The daily activity of the nurse in clinical research: an experience report*

O COTIDIANO DO ENFERMEIRO EM PESQUISA CLÍNICA: UM RELATO DE EXPERIÊNCIA

LA RUTINA DEL ENFERMERO EN INVESTIGACIÓN CLÍNICA: RELATO DE EXPERIENCIA

Daniele Fernandes de Aguiar[1], Karla Gonçalves Camacho[2]

ABSTRACT

The present study is a report on the authors' experience working nurses in a randomized, blinded, phase III clinical trial, developed at Escola Nacional de Saúde Pública Sérgio Arouca / FIOCRUZ / RJ. This study describes the participation of nurses in the implementation of a clinical trial, highlighting their importance in this new field of work. The authors state the rigorous implementation of the clinical trial by the nurse, aiming to prevent errors, biases and failures; as well as the commitment to the authenticity of data collection, attention and respect to the rights and welfare of the study subjects. Nurses are not only able to perform with quality their usual patient-related tasks, but also research activities in health science, such as participating in clinical trials, monitoring, supervision and professional training.

KEY WORDS

Nursing.
Clinical trial.
Clinical protocols.
Practice guideline.

RESUMO

O presente artigo consiste no relato de experiência das autoras como enfermeiras de um ensaio clínico randomizado, cego, de fase III, realizado na Escola Nacional de Saúde Pública Sérgio Arouca / FIOCRUZ / RJ. Relata as atividades do enfermeiro na operacionalização de uma pesquisa clínica e destaca a sua importância neste novo campo de trabalho. Menciona a rigorosa implementação do protocolo clínico pelo enfermeiro, visando prevenir desvios, falhas e vieses, assim como o compromisso com a autenticidade dos registros, a atenção e o respeito aos direitos e bem-estar dos sujeitos. O enfermeiro pode exercer com qualidade atividades não somente assistenciais, como também de pesquisa, em áreas da saúde, como por exemplo os ensaios clínicos, através de monitoramento, supervisão e capacitação profissional.

DESCRITORES

Enfermagem.
Ensaio clínico.
Protocolos clínicos.
Guia de prática clínica.

RESUMEN

El presente artículo consiste en el relato de la experiencia de las autoras como enfermeras de un ensayo clínico randomizado, ciego, de fase III, realizado en la Escuela Nacional de Salud Pública Sérgio Arouca / FIOCRUZ / RJ (Brasil). Relata las actividades del enfermero en el marco del proceso operativo de una investigación clínica y destaca su importancia en este nuevo campo de trabajo. Menciona la implementación rigurosa del protocolo clínico por parte del enfermero, apuntando a prevenir desvíos, fallas y deslices, así como el compromiso con la autenticidad de los registros, la atención y el respeto a los derechos y al bienestar de los sujetos. El enfermero está calificado para ejercer otras actividades además de las típicas de carácter asistencial. Puede, por ejemplo, trabajar también en investigaciones en el área de salud, como los ensayos clínicos, a través del monitoreo, supervisión y capacitación profesional.

DESCRIPTORES

Enfermería.
Ensayo clínico.
Protocolos clínicos.
Guia de práctica clínica.

[1] Graduated from *Escola de Enfermagem Anna Nery*. Master's student in Nursing at *Escola de Enfermagem Anna Nery, Universidade Federal do Rio de Janeiro*. Nurse and Clinical Research Monitor at *Escola Nacional de Saúde Pública Sérgio Arouca, Fundação Oswaldo Cruz*. Rio de Janeiro, RJ, Brazil. danifaguiar@ensp.fiocruz.br [2] Nurse-midwife. Graduated from *Escola de Enfermagem Anna Nery, Universidade Federal do Rio de Janeiro*. Master's student in Nursing at *Universidade do Estado do Rio de Janeiro*. Operating Manager of Clinical Research at *Escola Nacional de Saúde Pública Sergio Arouca, Fundação Oswaldo Cruz*. Rio de Janeiro, RJ, Brazil. kgcamacho@ensp.fiocruz.br

Portuguese / English: www.scielo.br/reeusp

Received: 06/30/2008
Approved: 04/15/2009

INTRODUCTION

Clinical research can be defined as a systematic study that follows scientific methods applicable to human beings, called volunteers or subjects, who can be healthy or ill, according to the research phase[1].

Clinical research, clinical trial or clinical study are different terms used to designate this scientific research process involving human beings. As a results, clinical researchers (or clinical investigators) can obtain new scientific knowledge on drugs, procedures or methods to approach problems that affect human health[2].

To develop clinical research, international rules need to be followed, which are registered in *Good Clinical Practice*, a set of ethical and scientific standards and orientations[1]. This document provides a standard for clinical research design, conduction, accomplishment, monitoring, auditing, registers, analyses and reports, guaranteeing the credibility and precision of the reported data and outcomes, as well as the protection, integrity and confidentiality of study subjects' rights.

In view of our experience in phase III (using placebo) of a randomized clinical trial[a], carried out at *Escola Nacional de Saúde Pública Sérgio Arouca (ENSP) / FIOCRUZ*, located in Rio de Janeiro, and because this professional area is on the rise for nursing, we aimed to report on nursing activities in putting in practice a clinical research and highlight its importance in this new work area.

Little discussion on the theme has occurred in nursing, mainly in undergraduate programs, because this is a recent activity area for these professionals. In Brazil, the evidence-based practice movement is incipient in nursing and most available literature is foreign[3]. At the same time, though, the potential development of this area is perceived, which increases the possibility of expanding our professional practice.

When exploring diseases and administering symptoms from a physiology focus, subjects like wound treatment, pain, feeding and rest-related aspects, immunity responses and particularly the control and interpretation of vital signs can constitute the target of clinical research by nurse-researchers[4].

In Brazil, the trajectory of clinical research is recent. The first activities were developed in the 1980's[5]. The most important Brazilian regulations were issued in the 1990's and the start of the 21st century, such as Resolutions 196 / 96 and 251 / 97 by the National Health Council (CNS), among others.

National Resolution 196 / 96, published by the Ministry of Health's CNS, regulates any research involving human beings. Brazilian researchers should not only respect national laws, but also work in accordance with the National Research Ethics Commission (CONEP) and Institutional Review Boards (IRBs), besides respecting international Good Clinical Practice.

When involving drugs, the basic goals of clinical research are to verify the effects, safety and tolerance; report on adverse effects and analyze the absorption, distribution, metabolism and excretion of active principles, with a view to determining the product's effectiveness and safety. It should be reminded that, in order to clinically study a drug in human beings, it should already have been approved in pre-clinical tests, that is, safety aspects are assessed in laboratory animals before applying the drug to human beings[1,6].

Clinical research is ranked as phase I, II, III and IV, and human beings' participate as early as phase I, always considering the "randomization" process, which serves to allocate the study subjects to the treatment or control group, using probability as a factor to reduce partialities or trends[1,6].

...the goal of phase III research is to compare both treatments and determine the superiority of one of both.

The research in question, in which we authors were active, refers to phase III. In this type of research, large multicenter studies are accomplished, whose design is similar to the pilot study. Between 300 and 3,000 subjects with the disease under analysis are followed for a period ranging from two to four years, generally in comparison with other existing treatments for the same problem[2,6].

If no treatments for the study problem exist yet, the use of the new drug will be compared with the use of *nothing*, i.e. a substance (gelatin or flour) without any pharmacological effect on the organism, which is called placebo. During this phase, the researchers hope to obtain further information about drugs' safety, effectiveness and interaction. Thus, when receiving the habitual treatment, the patient will be treated with what specialists consider to be the best at that time. If the patient receives the new treatment, (s)he will receive the alternative specialists consider to offer significant advantages in comparison with the habitual treatment[2,6].

Hence, the goal of phase III research is to compare both treatments and determine the superiority of one of both. The results obtained from research in this phase offer the information needed to elaborate the product label and information leaflet. The analysis of the obtained data can lead to the registry and approval of the new drug or procedure by health authorities for commercial use[2,6], taking the research to phase IV, involving the product's pharmacovigilance.

According to international Good Clinical Practice, to adequately conduct a clinical trial, a team of well-trained professionals is needed (physicians, nurses, pharmacists,

[a] Randomized clinical trials are considered the best research design to assess the effectiveness of health interventions and, therefore, represent the *gold standard* in evidence-based medicine[3].

statisticians, nursing and informatics auxiliaries, psychologists, among others), as well as a place where this research will be accomplished.

This physical space and its organization should be sufficient to comply with all demands of the protocol, ranging from assistance to the research subjects to the safekeeping of the drugs under study and all documents involved.

In general, all of these conditions are present at so-called *research units* or *centers*, organized at universities or in private spaces. No matter where, there will always be a responsible researcher, generally a physician or dentist, who is in charge of all clinical research procedures.

In view of the above, nurses active in clinical research perform different but little defined activities while conducting a study protocol. Hence, nurses need to be prepared and trained to deal with subjects and activities related to this area. The language of protocols, regulatory entities and subjects' particularities justify the need for specialized professionals who are committed to the clarity of the obtained data and the safety of the study population[7].

This theme, although not widely mastered yet in nursing, is relevant and should be discussed as a new professional activity option in a specific activity area. For this purpose, new knowledge and constant technical-scientific improvement are fundamental, which are basic factors to permit nurses' participation in increasingly complex clinical studies in view of current technological advances[8].

The emerging need for nurses to update their technical-scientific knowledge will certainly entail positive influences for their professional activities due to the incorporation of new knowledge. If transmitted to other nursing team members, this will also contribute to better care delivery, benefiting everyone involved in care practice[8]. Thus, we hope to contribute to future scientific research about nurses' participation in clinical studies.

We also intend to describe and characteristic possible activities for clinical research nurses and to promote knowledge among students, teachers and even nursing professionals about this group of workers. This theme can be included into the theoretical contents offered in undergraduate and graduate nursing programs.

NURSES' ACTIVITIES IN CLINICAL RESEARCH: OUR EXPERIENCE

Clinical research demands the strict observation of its design. The initial step, essential for the development of clinical studies and achievement of the proposed objectives, is to select the research subjects, which closely depends on the inclusion and exclusion criteria.

This universe differs from nursing care in the hospital context, in which subjects are absorbed by the Health System. In clinical research, not all patients can be included in the research, but only those corresponding to the pre-established criteria in the protocol. And, depending on its peculiarities, the selection phase becomes very difficult and involves many exclusions.

In this process, an adequate method needs to be used to select and follow the subjects, and the implications of this selection and possible interventions and outcomes for the Clinical Research Unit need to be presented. It is highlighted that the studies' expected final result is the production of reliable data, which the entire scientific community can accept.

The professionals involved need to program and plan their activities. Initially, they should know about their daily responsibilities, possible degree of integration and interface with other research components, and get familiar with the work tools and all research conductions protocols.

In this clinical research universe, we nurses can be active as monitors, collaborators or coordinators. Until date, in Brazil, the principal investigator can only be a physician or dentist.

In the blind, phase III and multicenter randomized clinical trial we participate in at ENSP/FIOCRUZ, we served as monitors in 2007 and 2008. In this function, our main concern is the strict implementation of the clinical research, controlling and preventing diversions, errors and bias; seeking authentic records; and guaranteeing attention and respect for subjects' rights and well-being.

It is our work to monitor the correct conduction of the protocol, previously approved by the IRBs of the involved institutions, CONEP and ANVISA (National Health Surveillance Agency); clarify potential participants' doubts, so that they can consciously decide whether they want to be part of the research; and identify points in the protocol that can be adjusted so as to optimize the selection process.

To preserve the specific study and mainly its subjects, we cannot provide information about the partial results and/or outcome. Moreover, we do not intend to describe it here, but to emphasize nurses' participation in clinical research, independently of the theme under analysis.

For nurses, the starting point when putting in practice clinical research is to observe the inclusion and exclusion criteria, as they define among volunteers which subjects will be selected for the research. This process is called capturing or clinical screening.

In this step, we assess the results of pertinent laboratory tests, apply the first Free and Informed Consent Term and, with the subjects and their legal representatives' approval (in case they are under-age or suffer from some mental disorder that substantially decreases their decision-making ability), we provide for and supervise the collection of biological material for more specific tests necessary for the research.

After the collection, we condition and store the biological material into the Unit's Cold Chain (CC) at an appropri-

ate temperature, which should be connected with an energy generator. This is a constant concern for nurses, as temperature variations can lead to the loss of all existing material at the research center and, consequently, cause harm and backward movements in the research.

Most studies published about the cold chain refer to immunobiological agents/vaccines, but the same knowledge also applies to clinical research. Hence, the integrity of the CC needs to be maintained, guaranteeing the storage, conservation, distribution, transportation and handling process of the materials for use and/or already collected, with a view to maintaining their original characteristics[9]. This challenge demands complete integration among all team members, mainly nurses.

Thus, we supervise refrigerator and freezer temperatures during the entire work shift and register levels and any changes with their possible justifications on a monthly control map. This is filed in a database together with all other research data. Next, the multidisciplinary team discusses with a view to the adoption of strategies and association with probable risk or seasonal factors, so as to put in practice control measures in real time to prevent other events and guarantee normality levels.

This measure allows for quantitative result analyses through specific statistical software, comparisons with results obtained at other collaborative research units and fieldwork quality monitoring.

We are also responsible for sending biological material and subject registration documents through the transportation system, which goes from the collaborative unit to the laboratory and the data analysis unit; we certify the activities performed in the field, comparing them with the pre-established protocol; we periodically perform the descriptive analysis of the information contained in the database; and we train new professionals who want to act in clinical research when the team needs to be expanded or a team member needs to be replaced.

Support teams are available, which include: transportation of biological material collected from the participants in ideal conditions for sample preservation; transportation of biological material collection kits, documents and the drug under analysis to the units; as well as laboratory analysis teams and teams to insert registers into the information system, everything managed by nurses.

We are in constant contact with these teams through one person responsible for supervising all collaborative units, generally the coordinating nurse, so as to monitor and speed up test result releases and partial reports.

About the subjects, when volunteers finally fit into the prerequisites established by the study protocol, they become research subjects and voluntarily submit themselves to the intervention with the active principle or placebo, through their random allocation (depending on the research design), during a preset period. Next, together with their legal representatives, if necessary, they sign the second free and informed consent term.

We follow the random allocation process and monitor adherence to the study since the start of the intervention, exclusions and possible dropouts, registering all data in control worksheets. We are responsible for storing, administering, accounting for and returning the research product, besides registering clinical problems and adverse events throughout the intervention period.

Adherence to the proposed treatment is one of the main concerns in clinical research, as it remains unclear why one subject group strictly follows the recommendations of the professional who dispenses the drug under analysis (nurse monitor), while another does not value treatment and takes it sporadically, despite the guarantee that members can cease their participation at any time. It should be reminded that all participants voluntarily agree with the intervention, are informed about the research and receive clarifications about their doubts before, during and after any procedure.

What the subjects inform during treatment is not always true, but we respect their participation without manipulating information or asking confirmation questions. As a strategy though, at the end of treatment, we ask participants to return the product, so as to calculate and verify whether self-reported adherence data coincide with calculations. We also record volunteers' information about the occurrence of clinical problems, adverse events and whether they are taking the medication in accordance with the medical prescription.

Based on the theoretical framework of social representations, the patient's understanding of the treatment is considered submitted to a personal elaboration process, aimed at translating medical information into a language that makes sense. This knowledge acquisition activity does not occur passively, with the subject accumulating the presented information. The person uses pre-existing knowledge and constructs an information map that will serve as a guide for conduct[10].

Thus, alliances should be established, that is, bonds between health professionals and subjects, as a form of guaranteeing the team's and, consequently, the prescribed treatment's credibility[10].

Therefore, monthly meetings are scheduled with each patient and weekly meetings with the team, in order to discuss old intervention cases and new insertions, so as to follow the entire course of the research for each subject, verifying the moments before, during and after the intervention, until the final outcome of the event under analysis. This strict follow-up aims to assess the efectiveness of the intervention. Whenever possible and necessary, we participate in discussion sessions with the entire team, including the principal investigator, to assess descriptive results, verify preliminary data produced from the database and guarantee the quality of our fieldwork.

At these moments, when specialists in the area are present, who were invited on that occasion, we use the opportunity to jointly analyze the effectiveness of the strategies the team uses to approach the study subjects and, if necessary, we adopt new procedures and work methods.

Thus, it is clear that our tasks as clinical research nurses include not only care activities, but also management and continuing education. Besides, we are involved in individual and/or group studies of scientific articles, mainly from international sources, about the project theme and prepare research sub-projects related to the main theme.

Constant training and accumulated experience improve the conduction of the research. We know that we should control our enthusiasm and self-confidence though, with a view to avoiding diversions in the conduction of research due to mere carelessness.

Our experience as clinical research nurses has demonstrated considerable value in this work of actively recruiting research subjects and monitoring their participation in the research.

FINAL CONSIDERATIONS

Nurses' daily work in clinical research differs from the habitual care model. Nevertheless, the same dedication and responsibility is needed.

This is a new and very interesting work area, as it demands continuous improvement and multidisciplinary teamwork, with good interaction among all participants (collaborators).

In practice, though, nurses assume responsibilities that have not been standardized yet, fundamental for conducting clinical research, such as selecting subjects, following them during the intervention and monitoring them until the end of the research.

Hence, further research is needed about nurses' participation in clinical trials and these professionals need to report on their daily experience, with a view to the sharing of ideas about a rich and very expressive area in the technological world we live in.

It should be clarified that no conflict of interest was involved in the elaboration of this paper.

REFERENCES

1. Lousana G. Pesquisa clínica no Brasil. Rio de Janeiro: Revinter; 2002.
2. Sociedade Brasileira de Profissionais em Pesquisa Clínica. Manual sobre pesquisa clínica voltado para o paciente [texto na Internet]. 2007 [citado 2008 fev. 23]. Disponível em: http://www.sbppc.org.br/asbppc_manual_publico_leigo.php
3. Galvão CM, Sawada NO, Mendes IAC. A busca das melhores evidências. Rev Esc Enferm USP. 2003;37(4):43-50.
4. Alves LMM, Nogueira MS, Godoy S, Cárnio EC. Pesquisa básica na enfermagem. Rev Lat Am Enferm. 2004;12(1):122-7.
5. Lousana G. Boas práticas clínicas nos Centros de Pesquisa. Rio de Janeiro: Revinter; 2005.
6. Brasil. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (ANVISA). Considerações e definições para pesquisa clínica [texto na Internet]. Brasília; 2007. [citado 2008 fev. 23]. Disponível em: http://www.anvisa.gov.br/medicamentos/pesquisa/def.htm
7. Brasil. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (ANVISA). Ensaios clínicos: princípios e prática. Brasília: Sobravime; 2006.
8. Souza P. O enfermeiro e a gerência na pesquisa clínica: um estudo sobre a sua inserção [dissertação]. Rio de Janeiro: Escola de Enfermagem Anna Nery, Universidade Federal do Rio de Janeiro; 2006.
9. Aranda CMSS, Moraes JC. Rede de frio para a conservação de vacinas em unidades públicas do município de São Paulo: conhecimento e prática. Rev Bras Epidemiol. 2006; 9(2): 172-85.
10. Bakirtzief Z. Identificando barreiras para aderência ao tratamento de hanseníase. Cad Saúde Pública. 1996;12(4):497-505.

Correspondence addressed to: Daniele Fernandes de Aguiar
Rua Edith de Jesus Moraes, 252 - Jd.Iguaçu
CEP 26281340 - Nova Iguaçu, RJ, Brazil