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Informed Consent for Drug Trial: A Systematic Study

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Abstract

Two hundred seventy five potential recruits to a double blind clinical trial comparing the efficacy of alprazolam with diazepam and imipramine in generalized anxiety disorder and major depression respectively were provided information about the trial in a standard manner. Except two subjects all others expressed clear choice about their participation. 62% of the subject consented for the trial, 37% refused for various reasons. Two subjects expected the treating doctor to decide for them. 15% of the subjects asked for further details before giving their choice. Comparison of the consenting and non-consenting subjects did not reveal any significant differences with respect to socio-demographic and clinical variables. The findings suggest that patients can express clear choice for drug trial provided sufficient information is given to them for making a choice.

Key words -
Informed consent,
Drug trial

Ethical issues are gaining increasing prominence in biomedical research in recent years. It is imperative on the part of the investigators to obtain valid informed consent from subjects participating in research [1]. The elements of a legally valid consent include voluntaries, provision of information, competency and understanding [2]. Several articles from the West have addressed themselves to the various aspects of informed consent. These include, the process of inform consent as practised by investigators [3], the adverse influence of informed consent in research [4], [5] establishing standards of competency [6], informed consent with respect to specific issues like ECT [7], psychotherapy [8], psychotic patients [9] and patients with senile dementia [10]. Some of the problems that have been discussed with respect to obtaining consent include problems of conveying information to subjects, impaired competency, subjects' difficulty in grasping the difference between research and treatment situations, subjects' failure to retain information for long periods of time and the tendency of investigators to offer technical explanations that are difficult for subjects to comprehend [3]. The views on informed consent are divergent [3] and some professionals have raised the issue of doing away with informed consent [11].

In sharp contrast to the West, there is limited published work on informed consent from India and other developing countries. It is impressionistically believed that people from underprivileged background cannot comprehend the components of informed consent. The authors recently carried out an opinion survey of 5000 medical professionals on issues pertainign to medical ethics through a mailed questionnaire [12]. 40% of the respondents noted patients' inability to

understand informed consent as a major constraint in the Indian setting. Considering these impressionistic opinions, a systematic study in this area was carried. An ongoing clinical trial provided an opportunity to study this important issue.

The aims of the present study were

(a) to systematically understand the responses of patients when information about a clinical trial is provided as part of the informed consent procedure.

(b) to understand the nature of variables that distinguish between consenting and non-consenting subjects.

Methods

This study was carried out as part of a multi-centre double blind trial comparing the efficacy of alprazolam, a triazolobenzodiazepine, with diazepam in generalized anxiety disorder, and with imipramine in major depressive disorder (without psychotic or melancholic features) as diagnosed by DSM-III [13]. The study being reported was carried out at the National Institute of Mental Health & Neuro Sciences, Bangalore India. Information about the nature of the clinical trial was prepared in English (appendix I) and the local and regional languages. The information included nature of the trial, duration, follow up, biochemical investigations, voluntary choice to participate, right to opt out of the trial at any stage without having to give any reason and that opting out of the trial will not bias subsequent treatment. This standard information was read out to all potential recruits to the trial as part of the screening procedure. To ensure comprehension, the information was read out slowly and subjects' immediate recall tested. If the patients had not understood the information, further information was provided. The responses given by the patients were recorded verbatim, and categorized into 8 categories. Socio-demographic and certain clinical variables were also collected. Data was collected from 275 patients.

Results

Socio-demographic and clinical characteristics of the sample are shown in Tables 1 and 2.

Table 1 - Sociodemographic characteristics of the sample (n=275)

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(Percentages in paranthesis)

Table 2 - Clinical characteristics of the sample (N=275)

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There was a relative over representation of patients who were single, literate and of urban background. With respect to clinical characteristics, there was a higher proportion of depressives. Two thirds of the patients had an illness of more than one year duration. Nearly three fourths of the patients had received earlier treatment for their complaints.

Table 3 shows the sexwise distribution of patients responses

Table 3 - Distribution of patient's responses to informed consent for drug trial

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Except two subjects (response 8), all others expressed a clear choice in response to the information provided. However the information had to be presented more than once so that patients could understand the different components of the clinical trial. 62% of the subjects (responses 1 and 2) agreed to the clinical trial without asking any further questions. 37% (responses 3-7) refused to participate due to various reasons. These included problem of coming from long distance, inability to maintain appointments ("cannot get leave from work", "Cannot leave children at home" "have got an exam coming" etc), and apprehension about possible added risk from the trial drug. 15% of the subjects (responses 2 and 3) asked for further details regarding the trials ("How effective is the new drug?" "how effective is the regular drug? "what are the side effects of the new drug and regular drug?", "What have been the results of your study so far?" etc.). Among the subjects who asked for more details, 3% refused to participate ("let me try to regular drug first"). Only two subjects refused to participate without giving any reason.

A comparison was carried out between the consents (N=143) and non consents (N=130) .
The two subjects who expected treating doctor to decide for them were excluded for this analysis
on the different socio-demographic and illness variables using chi square tests and t-tests depending on the nature of the variables. There were no differences between the two groups with respect to age, sex, marital status, education, occupation, diagnosis, duration of illness and past psychiatric treatment.

Discussion

The results of the present study do not support the contention that informed consent does not have relevance in the Indian setting. Ninety nine percent of the subjects in the present study expressed a clear choice regarding participation in the drug trial after provision of informed consent information. Patient's level of understanding would seem to be related to the amount of information that is provided rather than to their background characteristics. Reicken and Ravich [14] found that 28% of patients participating in research in Veterans Administrations hospitals were unaware of their participation in research. Unawareness was not related to personal characteristics but was related to the incompleteness of information provided, less amount of time investigators spent in explaining the research, and explanation offered by hospital personnel other than the investigators. Alfidi [15] in a study of patients undergoing angiography, noted that most of the patients appreciated an explanation of the procedure. These findings highlight the need for medical professionals to inform their subjects regarding the nature of the procedure being carried out so that individuals are enabled to participate in the decision making.

There are, however, controversies in the literature as to the amount of information to be provided [16]. Some professionals argue that it is impossible for the clinican to provide the patient with every bit of information. The clinical must select and provide the pertinent information [17].

In the present study, a tendency was noticed on the part of our subjects to be unduly cooperative as indicated by the percentage of consenters. Even among the non-consenters, majority of them refused participation apparently because of the difficulty in coming from long distances. One of the reasons for this excessive cooperation seems to be borne out of the hope that a recently manufactured drug might have better therapeutic efficacy. Another more important reason for this appears to be the quality of faith inherent in the doctor-patient relationship in our country. In the light of this, it is particularly important for investigators to refrain from exploiting the doctor-patient relationship to induce subjects for research participation.

Certain methodological considerations limit the generalizability of the study. The sample studied was not entirely representative of the general population. Particularly the proportion of patients from the urban background were over represented. It would be interesting to see how a predominantly rural population would respond to this type of enquiry. Future studies could also attempt to quantify the amount of recall of information that is provided.

In conclusion it is emphasized that all clinical investigators especially from developing countries provide adequate information to subjects participating in research without bias to their background so that they are enabled to exercise their free and informed choice for participation in clinical trials.

Appendix-I

Informed Consent-Information to Patients

Dear

I would like to give you the following information about the new drug.

You have come to us for your problems of which has been diagnosed as anxiety/depression. This is usually treated with the drug diazepam/imipramine. If you agree to take part in this study you will be treated with one of the two drugs. As part of the study you will be seen regularly for four/six weeks and your progress assessed in detail. In addition laboratory tests will be carried out to know the bodily effects of the drugs. The same team of doctors will see you during the follow up period.

You are free to join the study. If you join the study you will be seen as outlined above and given the drugs free of cost. If you were not to join the study if you were to decide to stop taking part in the study, you can do so at any time without having to give any reason. We will be able to answer any questions you would have throughout the study period.

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