Informed Consent as Viewed by Patients Participating in Cardiology Drug Trial

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Abstract

Background: In clinical tests, the Informed Consent is critical to preserve the ethics, but due to its high complexity level, it cannot be fully understood. This study assesses the Informed Consent as viewed by patients.

Objective: We addressed the issue of what do patients understand about the studies based on the IC.

Methods: We invited participants of outpatient clinical drug trials phase II, III and IV to answer a questionnaire with 29 questions, such as: why have you accepted to participate? Did you read the Informed Consent before signing it? By signing it, were you sure you have fully understood it? Eighty individuals (20 women and 60 men) showed up, from 106 patients. The variables of each question were considered as often as they appeared. The comparison of the averages among the groups was made by t tests of Student or Wilcoxon; and for associations, Chi-square or Likelihood Ratio, or Fisher's exact test..

Results: Ages averaged 58.7 ± 9.3 years. Concerning their reasons to taking part in the survey, 66.2% pointed out their own benefit; 42.5%, for science's sake; 25.0% claimed they were doing so at their doctor's request; 50% did not understand the Informed Consent properly; and 32.9% did not read it, but signed it. Among those who were administered placebo after randomization (n = 47), 66.7% did not understand the meaning of the informed consent. A strong correlation between failure to understand the meaning of placebo with literacy level (p = 0,02) was verified, which is an evidence that the smaller is the literacy level, the smaller is the understanding level.

Conclusion: The Informed Consent is poorly understood by patients and for some of them, trusting a doctor affected their decision in taking part in the clinical trial with drugs. Their literacy level also influenced their understanding of the term "placebo". (Arq Bras Cardiol 2010; 94(1) : 4-9)

Key words: Randomized controlled trials as topic; informed consent; comprehension; ethic.

Introduction

Trials with human beings are still critical, mainly in cardiology, as new drugs are usually for continued use. In Brazil, there was an increase in the number of sponsored trials, after the Brazilian Health Council authorized trials with human beings (CNS/MS 196/96)[1]. Then, the Informed Consent was introduced. The Informed Consent is a document that contains information on the study and the responsibilities involved. The Informed Consent is often taken for granted. Sometimes it is even viewed as a disclaimer[2]. Investigators may also be faced with a conflicting double role (doctor/researcher)[3,4], besides the power he has on the patient, taking into account the asymmetrical relationship among them[5,6].

One of the challenges posed in the 21st century is not allowing the power of technology to gain importance over the respect to people dignity, mainly in developing countries[7]. Cardiology presents an expressive number of studies in this area, which explains why we seek to assess, in these first 10, 12 years after the establishment of Ethics Committees in Brazilian hospitals, how the individuals participating in scientific trials view a study, starting with the Informed Consent, and which explanation given by those who develop the trial. We conducted this study by means of cross-sectional descriptive exploratory research, with qualitative and quantitative approach.

Methods

The study was conducted in a public hospital in the city of São Paulo, specialized in cardiology and educational and research activities. After the approval of the Ethics Committee for research in an institutional database of patients participating in clinical trials, we found phase II, III and IV of drug studies, conducted in specialized outpatient care from 2002 to 2006, with or without placebo. Then, we selected all clinical trials from 6 , which we deemed appropriate to these characteristics, which were conducted in that hospital in that period. In order to participate, the individuals should have used placebo at least in the washout period, or in comparison to the drug under trial, and they

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should have been randomized in the trial.

Data collection instrument

The data were collected from interviews and reference to patients' files. As there is no specific form to assess the interpretation of an Informed Consent, we drew on questions that could assess the understanding of the content and meaning of words. The questionnaire contained 29 items, including general information data and specific multiple-choice questions and open-ended questions. Besides the general characteristics of individuals, we assessed their literacy level considering the following levels:

1) elementary/middle education;

2) high school; or

3) higher education, considering complete or incomplete studies. As to the specific understanding matter, both in the trial itself and in the use of placebo, the individuals were submitted to an objective questionnaire which included the following questions and options:

I) Who invited you to take part in this trial? Options: 1 - researcher; 2 - another patient; 3 - nurse; 4 - secretary; 5 - others;

II) Was the inviter a contributing factor for you to take part in the trial? Options: Yes or No;

III) How were you contacted to come to the hospital to take part in the trial? Options: 1 – by telephone; 2 – in person; 3 - others;

IV) Were you told that you would take part in a trial? Options: Yes or No;

V) Why did you accept to take part in the trial? Options: 1 – for science's sake; 2 – for my own benefit; 3 – because my doctor asked me to; 4 – because my doctor told me it would be good to me; 5 – because I feared not being assisted or losing my turn; 6 – because this is a public hospital; 7 - other.

The following were yes or no questions: VI) Were you informed about how important is the trial? VII) Of the potential risks and distresses that could arise due to the trial? VIII) Of treatments other than those included in the trial? Then, the questions were specifically directed to the Informed Consent: IX) When you decided to take part in the trial, did you sign any documents? X) Have you read the document before signing it? XI) Did you discuss the Informed Consent with the researcher? XII) Upon signing the Informed Consent, were you sure you have understood what the Informed Consent explained? They also answered to the following: XIII) If you were not sure of having understood it, what did you do? Options: 1 – you signed it even though you had not understood it; 2 – you asked explanation from the researcher ; 3 - other.

Then, the following yes or no questions were asked: XIV) Were you provided with a copy of the document? XV) Did you understand what "placebo" meant?

Then, an open ended question was made: XVI) What did you understand (or not)?

Then, the following yes or no questions were asked: XVII) Did you know you could take a pill with no effect for some months? (this question applied only to those patients administered placebo as a treatment); XVIII) Was it important for you to have taken part in a trial? Why? (free answer).

Statistical analysis

The quantitative variables were analyzed in terms of averages and standard deviations. The classifying variables were presented in tables containing absolute (n) and relative (%) frequencies.

In order to check whether there was association among some issues, the potential associations of these variables were analyzed through Student's t test, Chi-square or Likelihood Ratio, or Fisher's exact test, as applicable[8]. The statistical analysis was conducted with the support of the software SPSS version 15.0 (SPSS Inc., EUA). The values $p < 0,05$ were considered statistically significant for the analysis. As for the analysis of descriptive data obtained through direct contact of researchers with patients by means of open-ended questions, we used the content analysis proposed by Bardin[9].

Focal group

In order to complement the data obtained through the qualitative and quantitative survey, especially to confirm patients' understanding of the term "placebo", we decided to build a focal group, once it is widely used technique intended to obtain data from previously planned discussions, where participants express their experiences, values, beliefs, attitudes and social representations on specific questions[10]. This technique is particularly appropriate when the interviewer has a number of open-ended and multiple-choice questions and wishes to encourage participants to explore a subject of extreme importance for them, in their own words and following their own priorities[11]. We also sought to get answers that could easily explore and clarify opinions and viewpoints by speaking their language, considering their perceptions on the subject, as compared to others' views[12].

Results

The studies in which patients participated were high blood pressure and ischemic heart disease treatments. Individuals included in the clinical trials likely to be located and those who would easily accept this survey were selected. Eighty individuals were interviewed in the second half of 2006, from 6 months to 4 years after the completion of the trial in which they participated to the interview. Out of these patients, 69 participated in studies with placebo, or in a washout phase, or as a comparison to the drug under trial during the active treatment phase—which means that the term "placebo" was written in the Informed Consent. From the individuals, 47 had effectively received placebo in the active treatment phase – the general characteristics of the patients are on Table 1. An expressive number of individuals—51 (63.8%)—did not completed elementary/middle education or were even self-declared as illiterate. Most of them (52.5%) were not engaged in any professional activity. Table 2 shows the answers concerning the patients' reason to taking part in the clinical trial. It was crystal clear in patients' perception that they feel benefitted by taking part in a study, as 66.2% stated they had taken part for their own benefit.

Table 1 – Social and demographic characteristics of individuals

Characteristics	n	%
Gender		
F	20	25,0
M	60	75,0
Literacy level		
Illiterate/incomplete elementary/middle education	51	63,8
Complete middle school/Incomplete high school	9	11,2
Complete high school and incomplete higher education	12	15,0
Complete higher education	8	10,0
Marital status		
With partner	64	80,0
Without partner	16	20,0
Professional activity		
No	42	52,5
Yes	38	47,5
Working status		
On leave	1	1,2
Retired	30	37,5
Homemaker	11	13,8
Working	38	47,5

Table 2 – Spontaneous answers about reasons to take part in the trial

Reasons	n	%
For science's sake		
No	46	57,5
Yes	34	42,5
For their own benefit		
No	27	33,8
Yes	53	66,2
Because their doctor asked them to		
No	72	90,0
Yes	8	10,0
Because their doctor told them it would be good for them		
No	68	85,0
Yes	12	15,0
For fear of not being assisted or losing their turn		
No	77	96,2
Yes	3	3,8
Because it is a public hospital		
No	72	90,0
Yes	8	10,0
Other		
No	75	93,8
Yes	5	6,2

Data related to the Informed Consent

Specifically concerning the Informed Consent (Table 3), 25.0% of individuals declare they have not received any type of information on the importance of the trial to which they were invited to take part, and almost half (42.5%) was neither informed of the risks nor the distresses involved. Worth of note is that the guarantee of confidentiality, which is critical during a trial, was not known by almost half of individuals (47.5%). On the other hand, only 67.1% have read the Informed Consent before signing it, and 52 individuals (65.0%) did not discussed it with the researcher. When asked about their understanding of the information contained in the Informed Consent, 50.0% of individuals did not understand the content or the information explained by the researcher. More importantly: even though they did not understand the information contained in the Informed Consent, 39 individuals (97.5%) signed it.

The meaning of "placebo"

When the 69 individuals were asked about what they understood from "placebo", 46 interviewees (66.7%) declared they have not learned about it. When asked about what they understood from it, 47.8% confirmed they did not know what "placebo" means and 18.8% have misleading beliefs as to its meaning. Therewith, we observe that only 20.3% of interviewees understood its meaning. We also observed that 13.0% of participants did not remembered the information they read when the interview was applied. As to the associations among the characteristics of individuals and their answers on the term "placebo", Chart 1 shows that the literacy level was not necessarily a contributing factor to the patients' understanding ($p = 0.02$).

Discussion

There are several aspects related to the individuals' perception while taking part in a clinical trial. This study confirms and brings forward key concepts to implement Informed Consent application strategies to those patients with lower literacy levels, especially the ones coming from public institutions. As to the educational level, most interviewees were illiterate or had dropped out elementary/middle school (63.8%). Souza[13] observed similar results, in data collected from 793 patients invited to take part in clinical trial protocols conducted in public and private institutions. In this study (53% males, averaged 58.2 years of age), the prevailing literacy level among the 444 individuals (96%) from public institutions was similar to our sample. Therefore, this is a sign of the high educational debt in Brazil, where 47% of Brazilians, aged between 14 and 64, did not complete grade 8 of middle school[14]. Among the ones who completed it, only 11% are considered fully literate[15]. That impacts in the clinical trial, once many patients may not be able to read and understand the Informed Consents[16]. According to Resolution 196/96[1], the informed consent must be applied to the individuals participating in the trial, which often requires reading it aloud,

Table 3 – Frequency of explanations provided by researchers on the information contained in the Informed Consent, as answered by the individuals.

Explanations given	n	%
Importance of the trial		
No	20	25.0
Yes	60	75.0
Risks and distresses		
No	34	42.5
Yes	46	57.5
Existence of treatments other than those included in the trial		
No	66	82.5
Yes	14	17.5
Guarantee of confidentiality		
No	38	47.5
Yes	42	52.5
Reimbursement of expenses		
No	2	3.3
Yes	59	96.7
Indemnification for damages or problems		
No	37	46.2
Yes	43	53.8
The individual could give up at any time		
No	19	23.8
Yes	61	76.2

explaining verbally and interacting, by means of dialogues, with the doctor delivering the Informed Consent. That applies mainly to outpatient studies, once there is sufficient time for researchers to dedicate to this application. In a study on acute myocardial infarction requiring immediate treatment, for instance, something different occurs: in this circumstance, more often than not, information are verbal and not read, at least by the patient. Because of that, and to the natural inhibition of those with lower literacy level, such individuals will hardly let the others know they do not understand what they are reading, that it, they read but fail to understand.

This study could successfully detect the problem of misleading interpretation, irrespective of which questionnaire was used. Such a distressful situation is not only restricted to our country and culture: A systematic review of 12 studies, conducted by Flory and Emanuel[17], revealed that participants with high level of literacy or reading skills presented significant superior understanding levels ($p < 0,05$). In our study, as to the reasons to participate, we observed that most of them (66.2%) did that for their own benefit, and for the science's sake (42.5%). Comparing the data of this study with those of Sakaguti[18], we found that, although the author has studied 50 individuals assisted in the units managed by the City Office of Health and the Dentistry School of the University of São Paulo, the results agree on the main reasons why the individuals accepted to take part in the clinical trials. In this study, 68% of individuals accepted to take part for their own benefit, 18% for science's sake and 2% upon their doctor's request. Another aspect stands apart: from a study with 35 patients participating in clinical trials sponsored by the pharmaceutical industry in oncology centers in Mexico, 46% of patients accepted to take part in the trial and signed the informed consent to have access to the treatment, 29% did so to release

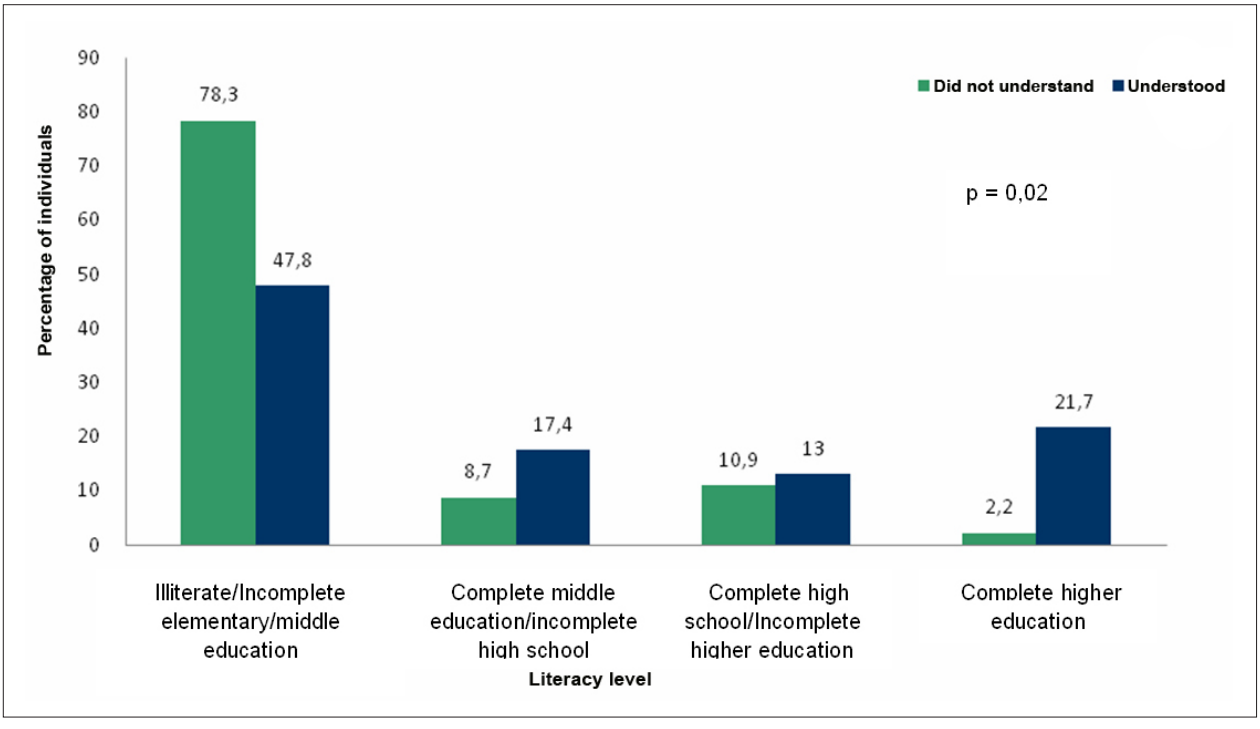

Chart 1 – Understanding of the term "placebo", in the informed consent, and association to the literacy level in 69 individuals.

the doctors and the hospital from any accountabilities none of them thought the informed consent would serve to protect them as patients[19]. Also in our study, 25% of individuals accepted the invitation to take part in the trial upon their doctor's request or recommendation. The words of a doctor may change the course of life or exercise great influence on a patient's[20] decision, not to mention the permanent possibility of conflicts of interest in trials sponsored by the pharmaceutical industry[21,22].

Data related to the Informed Consent

There is a huge variation in patients' understanding of the Informed Consent, which may also be due to the various information provided by investigators. In our study, 25% of individuals declare they have not received any type of information on the importance of the trial, and almost half (42.5%) was neither informed of the risks nor the distresses involved. The same is true as to other existing treatments – 66 individuals (82.5%) did not receive such information. These individuals may have had difficulties in recalling this information, due to the interval between the trial and the interview. Then, an effective communication between the doctor and the patient is extremely important to deliver effective information upon assigning an Informed Consent. Thus, we may infer that the way through which the doctor communicates with patient influences their judgment on the risks, benefits and barriers to take part in the study[23].

Professionals often consider the informed consent a statutory requirement, but not a means to afford autonomy to the individuals[24]. The complex information found in the Informed Consent, as well as the technical terms and the excessive number of pages, are contributing factors to prevent it from being properly understood[25,26]. Although our study has not analyzed the terms used in the performance of clinical trials, literature is unanimous in recognizing the "literary abilities" of individuals as a determining factor in the understanding process. Participants with insufficient "literary abilities" understand a minimum quantity of information contained in the Informed Consent[27].

Insights on the term "placebo"

As to the meaning of "placebo", the specific question was asked to 69 (87%) individuals—from 80—whose trials included the word "placebo" in the Informed Consent. When asked about they have understood or not from the meaning of placebo, almost half of them confirm they did not understand the meaning of this word (47.8%) or hold misleading beliefs as to its meaning (18.8%). Therewith, we observe that only 20.3% of interviewees understood its meaning. Moodley et al[28] interviewed 334 individuals from 4 to 12 months after a study conducted in South Africa to test the vaccine for influenza. Data reveal that, although 91% declare to have understood the explanation about study, 81% did not understand the meaning of the word placebo.

Final insights and constraints

The Informed Consent is still poorly understood and for individuals, trusting their doctor is critical to their decision to take part in a clinical trial with drugs. We could also verify the influence of the literacy level of individuals in understanding the term "placebo", strongly suggesting that some words and expressions presented in the Informed Consent are still very complex and fail to fulfill the need they are supposed to. A wide range of strategies may be used to improve participants' understanding, but these are not being tested yet. In the systematic review conducted by Flory and Emanuel[17], who addressed the interventions used to improve participants' understanding of the informed consent, some methods seem to be more effective than the others in this process.

We a in recent process of application of a structured Informed Consent. The assessment made in this study focused on sponsored trials, in which informed consents are usually more structured than those of independent trials. On the other hand, a huge number of pieces of information prevent the participants from properly understanding the trial. Such difficulties of understanding, however, are not only found in Brazil. Rather, they are found in many other countries. Lastly, the sample of 80 patients may be considered small to get accurate information on this subject. It is also true that the questionnaire applied, which is not a specific one, may pose constraints to the study. Nevertheless, specific questions on and Informed Consent understanding were direct and objective. Despite these constraints, this information has never been introduced before, and we conducted a quantitative analysis with this material. The confirmation of interpretation data by the individuals taking part in the survey, through other interviewing techniques, will certainly bring greater contribution to corroborate these results, which is included in a future analysis for this study.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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