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Knowledge of Informed Consent among Healthy Volunteers Participating In Bioavailability / Bioequivalence (BA/BE) Studies

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Article

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ABSTRACT

Bioavailability/Bioequivalence studies are special type of clinical trials conducted to establish that the generic drugs are equivalent to the innovator drugs and mostly healthy volunteers participate in these studies. The volunteers must be enrolled in BA/BE studies only after obtaining a written, informed consent. There are reports that the study subjects often fail to understand the important aspects of the study even after informed consent. Hence this project was executed to assess the knowledge of informed consent among healthy volunteers who participate in BA/BE studies. The study was conducted among the volunteers visiting CROs to participate in BA/BE studies. A questionnaire containing 20 questions selected from ICH-GCP was used to assess the knowledge of informed consent. Each correct answer was given a score of 5. The volunteer's knowledge of informed consent was categorized as excellent, good, average and poor based on the total score they obtained, excellent – 80 and above, good – 60 to 75, average – 40 to 55 and poor – 35 and less. In this survey, a total of 100 volunteers participated. Among them, 63 were men and 37, women. 12 volunteers scored less than 35 and they were categorized to have poor knowledge of informed consent and 30 volunteers scored average. 22 volunteers had good knowledge and 36, excellent knowledge of informed consent. It is evident that many of the volunteers have scored more than average in the assessment of their knowledge of informed consent. However to certain essential questions on informed consent, their answers were not found to be satisfactory and hence there is a need to educate the researchers and volunteers on the importance of informed consent in BA/BE studies.

INTRODUCTION

Clinical trials are research studies conducted among volunteers to find better ways to prevent, screen for, diagnose and treat a disease and are conducted in both patients and healthy volunteers. Phase II, III and IV clinical trials are carried out in patient population whereas phase I trials and Bioavailability / Bioequivalence (BA/BE) studies are mostly done in healthy volunteers [1,2]. BA/BE studies are special type of clinical trials conducted as a part of the regulatory requirement of establishing the equivalence of generic drugs to the innovator drugs [3]. India has become an important site for the international and national pharmaceutical companies for conducting BA/BE studies and lot of healthy volunteers participate in such studies.

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Healthy volunteers have to be enrolled only after obtaining the written, informed consent, after fully explaining the study procedures, benefits of participation, side effects of the drugs and risks in a manner in which they can understand. Informed consent is defined as a process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed and dated informed consent form [4].

There are few studies that have reported that study subjects often fail to understand important aspects of the research even after informed consent [5,6,7] such as the purpose of the study, its risks and benefits, that participation is voluntary, and that they have the right to discontinue participation. BA/BE studies being non-therapeutic studies with no direct benefit to the volunteers, it is seen that they participate in these studies only because they are given monetary compensation.

It is important to ensure that these volunteers participate in studies only after fully understanding the study procedures and risks and hence this project was executed to assess the knowledge of informed consent among the healthy volunteers who participated in BA/BE studies.

Objective of the Study

The objective of the study was to assess the knowledge of informed consent among the healthy volunteers participating in BA/BE studies.

METHODOLOGY

The study was conducted in a Chennai based CRO after obtaining approval from the Institutional Ethics Committee of Chettinad Hospital and Research Institute, Kelambakkam, Chennai. The criteria for inclusion of the volunteers in the study were a) they should have participated in at least one BA/BE study and b) they should be able to read and write.

The volunteers were enrolled in the survey after getting informed consent. They were not unduly influenced and they were given a chance to refuse to participate in the survey. The details regarding their gender, educational qualification, previous experience in participating BA/BE studies, duration of participation and the number of years of participation were obtained. The duration of informed consent session (longest, shortest and average) in their experience was also obtained from them.

Knowledge of informed consent was assessed through a questionnaire containing 20 questions selected from ICH-GCP that is provided in table 1. The questionnaire was made in English and Tamil. The volunteers were given adequate time to read the questions and answer.

Each correct answer was provided a score of 5. The maximum possible score was 100 and the minimum, 0 (Zero). The volunteer's knowledge in informed consent was categorized as excellent, good, average and poor based on the total score they obtained, excellent - 80 and above, good - 60 to 75, average - 40 to 55 and poor - 35 and less.

RESULTS AND ANALYSIS

In this survey, a total of 100 volunteers participated, among them, 63 were men and 37 women. They belonged to the age of 18 to 30 years. 51 volunteers had education up to graduation, 13 were diploma holders and 36 had education till 12th standard. 73 volunteers had participated in 6 or more BA/BE studies and 27 volunteers between 3 and 5 studies. 28 volunteers had been participating in BA/BE studies for less than 2 years and the remaining from 2 to 4 years. 51 of the 100 volunteers had expressed that they participated in BA/BE studies for the monetary benefit and the remaining 49 volunteers not for monetary benefit. Among the 100 volunteers, 47 did not know what a BA/BE study was.

Duration of Informed Consent Session

The results obtained from the volunteers regarding duration of the informed consent session were analyzed and the mean, mode and standard deviation were derived. The data is presented in table 2 and figure 1.

The shortest duration of informed consent ranged from 4 to 15 minutes for males. 51 male volunteers out of 63 had stated that10 minutes or less as the shortest informed consent session they attended. The longest duration ranged from 20 to 40 minutes, but only 6 had the longest duration beyond 30 minutes and the remaining 57 had 30 minutes or less. On average, for males, informed consent process lasted from 10 to 20 minutes.

For females, the shortest informed consent process lasted from 6 to 18 minutes, longest from 25 to 45 minutes and on average, it was from 15 to 20 minutes. 24 out of 33 females had 20 minutes as the average duration of informed consent process.

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Table 1: Informed Consent Assessment questionnaire for volunteers participating in BA/BE studies

	Questions	No. of Correct responses
1.	Do you know what informed consent is?	60
2.	Is Informed consent form a document, you are instructed to sign by the investigator?	30
3.	Is Informed consent form written only in English?	76
4.	Do you have to know how to read and write if you want to give consent?	70
5.	Does informed consent form give details regarding how the study is going to be conducted?	52
6.	Does informed consent form need to be approved by Ethics Committee?	54
7.	Do you think, if you are not available to sign the informed consent form, you can authorize somebody else to sign on your behalf?	53
8.	Does BA/BE study involve research?	62
9.	Will you receive the copy of the signed informed consent form while you are participating in BA/BE study?	60
10.	Will there be any personal benefit if you participate in a BA/BE study other than compensation?	72
11.	Can you withdraw your consent during the study without informing the reasons once you sign the consent form?	38
12.	Will you get free medical treatment and compensation if you suffer with study related injuries?	51
13.	If compensation is not provided to you as promised, can you make a complaint to Ethics committee?	62
14.	Do you need to personally date the informed consent form apart from signing it?	52
15.	Will there be information about the side effects of the drug in the informed consent form?	53
16.	Will you get serious adverse events when you participate in BA/BE studies?	49
17.	Is there a chance of death while you participate in a BA/BE study?	44
18.	Will your personal and medical details such as habits and lab results be shared with your family members?	31
19.	Will you be given sufficient time to study the informed consent form, think and decide on participating in a BA/BE study?	40
20.	Can you ask questions to clarify your doubts regarding the study before you give consent?	57

Table 2: Duration of informed consent session

	Male			Female			Entire 100 volunteers		
	Shortest	Longest	Average	Shortest	Longest	Average	Shortest	Longest	Average
Mean	9.14	27.81	14.52	12.09	32.00	18.64	10.16	29.25	15.94
SD	2.28	4.10	2.80	3.22	5.73	2.26	2.98	5.11	3.27
Mode	10.00	30.00	15.00	15.00	30.00	20.00	10.00	30.00	15.00

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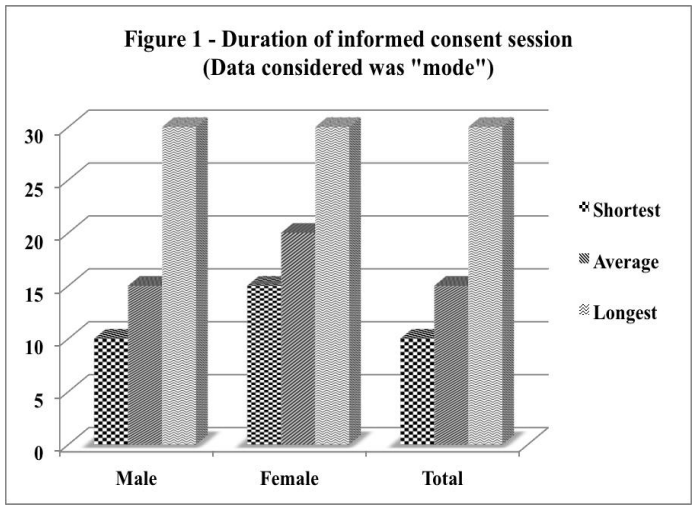
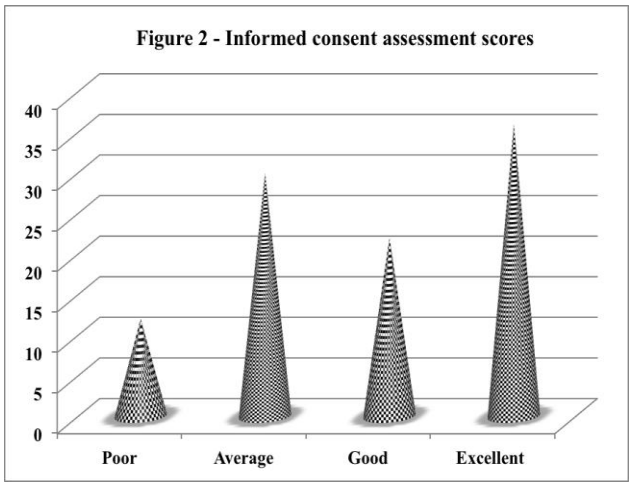


Knowledge of Informed Consent

The answers to the questions were scored and the volunteers were categorized according to the total scores they obtained. The number of correct responses for each of the 20 questions is provided in table 1 and the categorization of the volunteers is presented in table 3 and figure 2.

Table 3: Assessment scores

Scores	No. of volunteers
35 and less (Poor)	12
40-55 (Average)	30
60-75 (Good)	22
Above 76 (Excellent)	36
Total	100



None of the volunteers scored 100 or 0. 12 volunteers scored less than 35 showing poor knowledge of informed consent. 30 volunteers scored between 40 and 55 having average knowledge. 22 volunteers had good knowledge and 36, excellent knowledge.

DISCUSSION

This study was conducted to find out to what extent the participating volunteers know about informed consent and how long they were in the informed consent process before deciding to participate in a BA/BE study.

It was found that the shortest informed consent process ranged from 4 to 18 minutes for the entire 100 subjects and on average it was from 10 to 20 minutes. ICH GCP states that the subjects should be given ample time to think and take decision on whether to participate in a research or not [8]. The duration of informed consent is not specified in guidelines and literature and it is stated that enough time should be given to the subjects to decide [9]. But, it may be difficult to explain the study procedures, interact

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with volunteers, clarify their doubts and get their signatures in the consent form within 10 or 15 minutes. But when the same volunteers repeatedly participate in BA/BE studies, the informed consent process would have become a routine for them.

In this study, many of the volunteers have been assessed to have substantial knowledge of informed consent, as indicated by the scores. Only 12 volunteers have scored poor and the remaining 88 volunteers' average, good or excellent. However, there are important questions that are critical to assess the knowledge of informed consent. All the volunteers had already participated in BA/BE studies, but 40 of them have responded that there were not aware of informed consent.

During informed consent process, the consent form is distributed to the volunteers and they are given sufficient time to read and clarify their doubts. And only after their doubts are cleared, they sign the consent form expressing their willingness to participate in BA/BE study. There should not be any undue pressure from any of the study related personnel to sign [10]. But 70 of 100 volunteers have stated that they were instructed to sign the informed consent by the investigator and this shows that they sign the consent form without knowing about the study details. Informed consent should be obtained in the language understandable to the participating volunteers and informed consent form should be available in English and other local vernacular languages [1]. In this survey, 76 volunteers were aware that the consent form was available in languages other than English, whereas 24 volunteers were not aware of it.

In clinical trials in which therapeutic benefit is possible, both literate and illiterate subjects can participate and where illiterates participate, legally acceptable representative of the subject or impartial witness signs the consent form on behalf of the subject. But in case of non-therapeutic studies such as BA/BE studies, where there is no direct benefit to the participating volunteers, only literate subjects can participate [10]. Such a restriction is to prevent exploitation of the illiterate volunteers. In this survey, 70 volunteers were aware that only literates could participate in BA/BE studies. Ethics committee approved informed consent forms should only be used to obtain informed consent from subjects [8] and 54 volunteers were aware that informed consent documents should be prior approved by ethics committees and 46 were not aware of it.

After the volunteer and investigator sign the informed consent form, the study personnel shall photo copy the form and provide a copy to the volunteers [11]. All the subjects who participated in studies would have experienced this practice, but in this study, only 60 volunteers had informed that they should be issued a copy and other 40 had opined the other way. This indicates that the practice of issuing the copy of informed consent form is not routinely practiced in CROs. According to Good Clinical Practice and guidelines for BA/BE studies, a volunteer participating in a research study can withdraw his / her consent any time during the study even without revealing the reason for withdrawal [10,12]. But 62 out of 100 volunteers in this survey did not know this fact. The participating subjects should receive free medical treatment for any adverse event that can occur during the study and this should be made known to the volunteers during the informed consent session, but 49 volunteers did not know that they would get free medical treatment for adverse events. As per guidelines, the volunteers not only need to personally sign the informed consent form, but also personally date it [10]. In this survey, 48 volunteers were not aware of this. BA/BE studies are conducted for the drugs that are already available in the market and are not new drugs. Still, a subject while participating in a study may get serious adverse events. Serious adverse event is any adverse event that is life threatening or results in death, or hospitalization of the subject, disability. However, 51 and 56 subjects were not aware that they might suffer with serious adverse event or death respectively.

The informed consent form and the subject information sheet should provide the adverse events of the drug tested, risks and discomforts of participating in a BA/BE study [1,10]. After getting thorough information about all these, the volunteer signs the consent form. But only 53 volunteers knew that the side effects of the drugs are provided in the consent form. Remaining 47 did not know that these would be listed in consent form. The subject related details including the identity and personal details shall be kept confidentially and shall not be shared with others including their family members as per the guidelines [1,4,10]. But only 31 volunteers have expressed correct answer to the question on this aspect and 69 volunteers were of the opinion that the information could be shared with family members.

CONCLUSION

It is evident from this study that 88% of volunteers who participated in this survey have scored more than average in the assessment of their knowledge of informed consent. However their answers for certain important questions on the consent were not found to be satisfactory. And also the duration of informed consent process is not adequate to comply with the procedures defined in guidelines. The results suggest that there is a need to stress the importance of informed consent and educate the researchers and volunteers on the procedures of obtaining informed consent in BA/BE studies.

DECLARATION

The project was the original research work carried out by the authors in a CRO and its name is withheld for confidentiality as per the terms of agreement with the CRO. This was not funded and the authors personally met the expenses.

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