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ORIGINAL RESEARCH

Scientific research with individuals post stroke: difficulties in recruitment, allocation and adherence on two different protocols of physiotherapy intervention

Pesquisas científicas com indivíduos pós Acidente Vascular Encefálico: dificuldades no recrutamento, alocação e aderência em dois diferentes protocolos de intervenção fisioterapêutica

Las investigaciones científicas con sujetos que sufrieron accidentes cerebrovasculares: dificultades para el reclutamiento, destinación y adherencia en dos diferentes protocolos de intervención fisioterapéutica

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ABSTRACT | This study analyze the difficulties in recruitment, allocation and adherence of individuals with hemiparesis after stroke in the development of two randomized clinical trials (RCTs). For this, data were extracted from two RCTs that investigated patients with hemiparesis due to stroke, living in Florianópolis, aged over 40 years. RCTs interventions were based to task-oriented training and were performed evaluations at three different times (pre, post, follow-up). The sample calculations determined the need of 54 participants for Study I and 36 for Study II. The quantitative data were analyzed using descriptive statistics and qualitative information through the content analysis. It was found that of 127 potential participants, it was not possible to contact 18.1%, and 5.5% came to death. In preselection 6.3% were hospitalized/bedridden, 7% had no interest and 4.7% were unable to transport. During allocation 33% were excluded for not meeting the eligibility criteria. Among 32 patients who remained in the study, 16% missed the Study I and 2.5% the Study II. Wrong contact data, lack of resources for transportation, eligibility criteria and lack of interest were the factors that hindered the recruitment of subjects. Therefore, we suggested that the relations improvement between research centers and institutions, the proper recording of contacts, access to clinical records, the availability of financial resources to support the recruitment and transportation and increased funding for RCTs can improve the viability of this type of study in Brazil.

Keywords | Patient Selection; Clinical Trials as Topic; Paresis.

RESUMO | Este estudo busca analisar as dificuldades no recrutamento, alocação e aderência de indivíduos com hemiparesia pós AVE no desenvolvimento de dois Ensaios Clínicos Randomizados (ECR). Para tanto, foram extraídas informações de dois ECR que investigaram pacientes com hemiparesia devido ao Acidente Vascular Encefálico (AVE), residentes na Grande Florianópolis, com idade superior a 40 anos. Nos ECR foram realizadas intervenções baseadas no treinamento orientado à tarefa e avaliações em três momentos distintos (pré, pós, seguimento). Os cálculos amostrais determinaram a necessidade de 54 participantes para o Estudo I e 36 para o Estudo II. Os dados quantitativos foram tratados através da estatística descritiva e as informações qualitativas através da análise de conteúdo. Verificou-se que dos 127 potenciais

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participantes, não foi possível contatar 18,1%, e 5,5% vieram a óbito. Na pré-seleção, 6,3% estavam internados/acamados, 7% não tinham interesse e 4,7% não tinham condições de transporte. Durante a alocação, 33% foram excluídos por não atenderem aos critérios de elegibilidade. Dentre os 32 pacientes que permaneceram nos estudos, 16% faltaram ao Estudo I e 2,5% ao Estudo II. Dados de contato equivocados, falta de recursos para transporte, critérios de elegibilidade e ausência de interesse foram os fatores que mais dificultaram o recrutamento dos indivíduos. Portanto, pode-se sugerir que a melhora entre os centros de pesquisa e as instituições, o registro adequado dos contatos, o acesso aos registros clínicos, a disponibilidade de recursos financeiros para auxílio ao recrutamento e transporte e o aumento do financiamento para ECR podem melhorar a viabilidade deste tipo de estudo no Brasil.

Descritores | Seleção de Pacientes; Ensaios Clínicos como Assunto; Paresia.

RESUMEN | Esta investigación tuvo por objetivo analizar las dificultades en el reclutamiento, destinación y adherencia de sujetos con hemiparesia post accidente cerebrovascular (ACV) en el desarrollo de dos Ensayos Clínicos Aleatorizados (ECA). Para eso, se recolectó informaciones de dos ECAs los que hicieron estudios con pacientes portadores de hemiparesia debido al ACV, que vivían en la ciudad de Florianópolis, Brasil, con edad superior a 40 años. En los ECAs se han hecho intervenciones basadas en la capacitación orientada a la tarea y evaluaciones en tres ocasiones distintas (pre, post, seguimiento). Los cálculos de la muestra determinan la necesidad de 54 participantes para el Estudio I y 36 para el Estudio II. Los datos cuantitativos se han tratados a través de la estadística descriptiva y las informaciones cualitativas a través del análisis del contenido. Se han comprobado que de los 127 potenciales participantes, no ha sido posible contactarse con el 18,1%, el 5,5% fallecieron. En la preselección, el 6,3% estaban hospitalizados/encamados, el 7% no tenían interés y el 4,7% no tenían condiciones de transporte. Durante la determinación, el 33% han sido excluidos por no cumplir los criterios de elegibilidad. Entre los 32 pacientes que han permanecido en los estudios, el 16% no han comparecido al Estudio I y el 2,5% al Estudio II. Los datos de contacto equivocados, la falta de recursos para el transporte, los criterios de elegibilidad y el ausente interés en participación han sido los factores que más causaron dificultades al reclutamiento de los sujetos. Por lo tanto, se puede hacer una sugerencia a la mejora entre los centros de investigación y las instituciones, el registro adecuado de contactos, el acceso a los registros clínicos, la disponibilidad de recursos financieros para auxiliar en el reclutamiento y transporte y el aumento de los fondos para la ECA pueden ayudar a mejorar la viabilidad de este tipo de estudio en el Brasil.

Palabras clave | Selección de Pacientes; Ensayos Clínicos como Temas; Paresia.

INTRODUCTION

Clinical research, especially randomized clinical trials (RCTs), has the potential to provide real evidence regarding the effects of different treatments in health care. It is possible for records that hold information about the problems encountered in the recruitment and retention of patients, for purposes of performing clinical trials, to afford assistance in terms of developing strategies to overcome such challenges[1].

Recruitment refers to the process of selection that begins with communication between the researcher and potential participants, the objective of which is to obtain a representative number of the target population so to meet the demands of the sample size and the power of the study. Patient association or retention is the process of maintaining participants within the study[2].

Recruiting patients may be considered one of the most difficult aspects of the research process[3,4]. Half of all clinical trials fail in their objective to meet the quantitative sampling target[5]. Such difficulty in recruiting or retaining participants can have a negative effect on the statistical power of the study, leading to inconclusive results, increasing the evaluation duration, delaying the response of an appropriate intervention or resulting in a premature termination of the tests[3-6].

Clinical studies involving post-stoke (cerebrovascular accident) participants may experience several difficulties in recruitment, the main reasons being due to a lack of desire to participate, complex protocols, strict eligibility criteria, exhaustive testing and lack of resources, such as transport for the participants[4].

Information regarding the adherence and permanence of the participants is important; this is because it reflects the suitability of a treatment towards the target population and must be considered while developing appropriate training protocols[6]. With this in mind,

the objective of this study was to examine difficulties in terms of the recruitment, allocation and adherence of patients with post-stroke hemiparesis while developing two RCTS.

METHODOLOGY

The data analyzed in this article were provided by two RCTS, approved by the Committee for Ethics in Research in Humans, registered under the *Brazilian Registry for Clinical Trials* (ReBEC) and developed by the *Laboratory for Motor Control*, at the State University of Santa Catarina (UDESC) between November 2010 and November 2011.

The participants who showed post-stroke hemiparesis lived in Greater Florianópolis, they were over 40 years of age and had been identified at the Municipal Physiotherapy Clinic of Biguaçu/SC, the *Catarinense* Rehabilitation Center, the CEFID/UDESC Clinical Physiotherapy School and the "Health Care for Persons after a Cerebral/Encephalic Vascular Accident" extension project, totaling 127 individuals.

Individuals were recruited in order to participate in two RCTS, who used interventions based on task-oriented training with a view to improve paretic upper limb activity. Evaluations were performed in three distinct periods: pre-, post-training and follow-up.

After the data collections were completed, analysis began regarding the difficulties encountered during the recruitment, allocation and adherence of participants during the interventions proposed by the RCTs.

Study Descriptions

The quantitative samples from studies I and II were delineated according to criteria appropriated to experimental research in the health area[7], this in accordance with the following equation: $n=Z^2\times S^2\div d^2$, in which "n" is the sample size, "Z" is the number of standard deviations, "S" is the value of standard deviation and "d" is the difference in acceptable tolerance. After applying the compensation percentage for possible sampling losses, the sample calculations determined that 54 and 36 participants would be needed for studies I and II, respectively. This number represented approximately 70% of the 127 subjects who were identified as candidates to participate in the research.

Study I examined the effects of training with a mirror associated with symmetric functional tasks and systematic progression compared to the control group. The training was based on visual feedback through the mirror *(Mirror Therapy)*, in which the mirror is positioned at right angles between the two upper limbs, the individual is then advised to carry out simultaneous bilateral and symmetrical movements with their hands, while watching their arm's reflection in the mirror[8].

Study II assessed effect-oriented training on bilateral tasks during upper limb function recovery in patients with hemiparesis, compared to conventional physiotherapy. Intervention was based on bilateral training aiming at including the paretic upper limb (UL) in daily life activities.

Individuals who were in the chronic phase following a unilateral stroke (≥6 months post-stroke) were included in studies I and II. Those capable of performing rudimentary holding tasks, with moderate impairment of the UL, were included in Study I (between 30 and 49 points by the Fugl-Meyer-Scale (FMS)); Study II included those with severe impairment (<30 FMS points).

The following individuals were excluded: those who had other neurological disorders, orthopedic problems in the upper limbs that interfere with their function, bilateral impairment, painful shoulders, difficulty in understanding simple commands and for already being a member of other study involving the upper limbs.

All clinical evaluations for studies I and II were performed by trained physiotherapists. The interventions were performed at the participant's home or at the CEFID/UDESC Clinical Physiotherapy School. Follow-up assessments were performed two weeks after the interventions were completed.

Information extraction procedures

Information regarding the encountered difficulties were taken from the data, from studies I and II, related to the stroke history (occurrence date, number of incidents, affected side) and the clinical condition (dialog establishment, ability to speak, walk, move the impaired arm and pick up objects with the affected hand). After this information was processed, the participants were evaluated by way of interview over the telephone or through personal contact, which focused on the participants' difficulties.

Information handling

The variable analyses from studies I and II were handled by means of descriptive statistics (mean, standard deviation and percentile). The information collected during the telephone interviews were handled through a content-analysis technique, this was performed so as to describe the reported information and to allow knowledge to be inferred relative to response interpretation conditions[9]. Following the data systematization, the information content to be categorized into thematic blocks was selected.

The difficulties encountered during the RCTs (studies I and II) were evaluated by means of 'a priori' established categories. This procedure's adoption made it possible to understand the difficulties and extract the most significant elements by means of systematizations and objectivations which provided inferences regarding the processed information[9]. For both, the categories were defined as: a) recruitment; b) allocation, and c) adherence (Table 1).

Table 1. Study Feasibility Categories

Clinical Study Feasibility	
Recruitment	Telephone access number and evaluation scheduling, interest and difficulties to reach the evaluation location, individuals who are bedridden hospitalized or had passed away
Allocation	Inclusion and exclusion criteria, random drawing and allocation of experimental and control groups
Adherence	Acceptance (Term of Free and Informed Consent); Presence and permanence (attendance during evaluation and intervention sessions and reason for absence)

RESULTS

Recruitment

Figure 1 shows the recruitment difficulties. The first difficulty came from incorrectly reported phone numbers or it being impossible to contact the individuals (18.1%). During the pre-selection, 7.2% of the total number of individuals demonstrated no interest in participating, 6.3% were hospitalized or bedridden and 4.7% reported difficulties with transportation.

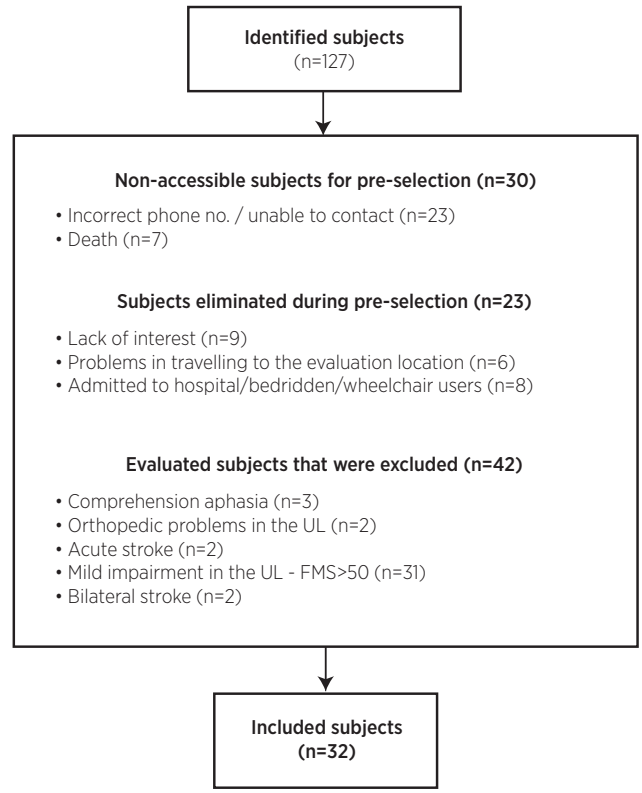

Figure 1. Schematic representation of patient recruitment

Allocation

Following the assessments, 42 individuals (33% of the total) were excluded because they did not conform to the eligibility criteria. Of these, 31 were excluded because they had a light impairment of the UL (FMS>50) (24.4% of the total and 73.8% of those excluded by the eligibility criteria).

16 individuals with moderate motor impairment and 16 with severe motor impairment of the UL were eligible to participate in studies I and II, these were randomly divided into the experimental group (EG) and the control group (CG) (Figure 2). The randomization was based on a sequence of computer generated random numbers that were placed inside numbered and sealed opaque envelopes.

Adherence

According to the protocol established in Study I, each participant, from both the EG and the CG, should perform one-hour sessions three times a week for four weeks, totaling 12 practice hours. In Study II, each participant should perform one-hour sessions five times a week for two weeks, totaling 10 practice hours.

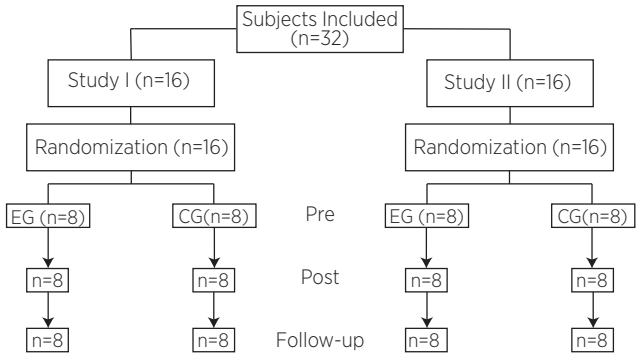

Figure 2. Allocation of subjects from the studies

The total number of sessions in Study I was 192 (12 sessions per patient), out of which 32 were missed, representing 16% of the total. Among the recorded reasons for the absences were: patient illness (28.1%), deaths in or problems with the family (18.7%), forgetfulness (12.5%), medical appointments (9.3%), unscheduled trips (9.3%) and house moving (6.2%).

Study II totaled 160 sessions (10 sessions per patient) with four absenteeisms, representing 2.5% of the total. Medical appointments were the only recorded reason for these absences (100%). Only two patients in this study who attended appointments at the CEFID/UDESC Physiotherapy clinic did not miss a session. The other participants were treated at home.

These absences were resolved through timetable rescheduling. All 32 patients had the same number of sessions as per the proposed interventions. No individual abandoned or withdrew from the treatment.

DISCUSSION

Recruitment

Data from the Brazilian national health system, DATASUS[10] and the Brazilian Institute of Geography and Statistics[11] have shown that during 2010 and 2011 the total population in Greater Florianópolis was 877,116 people. The hospitalization rate caused by stroke in the region's hospitals was 8.1%[11], which represents 71,046 individuals who were interned during this time in Florianópolis. Among these, only 127 individuals registered themselves on the contact waiting lists at the clinics for this research. The assumption is that the reduced number of patients identified is either because the researchers failed to obtain access to the records for stroke individuals that are made available by DATASUS, thereby limiting the patient list submitted through the Polyclinics in Florianópolis to the CEFID Clinical Physiotherapy School and/or the long list at the Catarinense Rehabilitation Center, where patient registration data might not have been recorded.

The fact that incorrect phone numbers were given proved to be the greatest factor that hindered recruitment. It is likely that the patients did not update their data or health professionals responsible for re-registering individuals did not do so correctly. This failure to obtain patient registration data from rehab clinics reflects the lack of training of the health professionals at these units - who are the first contact for patients in terms of gathering important data. As a result, 18.1% of individuals could not be contacted due to registration errors.

Among the main obstacles encountered in recruiting patients, it is possible to highlight the lack of direct access to the data of patients who had high hospitalization rates, this in order for them to be referred to rehab clinics or health centers, and the lack of connection between clinics and research centers. As a strategy, the research projects could be extended to hospitals, which are responsible for first contacts and follow-up of patients in the first few months. In addition, many patients end up not going through the Brazilian National Health Service (SUS) network for many different reasons, such as: transportation difficulties to the consultation locations, difficulties to physically move, by being bedridden or hospitalized, lack of family support, delays in being seen, among others[6,12].

One of the main reasons for non-participation in studies I and II was found to be the difficulty in terms of transport. As a result, some individuals reported to not be interested, but actually they were not able to get to the location where the evaluations and interventions were held. Similarly, another study[4] reported that the lack of resources for transportation was singled out as the main barrier to post-stroke individuals' participation and presence during research projects in Brazil. Among the 150 patients who were selected for clinical trials, 40% did not participate because of transport difficulties, while 32% missed their sessions because of the same difficulties, thereby compromising adherence. In contrast, in this study, such absences were minimized because most patients had their treatment at home and all participants completed all evaluation and treatment stages. Transportation difficulty was only a factor for a few evaluations during the pre-selection (4.7%) and for some appointments that were performed at the clinics.

Meanwhile, the costs incurred from commuting to the patient's homes were bore by the researchers themselves.

A study involving post-stroke individuals in Australia[13], which provided transportation for patients throughout the intervention period, had a recruitment rate of 51%; the rate for this study was 25.2%. Research performed in developed countries depend not only on investment for patient transport, but also on financial compensation for patients who decide to be involved in the surveys, which means that participation is even greater. In Brazil, the difficulty in finding funds for transportation and/or to pay a technician to perform the recruitment hinders the progress of many studies. However, although it might be said that there is lack of resources for investment in research, it should be noted that often financial resources do exist, but they are used for other purposes. During other RCTs, conducted at the patients' homes, it was observed that only 3 of the 20 subjects treated would have had the means to travel, if the test had not been performed at home[14].

As a result, it is possible to suggest that providing transport for patients would increase recruitment and retention rates[4], but would not completely solve the problem. This possibility is based on the fact that family attitude often ends up discouraging the retention of these patients in research groups, this happens due to the families not accompanying them to sessions, not encouraging them to participate and restricting them, this could be due to fear or for ignoring the importance of these studies in terms of improving rehabilitation. Sometimes, the patient is able to take the bus, but the family does not allow this to happen.

One study on the difficulties in patient recruitment rates for those with Parkinson's disease in an RCT reported that one of the main obstacles to recruitment, in addition to the lack of financial resources for transport to the training location, was the lack of interest and by not being accompanied[6].

The lack of interest regarding participation can come from a lack of financial resources, low or a lack of family encouragement, a lack of instruction regarding the importance of treatment and no motivation, which is caused by the depression that the disease itself causes. One study, which involved 3,626 post-stroke patients in the United States, observed that only 6% of individuals agreed to participate in the study, even when reimbursement of expenses for transportation, parking and food was available[3].

Allocation

In this study, 33% of the total number of individuals were excluded due to not meeting the eligibility criteria. This barrier was imposed by the researchers themselves in order to make the study even more thorough, the final objective being to reduce the biases caused by interested individuals being excluded.

Similarly, during recruitment for one RCT, after selecting 552 patients, only 49 were eligible[15]. Other research project selected 582 stroke patients, and from these, only 100 (17%) were eligible[16]. Whereas, in another study which identified 150 stoke patients, 77% were excluded because they did not meet the inclusion criteria as defined in that study[4]. It soon became clear that eligibility criteria constitute a factor that contributes to patient recruitment and allocation limitation, despite both being necessary in order to achieve more consistent results.

Adherence

Studies I and II showed that those subjects who had their own car and those who underwent treatment in their own homes missed less sessions. The largest number of missed sessions in Study I was due to the fact that there were four weeks of intervention and most patients did their intervention sessions at physiotherapy clinics. In Study II, the reduced number of absences, compared with Study I, may have been a result of the fact that there were only two weeks of intervention and only two patients received their treatment at the clinic; the others received home treatment.

The researchers encouraged participant attendance at the sessions through motivational exercises with progression, patient-centered functional goals and activities performed with real objects. The team's characteristics, in terms of their welcoming attitude and friendliness, created a trusting atmosphere that is essential for promoting patient motivation and retention during RCTs[7].

The fact that there were home visits in this study also resulted in there being the fewest absences during the interventions. However, the physiotherapists who performed the patients' home training pointed out some difficulties, namely: difficulty in accessing the patients' residence, due to road construction, difficulty in loading the required material, households elements that made patient concentration difficult and households located in high crime neighborhoods.

Based on all the data, it is possible to understand that, in order to achieve the greatest participation from post-stroke individuals in an RCT, the best method would be to perform interventions at the patient's residence. However, given all the difficulties already referenced, especially those that note that many pieces of necessary equipment are not portable, it seems that offering indiscriminate in-house interventions would produce incomplete results.

CONCLUSION

Incorrect contact information, lack of transportation resources, stringent eligibility criteria and lack of interest were the factors that most hampered the recruitment of individuals. Despite the aforementioned difficulties, performing RCTs must be encouraged. Closer contact between health managers and researchers is required, because if more accurate information about registered stroke patients in cities and hospitals is obtained, it can provide, among others things, greater accuracy regarding contact records. In order to improve adherence, home interventions and patient-centered goals were determining factors, despite the various constraints that may occur. However, funding to supply a member of staff for recruitment at the hospital and resources being made available by financial agencies for longer periods of time can still improve the viability of this type of study in Brazil.

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