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Barriers and facilitators to participation in clinical trial among lymphoma patients from Sun Yat-sen University Cancer Center in China

An observation study

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Abstract

Recruitment rate of clinical trials in cancer patients is pretty low in China. Little is known about factors influencing trial recruitment in Chinese cancer patients. The aim of present study is to evaluate the barriers and facilitators to participation in clinical trials among lymphoma patients in China.

From December 2014 to August 2015, the survey was carried out in the Department of Medical Oncology in Sun Yat-sen University Cancer Center. A self-made questionnaire was used among lymphoma patients (N = 331) to evaluate their attitude toward clinical trials. The questionnaire included 2 parts: patients' basic information and whether they were willing to participate in future clinical trials and their reasons.

There were 53.5% patients willing to participate in clinical trials. The most common reasons were thirst for new treatments, trust on hospital and doctors, the idea that clinical trials may be more effective than conventional therapy, and to get more management and monitoring. The following patients are more likely to participate in clinical trials: patients who have children ($P = .019$) or spouse ($P = .037$), cannot afford treatment cost ($P = .019$), have tumor relapse ($P = .045$), and cared about the medical development ($P = .032$). Patients who have little knowledge of clinical trials are less likely to participate in clinical trials ($P = .047$).

Popularization of knowledge about clinical trial is helpful to improve clinical trial participation in Chinese lymphoma patients.

Abbreviation: DLBCL = diffuse large B cell lymphomas.

Keywords: acceptance, clinical trials, lymphoma, willingness

1. Introduction

Lymphoma is among the leading causes of cancer-related deaths in China.[1] It was reported that about 88,200 people were diagnosed as lymphoma in China and about 52,100 people died from the disease in 2015.[1] Though the prognosis has been improved by chemotherapy and target therapy,[2] for lymphoma patients who fail to receive standard treatment, clinical trial is the first recommendation. However, patient recruitment to clinical trials is a big challenge in China.[3] There is no available data about recruitment rates of lymphoma patients in China. According to our experience, <10% of all cancer patients actually participate in clinical trials throughout the course of their treatment.

Basically, factors that may affect patients' recruitment include physician-, patient-, and system-related factors.[4] Recently, there was an analysis of barriers to recruit African American patients into research. Russell KM et al found that patient altruism and healthcare professionals' attitudes were strong driving forces to motivate patients to participate in clinical trials.[5] Barriers that prevented patients for clinical trials included increasing demands of more complex trials, limited healthcare resources, unease about randomization, fear of potential side effects, the idea that clinical trials are not appropriate for serious diseases, and fear that trial participation may have a negative impact on the patient-doctor relationship.[5] Patient mistrust of the healthcare system and inconvenience of study protocols have been identified as additional barriers.[6] Most cited studies were from the United States. There is a need for understanding such factors in China, since international multicenters clinical trials grow rapidly in China. The recruitment rate of patients into clinical trials in Singapore was much lower than that in western countries.[7] Little is known about the recruitment rate of clinical trials in China. A better understanding of barriers and facilitators in China will permit implementation of interventions to improve future trial recruitment.

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2. Patients and methods

2.1. Patient recruitment

From December 2014 to August 2015, a survey on the cognition and willingness to clinical trials was carried out in patients from the Department of Medical Oncology in Sun Yat-sen University Cancer Center. We are working in the lymphoma sections and it is therefore convenient to carry out the survey in lymphoma patients. Here in this study we only enrolled lymphoma patients. The inclusion criteria were lymphoma patients, older than 18 years, and capable of providing informed consent. The aim of the study is to find out the enrollment rate in clinical trial in Chinese lymphoma patients. Furthermore, we will explore why the patients agree or reject to participate in the clinical trial.

2.2. Questionnaire

We designed the questionnaire based on the previous reports on patients' willingness to participate in clinical trials. The questionnaire included 2 parts. The first part was patients' basic information. In the second part, patients were asked if they were willing or unwilling to participate in future clinical trials and the reasons (Supplementary material 1, http://links.lww.com/MD/B871).

2.3. Sample size

There is no preset sample size. We prospectively collect lymphoma patients from December 2014 to August 2015.

2.4. Survey

The questionnaires were distributed and recollected by the clinical research nurses. We totally distributed 331 questionnaires by using the anonymous questionnaire survey method and 331 questionnaires were recollected.

2.5. Statistical analysis

All statistical analyses were performed by Statistical Package of Social Sciences 13.0 software. P value $< .05$ was considered to be statistically significant. The chi-square test was used to compare the clinical data.

2.6. Ethics, consent, and permissions

All patients provided written informed consent. Study approval was obtained from independent ethics committees at Cancer Center of Sun Yat-sen University. The study was undertaken in accordance with the ethical standards of the World Medical Association Declaration of Helsinki.

3. Results

3.1. Basic information

A total of 331 lymphoma patients were approached. Of these, 177 (53.5%) verbally agreed to participate in clinical trial. One hundred fifty four (46.5%) disagreed to participate. Details of participants' basic characteristics are summarized in Table 1. About 54% of the patients had diffuse large B cell lymphomas (DLBCL) and the rest different subtypes including NK-T lymphoma, mucosa-associated lymphatic tissue lymphoma, and Burkitt lymphoma. We combined the rest subtypes as "Others" since the number of patients in each subtypes was small. There was no significant difference found between patients who agreed or disagreed to participate in clinical trials in terms of gender, living environment, annual income, religious belief, source of medical reimbursement, source of knowledge about clinical trial, relatives in the healthcare systems, optimistic or pessimistic attitude to treatment, and duration of illness.

The following patients were more likely to participate in clinical trials: those who have children or spouse (with children $P = .019$, with spouse $P = .037$), patients who cannot afford treatment costs ($P = .019$), relapse ($P = .045$) and those who cared about the medical development ($P = .032$). Patients who have little knowledge of clinical trials were less likely to participate in clinical trials ($P = .047$).

3.2. Factors facilitating decision to participate in clinical trials

The reasons facilitating decision to participate in clinical trials were listed in Table 2. The top 5 reasons include: thirst for new treatments (100.0%), trust on the hospital (96.6%), trust on doctors and their advice (96.0%), the idea that clinical trials may be more effective than conventional therapy (76.3%), expectation/hope of better treatment by doctors/staff (72.3%).

3.3. Barriers to trial participation

Barriers to trial participation are listed in Table 3. The top 5 reasons were lack of knowledge about clinical trials and did not want to try (94.2%); concern about the side effects and safety (93.5%); worry about the effectiveness of new drug (81.8%); the idea that the relevant laws and regulations were imperfect and the rights of patients could not be guaranteed (76.6%); and the idea that clinical trials were not necessary (60.4%).

4. Discussion

This is the first study to investigate the recruitment rate of clinical trial in Chinese lymphoma patients. We used a self-made questionnaire which covered the basic information and patients' willingness to participate into clinical trials. Furthermore, we tried to find out factors that may facilitate participation or prevent patients from participating the clinical trials.

We found that only half of the patients were willing to participate in future clinical trials. A previous study from Arabia showed that 54.1% (1081/2000) of patients agreed to take part in clinical trials,[8] which was similar to our result.

Our study confirmed findings from previous studies in identifying factors for both barriers (fear and uncertainty about new drugs and mistrust of system) and facilitators (trust in physicians and prior positive experience with trials).[4,5,9] We found new factors for both barriers (lack of knowledge about clinical trials and did not want to try, concern about the side effects and safety, the idea that the relevant laws and regulations were imperfect and the rights of patients could not be guaranteed, no need to participate in clinical trials); and facilitators (want to get more management and monitoring) among our participants. The effect of religious beliefs on clinical trial recruitment is controversial. Some showed that it was a barrier[7] whereas the other showed that it facilitated the participation.[8] In present study, we found that religious beliefs had no impact on the clinical trial recruitment. However, we needed to know that only a small group of patients (11.5%) have religious beliefs in China.

Table 1

Clinical characteristics of 331 lymphoma patients.

Characteristics	Agreed group N = 177, %	Disagreed group N = 154, %	*P* value
Age (Mean ± SD)	46.9 ± 1.18	43.8 ± 1.31	
≤30 y	28 (15.8)	38 (24.7)	
31–60 y	105 (59.3)	91 (59.1)	
>60 y	44 (24.9)	25 (16.2)	.046
Gender			
Male	114 (64.4)	93 (60.4)	
Female	63 (35.6)	61 (39.6)	.261
Marital status			
Not married	18 (10.2)	27 (17.5)	
Married	159 (89.8)	127 (82.5)	.037
Have children			
Yes	158 (89.3)	124 (80.5)	
No	19 (10.7)	30 (19.5)	.019
Living environment			
Rural	51 (28.8)	33 (21.4)	
Town	37 (20.9)	37 (24.0)	
Urban	89 (50.3)	84 (54.5)	.299
Educational level			
Elementary school	39 (22.0)	17 (11.0)	
Middle and high school	83 (46.9)	71 (46.1)	
College and bachelor degree	52 (29.4)	59 (38.3)	
Master's degree and above	3 (1.7)	7 (4.5)	.018
Occupation			
Enterprises and institutions	19 (10.7)	28 (18.2)	
Business services	15 (8.5)	18 (11.7)	
Farmers or workers	42 (23.8)	21 (13.6)	
Retired	35 (19.8)	17 (11.0)	
Students	6 (3.4)	15 (9.7)	
Teacher or medical staff	26 (14.7)	25 (16.2)	
No occupation	34 (19.3)	30 (19.4)	.001
Treatment			
Initial treatment	111 (62.7)	111 (72.1)	
Retreatment	66 (37.3)	43 (27.9)	.045
Economic situation			
Treatment costs can bear	115 (65.0)	117 (76.0)	
Treatment costs cannot bear	62 (35.0)	37 (24.0)	.019
Annual income, RMB			
<10,000	64 (36.2)	60 (39.0)	
10,000–50,000	74 (41.8)	50 (32.5)	
50,000–100,000	24 (13.6)	28 (18.2)	
>100,000	15 (8.5)	16 (10.4)	.317
Religious belief			
Yes	18 (10.2)	20 (13.0)	
No	159 (89.8)	134 (87.0)	.264
Have insurance or not			
No	30 (16.9)	32 (20.8)	
Yes	147 (83.1)	122 (79.2)	.227
Understanding clinical trials			
Not at all or a little	138 (78.0)	132 (85.7)	
Very much or generally	39 (22.0)	22 (14.3)	.047
The way to know about clinical trial			
The hospital or flyer	135 (76.3)	106 (68.8)	
No	42 (23.7)	48 (31.2)	.082
Concerned about medical knowledge			
Yes	82 (46.3)	55 (35.7)	
No	95 (53.7)	99 (64.3)	.032
Have relatives in the medical industry			
Yes	69 (39.0)	58 (37.7)	
No	108 (61.0)	96 (62.3)	.447
The attitude to treatment			
Positive	173 (97.7)	154 (100.0)	
Negative	4 (2.3)	0 (0.0)	.080
Duration of illness			
≤6 mo	58 (32.8)	62 (40.3)	
6 mo to 1 y	49 (27.7)	43 (27.9)	
1–3 y	47 (26.6)	36 (23.4)	
>3 y	23 (13.3)	13 (8.4)	.245
Psychological stress after illness			
Not at all or a little	48 (27.1)	58 (37.7)	
General or very much	129 (72.9)	96 (62.3)	.045
Histology subtype			
Diffuse large B cell lymphoma	100	80	
Others	77	74	.407

Table 2

Reasons for 177 lymphoma patients to agree with clinical trials.

Factors	Number (%)
The desire to try new drugs and early acceptance of new treatments	177 (100.0)
Trust on the hospital	171 (96.6)
Trust on doctors and doctor's advice	170 (96.0)
Clinical trials may be more effective than conventional therapy	135 (76.3)
Want to get more management and monitoring from doctors	128 (72.3)
Make a contribution to medical research	111 (62.7)
Free use of drugs	96 (54.2)
Advice from others	73 (41.2)
Fear of discrimination	61 (34.5)
No other effective treatment	58 (32.8)
Fear that refusing to take part in clinical trials will influence the relationship between themselves and doctors	36 (20.3)

The following patients were more likely to participate in clinical trials: those with children or spouse, those who cannot afford treatment costs, who have a relapse and cared about the medical development. It meant that financial incentive was one of motivations for clinical trial participation. Previous studies also showed that financial incentive, such as no need to pay for new drugs was facilitator.[3,4,6,7,10]

Patients who lacked awareness about the trials were less likely to participate in clinical trials. This is consistent with previous reports.[7,11] Therefore, to improve clinical trial participation in Chinese lymphoma patients, we need to popularize the clinical trial related knowledge.

The limitation of present study is the self-made questionnaire. However, there is no available standard questionnaire to evaluate patient's willingness for clinical trials. The questionnaire we used is based on previous reports in western countries.[8,10,12] Furthermore, we modified it with some Chinese characteristics, such as the insurance status. The insurance policy in China is totally different with that in the western countries. In China, there were health insurance, public refunds, new rural cooperative medical system, social security, labor protection, and business insurance. Moreover, a good number of patients have no insurance and have to bear the expense themselves. The new rural cooperative medical system has characteristics specific to China. This policy applies only to Chinese citizen in rural area. In this system, all people pay a certain amount of money per year to the country; in the event of a major illness (including cancer), patients can get certain percentage of reimbursement from country. The amount of money paid and the percentage of insurance cover differs in different cities.

Table 3

The reasons for 154 lymphoma patients refusing to participate in clinical trials.

Factors	Number (%)
Lack of understanding of clinical trials, do not want to try	145 (94.2)
Concerned about the side effects and safety of clinical trials	144 (93.5)
Worry about the effectiveness of drugs	126 (81.8)
Concern that the relevant laws and regulations are imperfect, patients' rights cannot be guaranteed	118 (76.6)
Consider their condition does not need to participate in clinical trials	93 (60.4)
Feel like a white mouse	90 (58.4)
Worry about additional fee	50 (32.5)
The advice of others	28 (18.2)
Worry about personal information leakage	21 (13.6)
Reading consent terms, procedures are lengthy so do not agree	20 (13.0)
Previous treatment failure	16 (10.4)
Worry about being looked down upon	8 (5.2)
Distrust on the hospital	6 (3.9)
Distrust on doctors	4 (2.6)

The second limitation is the single-institution participation. External validation of the questionnaire is necessary. Finally, this study only enrolled lymphoma patients. In future studies, we will explore the patients with other diseases.

5. Conclusion

This study suggests that the desire to try new drugs, benefit to themselves, and the trust on hospitals and doctors are the main motivation or attraction for patients to participate in clinical trials. And safety concern, not understanding the clinical trials, and inconveniences associated with the trial set-up are the main reasons to refuse clinical trials. Despite some shortcomings, this is the first study to explore the barriers and facilitators to participation in clinical trial among lymphoma patients in China. Popularization of clinical trial knowledge is helpful to improve clinical trial participation among Chinese lymphoma patients.

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