Recruitment and enrollment in a randomized clinical trial of mandibular two-implant overdenture

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PURPOSE. The purpose of this study was to evaluate the effectiveness of a promotion campaign for subject recruitment and selection, and reasons of withdrawal from a prospective clinical trial of mandibular two-implant supported overdenture. **MATERIALS AND METHODS.** The subjects of this study were participants in a randomized controlled clinical trial for investigating prognosis of implants and overdentures with attachments. Recruited subjects were classified by gender, age, and participation motives. Withdrawal rate of the participants before and after enrollment were evaluated. **RESULTS.** 177 patients were recruited and 51 patients were enrolled for the trial. Among them, 40 participants eventually took part in the trial. 116 subjects (65.5%) were recruited by advertisement and 61 (34.5%) were referred by patients of the hospital or local clinics. Regarding recruitment effectiveness, newspaper recruited the largest number of participants. With respect to referral patients, the proportion of our hospital patients was higher (37/61). Subjects in their 70s comprised the largest proportion (22/51). The male to female ratio was similar (25:26). Final withdrawal rate of all subjects were 74.0%. Among the reasons for withdrawal from enrollment (n=126) presence of remaining teeth and lack of motivation were the most common reasons. **CONCLUSION.** To facilitate recruitment of clinical trial subjects and improve enrollment rate, it is important to obtain a sufficient number of researchers, perform promotion activity with diverse strategies, cooperate with local dentists, increase the research funding, and alleviate subjects' fear against clinical trials by thorough consultation. ***[J Adv Prosthodont 2013;5:204-8]***

KEY WORDS: Mandibular implant overdenture; Clinical trial; Recruitment; Enrollment

INTRODUCTION

The value of clinical trial depends on the reliability of the study results. A well-designed clinical study helps clinicians select the most appropriate treatment option. The development of evidence-based medicine guides the best methods to increase reliability of clinical trials.

The randomized clinical trial (RCT) is regarded as the most reliable method of clinical study. However, clinical trials on patients require substantial amount of cost and time.[1] In addition, recruitment of subjects and execution of the experiment are difficult. Many researchers overestimate the pool of qualified participants. Even when the patient pool for the specific disease is sufficient in the institution where researcher belongs to, the number of screened patients who eventually enroll is frequently much less than the researcher's expectation.[2]

Various recruitment approaches have been proposed and effective recruitment interventions vary according to the type of clinical trial and target groups. Even after enrollment, subjects are often excluded from clinical trials due to various reasons. First, types of the recruitment

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interventions were not systemically set. Second, not many studies properly plan for the recruitment and withdrawal of the subjects. Finally, different recruitment approaches are required for each clinical trial depending on the unique characteristics of the disease of focus. Although clinical research is becoming more important, not many studies have proposed guidelines for encouraging recruitment and participation of subjects based on clinical trial experiences, especially in the prosthodontic field.[1] Therefore, this study aims to comparatively evaluate effectiveness of the promotion campaign during subject recruitment and selection process and reasons for withdrawal of a prospective clinical trial of mandibular two implant supported overdenture.

MATERIALS AND METHODS

Subjects of this study were participants of a randomized controlled clinical trial for investigating prognosis of implants and prostheses. This study was designed to place two implants in the mandible on patients with edentulous upper and lower. After healing period, two different ball attachments were connected to the fixtures.

This study was approved by the Institutional Review Board of Korea University Medical Center (KUMC) Guro Hospital (approval No. MD 1036) and was granted by the Korea Health Industry Development Institute (grant number A100669).

The disease of focus in this study was maxillary and mandibular edentulism. Inclusion and exclusion criteria were as follows:

Inclusion criteria of the subjects

- Complete edentulous patients or complete denture wearer in the mandible and maxilla
- Complete denture wearer with adequate occlusal plane, occlusal relationship, and lack of severe attrition of the artificial teeth
- Absence of prolonged disorders such as TMJ disorders and soft tissue lesions
- Motivated adults younger than 85 years old and
- Available residual alveolar ridge in the lower anterior region is 10 mm or more in height with sufficient buccolingual width
- Patients who consented to participate in the clinical trial and signed on the subject consent form

Exclusion criteria

- Pregnancy
- Recent history of myocardial infarction
- Uncontrolled systemic disease and bleeding disorders
- Presence of mental illness or when mental illness is suspected
- Hypersensitivity to implant materials
- Ethically inappropriate or when the subject's participation may affect results of the clinical trials at research director's discretion
- When performing implant surgery is difficult for the patient

Participants' treatment expenses were exempted by the government research grants except for fabrication of complete denture. Patient's existing dentures were relined or rebased and new complete denture was fabricated at the patient's expense when repair of the denture was not advised.

We assumed a confidence level of 95% and power of 80%, so 48 subjects were selected. Oral examination was conducted on applicants who met eligibility criteria at the preliminary telephone interviews. Phone interviews included simple questions to find out if they were aware of details of the clinical trial, current oral health status, and purpose of the application.

Interventions to promote recruitment were publishing health-related articles in the daily newspapers through the public relations department in the hospital, conducting interviews with dental newspapers, giving education sessions on denture use and maintenance, educating at local senior citizen welfare centers, and presenting posters in the hospital. Patients who were introduced by affiliated local dental clinics or subjects who were taking part in other clinical trials were also included in the study. Recruited subjects were classified by gender, age, and participation motives. Withdrawal rate of the participants before and after the enrollment were evaluated. In addition, withdrawal rate according to the reasons of withdrawal were calculated and compared.

RESULTS

A total of 177 patients were recruited. 51 patients met the selection criteria and were enrolled for the trial. Among them, 40 patients actually participated in the clinical trial.

Regarding types of recruitment interventions, 116 subjects (65.5%) were recruited by the advertising campaign and 61 patients (34.5%) were referred from patients of our hospital or local clinics. Regarding promotion effectiveness, newspaper promotion recruited the largest number of subjects, followed by internet articles and "education session on a denture". Printed advertisement such as posters recruited the least number of subjects. With respect to referred patients, the proportion of our hospital patients was higher (37/61), followed by referral patients from other hospitals or local clinics and those introduced by participants of other clinical trials (Fig. 1). Ages of the subjects ranged from 50s to 80s and subjects in their 70s occupied the largest proportion (22/51) (Fig. 2). The male to female ratio was similar (25:26) (Fig. 3).

Final withdrawal rate of all subjects were 74.01%. Withdrawal rate of patients who were recruited by advertisement (87.9%) was higher than those of referred patients (57.4%) (Table 1). Reasons of withdrawal from enrollment (n=126) were lack of motivation, treatment expenses (for fabrication of new complete dentures), presence of remaining teeth, systemic disease, long distance from participants' residence, lost contact, inadequate residual alveolar bone, poor oral hygiene, and decision to receive an alternative

Table 1. Applicants and withdrawal ratio in the study

Recruitment interventions	Type	Recruited	Enrolled	Withdrew	Withdrawal rate (%)	
Advertisement (116)	Newspaper	49	5	44	89.8	
	Internet	26	4	22	84.62	87.9
	Education	26	2	24	92.31	
	Poster	15	3	12	80	
Referral (61)	In clinic	37	16	21	57.75	
	Local clinic	18	9	9	50	57.4
	Participant of other trials	6	1	5	83.33	
		177	40	131	74.01	

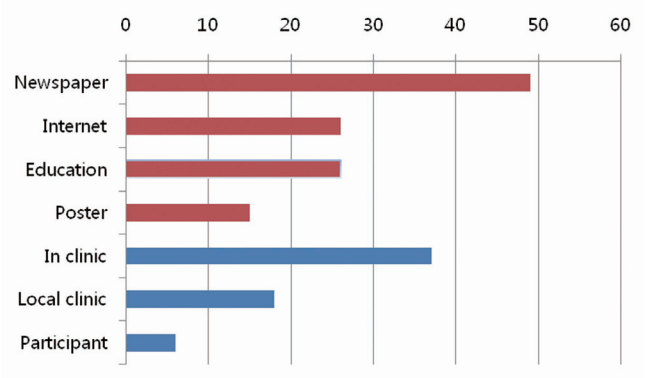

Fig. 1. The number of participants according to recruitment approaches (n=177).

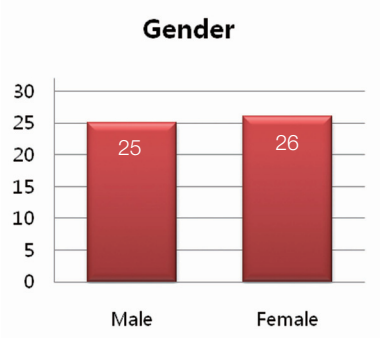

Fig. 3. Gender distribution of participants (n=51).

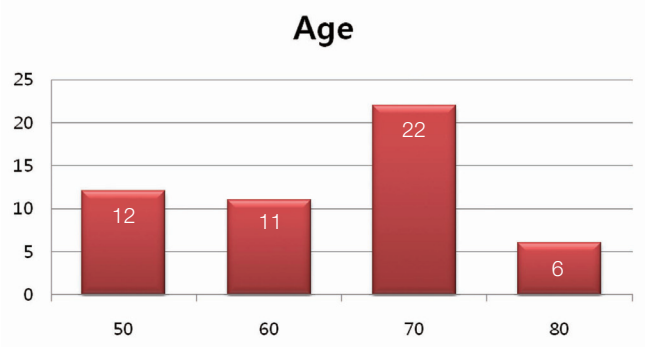

Fig. 2. Age distribution of participants (n=51).

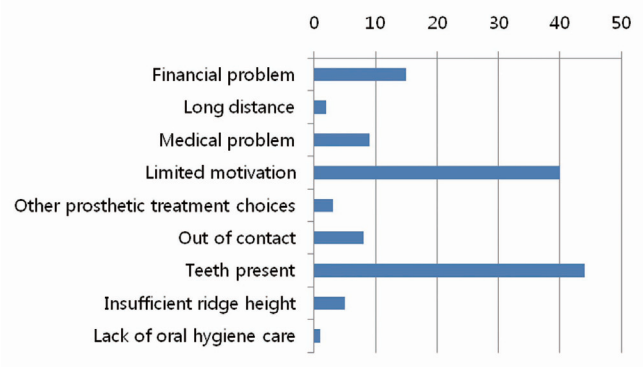

Fig. 4. Reasons for exclusion from this study (n=177).

treatment. Among them, presence of remaining teeth and insufficient motivation were the most common reasons. Insufficient motivation was due to fear against implant surgery and uneasiness for multiple visits to finish the treatment. However, details of insufficient motivation were not classified. Major reasons of withdrawal after enrollment (11 subjects) were because of deterioration of general health (5/11) and insufficient motivation (3/11) (Fig. 4).

DISCUSSION

One out of three patients who wears a conventional complete denture is not satisfied with the denture.[3] This is especially true with the lower denture. Two implant supported overdenture in the mandible is recognized as "the first treatment of choice" at the two consensus conferences for complete edentulism.[4-6] Patient satisfaction is exceptionally

high with this treatment modality. An implant supported overdenture is the optimally compromised treatment option. It overcomes the disadvantages of mandibular complete denture and does not require extensive surgery with reasonable expenses. This study started from the realization that many conventional denture wearers can be recruited as subjects because of discomfort of their dentures. The high proportion of denture wearers in our hospital was expected to be advantageous to recruit subjects.

Walton and MacEntee[1] recruited 86 subjects from 220 applicants at their prospective study on the mandibular implant supported overdenture. Patients from their university hospital occupied a high proportion (57%) of the final subjects and enrollment rate was 77%. Less people applied by advertisement or referral. This study was the good example of a clinical trial with sufficient patient pool. However, it is very unusual to have a good research environment like this. Walton and MacEntee[2] offered free implant treatment to edentulous patients. They expected people who were not satisfied with their full dentures would readily accept the offer. However, 30% of the subjects rejected implants for various reasons. The major reason was a difference of recognition about the treatment by researchers and subjects.

Many researchers with experiences in clinical trials agree that the most important factor for success of the research is recruitment of subjects[1,7] and that most mistakes were overestimating the number of subjects they can recruit. In other words, many fewer people in the subjects' pool end up joining the clinical trials as subjects. A systematic review of various recruitment interventions by UyBico *et al.*[8] found that secondary barriers included distrust of research, lack of confidentiality, fear of safety, schedule conflicts, poor access to medical care, lack of knowledge, language, and cultural differences.

Most edentulous patients were elderly people. Recruitment of older people is more challenging than recruitment of other age groups. McHenry *et al.*[9] reported that clinical trials of old adults are faced with more difficulties. Barriers of recruitment were distrust, inconvenient transportation, caregivers' burden, general health status, indifference, decrease of cognition and sensation, and physical and mental weakness. This study found similar reasons of withdrawal from enrollment.

Accurate assessment and diverse strategies are required on the barriers of the recruitment for successful recruitment and high enrollment rate. Galbreath *et al.*[7] described factors for successful recruitment of subjects: securing key study personnel in charge of the research; provision of an educational program to increase understanding of the clinical trial process; and allocating sufficient time. Nasser *et al.*[10] stated that access to an adequate number of persons who fit the study inclusion criteria and professional and intensive recruitment process are two key factors to improve subject participation. UyBico *et al.*[8] reported that although promotion is effective in recruiting subjects, efficiency is questionable due to the cost and low enrollment rate. According to their systematic review, however, the most commonly attempted recruitment interventions included social marketing and interaction with community organizations or meetings in most studies. A dental hygienist was designated as a key study personnel and supervised recruitment processes and promotion activities in this study. Although promotion and education by the key study personnel was effective in recruiting applicants, enrollment rate was not high. Therefore, recruiting as many participants as well as high enrollment rate are crucial for successful clinical trials.

Caldwell *et al.*[11] evaluated recruitment strategies in their systematic review. They found that types of clinical trials, recruiters, incentives, and methods of providing information were factors affecting success of recruitment. Recruiter differences did not seem to affect recruitment. Interestingly, the internet database was more efficient than a paper-based database (with shorter time required for data collection and more patients being exposed to the trial). In addition, monetary incentives increased recruitment although the difference was not statistically significant and there is a risk of adverse effect.[11,12] Conversely, subjects were recruited without provision of any financial gain in this study except treatment expenses for implant placement and attachment connection. Although opinions varied widely, financial incentives have a risk of lowering confidentiality of the treatment and can jeopardize trial results. Thus, we decided not to provide monetary incentives in spite of difficulty in recruitment.

Caldwell *et al.*[11] stated that the most efficient recruitment strategy was giving a series of educational sessions and engaging participants in the learning process using various methods of delivering the recruitment material. They also predicted that interactive internet-based strategy will be useful method to provide information. However, this literature was based on evidence in the medical field and may not be directly applicable to dental field. As in this study, enrollment rate of participants at the education sessions such as denture class was not high on the contrary to our expectation. This was because most subjects were senior citizens; younger caregivers were more likely exposed to details of the clinical trial process or educational materials; and patients were already aware of the target disease of edentulism by experience rather than learning by educational sessions.

Bader *et al.*[13] reported their personal experience of carrying out clinical trials by setting up diverse strategies for recruitment. We expected that most subjects could be recruited from the patients at our hospital at the early stages of the study. However, recruitment of participants did not proceed smoothly and various recruitment strategies were employed. We conducted denture educational sessions to educate and recruit potential participants in the community. Participants were also recruited by referral from affiliated hospital or clinics. Among the various approaches, enrollment rate was highest in patients of our hospital and referral patients from community hospitals and clinics. This

shows that decision and recommendation of dentists with professional knowledge played a key role in recruitment success.

The most common reasons for withdrawal from the trial were presence of remaining teeth and lack of motivation. Patients with remaining teeth either did not thoroughly understand the details of the trials or do not wish to extract remaining teeth. Insufficient motivation was due to misunderstanding that no surgery was involved in the trial, fear against surgery, and uneasiness for multiple visits to finish the treatment. These factors seemed to be barriers for elderly participants as mentioned before. Education and instruction by sufficiently trained professionals will improve enrollment of participants to increase patients' understanding on the clinical trial process and reduce fears against treatment.

Expenses for fabricating new denture occupied large proportion of the reason of withdrawal (15/126). Other minor reasons of withdrawal include excessive resorption of the mandible and systemic disease. Considering the older age of participants in this study, several patients' general health suddenly deteriorated after enrollment. One participant concealed his general health condition and was discharged from the trial after the health condition was discovered. Although enrollment would have been increased if financial incentives had been provided during the clinical trial, it will require an enormous amount of money. It is the researcher's task to achieve excellent outcomes from clinical trials with limited budget.

CONCLUSION

To facilitate recruitment of clinical trial subjects and improve enrollment rate, it is important to obtain a sufficient number of researchers, perform promotion activity with diverse strategies, cooperate with local dentists, increase the research funding, and alleviate subjects' fear against clinical trials by thorough consultation

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