adversos en la atención sanitaria: un enfoque sistémico. Comité Europeo de la Sanidad. Comité de expertos en la gestión de la seguridad y la calidad de la atención sanitaria. Consejo de Europa CDSP Estrasburgo, 2004, 41.
6. Aranaz, JM Estudio Nacional sobre los Efectos Adversos ligados a la Hospitalización. ENEAS 2005. Madrid: Ministerio de Sanidad y Consumo; 2006.
7. Declaración de profesionales por la seguridad del paciente. Agencia de calidad del Sistema Nacional de Salud. España [accessed June 13, 2006]. Available from: http://www.asoc-aen.es/web/docs/DeclaracionSeguridad06.pdf.
8. La seguridad del paciente en siete pasos. Agencia Nacional para Seguridad del Paciente (NPSA). Sistema Nacional de Salud (NHS). Reino Unido [accessed June 13, 2006]. Available from: http://www.infodoctor.org/Seguridad.pdf.
9. Cohen MR, Smetzer JL, Tuohy NR, Kilo CM. High-alert medications:safeguarding against errors. In: Cohen MR, editor. Medication errors. 2nd ed. Washington (DC): American Pharmaceutical Association; 2007. p. 317-411.
10. Institute for Safe Medication Practices. ISMP's list of high- alert medications. Huntingdon Valley (PA): ISMP; 2007. Available from: http://www.ismp.org/Tools/highalerttmedications.pdf.
11. Grupo Español para el desarrollo de la Farmacia Oncológica (GEDEFO). Prevención de errores de medicación en quimioterapia [accessed September 24,2005]. Available from: http://www.amgen.es/amgen2/grupos Errores_medicacion.htm.
12. Cajaraville G. Errores de medicación en oncología. XLV Congreso Nacional de Farmacia Hospitalaria. 2000;3:165-70.

13. Estadísticas de cáncer de los Estados Unidos, 2004. Rev Panam Salud Publica. [online]. 2004, 15, (3) p. 202-3 [accessed May 23, 2006]. Available from: http://www.scielosp.org/scielo.php?script=sci_arttext&pid=S1020-49892004000300012&lng=en&nrm=iso.
14. López-Abente G, Pollan M, Aragonés N, Pérez Gómez B, Hernández Barrera V, Lope V, et al. Situación del cáncer en España: incidencia. Anales Sistema Sanitario Navarra [online]. 2004, 27 (2) p. 165-173 [accessed May 23, 2006]. Available from: http://wwwscielo.isciii.es/scielo.php?script=sci_arttext&pid=S1137-66272004000300001&lng=es&nrm=iso.
15. Otero López MJ, Codina Jane C, Tames Alonso MJ, Pérez Encinas M. Errores de medicación, estandarización de la terminología y clasificación. Farm Hosp. 2003;27:137-49.
16. Committee on Quality of Health Care in America, Institute of Medicine. To err is human: building a safer health care system. Washington: National Academy Press; 2000.
17. Protti D, Catz M. The HER and patien safety: a paradigm shift for healthcare decision-makers. Electronic Healthcare. 2002;1:32-41.
18. Bates DW, Spell N, Cullen DJ, Burdick E, Laird N, Petersen LA, et al. The costs of adverse drug events in hospitalized patients. Adverse Drug Events Prevention Study Group. JAMA. 1997;277:307-11.
19. Sistemas de registro y notificación de incidentes y eventos adversos. Madrid: Ministerio de Sanidad y Consumo; 2005.
20. Michelagnoli MP, Bailey CC, Wilson I. Potencial slavage therapy for inadvertent intrathecal administration of vincristine. Br J Haematol. 1997;99:364-7.
21. Stein J, Davidovitz M, Yaniv I, Ben-Ari J, Gamzu Z, Hoffer E, et al. Accidental busulfan overdose: enhanced drug clearance with hemodialysis in a child with Wiskott-Aldrich syndrome. Bone Marrow Transplant. 2001:21:551-3.
22. Tejal K, Gandhi MD, Sylvia B, Bartel R, Lawrence N, Shulman MD, et al. Medication safety in the ambulatory chemotherapy setting. Cancer. 2005;104:2477-86.
23. Goyache Goñi MP, Vicario Zubizarreta MJ, García Rodríguez MP, Cortijo Cascajares S, Esteban Gómez MJ, Herreros de Tejada A. Errores de prescripción en citostáticos: análisis de sus causas y propuestas para prevenirlos. Farm Hosp. 2004;28:361-70.
24. Diaz-Carrasco MS, Pareja A, Yachachi A, Cortes A, Espuny A. Errores de prescripción en quimioterapia. Farm Hosp. 2007;31:161-4.
25. Sánchez Gómez E, Fernández Lisón LC, Giménez Castellanos J, Martín Fernández N, Marín Ariza I, Ynfante Milá JI. Evaluación de errores en prescripciones antineoplásicas. Seguim Farmacoter. 2003;1:105-9.
26. Aguirrezábal Arredondo A, Álvarez Lavín M, Yurrebaso Ibarreche MJ, Vilella Ciriza ML, Elguézabal Ortúzar I, Goikolea Ugarte FJ, et al. Detección de errores en la prescripción de quimioterapia. Farm Hosp. 2003;27:219-23.