

Patients' Motivation about Clinical Trials: A Local Perspective from Turkey

Türkiye'de Hastaların Klinik İlaç Araştırmaları Hakkındaki Görüşleri

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Abstract

Objective: To investigate attitudes concerning clinical trials amongst potential Turkish research participants.

Patients and Methods: This is a survey of 504 Turkish patients who applied to 4 research and education hospitals in Istanbul, Turkey in March and April 2008. Attitudes and knowledge of the patients concerning clinical trials were measured.

Results: Of the 504 patients, 62.3% were male and the mean \pm SD age was 36.8 \pm 14.0 years. Most of the respondents (88.3%) believed that the new drugs should not be used directly on human beings without being tested on human subjects and 52.2% thought that clinical trials were being performed in Turkey. 97.8% of the patients believed that new drugs should be developed, 71.4% specified that the new drugs should be tested on human subjects during the research period, 84.5% mentioned that apart from clinical trials they could not use a drug that had never been tested on human beings. Only 28.6% of the respondents believed that clinical trials could be performed on healthy human subjects. The educational status was an affecting factor for the patients' attitudes toward clinical trials. Only 7 (1.4%) patients in the survey participated in a clinical trial previously, but 33.7% of the survey group indicates that they may agree with participating in a clinical trial.

Conclusion: This survey presents first and valuable information about Turkish patients' attitudes for clinical trials. The results of this survey provide an understanding of Turkish patients' motivations, and supply information concerning recruitment and retention strategies. (*Marmara Medical Journal 2011;24:181-6*)

Key Words: Clinical phase studies, Patient motivation, Patient participation, Recruitment strategies, Turkey.

Özet

Amaç: Bu araştırmada Türk katılımcıların klinik çalışmalar hakkında tutum ve görüşlerinin ortaya konulması amaçlanmıştır.

Hastalar ve Yöntem: Türkiye'de 4 eğitim ve araştırma hastanesinde 504 hastaya uygulanan bu anket çalışmasında hastaların klinik çalışmalar hakkında tutum ve görüşleri sorulmuştur.

Bulgular: Beş yüz dört hastanın ortalama yaşları 36,8 \pm 14,0 ve %62,3'ü erkek idi. Katılımcıların çoğunluğu (%88,3) yeni ilaçların insan denekler üzerinde denenmeden doğrudan insan üzerinde kullanılmaması gerektiğine ve %52,2'si Türkiye'de klinik araştırmaların yapıldığına inanıyordu. Ayrıca, hastaların %97,8'i yeni ilaçların geliştirilmesi gerektiğini düşünürken %71,4'ü geliştirilme basamaklarında insanlar üzerinde denenmesi gerektiğini belirtmişlerdir. Hastaların %84,5'i insan üzerinde denenmemiş hiç bir ilacı kullanmayacaklarını ve %28,6'sı klinik araştırmaların sağlıklı bireylerde de yapılabileceğini belirtmişlerdir. Bu araştırmada hastaların eğitim durumunun, klinik çalışmalar hakkındaki görüş ve tutumlarını etkileyen bir faktör olduğu tespit edilmiştir. Ankette sadece 7 (%1,4) hasta daha önce bir klinik çalışmaya katılmıştır. Türk hastaların %33,7'si teklif edilmesi halinde bir klinik araştırmaya katılmayı kabul edebileceğini belirtmiştir.

Sonuç: Bu araştırmanın sonuçları, ilk defa Türk hastaların klinik ilaç araştırmaları hakkındaki görüş ve tutumlarını ortaya koyarak klinik araştırmaların tüm taraflarına önemli bilgiler sağlamaktadır. (*Marmara Üniversitesi Tıp Fakültesi Dergisi 2011;24:181-6*)

Anahtar Kelimeler: Klinik faz araştırmaları, Hastaların tutumu, Hasta katılımı, Hasta alım stratejileri, Türkiye.

Introduction

Clinical research is necessary for new drug development and human subjects are enrolled at different phases of clinical trials (CT).

Participation of the patients in CT is one of the main problems for investigators¹. Finalization of the CT needs more time than before and the participation of the eligible patients is relatively low². Besides, international pharmaceutical industry forces the

reduction of the duration and costs of CT, so developing countries such as India, Brazil, Argentina and Turkey are becoming more attractive to sponsor companies³.

Although the patient potential of the investigation site is crucial in the planning period of CT, there are few data about volunteer potential all around the world but no data is available from Turkey^{1,4,5}. Despite the lack of data about patient participation in CT, international and local media have a negative impact on the community for participating in CT^{6,7}.

Clinical trials are being performed in Turkey under international and local regulations since 1993⁸. According to updated regulations in 2008 and 2011 CT can be carried out in university and State education and research hospitals⁸. Turkey has a big population of 73.722.988, where Istanbul city population is the biggest (13.255.685) according to the polls of December 31 2010⁹. There are 111.211 active medical doctors and 1191 hospitals all around the country¹⁰. Eight

hundred and eighty three CTs are being performed (both recruiting and non-recruiting) at the time of this article was written¹¹.

In brief, there is a good potential in Turkey for CT but knowledge concerning patient attitude for participation is lacking. In this study, the attitudes of Turkish patients' to participation in a CT and identification of the factors influencing their attitude were investigated. Identification of the reasons behind Turkish patients' participation in CT will clarify the recruitment strategies. A questionnaire-survey was carried out on patients attending the out-patient clinics of 4 (3 State education and research and 1 university) hospitals in Istanbul.

Patients and Methods

In this research, a question survey technique with a questionnaire form consisting of 28 questions (27 closed and 1 open ended questions) was performed (Table I). The study was approved from

Table I. Survey questions

1. What is your name? (the name was used to address the patient during the survey, no identification data was saved)
2. What is your age?
3. Gender
4. Which is the last school you graduated from?
5. Do you have any information about clinical drug trials?
6. Can the drugs be used directly on human beings after preclinical trials without being tested on human subjects?
7. According to you how many human subjects are enrolled in clinical trials?
8. In which countries do you believe clinical trials are being performed?
9. Do you think CT are being performed on volunteers in Turkey?
10. Do you think that CT can be performed on healthy human subjects?
11. Which do you prefer? The drugs tested on Turkish subjects in the development period or the drugs tested on other nations' subjects in the development period?
12. What do you think about the safety of patients enrolled to clinical trials?
13. Apart from clinical trials, do you prefer to use a drug that has never been tested on human beings?
14. Apart from clinical trials, do you prefer any of your relatives using a drug that has never been tested on human beings?
15. Have you ever participated in a clinical trial?
16. Was informed consent given in the clinical trial that you participated in?
17. Did you read and understand fully the informed consent?
18. Did you have enough time to ask any of the questions in your mind to your physician?
19. Did your physician satisfy you concerning all of your questions and hesitations?
20. Have any of your relatives ever participated in a clinical trial?
21. Was informed consent given in the clinical trial that your relatives participated in?
22. Did your relatives read and understand fully the informed consent?
23. Did your relatives have enough time to ask any of the questions in their mind to their physician?
24. According to you, should the new drugs be developed?
25. Should the new drugs be tested on human beings in the development period?
26. Would you participate in a CT if your doctor asked you to?
27. Do you want your relatives to participate in a CT if their doctor asked them to?
28. According to you which of the following is/are the reason(s) of a person who participated in a clinical trial?
A. Benefit from a better treatment for his/her disease.
B. Having easier access to new treatments for his/her existing disease.
C. To obtain his/her medications without any charge.
D. For contribution of the development of science and medicine.
E. Helping other people suffering from the same disease.
F. He/she is interested in clinical trials or medicine.
G. Finding treatment for a terminal or severe disease.
H. Because the person had no other treatment option.
I. Because his/her physician recommended participation in clinical research.
J. He/she had information about the clinical trial.

each local ethics committee where the survey was performed. The questionnaires were filled by pollsters (Marmara University Medical School students) according to patients' answers by face to face interview in the out-patient clinics of 4 education and research hospitals in Istanbul (one university hospital: Marmara University Hospital and three State education and research hospital: Kartal Lütfi Kırdar, Haydarpaşa Numune, Zeynep Kamil) in March and April 2008. Primary inclusion criteria were the ability and willingness of patients to participate where there was no specific exclusion criteria.

There was a question in the beginning of the questionnaire (question #5 in Table I) asking if the patients' had information about clinical drug trials. If the patient responded "No" to this question, the pollsters gave brief information about CT, being careful not to affect the patients' answers for further questions. The survey procedure took approximately 5 to 10 minutes to complete for each patient.

The survey addressed 5 specific topics: (1) basic demographic information, (2) information from patients about their knowledge for CT (3) patients' previous participation to and their experience about CT, (4) attitudes of patients about participating in CT, (5) preferences of patients about the recruitment strategies of CT. No personal identification data were recorded.

All questionnaires (511) were examined for missing information and any questions that had not been answered were not included in the analysis. Obtained data from the study was analyzed by The Statistical Package for the Social Sciences (SPSS, version 11.0) software (using frequency and chi-square test) and $P < 0.05$ was considered statistically significant. Parametric data are presented as \pm standard deviation (SD). Categorical data are expressed as numbers and percentages (of the total number) for summarizing the data.

Table II. Basic characteristics of the patients in the survey*

Age (y) mean \pm SD	36.8 \pm 14.0 (15-83)
≤ 25	121 (24.0)
26-50	287 (56.9)
51-75	92 (18.3)
≥ 76	4 (0.8)
Total	504 (100)
Sex	
Male	314 (62.3)
Female	190 (37.7)
School qualifications	
Primary and Elementary School	197 (39.1)
High School and University	307 (60.9)
*Values are numbers (percentages).	

Table III. Responses of the patients' to survey questions (question numbers 9, 10, 15, 24 and 25)*

	Yes	No	No idea
#9. Do you think that CT are being performed in Turkey?	263 (52.2)	171 (33.9)	70 (13.9)
#10. Do you think that CT can be performed on healthy human subjects?	144 (28.6)	341 (67.7)	19 (3.8)
#15. Did you ever participate in a CT?	7 (1.4)	497 (98.6)	-
# 20. Have any of your relatives ever participated in a clinical trial?	15 (3.0)	454 (90.1)	35 (6.9)
#24. Should new drugs be developed?	493 (97.8)	9 (1.8)	2 (0.4)
#25. Should the new drugs be tested on human subjects in the development period?	360 (71.4)	120 (23.8)	24 (2.2)
*Values are numbers (percentages).			

Results

The study was completed by 504 patients in a two month period. The gender of the patients in the survey group was 314 (62.3%) male and 190 (37.7%) female. The mean \pm SD age of the patients was 36.8 ± 14.0 years (range, 15-83 years). Basic characteristics of the survey group are given in Table II.

Most of the patients (445 [88.3%]) believed that the drugs should not be used directly on human beings after preclinical trials without being tested on human subjects, where 38 (7.5%) of the survey group mentioned that the drugs can be used on human beings directly after preclinical trials without being tested on human subjects, and 21 (4.2%) patients had no idea about this question (#6).

The responses of the patients to the questions; (#9) "Do you think that CT are being performed in Turkey?"; (#10) "Do you think that CT can be performed on healthy human subjects"; (#24) "Should new drugs be developed?"; and (#25) "Should the new drugs be tested on human subjects in the development period?" can be found in Table III.

Almost all of the respondents (497 [98.6%]) had never been in a CT, only 7 (1.4%) patients had attended a CT previously (question # 15 in Table III). All of these 7 patients mentioned that they had filled informed consent before the CT they attended, and they had enough time to understand and evaluate the risks and benefits of the CT. Also all of them mentioned that they had asked their doctor all the questions they wanted before signing the informed consent.

There was a similar question (#20) to question number 15 asking if their relatives had attended a CT before and 15 respondents (3%) indicated that at least one of their relatives had attended a CT before, where most of them (454 [90.1%]) answered "No" to this question and 35 (6.9%) had no idea about the question.

Of the 504 patients, 226 (44.8%) mentioned that they would prefer the drugs tested on Turkish subjects in the development period if they had the chance to choose, where 156 (30.95%) preferred the drugs tested on other nations, and 122 (24.2%) patients had no idea or mentioned that "does not make any difference".

Answers of the question (#12) asking their beliefs about safety of CT showed that nearly half of the patients (264 [52.4%]) believed that the CT were not safe, where 212 (42.1%) patients thought that CT were safe (moderate to perfect), and 28 patients (5.6%) had no idea about the question.

Fifty two of the respondents (10.3%) indicated that apart from CT they could use a drug that had never been tested on human beings, and 16 patients (3.2%) could use the drug as an ultimate

Table IV. Responses of the patients' to survey questions (question numbers 26 and 27)*

	Yes ultimate remedy	No	No idea	As an
#26. Would you participate in a CT if your doctor asked you to?	170 (33.7)	294 (58.3)	29 (5.8)	11 (2.2)
#27. Do you want your relatives to participate in a CT if their doctor asked them to?	128 (25.4)	311 (61.7)	58 (11.5)	7 (1.4)

*Values are numbers (percentages).

Table V. Comparison of the responses by the patients' gender to survey questions 9, 10, 24 and 25*.

Gender	Yes	No	No idea
Question #9: Do you think CT are being performed on volunteers in Turkey?			
Male	156 (31.0)	118 (23.4)	40 (7.9)
Female	107 (24.2)	53 (10.5)	30 (6.0)
Total	263 (52.2)	171 (33.9)	70 (13.9)
Question #10: Can the CT be performed on healthy volunteers?			
Male	98 (19.4)	210 (41.7)	6 (1.2)
Female	46 (9.1)	131 (26.0)**	13 (2.6)
Total	144 (28.6)	341 (67.7)	19 (3.8)
Question #24: According to you, should the new drugs be developed?			
Male	305 (60.5)	8 (1.6)	1 (0.2)
Female	188 (37.3)	1 (0.2)	1 (0.2)
Total	493 (97.8)	9 (1.8)	2 (0.4)
Question #25: Should the new drugs be tested on human beings in the development period?			
Male	219 (43.5)	82 (16.3)	13 (2.6)
Female	141 (28.0)	38 (7.5)	11 (2.2)
Total	360 (71.4)	120 (23.8)	24 (4.8)

*Values are numbers (percentages).
** $p < 0.05$ when compared with the ratio of the answers of male gender.

Table VI. Comparison of the responses by the patients' gender to survey questions 26 and 27*.

Gender	Yes	No	No idea	As an ultimate remedy
Question #26: Would you participate in a CT if your doctor asked you to?				
Male	109 (21.6)	186 (36.9)	13 (2.6)	6 (1.2)
Female	61 (12.1)	108 (21.4)	16 (3.2)	5 (1.0)
Total	170 (33.7)	294 (58.3)	29 (5.8)	11 (2.2)
Question #27: Do you want your relatives participate to a CT if their doctor asked them to?				
Male	75 (14.9)	200 (39.7)	33 (6.5)	6 (1.2)
Female	53 (10.5)	111 (22.0)	25 (5.0)	1 (0.2)
Total	128 (25.4)	311 (61.7)	58 (11.5)	7 (1.4)

*Values are numbers (percentages).

remedy. Most of the patients (425 [84.5%]) responded "No" to this question (#13), where 16 (2.2%) had no idea.

Responses to a similar question to #13 -apart from CT do you want your relatives use a drug that had never been tested on human beings- (question #14) most of the patients 453 (89.9%) indicated "No", where 29 (5.8%) said "Yes" or 9 (1.8%) "As an ultimate remedy". Thirteen patients (2.6%) had no idea about this question.

The answers of the patients' for the question (#26) "Do you participate in a CT if your doctor offered" and a similar question (#27) "Do you want your relatives participate in a CT if their doctor offered them to?" are given in Table IV.

Comparison of the answers by the respondents' genders to the question numbers 9, 10, 24 and 25, are given in the Table V and question numbers 26 and 27 are given in the Table VI.

Table VII. Comparison of the responses by the patients' education status to survey questions 9, 10, 24 and 25*.

School qualifications	Yes	No	No idea
Question #9: Do you think CT are being performed on volunteers in Turkey?			
Primary and Elementary School	104 (20.6)	62 (12.3)	31 (6.2)
High School and University	159 (31.5)	109 (21.6)	39 (7.7)
Total	263 (52.2)	171 (33.9)	70 (13.9)
Question #10: Can the CT be performed on healthy volunteers?			
Primary and Elementary School	43 (8.5)	147 (29.2)	7 (1.42)
High School and University	101 (20.0)**	194 (38.5)	12 (2.4)
Total	144 (28.6)	341 (67.7)	19 (3.8)
Question #24: According to you, should the new drugs be developed?			
Primary and Elementary School	194 (38.5)	3 (0.6)	0 (0.0)
High School and University	299 (59.3)	6 (1.2)	2 (0.4)
Total	493 (97.8)	9 (1.8)	2 (0.4)
Question #25: Should the new drugs be tested on human beings in the development period?			
Primary and Elementary School	121 (24.0)	61 (12.1)	15 (3.0)
High School and University	239 (47.4)***	59 (11.7)	9 (1.8)
Total	360 (71.4)	120 (23.8)	24 (4.8)

*Values are numbers (percentages).
 ** p<0.05 when compared with the ratio of the answers of primary & elementary school graduates.
 *** p<0.001 when compared with the ratio of the answers of primary & elementary school graduates.

Table VIII. Comparison of the responses by the patients' education status survey questions 26 and 27*.

School qualifications	Yes	No	No idea	As an ultimate remedy
Question #26: Would you participate in a CT if your doctor asked you to?				
Primary and Elementary School	71 (14.1)	111 (22.0)	12 (2.4)	3 (0.6)
High School and University	99 (19.6)	183 (36.3)	17 (3.4)	8 (1.6)
Total	170 (33.7)	294 (58.3)	29 (5.8)	11 (2.2)
Question #26: Do you want your relatives participate in a CT if their doctor asked them to?				
Primary and Elementary School	62 (12.3)	108 (21.4)	25 (5.0)	2 (0.4)
High School University	66 (13.1)	203 (40.3)**	33 (6.5)	5 (1.0)
Total	128 (25.4)	311 (61.7)	58 (11.5)	7 (1.4)

*Values are numbers (percentages).
 ** p<0.001 when compared with the ratio of the answers of primary & elementary school graduates.

Comparison of the answers by the respondents' education status to the question numbers 9, 10, 24, and 25, are given in the Table VII and question numbers 26 and 27 are given in the Table VIII.

"According to you which of the following is/are the reason(s) for a person who participated in a clinical trial?" was the last question (#28) of the survey and the patients could choose one or more options as answer. The most (240 [47.6% of the patients mentioned]) chosen option was "Because of the person had no other choice". Other options that were chosen significantly were "Benefit from a better treatment for his/her disease" (232 [46.0%]); "Finding a treatment of a terminal or severe disease" (232 [46.0%]); "Having easier access to new treatments for his/her existing disease" (205 [40.7%]); "For contribution of the development of science and medicine" (203 [40.3%]); "Helping

to other people suffering from the same disease" (172 [34.1%]); "To obtain his/her medications without any charge" (148 [29.4%]); "Because his/her physician recommended participation in clinical research" (127 [25.2%]).

Discussion

Clinical trials are necessary for new drug development and eventually for human health and almost all (97.8%) Turkish patients in this survey believed that new drugs should be developed. The knowledge of patients' about CT was not much and generally the community did not lean towards CT because of the negative impact of the news in the written and visual media⁶⁷. In spite of the negative impact of media it is surprising that one third (33.7%) of the

patients' in this survey indicated that they might participate in a CT if their physician asked them to. This data is slightly over a similar survey performed in Germany (25% willingness to participate)⁵.

The awareness of the survey group about performance of CT in Turkey is well (52.2%) and over two thirds of the group (71.4%) believe that new drugs should be tested on human subjects in drug development. Also most of the patients' (88.3%) believe that the drugs should not be used directly on human beings after preclinical trials without being tested on human subjects. These data suggests that Turkish patients' knowledge and consciousness is sufficient concerning CT.

The patients and their relatives' prior attendance of a CT is less (4.4%) and this is due to the fact that Turkey is an emerging country in the clinical trial field, but the author thinks more patients will participate in CT in future because of the increasing trend in CT being performed in Turkey¹¹. All of the 22 patients (and their relatives) that previously participated in a CT had filled informed consent and the time given for the informed consent was enough for them and also all of them indicated that they had chance to ask all of their questions they wanted to about CT they participated in. Despite the number being small, this data shows that CT are being performed in Turkey in accordance with international and local regulations and ethical rules.

Almost half of the patients (44.8%) in this survey mentioned that they would prefer the drugs tested on Turkish subjects in the development period if they had the chance to choose. This is another awareness of Turkish patients about drug development and rational use of drugs. This might be because of the impact of genetic differences in the drug effects and Turkish patients prefer the drugs tested on Turkish subjects in the development period. Also the result of the answers of the Turkish respondents (84.5% answered "No") for the question (#13) "Apart from clinical trials, do you prefer to use a drug that had never been tested on human beings?" shows another consciousness about rational drug use.

Education is another factor affecting Turkish patients' attitude toward CT when data in the Table VII are considered, education level correlates with the awareness of the CT. On the other hand the effect of education level does not affect respondents' participation in CT even if it becomes the reverse in the responses of their opinion about their relatives' participation in CT.

Turkish patients in this survey believe that having no other treatment choice was the main reason for a person participating in a clinical trial. This may be due to the respondents' protecting themselves from the obscurity and potential dangers of the CT, and they may agree to participate in a clinical trial when they are in rigorous difficulty. Besides this, Turkish patients also believe that getting the advantage of a better treatment, having easier access to new treatments and contributing to the development of science and medicine may be the reasons for a person's participating in a clinical trial.

All of these data demonstrate that Turkish patients' attitude towards CT is good, but this survey was performed only in Istanbul and the attitudes of the patients' living in other cities

should also be analyzed. In addition, the condition of Turkish patients recruited to CT and their attitudes ought to be investigated. The position, situation and the feelings of the Turkish researchers' should also be investigated.

Conclusion

This survey presents first and valuable information about Turkish patients' attitudes concerning CT. One third of the patients willing to participate in a clinical trial in this survey is the most significant result. The results of this survey also provide an understanding of Turkish patients' motivations and information concerning the recruitment and retention strategies. In conclusion, Turkey has a rich potential for CT with regulations, hospitals, physicians, population and finally with the patients' perspective concerning CT.

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