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Perception of the informed consent form by participants in clinical trials

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Perception of the informed consent form by participants in clinical trials

Objective. To understand the perception of the participants in controlled clinical trials (CCTs) about the informed consent and describe the meaning of their participation in the research. **Methodology.** Qualitative study using the focus group technique. The sample was composed of 19 patients who participated in clinical trials about hypertension and coronary disease in a specialized cardiologic hospital located in the city of Sao Paulo. The methodological framework used was the content analysis. **Results.** Some of the participants were aware of the real objective of these studies while others had misperceptions. The reading of the informed consent is not always done and, when it is done, the patient does not understand it. The lack of understanding about the term "placebo" was mentioned by some participants. The motivation to participate was the personal benefit. **Conclusion.** This study shows that obtaining the informed consent in CCTs is complex and that there is the need to adapt the structure and application of this document, in order to protect the participants and improve the quality of clinical trials performed in the country.

Key words: informed consent, understanding, clinical trial, bioethics.

Percepción del término de consentimiento informado por los participantes de los ensayos clínicos

Objetivo. Comprender la percepción que tienen los participantes de los ensayos clínicos controlados (ECC) sobre el consentimiento informado y describir el significado de su participación en la investigación. **Metodología.** Estudio cualitativo que utilizó la técnica de grupo focal. La muestra estuvo constituida por 19 pacientes, quienes participaron en ensayos clínicos sobre hipertensión y enfermedad coronaria en un hospital especializado en cardiología en la ciudad de São Paulo. El referencial metodológico utilizado fue el análisis de contenido. **Resultados.** Algunos participantes tenían consciencia de la real naturaleza de estas investigaciones mientras otros tenían impresiones equivocadas. La lectura

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del consentimiento informado no siempre es realizada y cuando esta se hace el paciente no entiende su contenido. La falta de comprensión de lo que era el "placebo" fue mencionada por algunos participantes. La motivación en participar se centró en el beneficio personal. **Conclusión.** Este estudio muestra que la obtención del consentimiento informado en ECC es complejo y que hay necesidad de realizar adecuaciones en la estructura y aplicación del documento, con el fin de proteger a los participantes y mejorar la calidad de las investigaciones clínicas realizadas en el país.

Palabras clave: consentimiento informado; comprensión; ensayo clínico**;** bioética.

Percepção do termo de consentimento informado pelos participantes dos ensaios clínicos

Objetivo. Compreender a percepção que têm os participantes dos ensaios clínicos controlados (ECC) sobre o consentimento informado e descrever o significado de sua participação na investigação. **Metodologia**. Estudo qualitativo que utilizou a técnica de grupo focal. A mostra esteve constituída por 19 pacientes que participaram em ensaios clínicos sobre hipertensão e doença coronária num hospital especializado em cardiologia na cidade de São Paulo. O referencial metodológico utilizado foi a análise de conteúdo. **Resultados**. Alguns participantes tinham consciência da real natureza destas investigações enquanto outros tinham impressões equivocadas. A leitura do consentimento informado não é sempre realizada e quando esta se faz o paciente não entende. A falta de entendimento do que era o "placebo" foi mencionada por alguns participantes. A motivação em participar se centrou no benefício pessoal. **Conclusão**. Este estudo mostra que a obtenção do consentimento informado em ECC é complexo e que há necessidade de realizar adequações na estrutura e aplicação do documento, com o fim de proteger aos participantes e melhorar a qualidade das investigações clínicas realizadas no país.

Palavras chave: consentimento livre e esclarecido; compreensão; ensaio clínico; bioética.

Introduction

Clinical trial is a systematic study that is applied to every form of planned experiment and depends on the participation of human volunteers called research subjects to answer specific questions, although not yet covered by the literature.[1] Since the introduction of the Nuremberg Code[2] in 1947, the first international legal document related to research ethics, the voluntary consent and respect to the autonomy of the participants has been required in order to allow participation in these studies.[3] In Brazil, the Informed Consent form (ICF) is an ethical and legal requirement provided by the National Health Council Rule 466/2012,[4] which regulates research involving human beings in the country. This document is aimed at informing the participants about the objectives and procedures of the research, such as risks, benefits and alternatives. It also ensures people's autonomy, since it gives them the right to accept or not and stop their participation at any stage. Despite all the efforts to ensure the ethical rigidity based on Rule 466/2012,[4] this subject has concerned the researchers, institutions and research ethics committees because it involves the participation of vulnerable population.

Based on this information, ethical issues are raised in this research, especially in developing countries, where the participants are often people with poor socioeconomic condition and who accept this condition due to the difficulties to access healthcare services in the country.[5] In this context, the importance of the information provided by the researchers concerning the procedures involved in the research is highlighted, as well as the understanding by the participants of

the information described in the informed consent form.[6]

Despite its relevance for the clinical practice and safety of the participants, the application process of the informed consent form raises questions, because a large number of participants are incapable of understanding the details of the information in the document provided to them[7,8] and end up agreeing, often motivated by their socioeconomic condition and by what the clinical trial represents in the search for solutions to a healthcare problem.[9]

Furthermore, studies have shown that there are several circumstances involved that can limit the understanding of the participants, due to the lack of experience in relation to the unknown situation, anxiety, cultural and emotional barriers, relationship between patient, researcher and institution, as well as little understanding of the research procedures.[10,11]

In our country, the understanding of the information by the participants of clinical trials is still little known, despite the importance of the subject. Besides this, there is a lack of standardization in the literature concerning instruments to measure the understanding of the ICT, which makes it hard to compare the results.[7,12] Thus, the research in an attempt to clarify the difficulties and limitations involved in the understanding of this document in its entirety is justified, taking into account the subjectivity of the participants of clinical trials and relevance of this topic for healthcare professionals. In order to fulfill this knowledge gap, this study sought to learn the perception of the participants of clinical trials in relation to the informed consent form and describe the significance of the participation in the research.

Methodology

Descriptive and exploratory study with qualitative approach undertaken at a public teaching hospital specialized in cardiology. The following inclusion criteria were established: age between 20 and 80, to have participated in outpatient care clinical trials for the treatment of hypertension and coronary artery disease in the period from 2002 to 2006, to have used placebo after randomization or during the wash-out period (period in which the patient receives no treatment or the minimum treatment required for their safety before the randomization in the research),[13] to have been randomized in the clinical trial they participated, and to have agreed to participate in this research.

The subjects who had no memory of their participation in the selected clinical trials and/or did not agree to participate in this research were excluded. Each clinical trial carried out in the institution where the research was undertaken has a database. From this, the clinical trials for hypertension and coronary artery disease conducted from 2002 to 2006 were selected. And from there, 80 participants who met the inclusion criteria previously established in this research were selected. Next, the patients were divided into two groups, being group I composed of 47 patients who had participated in placebo-controlled clinical trials and group II composed of 33 patients who had participated in clinical trials in which the tested treatment was compared to another medication, but that also used placebo in the wash-out period. After this stage, 12 patients in each group were randomly selected according to the research criteria with the focus group.

The focus group was chosen for being a technique used to obtain data from the discussions previously planned, where the participants express their experiences, values, beliefs and attitudes about specific issues.[14] The discussion should be conducted by a facilitator in a private place in a period of approximately two hours. The records of the discussion are taken by the observers in writing and also through magnetic tapes.[14] Eight guiding questions were developed for the discussion with the groups: i) What is your understanding of a research? ii) What did it mean to you to participate in a research? iii) Did you have any doubts during the participation? iv) Why did you accept to participate? v) What do

you understand by consent form and what is its purpose? vi) Was the information in this document understood? vii) Did you read the document? viii) What do you understand by placebo? This question was discussed only with group I participants of group I, given that this information was not part of the consent form provided to group II, despite the wash-out period.

A meeting was held with each group in the second half of 2007 and these were recorded and later transcribed. Data analysis was performed using the content analysis.[15] In this technique, after the literal transcription, the pre-analysis, which is a stage of content organization aimed at systematizing the ideas, was carried out; next, there was the exploration of the material which basically involves the execution of categorization. And, at last, as the third stage, the analysis and the interpretation of the data were performed. The project was approved by the Research Ethics Committee of the Institution under number 1223/05, complying with the requirements of Rule 196/96, of the National Health Council. The anonymity of the participants was assured. Each participant received a copy of the informed consent form and another signed copy was filed.

Results

The study had the participation of 19 adults, eight from group I, with average age of 54.2 (±8.0) and 11 from group II with average age of 54.6 (±8.4). Concerning gender, 10 were male (52.6%) and nine female (47.4%). Most participants were illiterate or had only incomplete primary level of education. In order to better understand the results, the meaningful units were grouped into three themes: perception of the research, factors of motivation and consent, with their categories and subcategories respectively. The participants (P) are identified in the text with the numbering that was given to them in the transcription of the focus group.

From the first theme Perception of the Research, the following categories emerged: research of new medication, treatment and perception of human guinea pig. Concerning the research of new medication, it can be noted through the statements of the interviewees from both groups that they were aware of the participation in the test of a new medication. And also that the research might be aimed at discovering new treatment methods. *It is a work aimed at developing new medication or maybe even test a new type of medication* (P1, group II). *Its purpose is to discover new treatment methods, association of different drugs [...]* (P2, group I).

The research was considered by some participants a treatment with therapeutic purposes that can be the continuation of the conventional or a new one, and even a form of psychological treatment: *[...] it is the continuation of the treatment we were doing before, then it was great to me, it was good* (P4, group II); *I think that the research is a different form of treatment* (P5, group II); *To me, the treatment is also psychological* (P6, group II). It can also be noted that the perception of being a guinea pig for the test of a new medication continued, despite the information and signature of the informed consent form: *[...] it is like a guinea pig, we are participating to see if the medication will be good [...]* (P7, group I); *Being a guinea pig is to give your best. [...] because we could take the medication and it might not work at all* (P4, group I).

From the analyzed statements, the theme Motivation covers the following categories: own benefit, exchange relation, safety and attention, altruism, science progress and differentiated care. The personal benefit motivated the participation in the clinical trial due to the expectation of clinical improvement: *If that is very good, you are one of the first to be cured* (P1, group I); *[...] I participated to improve my health* (P2, group II); *I tried to invest in my improvement and would try everything to get better* (P8, group I). The exchange relation resulting from the participation was linked to their own benefit, contribution to scientific progress, and the assurance to continue the treatment in the institution where the research was undertaken: *[...] Within science, you have to*

accept because it is good for us, good for them who need it because they will discover new things (P7, group I); *[...] It is an exchange because it was benefiting me and I was helping* (P2, group II); *If you participate in the research, you can continue your treatment in the institution* (P7, group II).

In the interviewees' statements, it can be noted that they were also motivated by the chance of receiving better care and safety: *I participate in anything since there is care* (P4, group I); *[...] If there was a more serious problem, we would be informed* (P2, group I).

Altruism and the chance to contribute to the progress of science were expressed in the statements: *It was a way I found to pay back people, it was not only for me* (P8, group I). *When the research finished, I thought I had helped to develop a new medication for the disease I have* (P3, group II); *Regardless of finding or not the cure, somehow I helped the medicine* (P5, group I). The differentiated care and the more careful assessment make the participation beneficial: *[...] during the research, we have that care, we could say, a VIP care... [...]* (P3, group II); *During the research, I was more assessed than I normally be in an outpatient care. I performed more tests, and if there was anything more serious, I would have been informed* (P4, group I); *The appointments happened more often and I was more checked* (P7, group I).

As for the third theme, Consent, three categories emerged from the statements: purpose, document structure and information understanding. To some participants, the term consent is an institutional and not personal guarantee, besides being an exemption of liability on the part of the hospital: *[...] if it is not good, there is even a liability form of the institution that we sign [...]* (P3, group II). The document structure was divided into the subcategories: language and content. The statements show that the consent form is still a document with several technical terms, difficult words and many pages: *The words of the form need to be in a popular language* (P4, group I); *[...] they should simplify more what is written there because not everyone can understand [...]* (P6, group I); *[...] there are many pages, and that makes it harder [...]* (P4, group I).

As for the understanding, the following subcategories were identified: lack of interest for the reading and the understanding of the information. It is evident in the statements that often the consent form is not read, due to the trust relation established with the professionals. When there is an interest for the reading, they mention questions clarified by the team: *As I am curious, I asked him some of the words I could not understand [...]* (P7, group I); *I think there must also have a trust relation, so there would be no need to be reading and explaining too much* (P4, group I). Despite the difficulty in understanding the information contained in the document, the participants of both groups were aware of the risks involved in the research, as well as the insecurity related to the unknown. *I read the word, but I didn't understand what it meant* (P7, group II); *[...] you cannot fear [...]* (P8, group i); *[...] because it can either work, benefiting our problem, or it can also go wrong* (P9, group II). Some reports also show the relative lack of understanding of the meaning of the term placebo: *[...] For me, it was a spring placed in my heart* (P3, group I); *[...] it can have 70% of this, it can have less, or it can be nothing, only flour* (P2, group I); *It is a harmless pill, it doesn't do any good or bad* (P7, group I); *I didn't know what it was, only after a while I sought information* (P6, group I).

Discussion

Clinical trials depend on the participation of human beings in the evaluation of new drugs and procedures, before they are made available for public sale. Although studies of this kind are recent in our country, their number has increased, sponsored by pharmaceutical companies, especially in the cardiology field. This has only been possible due to the approval of guidelines

and rules that regulate studies that involve human beings in the 1990's. Based on this fact, concern with the participants has emerged, since they are vulnerable people when agreeing due to their socioeconomic conditions, low level of education and difficulty in accessing the healthcare services,[5,9] as seen in this research.

The results of this study indicate that most participants showed relative lack of understanding of the informed consent form and, as a consequence, of the objective of this research. Some were not able to differentiate research and treatment. In addition, the negative perception of being a guinea pig confirms the need for awareness on the part of the participants concerning their real role as research subjects in developing countries. To understand the research, people need to be able to receive, codify, retain and process the information. Besides, it should be considered that the reading of a text is an activity that involves attention, memory, understanding and cognition.[16]

Memory is the amount of information that people are able to process, constitute and register. In this sense, in order to understand a text, the reader activates the memory of the already known information and which will contribute to the construction of the meaning of the text read.[16-17] For this process to be effective, it involves short term memories that have the purpose of storing information during few hours, and long term memories that include both the capacity to remember words after a few minutes and to recognize features after years.[17] Furthermore, the understanding is inserted into the context of the decision making process, which is essentially subjective and subject to someone's beliefs, values and feelings when they are making decisions.

Another factor to be considered is related to the adequacy of the communication of the person interacting with the subject when inviting them to participate, which should involve not only the clinical research aspects, but also consider the specific characteristics and values of the person. For people to decide about their participation, they need time to understand the information, but if the decision is rushed, the participant may be disadvantaged by not clearly understand the meaning and the objectives of the research.[18] Furthermore, the complexity of the information, the use of technical terms and excessive number of pages in the composition of the consent form are factors that make the understanding of the participants harder. A recent study analyzed the readability rate of 10 consent forms used in an oncology outpatient care unit and showed that the degree of difficult in reading the document is incompatible with the educational level of the Brazilian population.[19] Also, the age and the educational level have been pointed out as important demographic predictors in the understanding of the document.[8,12,20]

The consent forms are frequently used in clinical research and are developed in different countries in the multicenter studies, and not adapted to the local context where the study will be conducted. In a research undertaken with researchers in the field of fertility regulation, 44% stated that the form was adapted and other 44% affirmed that it was translated and adapted. In 59% of the cases, the translations/adaptations had been performed by the researcher in charge.[21] Another interesting finding in this research is related to the participants not reading the consent form. It is assumed that this occurs due to the asymmetry in the relationship between participant and researcher. In addition, it needs to be considered that the subject does not often wish to make choices and delegates the decision to participate to the researcher. This relationship has a broad meaning since it is based on personal integrity and professional capacity, and therefore reading the document becomes irrelevant. Based on this, the performance of clinical research requires moral competence on the part of the professionals involved. A study carried out in Mexico with cancer patients showed that only 57% of them read the consent form and the others did not read it because they were illiterate and considered the medical explanation sufficient.[22]

The reasons for individuals to participate in the clinical trial may be mainly related to the

expected benefit for themselves and the science. These findings are corroborated in a study with cardiac patients who participated in clinical trials for acute and chronic diseases, in which it was expressed that the decision to participate is based on the provision of better treatment or follow ups, promotion of medical research, fear of refusing, besides others who had no specific reason.[18]
When someone does not understand the objective of the research and believes that the clinical trial can offer some benefit, there is the "therapeutic misconception" concept.[23] In this context, this benefit may not be reached and may only add future knowledge and benefits and not exactly a direct benefit to the current participant. During the period when the clinical trial occurs, the appointments, as well as the tests performance, are more frequent, which leads people to feel better cared for. This rigidity denotes results in the treatment, since it allows patients to express their feelings, receive more attention, besides having their complaints more valued, which is not possible in the conventional appointments in public institutions. This may satisfactorily contribute to dealing with the healthcare problems and establishing relationships.[24]

This research has some limitations that should be taken into consideration: the implementation of the focus group after completion of the clinical trial may have influenced the answers; the impossibility to analyze the readability rate of the consent forms, although they had been analyzed in relation to their content and complexity.

Conclusion. Through the interpretation of the meanings that emerged from the statements, the relative lack of understanding by some participants about the clinical trial was evident, highlighting their feeling of being used merely for research purposes, unaware of their rights and autonomy. The motivation to participate was based on the expectation of personal benefit for participants in both groups.

The study also showed the complexity involving the process of obtaining the consent form in developing countries and points out to the need for healthcare professionals to give more consideration to the understanding of this document by the participants of clinical trials, seeking changes not only to their structure but also to their application. Recognizing these limitations and having strategies to change them in favor of the research subjects are challenges to ensure the quality of the clinical trials performed, as well as the process to obtain the consent form in developing countries. When there is this awareness by researchers, the term guinea pig will probably stop being used by the participants. It is hoped that the findings of this research contribute to saving the respect to human dignity and to the protection of participants of scientific studies involving human beings as well as to the implementation of future longitudinal studies in order to expand the sample and place of research.

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