ITALIAN JOURNAL OF PUBLIC HEALTH

Focus on the activity of local ethic committees in Italy

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Abstract

Background: The continuing evolution of medical treatments and the loss of neutrality of medicine with respect to morality of human values have represented the major tracking elements towards settings of sharing of choices between society and medicine. Several concerns have been raised upon links between pharmaceutical corporations and researchers. Moreover, being in a learning environment, we must pay even more attention to these items because students appear to be at risk for unrecognized influence by marketing efforts. The aim of this study is to focus on the activities of a local ethics committee (LEC) and the characteristics of the protocols discussed in an Italian LEC during a three year period (2001-2003).
Methods: Three years of activity of a LEC were analysed by a questionnaire registering: main sponsorship, setting, technical characteristics of trials, outcome of the submission to the LEC, state of progress. Approved trials were followed-up until April 30th, 2005.
Results: A total of 345 protocols were discussed. 67.8% (n = 198) of approved protocols were submitted by a pharmaceutical corporation. 72.6% (n = 212) of studies approved in 2001 were still in progress in 2005. 91.3% (n = 73) of closed trials had a pharmaceutical corporation as their main sponsor. None of the submitted studies focused on prevention strategies.
Conclusions: These results show how important grants offered by pharmaceutical industries are, the efforts spent on therapy and the lack of investors in prevention.

Keywords: ethic committees, ethics, research, research supports

Introduction

The continuing evolution of medical treatments and the loss of neutrality of medicine with respect to morality of human values have represented the major tracking elements towards settings of sharing of choices between society and medicine, citizens and doctors. Ethics committees are places of natural expression for reflection on health and health-care. Several concerns have been raised regarding links between pharmaceutical corporations and researchers[1, 2] with impact on prescriptions,[3] and results in favourable publications4 as well as suggestions in clinical practice guidelines.[5] Moreover, being in a learning and teaching environment, we must pay particular attention to these items because, as already underlined, students appear to be at risk of succumbing to unrecognized influence of marketing efforts. [6] The aim of this study is to focus on the activity of a local ethics committee (LEC) and the characteristics of the protocols discussed in an Italian LEC during a three years period.

Methods

Setting

The Local Ethics Committee (LEC) of the Associated Hospital of Ancona and the local Public Health Authority (in an area of about 500,000 inhabitants), and its composition are reported.

Biomedical research protocols discussed by the LEC between January 1st, 2001 and December 31th, 2003 were included, approved trials were followed-up until April 30th, 2005.

Data collection

Data collection was completed by a questionnaire that recorded: year of evaluation, title of the trial, general and specific objective of the trial, type, purpose, phase (if experimental study), mono/multi-centric, national/international, promoter (pharmaceutical corporation, Local Public Health Authority, University, Governmental Authority, Others), anatomic main group (AMG) and therapeutic subgroup (TSG), setting, principal researcher. The questionnaires were completed

using the committee's archive of the first results of the examination, and eventual amendments. Complete anonymity of the trials has been assured by assigning an identification number to each study.

Definitions

The definitions used in this study are drawn from the Italian and European reference legislation. For anatomic main group (AMG) and therapeutic subgroup (TSG) codes, the anatomical therapeutic chemical (ATC) classification system was used.[7]

Activity assessment

The activity of the committee has been studied by analysing: the total number of evaluated studies, the number of closed studies (started at the beginning of the considered period and finished during the same period), the number of open studies (still in progress at the end of the considered period), the number of non started studies (studies which have received a negative judgement in first or second examination, or those suspended for revisions); the result of first submission (positive, negative, positive with reserve, suspended for revisions).

Statistics

Frequency distributions were calculated with MS Excel software. Differences between proportions were evaluated by the Chi-square test. For the analysis of trends over time the Cochrane-Armitage Chi-square test for trend was used.

Results

As provided for by the Italian legislation, the multidisciplinary of the considered LEC is guaranteed by the presence of: internal components (Medical School Head, Director of the Hospital Agency, Director of the Pharmacy Unit, a Nurses Representative, five clinicians with proven research experience, a Pharmacologist, a Biostatistician, a Legal Medicine expert); and external professionals (an expert in Law, an expert in Bioethics, a representative of Volunteers or Citizens Rights Associations, a General Practitioner, Local and Hospital Agencies Legal representatives).

A total of 345 protocols were discussed by the LEC during 2001-2003, with an increasing number of studies being submitted each year ($p < 0.05$). Pharmaceutical corporations were the main sponsors (64.1% of cases, n= 221), followed by local Public Health Authorities (7.5%, n = 26), Universities(7.3%, n = 25), Governmental Authorities (1.7%, n = 6), other subjects were responsible for the remaining sponsorships (19.4%, n = 67). 83.2% (n = 287) of protocols were approved unconditionally, 1.5% (n = 5) were approved under certain conditions, 1.5% (n = 5) resulted in withdrawal of the study proposal, and 4.4% (n = 15) were suspended. Only 9.6% (n= 33) of trials were rejected (after an eventual revision), with proportions varying from 8.1% (n = 8) in 2001 to 14.3% (n = 15) in 2002 and 7.1% (n = 10) in 2003 ($p = 0.654$). Sponsors of approved trials were mainly (67.8%) pharmaceutical industries (n = 198), followed by Universities (6.2%, n = 18), local Public Health Authorities (5.8%, n = 17), and Governmental Authorities (2.1%, n = 6), other subjects were responsible for the remaining (18.1%) sponsorships (n = 53). Approved trials were multicentric in 83.5% (n = 288) of the trials examined, ranging from 74.7% (n= 74) in 2001 to 92.2% (n= 130) in 2003 ($p = 0.853$). International trials represented 31.9% (n = 93) of those that had been approved, increasing from 22.4% in 2001 to 39.3% in 2003 ($p < 0.05$). 72.6% (n = 212) of approved clinical trials was started and were still in progress at the end of the considered period; of the 80 closed studies, 91.3% (n = 73) had a pharmaceutical corporation as the main sponsor. The difference between the proportion of closed studies sponsored by pharmaceutical corporations and that of closed studies submitted by other sponsorships was statistically significant. The number of the still in progress studies increased during the years ($p < 0.05$). Experimental studies represented the major proportion (69.3%, n = 239) of submitted protocols, but this proportion decreased during the three-years of study, from the 80.8% (n = 80) in 2001 to the 58.9% (n = 83) in 2003 ($p < 0.05$). Observational studies, on the other hand, have been the 25.2% (n = 87) of the total. Interventional procedures trials and in vitro ones were respectively limited to 2.9% (n =10) and 2.6% (n = 9). Among experimental studies, 62.8% (n = 150) were of phase III, 25.5% (n = 61) were of phase II, 10.0% (n = 24) were of phase IV and 1.7% (n = 4) of phase I. Table 1 summarizes the main scientific and technical characteristics of submitted experimental trials.

As far as Main Anatomic Groups are concerned (Table 2), we observed that 35.6% (n = 85) of experimental trials have dealt with antineoplastic and immunomodulating agents under the category AMG L, particularly cytostatic drugs (L01 therapeutic subgroup, n = 66), followed by, anti-infective agents for systemic use (14.2%, n = 34),

Table 1. Distribution of main purpose of discussed studies, per year (2001-2003).

Main purpose	2001		2002		2003		Total	
	N.	%	N.	%	N.	%	N.	%
Efficacy	41	51.2	30	39.5	37	44.6	108	45.2
Activity	15	18.8	23	30.3	16	19.3	54	22.6
Efficacy/Safety/Tollerability	18	22.4	9	11.8	21	25.3	48	20.1
Safety/Tollerability	-	-	4	5.3	3	3.6	7	2.9
Dose-Effect	1	1.3	9	11.8	4	4.8	14	5.9
Pharmacogenetic	-	-	1	1.3	2	2.4	3	1.3
Pharmacoeconomics	4	5.0	-	-	-	-	4	1.7
Bioequivalency	1	1.3	-	-	-	-	1	0.4
Total	**80**	**100.0**	**76**	**100.0**	83	100.0	**239**	**100.0**

Table 2. Distribution of Anatomic Main Groups of evaluated drugs, per year (2001-2003).

AMG – Anatomic Main Group		2001		2002		2003		Total	
		N°	%	N°	%	N°	%	N°	%
A	Alimentary tract & metabolism	11	13.8	2	2.6	3	3.6	16	6.7
B	Blood & blood forming organs	5	6.3	3	3.9	13	15.7	21	8.8
C	Cardiovascular System	4	5.0	10	13.2	4	4.8	18	7.5
D	Dermatologicals	-	-	2	2.6	-	-	2	0.8
G	Genito urinary system & sex hormones	-	-	4	5.3	4	4.8	8	3.3
H	Systemic hormonal preparations	-	-	-	-	2	2.4	2	0.8
J	Antiinfectives for systemic use	13	16.3	15	19.7	6	7.2	34	14.2
L	Antineoplastic & immunomodulating agents	25	31.3	27	35.5	33	39.8	85	35.6
M	Musculo-sketal system	3	3.8	2	2.6	4	4.8	9	3.8
N	Nervous System	10	12.5	2	2.6	5	6.0	17	7.1
R	Respiratory System	4	5.0	5	6.6	5	6.0	14	5.9
S	Sensory Organs	3	3.8	-	-	2	2.4	5	2.1
V	Various	2	2.5	4	5.3	2	2.4	8	3.3
	Total	**80**	**100.0**	**76**	**100.0**	**83**	**100.0**	**239**	**100.0**

particularly antiviral agents (n = 28), blood and blood forming organs (8.8, n = 21), and cardiovascular system (7.7, n = 18). Observational study submissions increased over the three-years study from 13.8% (n = 12) in 2001 to 59.8% (n = 52) in 2003 ($p < 0.001$). Among the observational studies, 19.5% (n = 17) had mainly a diagnostic purpose, 41.4% (n = 36) were of diagnostic/therapeutic interest, while 39.1% (n = 34) were mainly therapeutic.

None of the submitted studies focused on prevention strategies.

Discussion

Multidisciplinarity of the considered LEC is guaranteed by law, and experts from different backgrounds have been included in the study group, however, in contrast with other Italian, and international LECs, we have not a representative of the Church as a permanent member.[8,9,10,11] Moreover, questions concerning ethics committee members knowledge and education have been recently raised.[12] Differences in ethics committees may not only be limited to their composition resulting from different histories, cultural environments, and health organisations. Europe has been trying to overcome differences in ethics committees by adopting the Directive 2001/20/EC; this Directive aims at achieving a degree of harmonisation in research ethics committees (RECs) across Europe, including the time taken to assess a trial proposal and the kinds of issues a committee should take into account by establishing a clear, transparent procedure. The Member States had to apply these provisions, from 1 May 2004, at the latest. However different member states-have chosen to implement the directive in various ways; this has resulted in very different ways of structuring RECs, similar themes are present in all four cases, such as centralisation of control over RECs within member states, harmonisation of REC procedures across the EU and the increased role of political decision making with regards to such committees.[12] Despite that, similar problems continued to harm clinical research pathways in Europe and given

the considerable variation registered within Europe, it would be expected that similar difficulties exist for researchers wishing to conduct international studies. [13,14]

The present analysis outlines the activity completed in the considered period, with an average of 115 trials evaluated per year. Moreover, a percentage of 84.7% (n = 292) of approved trials is very encouraging. These results show the duration of experimental studies when considering that 72.6% (n = 212) of studies approved in 2001 was still in progress in 2005. On the other hand, a decreasing proportion of experimental studies, which represent the majority of approved trials registered in Italy overall, is quite worrying and might be compensated for by an increase in observational studies, which is in contrast to what is reported from other Italian LEC. [15,16] For the most part, experimental studies have been phase III (62.8%) and II (25.5%) trials, confirming an Italian national trend. Moreover, we have determined that more than one third of the experimental studies dealt with Oncological topics under the category AMG L, in particular cytostatic drugs (L01 subgroup), reflecting the important financial support provided to this medical specialty and the attention paid to it. We would like to express a particular appreciation for the 32.2% (n = 94) of trials promoted by non commercial boards: such as public hospitals, universities, research authorities, despite the poor governmental funding for research. In our local area, 64.1% (n = 221) of protocols were submitted by a pharmaceutical corporation, which is lower than that 75.4% registered for the same period in Italy (but considering only experimental studies).[15] We must underline the number of grants offered by pharmaceutical industries, which are responsible for the increase in submitted trials in the considered period. This massive sponsorship, however, is suspected to affect clinical practice, and these fears have been discussed by other Authors.[17,18] Moreover, the analysed data point out the long duration of experimental studies, even more when the submitting part is not a pharmaceutical corporation, which could represent another issue for reflection. Are clinical trials promoted by non pharmaceutical companies of different quality or do they organised differently, or is it a matter of enough contributions? Moreover, these numbers have given us the possibility to show the enormous efforts spent in therapy, and to recall the effects that this attention could have on medical students; but what about prevention? Prevention is not the same thing as cure, and it not necessarily uses drugs, but necessarily needs funding.

In Henan Province (China) malaria was reduced by 99% between 1965 and 1990 as a result of education, insecticide spraying of houses, the use of mosquito nets, early diagnosis and traditional medicine based on artemisinin, and is still decreasing in 2004.[19-21] Empowering, enabling people to increase control over the determinants of health and therefore to improve their health can be as just as important.22 Besides the importance and cost-effectiveness of prevention, none of the submitted studies focused on prevention strategies. The question is of whether and to what extent efforts should be made to prevent diseases rather than to accept the consequences of treating them. Should medical students be aware of the impact of prevention and health promotion? Should teaching hospitals, as well as other hospitals, be more actively involved in health promotion?

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