Physicians’ Reasons for not Entering Their Patients in a Randomized Controlled Trial in Japan

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RAHMAN, M., MORITA, S., FUKUI, T. and SAKAMOTO, J. Physicians’ Reasons for Not Entering Their Patients in a Randomized Controlled Trial in Japan. Tohoku J. Exp. Med., 2004, 203 (2), 105-109 —— Physicians’ not entering their patients can jeopardize the success of a randomized controlled trial (RCT). We used a survey to investigate the possible reasons why physicians who initially agreed to collaborate did not recruit any patients for an RCT being conducted in Japan. A total of 167 questionnaires were sent out and 122 responses were received. Main reasons for not entering patients were: concern about the detrimental effects on the doctor-patient relationship (51.8%), patients’ refusal (47.5%), complicated registration and follow-up procedures (34.9%), and not feeling comfortable recruiting their own patients (32.4%). Multivariate logistic regression made it clear that physicians who thought that registering their own patients would damage the doctor-patient relationship and who expected the RCT would fail were more likely to be uncomfortable entering their own patients. Moreover, physicians aged 50 years or older, who felt uncomfortable recruiting their own patients, and saw no advantage in participating in the trial, were more likely to view the enrolment and follow-up procedures as cumbersome. We conclude that training and a manual for obtaining informed consent and a face-to-face demonstration of patient registration/follow-up procedures for the potential participants are prerequisites for increasing physician participation in RCTs in Japan.

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Randomized controlled trial (RCT) is the main mode of clinical investigation to generate high-grade evidence in medical science. Physician participation, patient recruitment, randomization, well-designed follow-up procedures, data management, and satisfaction of both physician and patients with the trial activities, are the main ingredients of a successful RCT. However, every component needs to undergo careful scrutiny to minimize bias and to make the trial run smoothly. Physician participation is one of the most important components in an RCT. Obstacles to physician participation could increase the cost, workload and duration of the trial (Hunninghake et al. 1987; Swanson and Ward 1995). Previous studies found the following reasons behind physicians’ not entering their patients onto clinical trials: logistic problem, concerns regarding the doctor-patient relationship, difficulties obtaining informed consent, loss of professional autonomy, lack of proper incentives, dislike of frank discussions about uncertainty, concerns about the treatment used in this trial, lack of time, uninteresting research questions and doubt about the rationale of the trial itself (Taylor et al. 1984; Vinciguerra and Moore 1990; Ellis et al. 1999; Ross et al. 1999; Ellis et al. 2000). However, since the reasons given by Japanese physicians have not been reported yet, the objective of this study was to examine the reasons why physicians did not enter their patients in the CASE-J (Candesartan Antihypertensive Survival Evaluation in Japan) trial. This is an open-label, multi-center, randomized controlled trial designed to compare the incidence of cardiovascular events incurred by angiotensin II receptor antagonist (candesartan cilexetil) and calcium channel blocker (amlodipine besilate) users (Fukui et al. 2003). Enrollment for this trial began in Sept. 2001 and follow-up is to be completed in Dec. 2005.

MATERIALS AND METHODS

We conducted a questionnaire survey among the physicians who had initially agreed to participate in the CASE-J trial but eventually did not do so. Questionnaires were sent to a total of 167 physicians in January 2003, immediately after the patient recruitment period ended in December 2002. The questionnaire comprised two sections with 24 statements. Twelve questions in the first section asked about the physicians’ demographic and academic background and 12 questions in the second section explored the reasons for non-participation. In the second section, three questions addressed the physicians’ approach to their patients: whether they approached them about joining the trial, if they did, how many, and the patients’ reported reasons for refusal. The other nine were related to their personal reasons for not entering their patients and rated on a five-point scale (strongly agree, agree, neutral, disagree, and strongly disagree). This study was approved by the EBM Collaborative Research Center (Implementing body for the CASE-J Trial), Kyoto University.

Statistical analysis

Both bivariate and multivariate analyses were performed to identify the predictors of each of the reasons for not entering their patients into the CASE-J trial. For the multivariate logistic regression analysis, specific physicians’ attitude was considered as a dependent variable while demographic and academic background, and physicians’ attitudes towards CASE-J trial were considered as predictors. Each of the reasons for not entering their patients was modeled separately by transforming the five-point scale into a binary one (agree vs. neutral plus disagree). Statistical analyses were conducted with STATA statistical software (Stata Statistical Software Version 7 (intercooled), STATA Corporation, College Road, Texas, USA).

RESULTS

Demographics and academic background

The questionnaire was returned by 122 physicians (73.1% of the total). Table 1 shows the respondents’ demographic characteristics. Most of them were male (94.3%) with a mean age of
49.0 years, were qualified as either cardiologist or internist (81.0%), were working as private practitioners (75.2%), had been practicing medicine for an average of 25.6 years, had previously participated in a clinical study (81.2%), and were interested in participating in future trials (66.1%).

**Reasons for not entering patients**

Table 2 shows physicians’ reasons for not entering their patients. More than half of them were concerned about their doctor-patient relationship while nearly half of them said that they had approached their patients but nobody agreed to participate. More than one-third of them stated that the patient enrolment and follow-up procedures of CASE-J were cumbersome. Other reasons for not entering their patients were: (1) not feeling comfortable recruiting their own patients (32.4%), belief that differences in the efficacy of the treatments examined had already been established (22.0%), inability to find eligible patients to approach (17.2%), interest in drugs other than those used in the CASE-J trial (11.7%), lack of appropriate incentive for participation (11.6%), and possibility of failure of the trial (9.0%).
Patients' accounts of refusal to participate

Although 260 eligible patients were approached by 58 physicians (47.5% of 122 respondents) (average: 4.5 patients per physician), none of them agreed to participate. Physicians thought that uncertainty about the trial (48.1% of patients), lack of interest in a change of treatment (24.2%), inability to understand the significance of the trial (14.2%), and opposition from family member (13.5%) were the main reasons for patient refusal.

Predictors of physicians' reasons for not entering patients

Logistic regression analysis revealed that the physicians who thought that entering their own patients would have a detrimental effect on their doctor-patient relationship (odds ratio [OR]=3.2, 95% confidence intervals [CI]: 1.3-7.8, \(p=0.01\)) and who assumed that the CASE-J would fail (OR=6.8, 95% CI 1.8-30.7, \(p=0.01\)) were more likely to feel uncomfortable about patient recruitment. In addition, physicians aged 50 years or older (OR=2.9, 95% 1.1-7.8) \(p=0.03\), who felt uncomfortable recruiting their own patients (OR=4.3, 95% 1.3-11.7) \(p=0.005\), and saw no advantage in participating in the trial (OR=4.9, 95% 1.1-23.1) \(p=0.04\) were more likely to regard the enrolment and follow-up procedure as cumbersome. No other factors were significantly associated with the stated reasons for not entering patients.

DISCUSSION

This survey found that more than half (51.8%) of the physicians were concerned about the detrimental effects on their doctor-patient relationship and one-third (32.4%) were not comfortable even asking their patients to participate in the CASE-J trial. Multiple logistic regression analysis also demonstrated that physicians who thought that entering their own patients would hamper their doctor-patient relationship were more likely to feel uncomfortable entering their patient in the trial. These findings mean that they were not sufficiently motivated by the study design and alleged significance of the trial. Nearly half of the physicians (47.5%) said that their patients refused to take part in the trial due to the uncertainty, dislike of change in treatment, inability to understand the significance of the trial and family pressure. This indicates that many of the physicians may have been ill-equipped to obtain informed consent. In addition, it shows

<table>
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<tr>
<th>Causes of Non-Participation</th>
<th>Percentage of the Non-Participating Physicians (%)</th>
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<tbody>
<tr>
<td>1. Concerned about doctor-patient relationship</td>
<td>51.8</td>
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<tr>
<td>2. Approached eligible patients but the patient refused to participate</td>
<td>47.5</td>
</tr>
<tr>
<td>3. Procedures of patient enrollment and follow-up are cumbersome</td>
<td>34.9</td>
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<tr>
<td>4. Not comfortable recruiting own patients</td>
<td>32.4</td>
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<td>5. Efficacy of the two drugs is already different</td>
<td>22.0</td>
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<tr>
<td>6. Did not have any patients to approach</td>
<td>17.2</td>
</tr>
<tr>
<td>7. Interested in antihypertensive drugs other than the drugs in the CASE-J trial</td>
<td>11.7</td>
</tr>
<tr>
<td>8. No advantage in participation</td>
<td>11.6</td>
</tr>
<tr>
<td>9. High possibility to be a failed trial</td>
<td>9.0</td>
</tr>
</tbody>
</table>

* Denominators for each of the categories were based on the total number of data available for that category. Data did not sum up to 100 because of multiple choices.

* “Strongly agree” and “agree” were combined to generate these values.
that patient factors also play a part in physician non-participation. The limitation of this study is that it did not directly question the patients who refused to take part in this RCT, which could have provided a more complete picture. About one-third (34.9%) of the physicians characterized the data collection procedure as cumbersome, which probably means that they were not comfortable with the Web-based data transmission system offered by the CASE-J trial. Multivariate analysis indicated that physicians aged 50 years or older who were uncomfortable recruiting their own patients, and saw no advantage in participating in the trial, were more likely to consider the enrolment and follow-up procedure cumbersome. This implies that of the physicians, who initially intended to participate in this study, some were not properly motivated, especially those aged 50 years or older, who were not confident about the technical skill needed to perform remote data entry. In a previous study, we reported that physicians aged 55 years or older were more likely to use fax when both Internet and fax were available for data transmission (Rahman et al. 2004). This confirms that older physicians tend to shy away from Web-based clinical trials. The following measures may thus be useful for increasing the rate of physician participation in clinical trials. First, physicians targeted for a proposed clinical trial should be provided with detailed information about the study design and the significance of the trial well ahead of the start of the trial. Second, they should receive formal training or a standardized manual for obtaining informed consent. Third, demonstration, preferably in person, of the Web-based system, for the participating physicians before the start of the trial, and intensive teaching sessions for older physicians who tend to shy away from a Web-based system are essential.

Acknowledgements

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References


