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ORIGINALES

Assessment of new drugs in a tertiary hospital using a standardized tool

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Abstract

Objective: To describe the profile of new drugs evaluated by the Pharmacy and Therapeutics committee in a tertiary hospital using a standardized tool, the Guideline for the Introduction of New Drugs in the Formulary (GINF form), as main objective.

Materials and methods: Retrospective observational study of drugs was assessed during 2008-2011. Variables related to the drug, the request, and the result of the evaluation were collected based on information contained in the GINF form and in the assessment reports.

Results: 63 of 75 assessed drugs (84%) were included in the hospital formulary. Only one drug (1%) was included without any restrictions. The rest of them were included as therapeutic equivalents (23%) or under specific recommendations (61%). Half of the drugs (6) not included had insufficient evidence of effectiveness compared with current treatments. Haematology and Medical Oncology were found to be the most active medical services in the application process. There was a high prevalence of drugs that had more than one advanced clinical trial (phase III and/or phase IV). Furthermore, 28% of assessed drugs were associated with a financial burden of more than € 10,000 per year for our hospital. High-quality information was provided by applicants to the P&T committee for drugs that were finally included. However, the relationship between the information provided to the P&T committee and its decision was not statistical significance.

Conclusion: The requests received were primarily related to drugs intended for parenteral use and most of them were antineoplastic drugs. The medical departments most heavily represented were Haematology and Oncology.

KEYWORDS
Pharmacy and Therapeutics Committee; technology assessment; decision-making; formularies

Evaluación de nuevos medicamentos en un hospital terciario mediante el empleo de una herramienta normalizada

Resumen

Objetivo: Describir las características de los nuevos fármacos evaluados por la Comisión de Farmacia y Terapéutica (CFyT) en un hospital terciario mediante el empleo de una herramienta normalizada, la Guía para la valoración de Inclusión de Nuevos Fármacos, como objetivo principal.

Material y métodos: Estudio observacional retrospectivo de aquellos fármacos evaluados en el periodo 2008-11. Fueron recogidas variables relativas al fármaco, a la solicitud y al resultado final de la evaluación mediante la información contenida en las guías GINF y en los informes finales de evaluación.

Resultados: De los 75 medicamentos evaluados, 63 (84%) fueron incluidos en la Guía Farmacoterapéutica del Hospital. Únicamente 1 (1,3%) lo fue sin ningún tipo de restricción. El resto fueron incluidos como equivalentes terapéuticos (21,3%) o bajo recomendaciones específicas (61,3%). La mitad de los fármacos no incluidos (6) presentaban insuficiente evidencia respecto a su eficacia frente a los tratamientos habituales. Hematología y Oncología Médica se encontraron entre los servicios médicos más activos en la solicitud. Se observó un alto porcentaje de fármacos que disponían de más de un ensayo clínico en fase avanzada (III y/o IV). Por otra parte, el 28% de los fármacos evaluados se relacionaron con un impacto financiero superior 10.000 € anuales. Las guías GINF proporcionadas por los solicitantes a la CFyT se caracterizaron por la alta calidad de la información contenida en ellas. Sin embargo, la relación entre la información proporcionada a la CFyT y la decisión final de la misma no fue estadísticamente significativa.

Conclusiones: Las solicitudes recibidas pertenecieron principalmente a fármacos de administración parenteral, siendo la mayor parte de ellos antineoplásicos. Los servicios médicos más intensamente representados fueron Hematología y Oncología.

PALABRAS CLAVE
Comisión de Farmacia y Terapéutica; evaluación de tecnologías sanitarias; toma de decisiones; guía farmacoterapéutica

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Introduction

The lack of a selective nationwide registration policy for new drugs according to cost-effectiveness criteria[1] and comparative efficacy between those in the same therapeutic group have spurred the development of pharmacy and therapeutics (P&T) committees[2-6] as the key authority for regulating the approval of drugs for hospital use. The P&T committee constitutes one of the powerful elements in the process of ensuring the rational use of drugs in the hospital setting through a careful selection of drugs and their appropriate use.

At the same time, there is on the national level a certain degree of variability in the function of P&T committees,[7] which can lead to discrepancies and different levels of access to new therapies between different hospitals. In addition, the function of P&T committees can be influenced by changes in the registration and commercialisation of new drugs, as well as by financial and social factors that are present in the working environment of these institutions.[7-9] This problem has been lessened by the development of standardized tools with the goal of unifying criteria for requesting the inclusion of new therapies as well as for drug assessment. With this aim, different tools have been designed, including the Guideline for the Introduction of New Drugs in the Formulary (GINF form)[10,11] and the Method for Decision-Making and Drug Assessment (the MADRE procedure).[12]

Most previous national[4] and international studies[13-17] did not address the issue of the overall new drugs assessment and selection process in the hospital setting, along with factors that are potentially linked to the decision-making process. In a previous study by our group evaluated the P&T committee activity of our hospital, and the implementation of the GINF form during the time periods 2002-03 and 2004-07.[18,19]

Our objectives with this study are: 1) to describe the profile of new drugs evaluated by the Pharmacy and Therapeutics (P&T) committee in a tertiary hospital using a standardized tool, the Guideline for the Introduction of New Drugs in the Formulary (GINF form); 2) to evaluate the association between the quality of compliance and the GINF form, the level of scientific evidence, the budgetary impact, and the subsequent final decision made by the P&T committee; 3) to realize a comparative analysis with previous studies by our group.

Material and methods

This is a retrospective observational study about the characteristics of the request and decision-making process by the P&T Committee of a large teaching hospital during 2008–2011. All requested drugs were identified, by review of the GINF forms[10,11] along with the assessment reports based on the MADRE procedure,[12] from the Spanish Society of Hospital Pharmacists. These guidelines (GINF form) were revised by two clinical pharmacists and the discrepancies were resolved by consensus.

For each of the drugs evaluated, variables linked to the drug, the petitioner, the decision-making process, and the final result were assessed. The analysis of the GINF form was carried out in order to evaluate the quality of the information provided by the petitioner.

The variables compiled for each drug were: the therapeutic group according to the ATC classification system; the route of administration (oral, parenteral, or other); and the setting of administration (inpatients, outpatients, or mixed). Furthermore, the quantity and quality of scientific evidence used to support the use of the drug at the moment of the request were assessed.

Also, the following variables regarding the estimated budgetary impact the new request would have on the hospital setting were analysed: the number of patients that could receive the treatment in question; the costs of treatment; and the annual costs, in the case of chronic treatments.

Finally, following variables regarding the petitioner were compiled: the hospital department; the professional category (physician, resident, or department head); and the relative consensus regarding the request within the department (a petition from a single individual, a consensus request from a group of colleagues, or a consensus petition from the department head and colleagues). In addition, variables related to the process and results of the P&T Committee assessment for each drug were collected: inclusion or not in the formulary, and final category based on the GINF form. These categories address drug inclusion in the formulary and the cause related to the lack of inclusion or, in the case of a drug ultimately included, its positioning in the hospital formulary (e.g., as therapeutic equivalent or with specific restrictions). The GINF categories are listed in table 1.

We analyzed the quality of the requests received based on the percentage of compliance, taking into account the global score for all 25 items included in the GINF form as well as a score for ten of them considered to be strategically important. The latter information included 1) available scientific evidence regarding the efficacy and safety of the new drug; 2) the availability of an economic analysis for predicting the impact of including the medication on the hospital formulary; and 3) the primary advantages over alternative treatment options. The quality in compliance was categorised into three different levels. The criteria used to classify the quality of the information provided to the P&T Committee via the GINF form are summarized in table 2.

A statistical analysis using the chi-square test and Fisher's exact test for a 95% confidence interval was performed with the objective of identifying possible links between the quality of compliance with the GINF form, the level of scientific evidence, the budgetary impact,

Table 1. *Standardized categories in the Guideline for the Introduction of New Drugs in the Formulary (GINF form)*

Code	Description	n (%)
A2	Not included in the formulary due to indications for a pathology that does not requiere treatment in hospital or outpatient settings.	2 (3)
B1	Not included in the formulary fue to insufficient evidence to support a better effectiveness/safety as compared to the treatment currently used in the hospital.	6 (8)
B2	Not included in the formulary since the available evidence indicates a worse effectiveness-safety profile than the treatment currently used by the hospital	2 (3)
C1	The medication demonstrated comparable levels of efficacy and safety to those of alternative drugs that are currently used for the proposed indications. In addition, it does not provide any benefits in terms of cost-effectiveness or organisation and management of health care services, and so it was not included in the formulary.	2 (3)
C2	The medication has comparable levels of efficacy and safety to those of currently existing alternatives for the proposed indications. In addition, it provides no benefits in terms of cost-effectiveness. However, the analysis suggested that inclusion of this medication into hospital protocols could provide advantages for health care management. As such, it was included in the guide as a therapeutic equivalent for the currently used options, making the medication used in anytime due to the acquisitions costs.	16 (21)
D	Included in the formulary under specific recommendations.	46 (61)
E	Included in the formulary with no specific recommendations.	1 (1)

and the subsequent final decision made by the P&T committee.

Finally, for certain variables, a comparative analysis with previous studies[18,19] was performed in order to provide an overview of the P&T committee's activity during 2002–2011.

Results

A total of 75 drugs were evaluated. Of these, 63 (84%) were included in the hospital formulary. Table 1 summarizes the results of the final P&T Committee decisions based on the GINF category adopted. Only one drug out of the 63 included did not involve accompanying restrictions. For all other accepted drugs, the inclusion in the formulary implied specific recommendations or assignment as a therapeutic equivalent.

The mean and standard deviation of the number of drugs assessed each year during 2008–2011 was 19 (5), with a significant increase in the number of requests in 2010 (27). The percentage of drugs that were not included in the formulary was independent of the number of requests received. The requests received were primarily related to drugs intended for parenteral use (60%). Most of them were antineoplastic drugs (43%) and those acting on the bloodstream (17%). The remaining requests were concerned to the following ATC system groups: cardiovascular system (8%), antiinfectives (8%), alimentary tract and metabolism (6%), musculoskeletal system (6%), nervous system (6%), respiratory system (2%), various (2%), dermatologicals (1%) and genito-urinary system and sex hormones (1%).

The greatest percentage of inclusion (100%) was observed for drugs acting on the alimentary tract and metabolism and, on the musculoskeletal system, but related to a small number of requests (four in each group).

The majority of requests came from medical departments. The most heavily represented of these were Haematology (15%), Oncology (12%), and Nephrology (7%). In most cases, the requests were filled in by physicians, with consensus agreement with the department head and with colleagues (82%) within the unit. The hospital departments with a higher rate of inclusion in the formulary were Nephrology and Rheumatology (100%) in contrast with Cardiology (25%).

Table 2 shows the available scientific evidence, the quality of the GINF form compliance, and potential budgetary effects for all of the included and excluded drugs. We observed that a high percentage of drugs (60%) had more than one phase III or phase IV supporting the requested treatment indication. We also observed that a high percentage of drugs (52%) were supported by comparator- or active-controlled clinical trials. In contrast, meta-analysis at the time of the assessment was uncommon (11% of the drugs).

We observed a non-significant statistical trend between the quality of compliance with the GINF form and the rate of inclusion.

Most of the approved drugs (79%) had more than 18 items of global compliance in the request and more than 6 strategic items. Only one excluded request had high-quality compliance.

Regarding the economic assessment, the mean annual cost of treatment for all requested drugs was € 16,343.

Table 2. *Relationship between drug-related variables and new drugs included in the hospital formulary*

	n (%)	Included in hospital formulary	Rate of inclusion (%)	P value
Scientific evidence available at time of assessment*				
No clinical trial	13 (17)	12	92	NS
1 clinical trial	17 (23)	15	88	NS
> clinical trial	45 (60)	36	80	NS
All clinical trials placebo-controlled	15 (20)	12	80	NS
≥ 1 clinical trial *vs.* active comparator	39 (52)	32	82	NS
≥ 1 meta-analysis	8 (11)	9	82	NS
Quality of GINF form compliance**				
Level A (> 23 total items/yr > 8 strategic items)	18 (34)	17	95	NS
Level B (> 18 total items/yr > 6 strategic items)	24 (45)	20	83	NS
Level C (≤ 18 total items/yr ≤ 6 strategic items)	11 (21)	9	82	NS
Mean costs by patient-year or patient overall treatment*				
< € 1,000	25 (33)	20	80	NS
€ 1,000-€ 10,000	22 (29)	18	82	NS
> € 10,000	28 (37)	25	89	NS
No. of patients likely to benefit from new drug*				
1-10	31 (41)	27	87	NS
10-100	25 (33)	20	80	NS
> 100	19 (25)	16	84	NS

NS = Not statistically significant. T-test and chi-test were performed as described in the Material and methods section.
*Data available for all of the drugs assessed during 2008-2011.
**Data available for 53 of the drugs assessed during 2008-2011.

Globally, drugs involving a greater cost per treatment and those with the potential to be prescribed to a smaller number of patients had the highest rates of inclusion.

Data regarding the quality of compliance with the GINF form (ranked from level A to level C) and its association with the characteristics of the request showed a greater level of quality on those requests provided by physicians (36% level A); on requests coming from the Internal Medicine Department (100% level A); on requests regarding cardiovascular and dermatological drugs (75% and 100% level A, respectively); and on requests coming from consensus requests within hospital departments (50% level A). Lower levels of quality were observed on requests coming from department heads (67% level B) or from the Nephrology department (100% level B or C); on requests regarding drugs that act on the nervous system (33% level C); and on individual requests (100% level B).

A comparison of our data with previous studies from 2002–2007[18,19] showed an increase (10%) in the number of drugs assessed. Furthermore, as time passed, a trend toward a higher rate of inclusion in the formulary was noted (68% vs. 84%). In contrast, more positive resolutions were linked with specific restrictions (52% vs. 73%) or with therapeutic equivalences (12% vs. 25%).

Discussion

We observed a slight increase in the number of drugs assessed by the P&T committee over the course of the overall study period[8,19]. However, the number of annual requests during 2008–2011 showed the opposite trend. These data may correspond to the registration of new authorizations maintained by the U.S. Food and Drug Administration, which indicate possible stagnation in the number of authorized drugs over the past decade.[20] However, during the study period, there was a clear increase in the percentage of drugs included in the hospital formulary.

The strict compliance demanded by the GINF form[10,11] could be the cause for this situation, which would create an environment in which only those drugs with sufficiently solid scientific support would be petitioned.

In addition, the importance of the authorization of drugs as therapeutic equivalents or under specific conditions was emphasized in 92% of cases. This could be related to the current economic context as well as to the importance given to policies for the rational use of drugs in hospital settings. These policies, linked to the emergence of «me too» drugs, promote the use of therapeutic equivalence as a tool for managing the economic burden associated with drugs used to treat the same

pathology. However, despite the significant economic impact of the therapeutic equivalence statement in hospital procedures for the procurement of new drugs, this concept is not applied across the board by P&T committees as a standardized final category.[21]

At the same time, the dynamic clinical research on antineoplastic agents during the last decade and the major economic impact of these drugs on health care systems[22,23] explain their marked presence in the assessment performed by P&T committees directed toward improving drug efficiency. Another explanatory factor could be the preponderance of the antineoplastic drugs in the registries for authorizations of new drugs, as described by Kaitin and DiMasi.[20] This result is logically correlated with the high number of assessments derived from the Oncology and Hematology departments.

We also observed a higher degree of compliance with the GINF form for drugs that were ultimately included in the hospital formulary. Several different studies have examined the profiles of petitioners based on the final conclusions adopted in pharmacoeconomic evaluations.[4,24] In our study, this relationship could be explained by the fact that GINF forms with better compliance are based on a higher quality of scientific evidence and/or on economic impact studies, providing a better profile for later inclusion in the hospital formulary. Nonetheless, the relationship between the quality of the GINF form and the final decision adopted by the P&T committee failed to show statistical significance. This could be explained not only by an insufficient sample size, but also as a confirmation of the independent activity of P&T committee evaluators, instead of the data and evidence provided by applicants.

Our results agree with those previously published by our research team,[18,19] especially in terms of the growing activity of the P&T committee in the last decade and of the implementation of standardised methodologies.[10–12] When we compare our results with those obtained by Puigventós et al. in a nationwide study conducted in 2010,[4] we observe that the number of drugs assessed per year was even greater than the mean obtained for hospitals with more than 500 beds. Our percentage of inclusion in the formulary (75%) is slightly higher than the mean value observed in this study. However, the number of drugs included by our P&T committee under specific conditions or as therapeutic equivalents was also significantly higher. This could be explained by the long-term experience using the GINF form at our hospital, which determines a greater level of familiarity with and awareness of the evaluation process carried out by the health care professionals involved.[25]

The primary limitation of our study was that it was carried out in a single hospital. This limits our ability to extrapolate our results for application outside of our institution. Similar studies should be carried out in multiple institutions in order to compare the activity of P&T committees at different hospital settings, which would help identify those factors that might be linked to the assessment and decision-making process and its economic impact.

In addition, this study focused on the importance of carrying out studies to evaluate antineoplastic drugs in order to assess the conditions of use, the impact of therapeutic equivalence policies, and the quality of GINF forms or of requests associated with these drugs.

This study has provided three important findings: First, the requests received were primarily related to drugs intended for parenteral use and most of them were antineoplastic drugs. The medical departments most heavily represented were Haematology and Oncology.

Second, we observed a non-significant statistical trend between the quality of compliance with the GINF form and the rate of inclusion. Finally, there is an increased in the number of drugs assessed over time and a trend toward a higher rate of inclusion in the formulary but with specific restrictions or with therapeutic equivalences.

Disclosure

The authors have no conflicts of interest.

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