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DRUG UTILIZATION STUDIES: A TOOL FOR DETERMINING THE EFFECTIVENESS OF DRUG USE

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1 To evaluate the quality of the consumption of medicines in Spain, its potential efficacy, and its evolution during the last years, an assessment of the 'intrinsic value' of the most sold pharmaceutical specialities (amounting to more than 50% of total pharmaceutical market) was carried out.

2 A panel of five clinical pharmacologists classified medicines, according to their intrinsic value, in four groups: (i) 'high value' (41% of analyzed medicines in 1980); (ii) 'relative value' (12% in 1980); (iii) 'doubtful value' (3%); (iv) 'no value' (23%), and (v) 'unacceptable value' (21%).

3 Drugs were also classified according to their expected potential of use; and three groups were formed: (i) 'high' (32%); (ii) 'relatively high' (14%), and (iii) 'reduced' (10%). A fourth group of 'not applicable' (44%) in this classification was formed with pharmaceuticals considered unvaluable or unacceptable in the first classification.

4 The results of this study suggest that this kind of analysis may be a useful tool to evaluate the efficacy of drugs in the community, and to identify priorities and guidelines in the selection of drugs in each country.

Keywords Drug utilization efficacy of drugs selection of drugs

Introduction

In the recent years studies on drug utilization have become a potential tool to be used in the evaluation of health systems. Drug utilization has been defined as 'the marketing, distribution, prescription and use of drugs in a society, with special emphasis on the resulting medical, social and economic consequences' (WHO Expert Committee, 1977). One of the most important activities in this field, originally introduced in Scandinavia, is the development of consumption studies, in which the drugs prescribed are converted to 'defined daily doses' (DDD) based on the recommended daily dose, to indicate the actual numbers of treatments given. This technique has caught on enormously, and has proved very useful, especially in international comparative studies. Many countries have adopted it as their reference method (Anonymous, 1982; Øydvin, 1980; Baksaas & Lunde, 1981). Recently, an international comparison of the use of various groups of drugs, expressed in DDDs, has been published (Friebel, 1982) in which wide differences were identified among various European countries. Although the DDD methodology has proved to be a useful method for the quantitative comparison of the consumption of drugs among different countries, or in one country through the time, it has a limited potential role for the evaluation of the quality of drug consumption.

The efficacy of the use of drugs in a community can be investigated at different levels. One possibility may be to study the value of the drugs used. A reasonable intrinsic evaluation of a pharmaceutical speciality is possible in the majority of cases on the grounds of the existing international bibliography on efficacy and on side effects of the active ingredients contained. Pharmacokinetic considerations and the knowledge of possible drug interactions are also helpful in this kind of analysis. In addition, the expected potential of use of a drug can also be defined in very broad terms in a particular community. Thus, for example, although chloramphenicol has been shown to be effective in the treatment of a variety of infectious diseases, its expected degree of use is limited, as other antibiotics are preferred because of benefit/risk considerations. We present here the results of an assessment of the intrinsic quality and the expected potential of use of the pharmaceutical specialities most sold in Spain in recent years.

Methods

The consumption data source has been a data collecting system for drug utilization studies, based on the sales figures of more than 20 pharmacies and the most

important wholesaler in our country. Data obtained with this system are periodically validated through comparison with other data from other sources (*Consejo General de Colegios Oficiales de Farmacéuticos*, independent sources, *Centro Nacional de Información sobre el Medicamento* -CINIME-, and IMS) (Laporte *et al.*, 1981). The 400 most sold pharmaceutical specialities (both as number of units and as economical value) in 1970, 1975 and 1980 in Spain were identified. Milks and other alimentary products, toothpastes, and diagnostic products were excluded. The registered specialities whose composition varied during the 11 year period studied were considered as different products. Table 1 shows the number of pharmaceutical specialities assessed each year and the criteria which led to these figures. Two classifications of the 948 pharmaceutical products included in the study were made.

1. *Intrinsic value*

Five groups were formed:

(1) 'High value': products with no backing from controlled clinical trials, which are justified by their immediate and obvious effect (e.g. insulin for acute juvenile diabetes, vitamin B_{12} for pernicious anaemia, penicillin for certain infections), and products for which controlled clinical trials exist, supporting their clinical efficacy; the estimation term 'high' did not depend on the therapeutic index of each product (that is, on the ratio between therapeutic and toxic doses, or on the incidence of side effects), and was only based upon published data on controlled clinical efficacy.

(2) 'Relative value': pharmaceutical specialities that are irrational from a pharmacological and therapeutic point of view, because, together with a highly valid active principle, they contain one or more chemical entities with a rather doubtful therapeutic efficacy (vitamins, coenzymes, and so on), the addition of which is not supported by any published clinical data obtained by an adequately controlled clinical trial.

(3) 'Doubtful value': drugs for which a controversy is at present open in the international literature, about their long-term efficacy; this group included chiefly drugs used in the treatment of chronic conditions, such as oral antidiabetics and antiplatelet drugs.

(4) 'No value': those products for which no adequate controlled clinical trials exist, supporting their clinical efficacy; this group also included some products with 'high value' active ingredients formulated in an insufficient dose, even if for paediatric use.

(5) 'Unacceptable value': pharmaceutical specialities which, because of their composition, have a clearly unfavourable benefit/risk ratio under all circumstances.

2. *Expected degree of use*

Since the intrinsic value of a drug does not necessarily bear any relation to its expected degree of use (e.g. a cephalosporin would rarely be a first-choice drug in general community medicine; the majority of cancer chemotherapeutic agents are not of general use, though effective in some cases), we deemed interesting to examine also this parameter. Four groups were formed:

(1) 'High potential of use': drugs with a recognized activity in frequent or fairly frequent prescription situations.

(2) 'Relatively high potential of use': products with a recognized activity, but for which a better alternative exists (e.g. chloramphenicol in many conditions) or which are basically of hospital use (e.g. cephalosporins and aminoglycoside antibiotics), or which must be chiefly prescribed by consultants to carefully monitored patients (e.g.

Table 1 Number of pharmaceutical specialities assessed in 1970, 1975, and 1980, and criteria which led to these figures. (The total number of products assessed was 948).

	1970	*1975*	*1980*
Top products in number of packs sold*			
Number of analyzed products	369	377	375
Sales of these products (numbers of packs)	306×10^6	440×10^6	514×10^6
Top products in economical value*			
Number of analyzed products	380	385	375
Sales of these products (economical value in Ptas)**	14.6×10^9	35.8×10^9	64.3×10^9
Total number of analyzed products	528	557	510

* The 400 top products were identified, and some products (milks, toothpastes, diagnostic products, etc.) were excluded from analysis.

** Rate of exchange. 1970: 1 US $ = 69.7 Ptas; 1975: 1 US $ = 57.4 Ptas; 1980: 1 US $ = 71.7 Ptas.

the most used cancer chemotherapeutic agents, clofibrate, and oral anticoagulants).

(3) 'Limited potential of use': drugs rarely used in very particular circumstances (e.g. vitamin C, which should have no other indication than scurvy, which is particularly rare in our latitudes; less used antineoplastic agents, and so on).

(4) 'Not considered': this group includes the specialities which were considered of 'no value' or 'unacceptable value' in the intrinsic value assessment, and the degree of use of which was not therefore worth examining.

All specialities were assessed and classified according to the above criteria by a panel of five clinical pharmacologists who were blind about the sales volume of each product, at the Division of Clinical Pharmacology of the Universitat Autònoma de Barcelona. Decisions were taken by consensus.

Results

Table 2 shows the distribution of the pharmaceutical specialities examined for each year, according to their intrinsic value. A slight increase of the proportion of 'high value' specialities consumed during the 11 year period of the study, and a decrease of the proportion of 'unacceptable value' products can be seen.

Table 3 shows the distribution of the assessed products according to their expected degree of use. Here too, a slight trend to a more rational consumption can be noticed: there is an increase (even if irregular) of the proportion of pharmaceutical specialities with a high potential of use, to the detriment of the products excluded of this second assessment because of their non-existent or unacceptable value.

The proportions of the examined products according to their inclusion in the World Health Organization list of 'Essential Drugs' (WHO Expert Committee, 1977) and in the Catalan Formulary for General Practitioners (Comissió Redactora, 1980) in 1970, 1975 and 1980 are 24.0%, 27.8% and 34.5% respectively. Again, a moderate trend to a consumption of more rational drugs can be identified.

Table 2 Most sold pharmaceutical specialities in 1970, 1975, and 1980 in Spain: intrinsic value of the assessed sample.

Intrinsic value	*1970* (n = *528*)	*1975* (n = *557*)	*1980* (n = *510*)
'High value'	31.6	35.9	41.0
'Relative value'	9.7	10.9	12.2
'Doubtful value'	2.1	2.5	2.9
'No value'	19.3	18.1	22.5
'Unacceptable value'	37.3	32.9	21.4

Table 3 Most sold pharmaceutical specialities in 1970, 1975, and 1980 in Spain: expected potential of use of the assessed sample.

Expected potential of/for use	*1970* (n = *528*)	*1975* (n = *557*)	*1980* (n = *510*)
'High'	23.1	24.6	32.2
'Relatively high'	9.3	14.5	13.5
'Reduced'	10.8	9.7	10.2
'Not considered'*	56.8	51.2	44.1

* Because judged without intrinsic value or unacceptable.

Discussion

Studies of drug utilization have revealed wide geographical differences in the use of some groups of drugs. The methodology used in these studies has mainly consisted in the comparison of consumption using defined daily doses of the drugs consumed. This methodology has mainly been used in the Nordic Countries (Baksaas, 1978; Bergman, 1978; Stika & Vinar, 1980), in Northern Ireland (Baksaas, 1978, Bergman, 1978), and more recently in Spain (Laporte *et al.*, 1981) and in other countries (Friebel, 1982). The consumption of antidiabetics (Bergman, 1978), hypotensives (Baksaas, 1978), and psychotropic drugs (Stika & Vinar, 1980) has been particularly studied, and in these fields of drug therapy, as well as in others, the essential question arises—what is an optimal level of therapy? (Lunde, 1978). The DDD methodology has proved to be most useful in countries with a limited supply of drugs, and particularly in countries in which a small proportion of fixed-dose combinations are marketed. While the majority of Western European countries have a market of 10,000–30,000 trade names (Dukes, 1979), with a 35–50% of fixed-dose combinations, the Nordic Countries have a pharmaceutical supply of 1000–3000 trade names, with a lower proportion of fixed-dose combinations (Lunde, 1982). Therefore, it seems logical to speculate that a less stringent regulation for licensing drugs, as that existing in Spain, Italy, France, and Western Germany, may be associated with a pattern of drug consumption which is substantially less rational than that existing in countries with a more limited supply of drugs.

The assessment of the intrinsic value and the theoretical potential of use of the most sold pharmaceutical specialities seems to be the most adequate way to test the above suggested hypothesis. A similar analysis, in which an analogous classification was used, had been carried out in 1973 (Erill, 1974). This study focused on the supply of drugs, and not on the most consumed drugs. The value was found to be 'high' for 30.2% of the marketed pharmaceutical

specialities, 'relative' for 27.6%, 'limited' for 19.4%, 'null' for 9.6%, and 'unacceptable' for 13.2%. The results obtained in the present study indicate that the efficacy of the drugs most used in Spain is improving. In spite of this, the dramatic fact that still in 1980 only 41% of these drugs had any demonstrated efficacy must be pointed out. However, not only the relative efficacy of the drugs used is worthy of study, but also the way the potentially efficacious drugs are used. This would enable us to acquire an idea of the efficacy with which these drugs are used. This is much more difficult to measure. It requires studies on the way drugs are used, that is studies of self-medication, medical prescription, pharmaceutical dispensing and counseling, the final conclusion of which will depend on the patient's clinical history and present symptomatology.

Although the present study gives a description of the quality of a representative sample of the drugs consumed in Spain, it only provides a limited information about the effectiveness of the use of the efficacious drugs. If the possibility of the incorrect use of an efficacious drug is considered (which does not seem unreasonable), it would be naive to conclude that a rationalisation of the supply of drugs (by eliminating irrational, inactive and unacceptable drugs) would halve the pharmaceutical expenditure. The results here presented point out that not only the quantity of drugs that are used, but also their quality and the way they are used are problems to be dealt with in drug epidemiology. The more specific and appropriate is the use of a drug, the greater chance there is of the benefit/risk ratio turning out positive on the benefit side. It is our belief that regulatory restrictions by themselves can do little to improve the use of drugs. Only by a combination of regulatory, informative and educational actions, together with a general improvement of the quality of out-patient medical care in the National Health System, which is in the main responsible for drug prescription, can the use of drugs be more rational.

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