



**PATIENTS' ADHERENCE TO MEDICATION IN CLINICAL TRIALS**  
**ADESÃO DE PACIENTES À MEDICAÇÃO EM ENSAIOS CLÍNICOS**  
**ADHESIÓN DE PACIENTES A LA MEDICACIÓN EN ENSAYOS CLÍNICOS**

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**ABSTRACT**

**Objective:** check patients' adherence to medication in clinical trials. **Method:** this is a descriptive, quantitative, and cross-sectional study with 80 patients who participated in 6 multicenter trials conducted by an integrated research center by means of a questionnaire. Data were analyzed using the statistical tests *Student's t* and *Fisher's*. This study was approved by the Research Ethics Committee of Faculdade de Medicina de São José do Rio Preto (Famerp), under the Opinion 4007/2007. **Results:** we found out that there was a statistically significant relationship between education level and the issue of failing to take medication for some reason. We observed an association between those who stopped taking the study medication for any reason and the need for help to use the medication, showing that the person who says to need no assistance is that presenting the worst compliance with treatment. **Conclusion:** the nurse, as coordinator of clinical trials, must reinforce guidance to patients with low education level and stay tuned to reports of people who say they need no help. **Descriptors:** Adherence To Medication; Clinical Trial; Nurse.

**RESUMO**

**Objetivo:** verificar a adesão de pacientes à medicação em ensaios clínicos. **Método:** trata-se de estudo descritivo, quantitativo e transversal com 80 pacientes que participavam de 6 estudos multicêntricos de um centro integrado de pesquisa por meio de questionário. Os dados foram analisados por meio dos testes estatísticos *t de Student* e *Fisher*. Este estudo foi aprovado pelo Comitê de Ética em Pesquisa da Faculdade de Medicina de São José do Rio Preto (Famerp), sob o Parecer n. 4007/2007. **Resultados:** constatou-se que houve relação estatisticamente significativa entre o grau de escolaridade e a questão de deixar de tomar a medicação por algum motivo. Foi evidenciada associação entre quem deixou de tomar a medicação do estudo por algum motivo e a necessidade de ajuda para o uso da medicação, mostrando que quem diz não necessitar de auxílio é aquele que menos adere ao tratamento. **Conclusão:** o enfermeiro, como coordenador de ensaios clínicos, deve reforçar a orientação aos pacientes com baixo grau de escolaridade e ficar atento aos relatos das pessoas que dizem não necessitar de ajuda. **Descritores:** Adesão À Medicação; Ensaio Clínico; Enfermeiro.

**RESUMEN**

**Objetivo:** verificar la adhesión de pacientes a la medicación en ensayos clínicos. **Método:** esto es un estudio descriptivo, cuantitativo y transversal con 80 pacientes que participaban en 6 estudios multicéntricos de un centro integrado de investigación por medio de un cuestionario. Los datos fueron analizados mediante las pruebas estadísticas *t de Student* y *Fisher*. Este estudio fue aprobado por el Comité de Ética en Investigación de la Facultad de Medicina de São José do Rio Preto (Famerp), bajo la Opinión 4007/2007. **Resultados:** se constató que hubo una relación estadísticamente significativa entre el nivel educativo y la cuestión de dejar de tomar la medicación por alguna razón. Se observó asociación entre los que dejaron de tomar la medicación del estudio por cualquier razón y la necesidad de ayuda para el uso de la medicación, mostrando que los que dicen que no necesitan ayuda son los que menos adhieren al tratamiento. **Conclusión:** el enfermero, como coordinador de ensayos clínicos, debe reforzar la orientación a pacientes con baja escolaridad y estar atento a los relatos de las personas que dicen que no necesitan ayuda. **Descriptor:** Adhesión A La Medicación; Ensaio Clínico; Enfermero.

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## INTRODUCTION

In Brazil, clinical research is a relatively new area of activity, with an increasing interest of researchers from public and private institutions, especially pharmaceutical companies that have been developing new medicines. Multinational companies operating in Brazil, as well as national companies, acquired greater experience in conducting clinical trials involving new medicines, starting with studies at the stages III or IV and today they reach the stages I and II.<sup>1</sup>

This evolution took place by means of the initiative of industries that sponsored these studies and reflected the maturation of clinical research in Brazil, through the Resolution 196, enacted in 1996, from the National Health Council. The Resolution 251/97 from CNS is specific to researches on new pharmaceuticals, medicines, vaccines, and diagnostic tests, as well as clinical researches at the phases I, II, III, and IV.<sup>1</sup>

The study subject selection phase is crucial to conduct the clinical trial and reach the proposed objectives. This screening phase is closely dependent on the inclusion and exclusion criteria defined by the study protocol, and the nurse is a key part of this recruitment process. She/he can also take monitoring, collaborating, and coordinating functions in clinical trials, due to her/his academic training, which comprises technical and scientific knowledge, as well as skills regarding relationship with patients and their relatives. She/he should also have knowledge on the medicines from protocols and strategies to help improving adherence to treatment.<sup>1-4</sup>

The functions performed by the nurse in a clinical research involve many activities during the use of a protocol, such as: recruiting and monitoring patients, registering forms, managing and advising on medicines, as well as participating in research design, protocol implementation, discussion and interpretation of results, therefore, she/he needs to be prepared to deal with issues related to the area under investigation.<sup>5</sup>

The first contact between patient and research center occurs at the time of obtaining the free and informed consent term, when the researcher establishes a bond of relationship with the person, aiming to explain the objectives of the research to which she/he is being invited to participate.<sup>6</sup> In this process, the nurse plays an important role by ensuring that the term is obtained and that the protocol rules are observed,

developing strategies so that the study data are complete and meaningful.<sup>7</sup>

Adherence to treatment is defined and characterized when the medical or health advice coincides with the individual's behavior with regard to the habit of using medicines. That is, following the recommended changes in lifestyle and attending medical consultations.<sup>8</sup> This definition expresses the meaning of *compliance* in English, which implies patient's agreement with regard to recommendations, assuming that she/he knows the therapeutic alternatives and participates in decisions about her/his treatment.<sup>9</sup>

The medicines prescribed or other procedures from the research protocol must have the adherence of at least 80%, taking into account schedules, doses, and length of treatment. The factors that interfere with patients' adherence are varied, such as: access to the medicine, number of doses, adverse effects, patient's perception regarding her/his own illness, coping with her/his symptoms, relationship with the health professional, and understanding of her/his values and beliefs.<sup>10</sup> Having this in mind, this study aimed to check patients' adherence to medication in clinical trials.

The health professionals who work with clinical research perform various activities, such as: guidance with regard to the disease and medicines, monitoring of patients through periodic consultations to evaluate symptomatology, and therapeutic monitoring of drugs. It is crucial to identify the patients who do not show adherence to medication, in order to address the aspects that need to be improvement in the relationship between nurse/team and patient, which, besides helping, contribute to science in the development of new medicines that will benefit the population as a whole.

This study shows to be relevant for the nurse in that it will allow her/him to know the behavior of individuals during their participation in a clinical trial, because she/he will check the elements that help or not in adherence, contributing to new approach and persuasion ways, helping the multi-professional team in further studies. We notice that the difficulties faced along with the patients, at the time of adhering to medication, i.e. when they have to decide leaving the comfort of the medicine they know and control reactions to start using a new drug that has not been sold, yet, generating concern and suspicion that are reflected on the behavior of society when a new drug is made available on the market.

The object of this study is the behavior of the patient who participates in clinical trials instead of the medication effects. It seeks to understand her/his experience as a research subject according to education level, family support, need for help to take medication, length of use, strategies used to not forget, treatment importance, guidelines received, relationship with the professionals involved, and reasons to adhere or not to the proposed treatment and medication, and it is expected that the results point out the agents who facilitate or hinder patients' adherence to medication in clinical trials, helping the professionals who work in this area.

## OBJECTIVE

- Check patients' adherence to medication in clinical trials.

## METHODOLOGY

This is a descriptive, quantitative, and cross-sectional study conducted at the integrated research center (CIP) of a teaching hospital in the state of São Paulo, Brazil, which has a coordinating nurse and cared for an average of 45 patients per month, from 6 multicenter studies in the field of cardiology.

It relied on the participation of 80 patients who met the inclusion criteria: being over 18 years of age, attending the consultation of clinical researches in the field of cardiology in the months of January and February 2010, and signing the free and informed consent term.

Data collection was conducted by the nurse from CIP, by means of an interview with structured questions, at the time of the previously scheduled consultation. The interview had questions on gender, education level, family support, need for help to take medication, guidance with regard to the use, adherence to medication, reason for non-adherence, treatment importance, and the professionals who provided guidance.

First, data were grouped into a spreadsheet in the software *Microsoft Excel* and analyzed using the statistical tests *Student's t* and *Fisher's*. We regarded as significant difference the  $p$  value  $< 0.05$ .

The study was approved by the Research Ethics Committee of Faculdade de Medicina

de São José do Rio Preto (FAMERP), under the Opinion 4007/2007, and the research participants signed the free and informed consent term, complying with the rules of the Resolution 196 /96 from CNS.

## RESULTS

Out of the 80 patients who participated in the study, 50% were men and 50% were women; the average age was  $64.5 \pm 12$  years, most of them had only incomplete Primary Education (75%) and the average length of time using the investigational medication was 15.34 months.

Most patients had family support, 78.75% lived with another person. Regarding the need for help to use the medication, 68.75% reported they do not need it and all participants (100%) said they had received guidance to use the study medication.

As for the adherence to treatment, 90% reported they have never failed to use the medicine and 10% stopped taking it at some time. Among the subjects, 74.63% attributed their clinical improvement to treatment and 25.37% had some cardiac improvement, such as a decrease in dyspnea, fatigue after minimal efforts, and edemas. The majority (90%) received guidance on the importance of adhering to the study medication during their consultations, and the professionals responsible for this guidance were the nurse and physician together (52.50%), in 31.25% of cases only nurses and in 16.25% of cases only physicians.

The interaction between nurse and patient was regarded as good by 95% of subjects, and among the important points in this relationship we may highlight: keeping health (67.50%), helping in the proper use of medication (21.25%), and encouraging the conduction of proper treatment (11.25%). Some patients used strategies to avoid forgetting of the study medicines, and the most cited were: clock (73.75%), leaving them within easy reach (21.25%), and schedule (5.0%), according to Table 1.

Table 1. Presentation of the studied variables. São José do Rio Preto (SP), Brazil, 2011.

Variables	N	%
<b>Age (years)</b>		
50 to 60	17	21.00
61 to 70	50	63.20
71 to 80	13	15.80
<b>Gender</b>		
Female	40	50.00
Male	40	50.00
<b>Education level</b>		
Incomplete Primary School	60	75.00
Complete Primary School	13	16.25
Complete High School or Higher Education	07	8.75
<b>Family support</b>		
Yes	17	21.25
No	63	78.75
<b>Need help to use medication</b>		
Yes	25	31.25
No	55	68.75
<b>Length of time using the study medication</b>		
Up to 1 year	30	36.80
1 year to 2 years	50	63.20
<b>Guidance on the use of medication</b>		
Yes	80	100.0
No	–	–
<b>Stopped using the medication for some reason</b>		
Yes	08	10.00
No	72	90.00
<b>Treatment importance</b>		
Clinical improvement	50	74.63
Cardiac improvement	17	25.37
<b>Guidance on adherence to treatment</b>		
Yes	72	90.00
No	08	10.00
<b>Professional providing guidance</b>		
Nurse and physician	42	52.50
Nurse	25	31.25
Physician	13	16.25
<b>Good relationship with nurse</b>		
Yes	76	95.00
No	04	5.00
<b>Important points of the nurse-patient relationship</b>		
Keeping health	54	67.50
Helping in the proper use of medication	17	21.25
Encouraging proper treatment	09	11.25
<b>Strategy to avoid forgetting of medication</b>		
Clock	59	73.75
Easy reach	17	21.25
Schedule	04	5.00

Statistical tests showed that there was no association of non-adherence to medication between the following variables: age ( $p = 0.73$ ), gender ( $p = 0.71$ ), length of time using the medication ( $p = 0.56$ ), need for family support ( $p = 1.0$ ), treatment importance ( $p = 1.0$ ), whether received guidance on use and adherence ( $p = 0.59$ ), who provided guidance ( $p = 1.0$ ), whether there is a good relationship with the nurse during clinical research ( $p = 1.0$ ), the important points of nurse-patient relationship ( $p = 0.61$ ), and strategies to avoid forgetting to take the medication ( $p = 0.79$ ).

We observed a negative impact of low education level on adherence ( $p < 0.0005$ ), it is lower with incomplete Primary Education than in the other two levels (complete Primary Education or complete High School or Higher Education). We found out that there is no significant difference between the need for help to use the medication and education level ( $p = 0.27$ ). In the union between the two highest education level categories, when compared to incomplete Primary Education,  $p$

$= 0.025$  indicates a “negative” correlation between education level and need for assistance, i.e. a reversed association, those who seem to need more assistance say they do not need it.

## DISCUSSION

The profile of subjects participating in this study was similar to the findings of a cohort study conducted in a public university hospital, in the city of Porto Alegre, Rio Grande do Sul, Brazil, with patients undergoing clinical trials, who had an average age of  $60 \pm 11.1$  years and 50% were men<sup>11</sup>; it was also consistent with the results of a clinical trial conducted with elderly people followed up for 6 years, in California, USA, where age ranged from 72 to 91 years and 58.1% were men.<sup>12</sup>

Most patients reported that the physician and nurse guided with regard to the use of the study medication, however, the nurse was the most cited professional in terms of guidance a good interaction between them was

demonstrated. A study shows that the nurse plays the role of educator of the research subject, explaining about therapy and its benefits, objectives, and, also, adverse reactions and complications.<sup>13</sup>

Among nurse's duties in a clinical research team there lies controlling adherence to the study medication, using strategies such as periodic meetings between patients and the team and/or phone contacts in order to reinforce proper treatment.<sup>14</sup> This corroborates the results of this study as for guidance received and the importance of adherence to treatment.

There are factors directly interfering with patient adherence to medication, such as lack of access to the medicine, complexity, and lengthy treatment, high number of doses, adverse effects, the disease itself, and the person's coping. Another decisive factor is patient's reliance on prescription and, especially, on the healthcare team, which should develop attitudes and skills to use appropriate language and present attention during the consultation, an embracing care, and respect for the individual needs of each patient.<sup>10</sup>

Regarding the importance of the study medication, most patients reported feeling better after using it, especially in terms of cardiac function. A research on adherence to consultations and drug treatment in a clinical trial has shown that patients undergoing long-term follow-up had a loss in adherence, since they had more adverse events and a higher hospitalization rate.<sup>11</sup> In turn, in a literature review about adherence, it was observed that participants who do not adhere to treatments in clinical trials have worse prognoses.<sup>14</sup>

The management of a protocol by the nurse coordinating studies increases the safety and efficacy of a clinical trial. In addition, the nursing process comprises the diagnosis, planning, intervention, and evaluation and it must be performed in all activities.<sup>15</sup> This professional is able to play this role, due to her/his academic training, mainly by means of skills involving the relationship with patients and their relatives.<sup>3</sup>

Nurse's role as a coordinator requires that, along with knowledge specific to the area in which she/he operates (health, management, education, and research), she/he masters fundamentals of group dynamics and management, as well as a strong investment in self-knowledge. The professional who works with confidence and safety allows team members to have a more independent, autonomous, and reflexive action.<sup>16</sup>

Clinical research is a relatively new and interesting field that requires continued improvement and multidisciplinary teamwork, with good interaction between all participants. The nurse, besides following the entire process of random allocation, monitors adherence to the study medication, exclusions, and possible subject withdrawals, registering all data in control spreadsheets, provides storage, administration, accounting, and return of the product under investigation, besides registering clinical complications and adverse events over the entire intervention period.<sup>17</sup>

The nurse is increasingly getting involved in researches, identifying patients, their needs, and attending graduate courses, and these efforts contribute to the advance of knowledge in Nursing, favoring population's health, as well as scientific and technological innovation.<sup>18</sup>

## CONCLUSION

In this study, with patients from clinical researches, men and women participated on an equal basis, most of them with a length of study medication use ranging from 1 to 2 years, aged between 50 and 80 years, having incomplete Primary School, and living with relatives, especially the spouse. Most patients reported they do not need assistance to take medication, received guidance on its use, did not stop using it, had some cardiac improvement, received guidance mainly from the physician and nurse, had a good relationship with the nurse, and used the clock strategy to avoid forgetting to take the medicines.

It was found out that there was a statistically significant relationship between the education level and the issue of stop taking medication. Association was observed between those who stopped taking the study medication and the need for help, showing that those who say they do not need assistance are the ones with worst adherence to treatment, making clear the nurse and team's importance to provide guidance to patients with lower education level and to those reporting they do not need help to take the medication.

It is worth stressing the scarcity of published national and international papers about nurse's activities as coordinator of a clinical trial, demonstrating the need to conduct further researches on nursing interventions concerning the adherence of patients to medication and treatment.

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