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Special article

The adequacy of consent forms for informing patients entering oncological clinical trials

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Summary

The impact on 100 patients of information and consent forms signed prior to medical oncology clinical trials was evaluated by a survey at a subsequent visit. Only 40 patients believed that the purpose of the form was to explain the treatment. The form was listed as the major source of information by 12 patients while 52 listed a doctor and 26 a nurse. Although 21 patients believed that the form made them less anxious, 19 patients believed that it made them more anxious. Despite 80 patients reading all of the form, 60 claiming to understand all of it and 68 claiming that it contained adequate information, in tests of recall only 52 patients could name all of their drugs and only 4 all of the side effects. The number of drugs named correlated with how much of the consent form had been read ($p = 0.003$) and the highest education level achieved by the patient ($p = 0.0003$). Patients under 55 years had significantly better recall. Patients with a better ECOG performance status were more likely to find the form very helpful. Such forms may not ensure that the requirements for informed consent are satisfied.

Key words: clinical trial, informed consent, medical oncology

Background

In order to satisfy the requirement that patients make autonomous decisions about entry into clinical trials they must be given sufficient knowledge about the potential benefits and side effects of the treatment and the alternative treatments available [1]. Beauchamp and Childress highlight the change in the focus of informed consent from the obligation of the doctor to disclose the information, to the quality of the patients' understanding and consent [2].

Part of the process of providing the necessary information has been the use of written information and consent forms prior to participation in clinical trials. The value of this approach has been questioned with some studies highlighting the difficulties that patients have recalling this information while others have focussed on the problem of the readability of the forms [3–7]. Concern has been expressed that full disclosure written information may increase anxiety, suggest toxicities and even lead to the rejection of therapy [8]. On the contrary, other studies have found that detailed information has a positive impact on the treatment outcome [4, 9, 10].

We sought to determine the impact on patients of plain language, full disclosure, written information and consent forms given to patients prior to entry into clinical trials in medical oncology.

Patients and methods

Patients with cancer who had signed information and consent forms prior to entering international and Australian medical oncology clinical trials were evaluated when they presented for their next course of treatment. There were 18 different trials of chemotherapy treatments, the majority being phase II studies of single agents or combinations, but phase I and randomised phase II studies were also included. The information and consent forms were full disclosure, common language forms which had been written in a standardised format as approved by the ethics committee of the Peter MacCallum Cancer Institute, where this study was conducted. The information and consent forms are required to state the purpose of the study, the investigational nature of the study, alternative treatments, the procedures to be followed in receiving the drugs, including the investigations required, and presentation of all of known toxicities of the treatments. This prospective study of the impact of the consent form was approved by the ethics committee but a written consent form was not required.

A questionnaire was administered by the nursing staff of the day chemotherapy ward who also completed a second form scoring the patients on their recall of the information on the information and consent form. Demographic data were collected on the patients' primary language, level of education, occupation and performance status. Patients were asked a series of general questions, with defined options, on the purpose of the form, the timing of the information, the extent of the information provided and how much of the form they had read and understood. They were also asked how helpful they found the form, how anxious it made them feel about the treatment and from where they had received most of their information about the treatment. Open ended questions without categorised answers tested their recall of the chemotherapy drugs and their side effects.

BMDP Statistical Software was used to analyse the data base. Except where otherwise stated the Pearson Chi-square test for contigency tables (with Yates correction where appropriate) compared the first response with other responses combined.

Results

Of 105 consecutive patients entered into the survey, five were excluded. Four missed being surveyed on the second cycle and for one patient 8 months had elapsed between signing the consent form and receiving her second course of treatment. The patients had been enrolled in 18 different clinical trials and a wide range of age and educational levels were represented (Table 1). There was a median of 23 days (range 6–43 days) between signing the consent form and completing the survey.

Only 40 patients believed that the main purpose of the information and consent form was to explain the treatment, while 26 thought that it was to protect the doctor and 25 to protect the patient. Eighty patients claimed to have read all of the form, 11 just skimmed through it, 4 read only part of it, 2 could not remember how much of it they had read, while 2 of 3 who had replied that they had not read it, had it read and translated for them. Patients who read all of the consent form were more likely to be inpatients than outpatients (89% vs. 70%, $p = 0.046$), more likely to have English as their first language (89 vs. 44%, $p = 0.0001$), and were more highly educated (primary 33%, secondary 84%, tertiary 93%, $p = 0.0008$ Chi-square test for trend).

Ninety patients rated the information and consent form either very helpful or somewhat helpful. Patients with better performance status were more likely to rate the consent form as very helpful; 63% of ECOG 0, 48% of ECOG 1 compared with 27% with ECOG ≥ 2 ($p = 0.01$). Sixty patients claimed to understand it fully, 26 understood most of it, 7 some of it, while 1 could not understand any of it, 5 could not remember and 1 did not read it. Of the 28 patients with a tertiary education, 75% could name all of the drugs compared with 48% of the 62 patients with a secondary education and only 10% of the 10 patients with a primary education ($p = 0.0003$, Chi-square test for trend). There is a poorer association with the ability to remember the side effects, with only 43% of the 28 patients with a tertiary education remembering at least half of the side effects compared to 44% of the 62 patients with a secondary education and only 20% of the 10 patients with a primary education ($p = 0.37$, Chi-squared test for trend). Of patients with professional occupations, 89% were able to name all of their drugs compared to 38% of the remaining patients ($p < 0.0001$).

Of those who offered an opinion on the amount of information contained in the information and consent form, 14 thought it was too little, 5 too much and 68 just right. However, 19 patients felt that the consent form made them feel more anxious, 21 less anxious and 55 no different while 4 couldn't remember and 1 did not read it. Only 12 patients reported receiving most of their information about their treatment from the information and consent form, most receiving it from a health professional; 52 from a doctor and 26 from a nurse. Eight cited other books or pamphlets on cancer treatment, one a hospital overseas and one the local newspaper as their major source of information. Significantly more of 37 patients enrolled in three trials of paclitaxel (70%) obtained most of their information from the doctor compared to patients entered into other trials (41%) ($p = 0.01$).

Table 1. Patient characteristics.

Evaluable patients	100
Median age (range)	54.5 (27–78)
Sex	
Male	31
Female	69
Treated as	
Inpatient	62
Outpatient	38
Performance status ECOG	
0	28
1	48
2	20
3	3
4	1
Main language	
English	83
Other	17
Education	
Primary	10
Secondary	62
Tertiary	28
Occupation	
Unskilled	8
Blue collar	14
White collar	15
Professional	28
Home duties	32
Other	3

Most patients had several days between seeing the form and starting their chemotherapy. For 50 patients it was 7 or more days, 1 to 6 days for 36 and a few hours for 12 patients. Seventy-seven patients thought that the time interval was adequate, with only 3 believing it to be too short and 18 believing it to be too long.

Fifty-two patients could name all of the drugs (median number 2) in their chemotherapy regimen, 6 at least half, 5 less than half and 37 none. The number of drugs named correlated strongly with how much of the consent form had been read ($p = 0.003$) and the highest level of education achieved ($p = 0.0003$). The number of side effects listed varied depending on the complexity of the study but there were usually 4 or 5 major toxicities listed. Only 4 patients could remember all of the side effects listed on the consent form, 37 at least half, 32 less than half and 27 none. Only 3 patients could remember all of the drugs and side effects. Thirty patients experienced side effects which they thought

had been mentioned on the information and consent form but were not. Patients younger than 55 years could name significantly more drugs (p for trend = 0.002) and remember significantly more side effects (p for trend = 0.05), than older patients. All but 3 of the 37 paclitaxel patients (92%) remembered the name of their drug whereas only 29 (46%) of the patients on the remaining trials could name at least one of the drugs they were receiving ($p < 0.0001$). This could well have been due to the high level of media coverage associated with paclitaxel at the time of the study.

Conclusions

Both this study and a parallel study that we performed with patients receiving chemotherapy outside of a clinical trial confirmed Cassileth's finding that most patients did not realise that the information and consent form was primarily meant to benefit them [3, 11]. Although very few patients listed the information and consent form as their major source of information, if they had not fully read it, which can be their autonomous choice, their knowledge of their treatment was compromised. This suggests that the information and consent form was a more important source of information than the patients gave it credit for.

It is of great concern that in this trial and in other studies evaluating consent forms, the recall of information on the treatment and its side effects is poor [3, 11–13]. The correlation that we found between the understanding and recall of the form and educational level obtained by the patients may suggest that the information on the form is too complex, a finding previously described when testing such forms for readability [5, 6]. Another factor could be the time that patients have to study the form. This was not perceived by the patients as a problem in the current study where most had days to weeks between receiving the form and treatment. The time between reading the form and completing the survey did not differ greatly between patients being between 3 and 4 weeks as expected by the interval between chemotherapy cycles.

Although providing patients with information can lessen anxiety as it did in 21 patients in this study, anxiety levels were increased by the information and consent form in nineteen patients. This was less than the 42% found in our study of patients receiving chemotherapy off clinical trials and may reflect differences in patients who are prepared to enter clinical trial [11]. Certainly there has been debate on how much information a patient need be given in the context of a clinical trial, particularly if information will adversely impact on some patients, as we have found. It has been argued, for example, that patients prerandomised to the standard treatment control arm of a randomised clinical trial may be unnecessarily burdened by full information about both arms of the study [14]. A randomised trial of total disclosure compared to disclosure at the doctors' discretion found that total disclosure improved understanding but increased anxiety [8]. It is a fine line between patients' autonomy and paternalism in trying to serve the patients best interests and doing the patient no harm. We believe that we need to provide any information which could affect the patients' decision to participate in a trial; that is the treatment alternatives, the common side effects or rare but potentially serious side effects.

The fact that all of the patients in this study were entering clinical trials makes their lack of understanding more problematic but is in line with other studies. Patients participating in phase I trials were found to be motivated by the hope of therapeutic benefit but only a minority of patients understood that a phase I trial was a dose finding study [15]. Problems have been identified with phase I and II studies focussing on communicating effectively with patients when the goals of the investigator and the patient are different, there is a lack of knowledge in phase I studies of all of the side effects and there is a general lack of activity in phase II trials [16]. Strategies to ensure that consent is truly informed in these cases will involve analyses of the process of doctor patient communication [17].

Future studies will need to determine why the recall and understanding is so poor following the use of written full disclosure information and consent forms. Given that we allowed free access to other sources of information it may not be the presentation of the information that is at fault. For example, one study where patients received audiotapes of their consultations with their oncologist found that although this improved patient satisfaction it did not improve the recall of information and general tapes had a detrimental effect on recall [18].

Factors such as anxiety at the time of receiving the information or defense mechanisms such as denial may be the main factors responsible for defective recall. The information given about a trial may not be what the patient wants to know. This requires further investigation if the requirements for informed consent are to be satisfied.

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