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CELL THERAPY IN PATIENTS WITH PSEUDOARTHROSIS: COST ANALYSIS AND CONSEQUENCES

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ABSTRACT

The treatment of pseudoarthrosis is often long and with great financial and social cost. The aim of this study was to analyze the costs and consequences of stem cells application in patients with pseudoarthrosis. Methodology: This study is an economic analysis of costs and consequences. It was undertaken in a University Hospital from September 2008 to December 2010. The direct costs and time to fracture healing of eight patients were raised. Results: The follow up of patients after the procedure was for six months. From eight patients, seven were healed. The healing time was an average of 14.7 weeks. The direct costs of hospital treatment was R\$ 1,207.75. Conclusion: The results of this study are encouraging. The future challenge will be to increase the sample and evaluate the effectiveness of this procedure.

Keywords: Cost, Pseudoarthrosis, Stem Cells, Consequences, Nursing.



ORIGINAL ARTICLES

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INTRODUCTION

The development in the biomedical science allow new possibilities of treatment for many types of diseases. Among these treatments there is the cellular therapy, which is consisted on the use of stem cells (SCs) with the objective to regulate the regenerative process of the human body; directing and amplifying the repairing of the process and the substitution of the injured tissue⁽¹⁾.

In orthopedics, as well as other areas of knowledge, is searching for new possibilities of treatment to the diseases. And pseudoarthrosis is a disease that gets more and more attention from these professionals, since it has a considerable negative impact in quality of life of the patients and in the increase of direct and indirect costs related to the recurrent hospitalizations⁽²⁻³⁾.

Pseudoarthrosis is also known in the English language as *nonunion*; it happens when the bone healing ceases prematurely and does not continue unless there is some sort of intervention. It is also defined as a non-healed fracture documented by x-rays for more than 6 months or with a fracture that does not present any healing progression for a period beyond 3 months⁽²⁾.

Nowadays, there are many methods to treat pseudoarthrosis⁽²⁾ and the most used ones are: the decortication or osteoperiostal scaling, sponge autograft, BMP addition (bone morphogenetic protein), bone marrow and platelet growth stem cell concentrate, distraction of the bone callus with external holders, vascularized bone graft on bone loss, internal stabilization material, external stabilizers (external holders or orthoses), ultrasound, shock waves and electromagnetic fields.

The autologous bone graft is considered today the gold standard to treat pseudoarthrosis, because of its osteogenic, osteoinductive and osteoconductive proprieties, besides the fact to not cause any immunologic reaction of transmission of infectious illnesses. Despite this fact, its use is limited as it comes from an exhaustible source, and it also has consequences on the donating site of the craft (pain, sensibility alterations and scars), as well as having the quality of live altered depending on the age and general conditions of the individual⁽⁴⁾.

This study approaches the application of a bone marrow stem cell concentrate as a possibility of treatment of pseudoarthrosis, as it considers this treatment is a way of crafting which is less invasive than the traditionally used techniques in relation to the donor and receptor area and the data raised by the literature show us a higher efficiency.

Because of that, it is considered indispensable to perform a cost evaluation and consequences study about this procedure, since without a detailed analysis of all aspects involved in an intervention, such as costs and its consequences, mistaken decisions can be eventually adopted during the nursing practice, generating losses.

Aiming the patient during the healing process and the quality of life, the nurse engages into the process of innovation in science and technology, learning and understanding conceptually the field and involving with each and every stage of the life cycle of the products and processes, to lower the costs and maximize the clinical, therapeutic and assistant benefits⁽⁵⁾.

Therefore, to establish economical studies involving cost and consequences evaluation, even if just as descriptive, are an imperative to offer better sustainability to the complex decisions that involve the scarce resources located to the public health system in Brazil.

This research had as an objective to analyze the costs and the consequences of the application of stem cells in patients diagnosed with pseudoarthrosis.

METODOLOGY

It is an economical analysis of the cost and of the consequences when applying stem cells in patients with diagnosed pseudoarthrosis.

The analysis of cost and consequence (ACC) is one type of analysis of cost-effectiveness (ACE) that compares the costs (direct and/or indirect) and the consequences (averages in clinical units) of a certain intervention⁽⁶⁾.

In accordance to Resolution 196/96 of the Brazilian National Health Counsel (CNS, in portuguese), this research was submitted and approved by the Ethics in Research Committee of the Antonio Pedro Medicine College and College Hospital, protocol #108/09, CAAE: 0084.0.000.258-09.

The scenario was the Antonio Pedro College Hospital (HUAP, in Portuguese), located in the municipality of Niterói, in the state of Rio de Janeiro. The used units were the Clinical Research Unit, the Surgeon Center and the Orthopedics Ambulatory. The duration of this study was from September 2008 and December 2010.

The subjects were eight patients sent by the project named "The use of bone marrow on the treatment of pseudoarthrosis and delay of consolidation". The criteria of inclusion and exclusion of the patients were in accordance to the ones established abovementioned, which existed before this study.

The criteria of inclusion were: to be 18 years old or more; diagnosed pseudoarthrosis, not infected, in long bones, with spaces between fragments of a maximum of 10 millimeters, visible in simple x-ray in two incidents; pseudoarthrosis originated from closed fracture or an open one, treated with a plaster cast, plate, external holder or intramedullar bar.

Criteria of exclusion of the subjects were: patients that presented bone loss, or lack of contact spaces larger than 10 millimeters; patients without cutaneous cover on the focus of the fracture; angle deformity or pre-existent shortening that needed specific treatment; patients with active infection in the fracture.

The perspective of this study corresponded to the main source of financial support to medical assistance in Brazil, the Brazilian Unified Health System (SUS, in Portuguese). The costs seen here were the direct ones to the treatment.

The following stages were followed to the estimate of costs: (1) identification of relevant costs to the evaluation; (2) measurement of the used resources; (3) valuing the resources.

The costs raised in this study were the direct costs that involved those directly related to the health services that implied on immediate spending, of easy identification.

While analyzing the registered proceeding on medical records, the quantities of materials, medications, solution bottles used and hospitalizations were identified. After the identification, the data was analyzed and registered in Microsoft Excel version 2007 spreadsheets.

In this study, the consequence (outcome) analyzed was the time of consolidation of the fracture after the intervention.

The statistical analysis: it was calculated the average (standard deviation) and the median of the direct cost of the proceeding and of the period for the consolidation of the fracture.

RESULTS

Characterization of the Subjects of the Study

The sample was constituted of eight patients with pseudoarthrosis on the femur and tibia, which 87.5% (7) were males and 12.5% (1), females. The age varied between 21 and 59 years old, averaging 35.8 years old.

From the causes, 87.5% was originated in automobile accidents and the tibia corresponded to 75% of the fractured bones. Here, the period between the diagnose and the last treatment was, in average, 15 months. The patients stayed hospitalized for the proceeding for 24 hours,

in the majority of the cases, being discharged just after this period. It was not found any immediate or late adverse reaction after the proceeding.

Calculation of the treatment cost

The direct costs directly resulting from the interventions were calculated, specifically the hospitalization costs, complementary exams, medication, other inputs and professional honoraries. To the used resources, we attributed real costs based on their market values in 2009.

The unit costs of inputs were obtained through the consultation to the minutes of electronic trading performed by the HUAP and by the Health Prices Bank, of the Brazilian Ministry of Health (BPSMS, in Portuguese). The rate of a surgery room was calculated based on the Proahsa Bulletin, and the medical honoraries, on the SIGTAP – the Management System of the Table of Proceedings, Medications and OPM of the Brazilian Unified Health System. The calculation of the total cost was obtained multiplying the quantity and the unitary cost of services and inputs. Table 1 illustrates the direct costs of the treatment.

Table 1 – Direct costs of the Treatment – Niterói, 2009

#	DH	TSC	Med.	In	EXL	EXI	HP	Cost Total (R\$)
PC1	374.96	360.48	26.49	174.01	16.09	17.88	225.27	1,195.18
PC2	374.96	360.48	34.35	175.32	21.24	17.88	225.27	1,209.50
PC3	374.96	360.48	27.80	179.66	21.24	17.88	225.27	1,207.29
PC4	374.96	360.48	50.94	176.38	16.09	17.88	225.27	1,222.00
PC5	374.96	360.48	44.40	178.33	16.09	17.88	225.27	1,217.41
PC6	374.96	360.48	34.50	178.84	16.09	17.88	225.27	1,208.02
PC7	374.96	360.48	21.50	180.28	21.24	17.88	225.27	1,201.61

PC8	374.96	360.48	26.41	179.90	16.09	17.88	225.27	1,200.99
Average	374.96	360.48	33.30	177.84	18.02	17.88	225.27	1,207.75
SD	0.00	0.00	10.00	2.33	2.67	0.00	0.00	8.79
Minimum	374.96	360.48	21.50	174.01	16.09	17.88	225.27	1,195.18
Maximum	374.96	360.48	50.94	180.28	21.24	17.88	225.27	1,222.00
Median	374.96	360.48	31.08	178.59	16.09	17.88	225.27	1,207.66

Label: **DH** – Hospitalization Daily Rate; **TSC** – Surgery Room Fee; **Med** - Medications; **In** – Inputs; **EXL** – Laboratory Exams; **EXI** – Imagery Exams; **HP** – Professional Honoraries.

On Table 2 the direct costs are presented with each patient in relation to the time spent to fracture consolidation.

Table 2 – Treatment cost *versus* consolidation time – Niterói, 2009

Patient	Total Cost	Consolidation Time
PC1	1,195.18	24 weeks
PC2	1,209.50	03 weeks
PC3	1,207.29	16 weeks
PC4	1,222.00	16 weeks
PC5	1,217.41	12 weeks
PC6	1,208.02	12 weeks
PC7	1,201.61	20 weeks
PC8	1,200.99	Not consolidated
Average	1,207.75	14.71

Minimum	1,195.18	3.00
Maximum	1,222.00	24.00
Standard Deviation	8.79	6.70

Source: Study data 2010.

The average cost of hospital treatment to the application of molecular aspirate for the treatment of pseudoarthrosis per patient at the HUAP was R\$ 1,207.75 and a standard deviation of R\$8.79. The expected costs are at least R\$ 1,195.18 and no more than R\$ 1,222.00. The total cost is uniform, in other words, from all the analyzed cases there was no discrepancy.

The consolidation period was, in average, 14.7 weeks, with a standard deviation of 6.7 weeks, indicating a certain variation of the period of the treatment. The minimum time spent for consolidation was three weeks and the maximum of 24 weeks. Patient II had the shortest period and patients I and VII had the highest (Table II).

DISCUSSION

The results obtained related to the age of the studied group corroborated other studies: the average age of the patients involved was 35.8 years old, while in other studies^(7,8) was 36.6 and 40 years old, which allows us to affirm that the pseudoarthrosis affects a part of the population in a potentially productive age. This is strategic information, as it involves the professional absence, and then, it deserves maximum attention by the health professionals involved in the care of this patient. The earliest these patients are recovered, soon they will

go back to their daily routine and work, reducing the absenteeism and relieving financially the State.

Frequent hospitalizations and many times with a considerable duration increase even more the absenteeism. The delay in the treatment raises the risk to develop certain complications, raising, consequently the costs⁽²⁾.

Besides that, the loss in productivity of these patients during the period of incapacity as a result of pseudoarthrosis has negative effects over the economy. The impact over the family of the patient has also negative indirect effects. The indirect costs (missed work days, the transportation of the patient to the hospital, among others) related to the changes in the productive capacity of the individual and family members as a consequence of the process of sickness can be devastating⁽³⁾.

In this study, from the eight patients treated, seven were discharged after six months of treatment and did not need any other hospitalizations, demonstrating a reduction of the costs to the Health System and putting the patients back to society.

In Brazil there are no studies of economical evaluation of the cost and/or effectiveness of pseudoarthrosis treatment with a comparative effect like this one.

At this moment, there are many treatments for pseudoarthrosis and the cost of them depend on the chosen method. The international literature presents the costs of some treatments, including the one proposed here. Even though, they do not reflect the costs seen in Brazil, making inadequate any sort of comparison.

When referring to the time of consolidation of the fracture among different methods, a study⁽³⁾ with 111 patients with femoral pseudoarthrosis compared these methods evaluating the cure index and time. In this study, the patients were submitted to an average of two surgical proceedings, and the accompaniment average time after the appearance of the pseudoarthrosis was 62 months.

Among the 111 treated patients, 55 (49%) were cured and 56 (51%) were not. The analysis revealed a significant difference among the average age of the patients, being those who found the cure averaging 35.9 years old, versus those who did not succeed, averaging 42.9 years old ($p = 0,026$).

The initial treatment of the fracture did not have a significant impact on the result of the treatment of the pseudoarthrosis. Despite that, significant statistical differences were found among the different treatment methods after pseudoarthrosis was diagnosed.

The intramedullar bar (with and without adjunctive bone graft and/or electrical stimulation of the osteogenesis) was the most successful method for pseudoarthrosis. The patients treated with this procedure, 21 out of 45 (47%) were cured ($p = 0.031$). However, it was not clear if the bone graft and/or the electrical stimulation of the osteogenesis improved the result of this treatment.

In another study⁽⁹⁾ with 200 patients suffering from tibia fractures, they were evaluated which prognostics were associated with an elevated risk of reoperation after surgical treatment. And the pseudoarthrosis was the most frequent in treatments with plates (2.6%); with rod milled (8.0%); with shank milled (16.7%) and with plaster treatment (17.2%).

Studies that refer to a 100% consolidation in their case series are scarce. Here, the time of attendance was of six months and the patients were submitted to only one surgical proceeding for the treatment of pseudoarthrosis. The cure index was 87.5% with one non-consolidated case after treatment. And the average time spent to the consolidation was 14.71 weeks, corroborating with other studies^(7-8;10) that used a similar method.

Niedźwiedzki⁽⁷⁾ applied the same technique with 96 patients in three distinct situations (fracture, consolidation retardation and pseudoarthrosis) and reached a consolidation averaging 11.2, 12.8 and 13.6 weeks respectively, after the use of stem cells. Hernigou *et al.*⁽⁸⁾ obtained in his study an average time of consolidation of 16 weeks. While that, Healey

et al.⁽¹⁰⁾ got a consolidation of pseudoarthrosis in an average time of 19.8 weeks, besides the patients had a base disease or a sarcoma on the edge of the femur.

FINAL CONSIDERATIONS

The goals were reached analyzing the costs of the procedure of application of stem cells in patients diagnosed with pseudoarthrosis (R\$ 1,242.30), averaging consolidation in 14.7 weeks.

The time of consolidation was similar to other international studies that applied a similar method, being yet considered better than other studies that used routine treatment methods (plate, rod milled, shank milled and plaster). The direct costs of this procedure were relatively low, but yet unable to compare with the table of procedures of the SUS and not even with the international costs. Future studies are necessary to elucidate the questions that are persisting.

In relation to nursing, it is understood that to enable an assistance of superior quality to the patient, we must permanently search for a process of technical capacity, learning and researching, knowing new technologies, identifying your concepts, the incorporation, costs, consequences, concepts and even substitution. This way, the insertion of nursing into research with cell therapies opened a new field for the nurses, allowing to work in many areas of knowledge, such as an economical evaluation in health.

Thus, this study is covered in great relevance to raise the costs and consequences of this innovative proceeding, contributing in a near future so the SUS have subsidies to evaluate and incorporate this new technology to the treatment of patients of pseudoarthrosis.

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