Comparison of Research Ethics Committees of Buenos Aires and its Suburbs

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María Fernanda Sabio [1]

Abstract

The Research Ethics Committees (CEPs) are core pillars for the protection of human beings as subjects of clinical research. The objective of this work was to be aware of the difficulties of CABA's CEP (Ciudad Autónoma de Buenos Aires) and its suburbs, as well as to compare its operations. A semi-structured interview was conducted with 38 committees. Results were expressed in percentages for categorical and median variables, and in interquartile range of 25-75 (RIC 25-75) for continuous ones were used. We used Chi-square test or Fisher test in the comparison of categorical data, and for the quantitative ones non-parametric tests were used. No significant statistical differences were found between CEP of CABA and its suburbs, except for its conformation and operation age. Problems related to the lack of time, resources and recognition of the Committee's tasks by researchers and institutions were found.

Key words: Bioethics. Institutional review boards. Research ethics.

Resumo

Comparação dos comitês de ética em pesquisa de Buenos Aires e Conurbano Bonaerense

Os comitês de ética em pesquisa (CEP) são fundamentais para a proteção dos sujeitos de pesquisa. Este trabalho tem como objetivo conhecer e comparar o funcionamento e dificuldades dos CEP da Ciudad Autónoma de Buenos Aires (CABA) e do Conurbano Bonaerense. Neste estudo, se realizou uma enquete semi-estruturada a 38 comitês. Os resultados foram expressos em porcentagens para as variáveis categóricas e mediana e intervalo interquartil 25-75 (RIC 25-75) para as contínuas. Para a compreensão dos dados categóricos se utilizou o teste de qui quadrado ou do Fisher e para a comparação dos dados quantitativos, provas não paramétricas. Quase não foram encontradas diferenças entre os comitês da CABA e o Conurbano Bonaerense, exceto na sua conformação e quantidade de anos de funcionamento. Foram encontradas dificuldades por falta de tempo, recursos e reconhecimento das tarefas do comitê pelos pesquisadores e as instituições.

Palavras-chave: Bioética. Comitês de ética em pesquisa. Ética em pesquisa.

Resumen

Comparación de los comités de ética en la investigación de Buenos Aires y Conurbano Bonaerense

Los comités de ética en investigación (CEP) son fundamentales para la protección de los sujetos de investigación. Este trabajo tiene como objetivo conocer y comparar el funcionamiento y dificultades de los CEP que funcionan en instituciones de la Ciudad Autónoma de Buenos Aires (CABA) y el Conurbano Bonaerense. En este estudio, se realizó una encuesta semiestructurada a 38 comités. Los resultados se expresaron en porcentajes para las variables categóricas y mediana y rango intercuartílico 25-75 (RIC 25-75) para las continuas. Para la comprensión de los datos categóricos se utilizó el test de chi cuadrado o de Fisher y para la comparación de los datos cuantitativos, pruebas no paramétricas. Casi no se encontraron diferencias significativas entre los comités de CABA y del Conurbano, salvo en su conformación y cantidad de años de funcionamiento. Se encontraron dificultades por falta de tiempo, recursos y reconocimiento de las tareas del comité por parte de los investigadores y de las instituciones.

Palabras-clave: Bioética. Comités de ética institucionales. Ética en investigación.

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1. **Specialist** mariafernandasabio@gmail.com – Universidad Nacional de Quilmes, Comité de Bioética Htal. Nac. Dr. Alejandro Posadas, Buenos Aires/CF, Argentina.

Mailing Address
Pje. El chasque 6550. Buenos Aires, CABA, Argentina.

Conflicts of interest: the researcher is a member of a bioethics committee participating in the study

Research article

The research ethics committees (REC) are fundamental pillars in the protection of research subjects. The need for evaluation of the protocols by these committees first appears in the Declaration of Helsinki in 1975 [1]. Then, with the introduction of other standards - CIOMS [2] standards, International Harmonization Guides, Chapter E6 GCP [3] and new versions of the Declaration of Helsinki –the responsibilities and composition, operation of the committees, as well as its procedures started to be defined.

Under these standards, research ethics committees have an obligation to evaluate the research protocol from the methodological point of view, weighing risks and benefits to research subjects, ensuring that subjects are involved in the study on an autonomous, informed and protected way etc. However, information available in relation to creation, functioning and fulfilling of their obligations in Argentina is limited by the lack of a record. This flaw should be saved, given that knowledge about these organisms is central to improve its functioning, where necessary. For the RECs to work properly, on the one hand, it must be properly constituted (number of members and their formation); given that interdisciplinarity facilitates the diversity of perspectives and representation of the implicated [2] actors. On the other hand, they must have the resources, time, dedication and the right tools. The importance of a research that gives information about the REC is related to the role of these bodies: they are central when it comes to protect the research subjects.

In our country no previous studies were made to compare the ethics committees included in an institution (REC) of the autonomous city of Buenos Aires (CABA) and el Conurbano Bonaerense (area surrounding the autonomous city of Buenos Aires) in Argentina. Thus, this study investigates and compares the Constitution and obligations of the CABA and Conurbano Bonaerense RECs. This comparison could reveal unjustified differences. If so, the causes of these differences should be studied to avoid any type of discrimination by geographical matters.

One of the findings of this study is the similarity in the functioning of the CABA and Conurbano Bonaerense RECs. Some differences were found in the conformation and number of years of operation. What was found, what is most troubling is that several RECs claimed to have difficulties to perform their work for lack of time, resources, and recognition by part of the researchers and the institutions in which they are inserted. These difficulties must be addressed to ensure that these agencies do their jobs in the best possible conditions.

Objective

To describe and globally analyze the conformity and operation of RECs, according to their geographic location.

Materials and method

Population

Between 05/16/08 and 05/05/09 institutional of the CABA and Conurbano Bonaerense RECs stood out with at least one year of operation. The reason for choosing these RECs was the knowledge they have of their scope of work and the population that will be subject of investigation, as well as of the institution in which the study will be conducted.

Method for data collection

We used a semi-structured survey of 25 questions, the last of which was open. Contact with the RECs was carried out by telephone. When the invitation to participate was accepted, the questionnaire was sent by e-mail or delivered in person. Once the survey was answered, if the answers were unclear, we contacted again the person who had responded in order to resolve difficulties. It was also delivered to the participants an information sheet on the study, clarifying its methodology, objectives and funding and a commitment to confidentiality was signed, ensuring anonymity

Statistical analysis

Results are expressed in percentages for categorical and medium variables and rank interquartile range 25-75 (RIC-25-75) for continuous variables. The test of Chi-square or Fisher, and for comparison of quantitative data, nonparametric tests were used for the comparison of categorical data. The established level for comparisons was 0.05.

Study limitations

The results of this research cannot be generalized, since almost 50% of the RECs did not agree to participate. But given the precarious situation of the participants, it is suspected that those who rejected the invitation are in worse conditions.

Results

139 health institutions were contacted: 68 state-owned and 71 private. 70 were in the Autonomous City of Buenos Aires (CABA), of which 33 were private and 37 state-owned. In the Conurbano Bonaerense 28 private and 41 state-owned institutions were contacted, totaling 69. Through telephone contact, 70 institutions declared not having REC for evaluation of clinical trials, i.e., slightly over 50%. It is unknown how many of the institutions without REC carried out clinical trials, given that in Argentina there are the so-called independent ethics committees which are not inserted in institutions and that evaluated protocols by direct sponsors' request. The institutions without REC can take advantage of this approval to carry out investigations. The new laws of the CABA and Conurbano Bonaerense shall require protocols to be evaluated by RECs included in institutions, but at the time of this investigation, such laws had not been implemented.

Sixty-nine surveys were delivered: 2 institutions had REC but with <1 year of operation, 28 refused to participate in the work and 1 delivered the answers when the data had already been processed. Therefore, the analysis group was constituted by 38 institutions with REC. This percentage of little more than the total number of health institutions allowed confirming the difficulties for monitoring approved studies

Table 1 – Characteristics of CEPs – Legend: EAS = serious adverse advents*; CI= Informed consent*

Variables	Total RECS n=38 n (%)	CABA REC n= 25 n (%)	Suburban REC n=13 n (%)	P value
Private institutions	13 (34,2)	9 (69,2)	4 (30,7)	ns
Time of operation				
≥15 to 10 years	25 (65,8)	19 (76)	6 (46,2)	ns
9-1 years	13 (34,2)	6 (24)	7 (53,8)	ns
No. of members				
≤ 9	20 (52,6)	13 (52)	7 (53,8)	ns
≥10	18 (47,4)	12 (48)	6 (46,8)	ns
Frequency of meetings				
Monthly/biweekly	24 (63,2)	15 (60)	9 (69,2)	ns
Duration of meetings				
1-2 hrs	19 (51,4)	10 (41,7)	9 (69,2)	ns
≥ 3 hrs	18 (48,6)	14 (58,3)	4 (30,8)	ns
Works outside meetings				
1-2 hrs	8 (21,6)	3 (12,5)	5 (38,5)	ns
≥ 3 hrs	29 (78,4)	21 (87,5)	8 (61,5)	ns
Members remuneration (no)	32 (84,2)	20 (80)	12 (92,3)	ns
Operating procedures (yes)	25 (67,6)	17 (70,8)	8 (61,5)	ns
Total protocols evaluated/year	825 (100)	660 (80)	165 (20)	<0.0001
Pharmacological protocols evaluated/year	418 (50,6)	336 (81)	82 (19)	ns
Pharmacological protocols approved/year	369 (88,3)	292 (87)	77 (94)	ns
Frequency of submission of progress reports (semiannual/annual)	26 (70,3)	15 (62,5)	11 (84,6)	ns
Time for reception of EAS occurred in the center (≤ 72hrs)	15 (40,5)	8 (33,3)	7 (53,8)	ns
Amendments to CI (yes)	33 (91,7)	22 (91,7)	11 (91,7)	ns
Record of subjects included in the protocols (Yes)	13 (35,1)	8 (33,3)	5 (38,5)	ns
Assistance for taking CI	6 (16,2)	4 (16,7)	2 (15,4)	ns
Contact with subjects included in protocols (Yes)	9 (24,3)	5 (20,8)	4 (30,8)	ns

Of the 38 centers that answered to the survey (55% of the total number of centers with REC), 65.7% belonged to CABA and of the 28 centers that did not respond, 57.1% were CABA (p=ns). 34.2% of the centers that responded were private institutions and of the centers that did not respond some 42.8% (p=ns).

The global results according to the location of the centers (CABA vs Conurbano) are included in table 1. In CABA, 48%of the RECS had >15 years of operation, while no center in the suburbs had >15 years of operation. In 58.3%of the centers of CABA, the duration of the meetings was greater than ≥

3 hours compared to the suburbs (30.8%centers; P=NS).

Only in 6 centers members are remunerated. Of these, 3 (7.9%) centers remunerate only non-institutional members, and in the other 3, all members. In any of the centers, members of the Committee were exempted of their usual tasks.

A greater proportion of CABA centers devoted more hours to tasks related to the REC outside the schedule of meetings (>2 hours per week) than centers of suburbs(87.5% CABA vs 61.5% suburbs; p=ns).

Of the 825 protocols/year evaluated in the total sample, 80% were evaluated in CABA centers. Average protocols reviewed by Center in CABA was 19 (RIC 8-40) clinical trials in the suburbs of 11(RIC 4-17) (p=ns).

Since the creation of the RECs, 37.1% of the centers suspended at least one protocol for security reasons; in CABA, 39.1% vs suburbs 33.3% (p=ns).

Table 2 – Composition of CEPs

Variables	REC totals n=38 n (%)	CABA REC n= 25 n (%)	Suburban REC n=13 n (%)	Valor p'
Total average of members (RIC)	9 (7-12)	9 (7-12)	9 (8-10)	ns
Doctors average (RIC)	38 (100) 4,5 (3-6)	25 (100) 5 (4-6)	13(100) 4 (3-5)	ns
Nurses average(RIC)	24 (63,1) 1 (0-1)	16 (42,1) 1 (0-1)	8 (61,5) 1 (0-2)	ns
Psychologists average (RIC)	23 (60,5) 1 (0-1)	15 (60) 1 (0-1)	8 (61,5) 1 (0-1)	
Lawyers average(RIC)	33 (86,8) 1 (1-1)	21 (84) 1 (1-1)	12 (92,3) 1 (1-1)	ns
Social workers average (RIC)	17 (44,7) 1 (0-1)	8 (32) 0 (0-1)	9 (69,2) 1 (0-1)	ns
Methodologist average (RIC)	7 (18,4) 1 (0-1)	4 (16) 0 (0-0)	3 (23) 0 (0-1)	ns
Philosopher average(RIC)	13 (34,2) 0 (0-1)	8 (32) 0 (0-1)	5 (38,4) 0 (0-1)	ns
Representative of the community average (RIC)	26 (68,4) 1 (1-1)	18 (72) 1 (1-1)	8 (61,5) 1 (0-1)	ns
Religious average (RIC)	10 (26,3) 0 (0-1)	6 (24) 0 (0-0)	4 (30,7) 0 (0-1)	ns
Other average (RIC)	24 (63,1) 1 (1-2)	16 (64) 1 (1-3)	8 (61,5) 1,5 (1-2)	ns

Leyenda: RIC= Rango intercuartil 25-75; ns= no significativo

In all centers, the majority of the members of the Committee were doctors. (see table 2). An average of 9 members, half of them were doctors; in the RECs of CABA, the average of doctors was of 5 and in the suburbs, of 4 (p=ns). In the other 50% of the members, in most of the centers they were lawyers, representatives of the community, nurses and psychologists. The median of these members was of 1 in each center. The presence of social workers was higher in the RECs of the suburbs, than in the CABA.

Most of the RECs (n=22; 65%) expressed having difficulties tracking the protocols. The expressed difficulties are summarized in:

- Lack of recognition of the REC by researchers and/or the center authorities, as well as reluctance of researchers to respect REC's rules;
- Lack of personnel, resources and lack of organization of REC and time available of its members.

Discussion

This study illustrates through the results of time of operation, number of members, attendance to meetings and others, that the RECs of CABA are

more organized than those in the suburbs. The difference in the availability of standard operating procedures (SOPs) also shows that the RECs of CABA adhered to international and/or national standards that rule clinical research. The importance of operating procedures is unavoidable, since they control the conformation and the operation of the REC and that stipulate the procedures necessary to safeguard the security of participating subjects.

It can be noticed that there is a significant difference in the number of years of operation of the RECs: in the CABA these were created previously. It should be taken into account that National Law 24742 [4] on the establishment of ethics committees does not differentiate the RECs from clinical ethics committees, since it mandates the creation of committees with both functions. So it is unknown if the CABA RECs were initiated as clinical ethics committees and soon evolved to RECs.

The difference in the duration of meetings and the work done outside CABA and suburbs centers is explained by the amount of protocols evaluated according to the location of the centers (in CABA 660; in suburbs 165).

In terms of its conformation, the number of members who belong to the RECs is suitable. Different standards and rules vary as to the number of members making up a REC, but none stipulates one number less than 5, and none of the REC interviewed had fewer than 7 members. That is to say that no REC had fewer members than those required by law.

A flaw that could be observed is the dominance of doctors in the CABA and the suburbs RECs. The problem is that the RECs with a predominance of doctors tend to adopt the protocols easierly [5]. While there is a study that explains why this fact occurs, it is very likely that this is due to the fact that vocational training also involves a professional deformation; It is said that academic training often determines the look. This explains why the RECs 'should be multidisciplinary, as each discipline will bring its own point of view and knowledge, as they must also have a member of the community. The RECs must be understood as forums for reflection and analysis, whose purpose is to make decisions that ensure the safeguarding of research [7] subjects. To make them real forums, they must inevitably have people of diverse background and members of the community to ensure different perspectives, and those looks that should be represented on a balanced way [2]. An important point is that these RECs should not arrive at a consensus in the political sense of the term, i.e. that the negotiation should not be part of their work; the sort of consensus which should be reached must be based on rational argumentation of their members [8].

Related to this point, another flaw to be solved is the little presence of members of the community both in CABA and in the suburbs committees. This representative cannot be overlooked, since his function is to represent the position of the subjects participating in the study. All orientations on conducting of committees highlight the need and importance of this member.

Another important and underrepresented in the RECs is the methodologist of protocols. It should be recalled that the RECs cannot ignore the methodological feature of protocols, since a poorly designed study is not ethically acceptable.

A relevant difference between the RECs 'in CABA and in the suburbs is the amount of social workers: in latter they are best represented. This could be explained by the situation of poverty of people who attend the surveyed centers. Social workers are essential since the RECs should work with vulnerable people.

One of the points to take into account in this study was the difficulties of the RECs to perform their task of monitoring studies once approved. To learn about these difficulties, an open-ended question was made in which it was allowed that members could extend on the subject.

Since 2000, in the Helsinki Declaration, it is granted the right to the RECs of performing what is called monitoring of research studies. In Argentina, since 2008, the National Administration of Medicines, Food and Medical Technology (ANMAT), established by Provision 6550/08 [6,] makes mandatory this monitoring by all RECs. Although neither Helsinki nor the ANMAT defined in what the procedure consists, this might be to supervise the informed consent process, carry out a registry of patients admitted in each protocol, interviewing patients, review medical records, continuous observation of serious adverse events.

Many of the RECs claimed not to have difficulties, but the results of the study show the opposite. One of the most important data found is the difficulty of the RECs in the reception of the reports in advance of the protocols. These should be annual or semi-annual, but few RECs claimed to receive them with such regularity. This flaw makes difficult the follow-up work and could be taken as an indicator of the place that the RECs have occupied for researchers and institutions in which they are inserted.

As a result of the survey, it can be seen that few RECs receive immediate report of serious adverse

events that occurred in the center. It means that researchers are not communicating with RECs directly when difficulties arise in the research sponsored by some agency external to the institution in which it is performed (either the pharmaceutical industry, a university or some other agency). Most RECs will take knowledge of serious adverse events that occurred at the institution when the sponsor sends the report with data. On the other hand, few RECs have registration of patients included in protocols or which witness the making of informed consent and/or have contact with the subjects included in protocols. This shows that the field monitoring is not performed in almost any case. One possible explanation of this fact is that it was not defined in detail what the monitoring of protocols means, although there are recommendations that it be implemented [3]. The follow-up carried out in approved studies seems to be limited to documentation that sponsor sends to the REC (serious adverse events, amendments to the protocol etc.).

In order to carry out this follow-up, it is necessary to correct the lack of time, resources, and recognition of the functions of the RECs. On the other hand, the lack of remuneration is also a factor that influences the impossibility of performing the aforementioned monitoring.

On the other hand, the fact that 35% of the RECs have not recognized the existence of difficulties despite not performing the monitoring studies may be due to the fact that this follow up is recognized, as defined in this article, as part of the duties of the RECs. However, without this monitoring, the work of the RECs would be simply bureaucratic, since it would evaluate the conducting of a study, but would never verify if who evaluates has complied properly in the field. Monitoring is central to the work of the RECs and cannot, nor must be ignored.

This study also seems to suggest little relevance that the PRCs have for the institutions. In the open responses, one of the problems identified is the lack of collaboration of researchers. They confuse the ethical evaluation of protocols with a personal assessment. Another fact to highlight that was collaterally found in this study was the ignorance of the telephone operators of the surveyed institutions about the existence of the RECs and that most RECs had not assigned a physical place, but that they were operating in the service that belonged to the coordinator or president. Although not a direct product of the research, this data reaffirms the little importance of the REC to the institutions.

Final considerations

It is necessary that the role of the RECs be recognized by the parties involved. They cannot and must not be reduced to a merely bureaucratic place, whose sole purpose is to approve clinical research studies. Their main function is the protection of research subjects, and as a consequence also to continue the protection of the researcher and the institution in which the studies are carried out. For this reason, the evaluation that the RECs made of protocols is an important element

Data presented in this paper show that it is imperative to deepen state policies to ensure the work of these bodies. The presence of difficulties associated with the lack of recognition of the institutions in which the RECs are inserted, the lack of resources, the shortage of time available to perform the task and the lack of physical and administrative staff (secretary) is particularly worrying. The new laws of CABA [9] and of the Province of Buenos Aires [10] as the new Provisions of the ANMAT [11] are directed to solve the difficulties presented. New research will be needed to verify that these laws achieve its commitment.

References

1. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. [Internet]. 59th WMA General Assembly, Seoul, out. 2008 [acesso 17 jun. 2012]. Disponível: http://www.wma.net/en/30publications/10policies/b3/17c.pdf
2. Consejo de Organizaciones Internacionales de las Ciencias Médicas (Cioms). Organización Mundial de la Salud. Pautas éticas internacionales para la investigación y experimentación biomédica en seres humano. [Internet]. [aceso 17 jun. 2012] Disponível: http://unesdoc.unesco.org/images/0015/001512/151255s.pdf
3. International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human. ICH Harmonised Tripartite Guideline. Guideline for good clinical practice E6(R1). [Internet]. 1996 [acesso 17 ju.n 2012]. Disponível: http://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6_R1/Step4/E6_R1__Guideline.pdf

4. Argentina. Poder Legislativo Nacional. Ley 24742, de 18 diciembre de 1996. [Internet]. Comité hospitalario de ética, funciones, integración. 23 dez. 1996 [acceso 17 jun. 2012]. Disponível: http://www.ms.gba.gov.ar/sitios/ccis/files/2012/10/LEY24742ComiteHospitalarioEtica.pdf
5. Gracia D, editor. Profesión médica, investigación y justicia sanitaria. Bogotá: El Búho; 1998.
6. Argentina. Administracion Nacional de Medicamentos, Alimentos y Tecnologia Médica. Disposición ANMAT nº 6.550, de 5 de noviembre de 2008. Modifícanse las Disposiciones nº 969/07 y nº 5.330/07, relacionadas con el Régimen de Buenas Prácticas de Investigación en Estudios de Farmacología Clínica. 7 nov 2008 [acceso 17 jun. 2012]. Disponível: http://www.icba.com.ar/profesionales/investigacion/disposicionesanmat/08_6550_2008.pdf
7. Fernández de Urziano E; Lavilla Uriol P; Álvarez-Sala Walther R. Funcionamiento de un comité ético de investigación clínica hospitalario y después de la entrada en vigor del nuevo Real Decreto 223/2004 de ensayos clínicos con medicamentos. Rev Clin Esp. 2005;205(10):493-5.
8. Bertomeu MJ. Comisiones y comités de Bioética: una mirada retrospectiva. Perspect Bioéticas AM. 2001;6(11):35-42.
9. Argentina. Buenos Aires. Ley nº 3.301, de 2009. [Internet]. Ley sobre protección de derechos de sujetos en investigaciones en salud. 26 nov 2009 [acesso 17 jun. 2012]. Disponível: http://www.cedom.gov.ar/es/legislacion/normas/leyes/ley3301.html
10. Argentina. Gobierno de la Provincia de Buenos Aires. Ley no 11.044, de 6 de diciembre de 1990.[Internet]. Aspectos éticos de la investigación en seres humanos. [acesso 17 jun. 2012]. Disponível: http://www.ms.gba.gov.ar/sitios/ccis/files/2012/07/Ley11044.pdf
11. Argentina. Administracion Nacional de Medicamentos, Alimentos y Tecnologia Médica. Disposición ANMAT nº 6.677, 1 de noviembre de 2010. [Internet]. Apruébase el Régimen de Buena Práctica Clínica para Estudios de Farmacología Clínica. [acesso 17 jun. 2012]. Disponível: http://www.anmat.gov.ar/Comunicados/Dispo_6677-10.pdf

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