INVESTIGACIÓN ORIGINAL

# The effect of game-based exercise on infant acute lymphocytic leukaemia patients

*Efecto del ejercicio físico basado en el juego en la leucemia linfocítica aguda*

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| Summary |

**Objective.** To establish the effect of a game-based exercise programme on Physical Deconditioning Syndrome (PDS) in 5 to 12 year-old children suffering Acute Lymphocytic Leukaemia (ALL).

**Materials and methods.** This was a quasi-experimental study involving seven children being treated for ALL at the National Cancer Institute (NCI) in Bogotá, Colombia. Fitness determinants (aerobic capacity, muscle strength, flexibility, motor skills and proprioception) were initially assessed to establish their exercise regime category, classifying subjects into three levels. Post-intervention assessment at the end of the programme verified changes in such determinants.

**Results.** Seven children aged 5 to 12 years-old (9±2.13 years) suffering from ALL (4 girls and 3 boys) met the inclusion criteria. Most determinants underwent changes leading to an increase in patients' evaluation scores (except for muscle strength, which remained constant). Whilst determinant variation was important, a greater difference was found when the overall score was analysed (p=0.05), signifying that the intervention had changed these children's health status.

**Conclusion.** Game-based exercise was useful for managing PDS in 5 to12 year-old ALL patients and suggested new ways of providing an intervention concerning physical therapy. However, studies involving a larger target population and longer intervention time are needed to identify new findings in this field.

**Key words:** Physical Fitness, Exercise, Play and Playthings, Precursor Cell Lymphoblastic Leukemia-Lymphoma (MeSH).

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Resumen

**Objetivo.** Establecer el efecto de un programa de ejercicio físico (EF) basado en el juego sobre el Síndrome de Desacondicionamiento Físico (SDF) de niños con Leucemia Linfocítica Aguda (LLA) entre 5-12 años.

**Materiales y métodos.** Se realizó un estudio cuasi-experimental con la participación de siete niños tratados por LLA en el Instituto Nacional de Cancerología (INC). Se hizo una evaluación inicial de los determinantes de la condición física (capacidad aeróbica, fuerza muscular, flexibilidad, destreza motora y propiocepción) para establecer la categoría de intervención de EF, clasificando a los sujetos en tres niveles. Al finalizar el programa se ejecutó una evaluación post-intervención para verificar cambios en dichos determinantes.

**Resultados.** Siete niños con LLA (4 niñas y 3 niños) reunieron los criterios de inclusión, con edades entre 5 y 12 años (9±2,13 años). La mayoría de determinantes experimentó cambios en su puntuación, ascendiendo en calificación, a excepción del determinante de fuerza muscular, que se mantuvo constante. Si bien la variación por determinante fue importante, se encontró una mayor diferencia e impacto al analizar el puntaje global de la Batería evaluativa (p-valor 0,05), lo que representa que la intervención produjo un cambio en la condición de salud de los niños intervenidos.

**Conclusión.** El EF basado en el juego es útil para el manejo del SDF de niños con LLA entre 5-12 años y abre la puerta a nuevas formas de intervención fisioterapéutica. Sin embargo, es necesario implementar estudios con mayor número poblacional y tiempo de intervención que permitan identificar nuevos hallazgos en el área.

**Palabras clave:** Acondicionamiento físico, Ejercicio, Juego e Implementos de Juego, Leucemia-Linfoma Linfoblástico de Células Precursoras (DeCS).

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## Introduction

Acute Lymphocytic Leukaemia (ALL) is the most common malign disease in the infant population, accounting for around 25 % all types of cancer during childhood and about 75 % of all types of leukaemia in children (1). Even though advances to date regarding ALL treatment have resulted in high survival rates (>70 %), efforts today are focused on minimising treatment-related morbidity (2-4).

ALL treatment involves well-recognised osteomuscular and musculoskeletal complications, such as paraesthesia, reduced osteotendinous reflexes, muscular cramps, muscular weakness, reduced range of movement and an alteration in gross and fine motor performance, as well as pain, reduced expenditure of energy, fatigue, obesity, avascular necrosis, osteopenia, osteoporosis and learning alterations. These complications have important implications due to their association with high morbidity rates and social, psychological and financial consequences (2-8).

Complications arising from ALL may be aggravated by bed rest in these children, leading to Physical Deconditioning Syndrome (PDS) which reduces a person's physical condition. The pertinent literature suggests that all children being treated for ALL should be considered "at risk" as their aerobic physical capacity becomes reduced and they could gain weight excessively (3). New prevention and rehabilitation measures, such as a Physical Exercise (PE) programme, must be included for reducing the risk of relapse and maintaining a high quality of life for these patients. Since PE has a beneficial impact on all body systems by attenuating the effects of muscular atrophy, cachexia, suppressing the inflammatory response and increasing immunological function, thereby making it into a protective factor regarding new neoplasias (4,9).

Existent PE programmes highlight physiotherapeutic intervention in surviving patients, but do not focus on secondary prevention strategies. As the target population in this study consisted of 5-12 year-old children, it was important to involve practices allowing adherence to PE programmes, including game-based exercise. This study was thus aimed at establishing the effect of a game-based PE programme on PDS in 5-12 year-old all patients.

## Materials and methods

This was a quasi-experimental study aimed at establishing the effect of a game-based PE programme on PDS in 5-12 year-old children suffering ALL by evaluating each child's physical condition.

### Patients

Seven children were included in the study as they fulfilled the inclusion criteria: being aged 5 to 12 years, having a confirmed diagnosis of ALL, patients having been treated for ALL during the last two months at the National Cancer Institute (NCI), whether as inpatients or outpatients from January-April 2012. Children were excluded if they had severe pancytopenia, anaemia, severe thrombocytopenia, severe neutropenia, leukopenia, signs of respiratory difficulty, cardiac dysfunction (congenital or cardiotoxicity), active infection, pain rated above six on the Visual Analogue Scale (VAS) and recent surgery.

Indications and contraindications for PE were explained to each child and their families upon acceptance and giving approval by signing an informed consent form. The study was approved by the INC's Paediatric Medical Board.

### Physical condition

The physical condition of infant ALL patients was evaluated by using a battery of tests for evaluating their physical condition (10), which consisted of the following determinants: aerobic capacity, muscular strength, flexibility, motor skills and proprioception.

A specific evaluation tool was used for evaluating each determinant. Aerobic capacity was determined by using

the six minute walking test, muscular strength by testing for Gowers' sign and the number of abdominal repeats in a minute, flexibility by modified Sit and Reach test and specific retraction tests (Thomas, Kendal, Elly-Duncan tests, popliteal angle and hip adductor). Proprioception was evaluated by observing different body segments' stabilisation and displacement in bipodal, unipodal support, with and without visual feedback. Gross motor function measurement (GMFM) was used for measuring motor skills in the following categories: seated, bipedal, walking, running and jumping. The VAS was used for rating pain intensity.

The battery of tests was designed for differentially classifying the children. Level I was used with patients confined to bed for evaluating pain, specific retraction tests and GMFM module B, whilst level II was used for patients who could walk in their rooms, evaluating the foregoing plus aerobic capacity, testing for Gowers' sign, GMFM module D and proprioception. Level III was used for children able to walk around the INC, including those being attended as outpatients; all the evaluation tools were used in this case. The children were classified in a PE level adapted to their possibility of movement and clinical condition, in line with the results of the battery of tests.

### PE Programme

The PE programme consisted of three levels related to a patient's clinical state and PDS. The programme lasted three months and involved a child having been prescribed PE and activities according to each intervention level, as follows. Level I consisted of 50% Heart Rate Reserve (HRR), lasting 15 minutes and having 3 days/week frequency, involving activities such as: inspiratory breathing exercises, changing position in bed, bridge exercise, doing jigsaw puzzles, inserting beads necklace, drawing with different materials, tearing and cutting paper, throwing a ball from a prone position on the elbows and active-assisted exercises involving the upper limbs and trunk with the help of a ring. Level II involved 51-60% HRR, having a 4-5 times/week frequency and lasting 20 minutes; activities involved playing at statues, throwing a ball from both biped and sitting positions, walking around the room, creeping on a mat and kicking and catching a ball in biped position.

Level III involved 61-70% HRR, frequency being 4-5 times/week, lasting 30 minutes; it included activities such as throwing and transferring cards whilst on the knees, collecting and transferring objects located at different heights, medium-impact dance, throwing a ball above the head, play circuits, passing under a rope placed at different heights and games in a round. The activities in each level were based on those proposed by Caimán, Cortés and Melo (11).

Each participants' physical condition was evaluated again once the PE programme had ended, using the aforementioned battery of tests for determining the programme's effect on the children's PDS.

### Statistical analysis

Microsoft Office Excel (version 2010) was used for analysing the data, using descriptive statistics for each determinant involved in the evaluation, as well as for overall score. The R statistic was used for studying the difference in score between evaluations for each determinant of physical condition and then crossed with the number of interventions for each child. Non-parametric statistics (Wilcoxon's signed-rank test) were used for evaluating change regarding each component in the evaluation, as well as overall score.

## Results

Seven 5 to 12 year-old children (9±2.3 years) suffering ALL (4 girls and 3 boys) being treated by the INC's inpatient service met the inclusion criteria for participating in this study. Following an initial evaluation, five participants were classified in level II and two in level III. Once the intervention period had elapsed it was found that most determinants had undergone changes regarding their scores, thereby raising the rating (except for the determinant of muscular strength, as described in figure 1). Even though such progress was important, so too was maintaining the quality of movement; this meant that obtaining constant scores represented a clinical gain for the target population. Determinant variation was significant; however, greater difference and impact was found when analysing the overall score from the battery of tests (Figure 2).

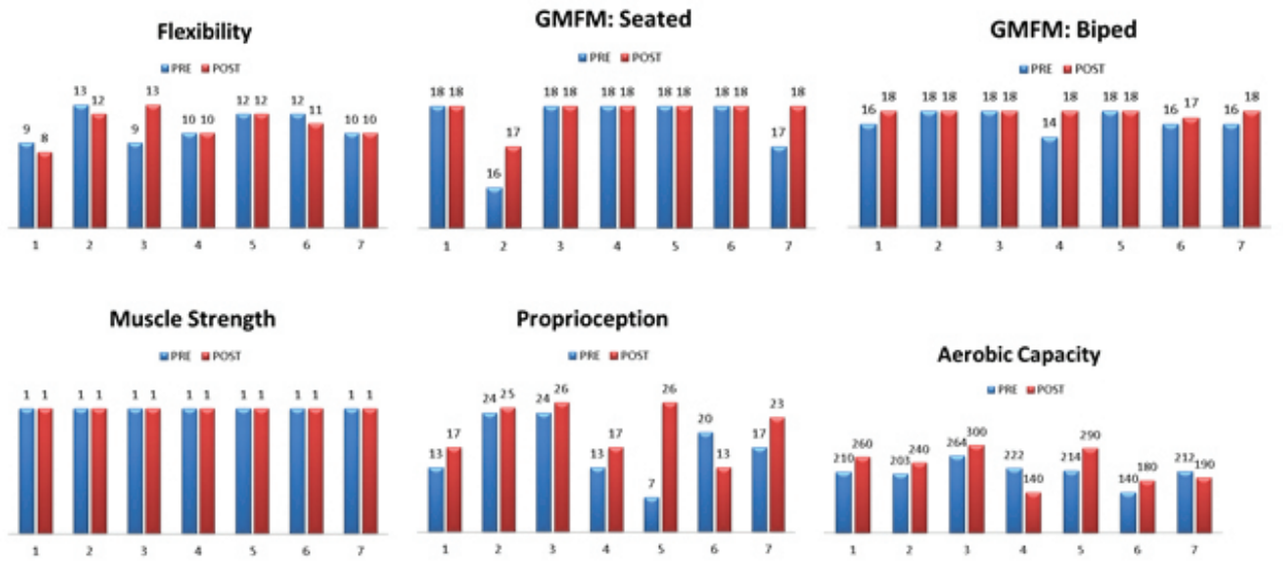


Figure 1. Difference in score between evaluations for each determinant of physical condition.
Source: authors.

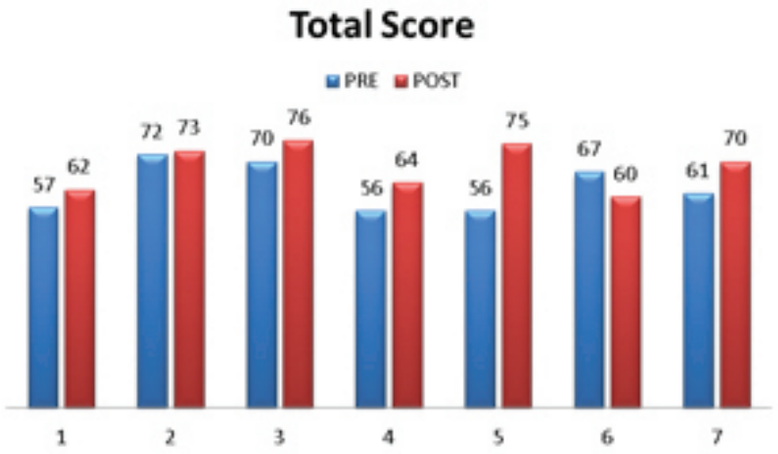


Figure 2. Difference in overall score between evaluations regarding the battery of tests.
Source: authors.

It was found that a greater number of sessions increased the difference between such evaluations, regarding determinants for proprioception and aerobic capacity when considering the influence of the amount of interventions (8.4±2.9 sessions) on the difference in score between evaluations, such qualities being important regarding the effects of PDS (Figure 3). Likewise, it was established that the effect of the programme was greater when considering the set of the five determinants, i.e. regarding "physical condition" (Figure 4).

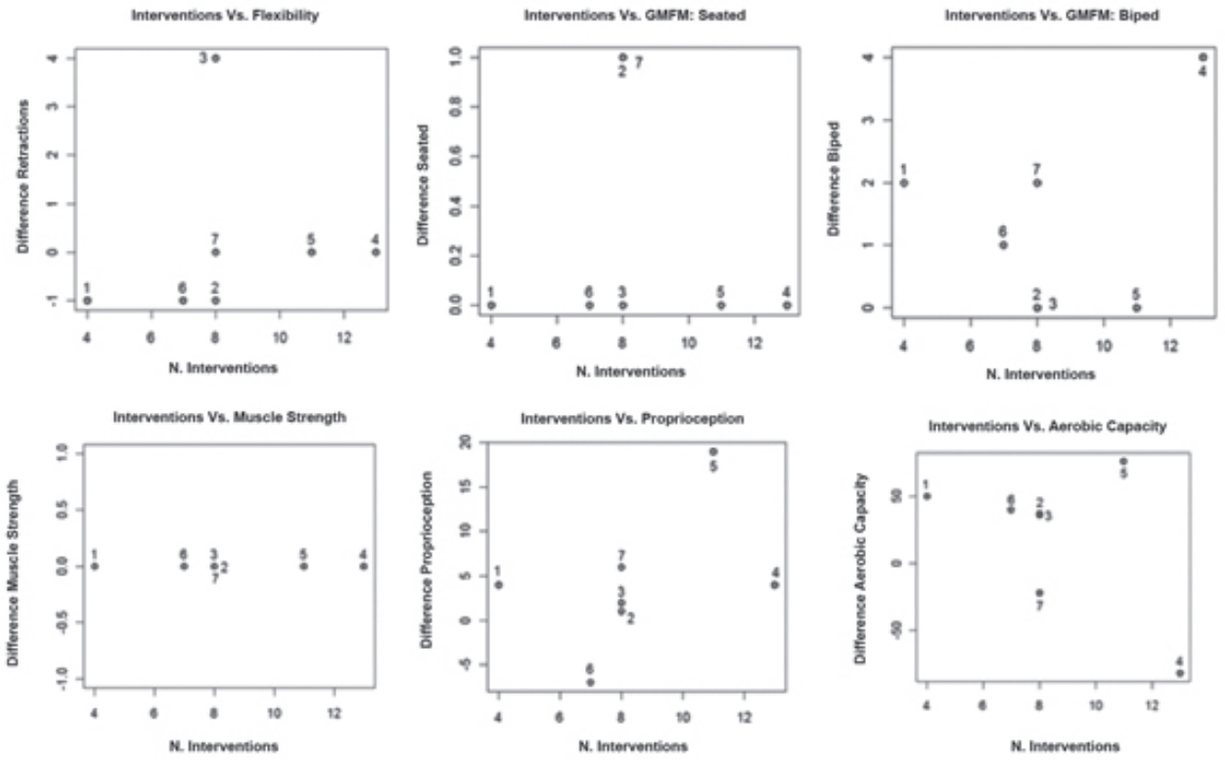


Figure 3. The influence of the amount of interventions on differences in score regarding the evaluation of each determinant of physical condition.
Source: authors.

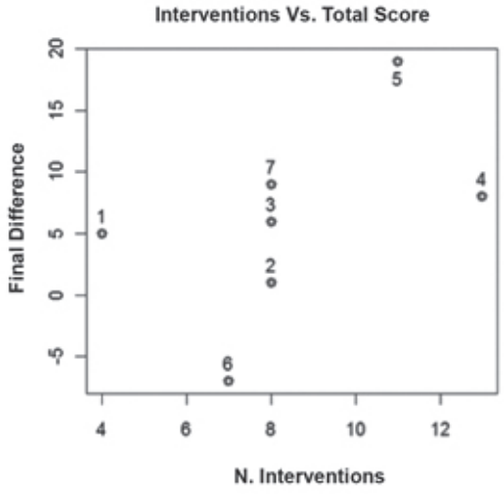


Figure 4. The influence of the amount of interventions on differences in overall score regarding the battery of tests.
Source: authors.

Grouping the determinants within a single concept ("physical condition": p-value for overall score on the battery of tests, using Wilcoxon's signed-rank test) revealed a statistically significant change (p=0.05), meaning that the intervention did lead to variation in the target children's health conditions.

Post-intervention evaluation classified three participants in level II and four in level III, finding that the children improved or maintained their initial physical condition, having great clinical significance given the negative effects of these children's treatment and their being bed-ridden.

## Discussion

The beneficial effects of PE have been described by several authors as providing coadjuvant therapy when treating cancer (3). Previous studies have involved small samples of infant ALL patients aged 4 to 15 years-old (2,3). The present study involved analysing seven 9 ± 2.13 year-old children diagnosed as suffering from ALL (such small population sample being due to variability regarding the length of the children's hospital stay).

Some PE-based interventions' authors have involved the patients' stage of chemotherapeutic treatment (2,3,5,6). The children in the present study were included in a PE programme based on physical condition and were evaluated by using a battery of tests for placing them in a level regarding their physical condition and determined the type of PE which they would be engaged in.

The intervention time used in other researches has ranged from 1.5-12 months, having 30-60 minute structured times and sessions lasting a minimum of 3 and maximum of 5 days per week (1-3,6,7,12). The present programme involved 3-4 days per week intervention frequency for each level, lasting a minimum of 15 and maximum of 30 minutes. The time taken for the activities depended on each patient's length of hospital stay, as well as their state of health, following a daily review of their haematological profile.

Previous studies have focused on evaluating and training this population's flexibility, aerobic capacity, muscular strength and gross motor performance (9), excluding proprioception as a determinant of physical condition (i.e. this quality was included in the present study).

A study by Gohar et al., (6) included activities for training aerobic capacity such as riding a bicycle, walking and dancing; better states of health were reported for the children following the intervention period and greater tolerance regarding future cycles of chemotherapy. Activities aimed at aerobic capacity in the present study involved play-based strategies which led to identify significant differences between evaluations and establish a directly proportional relationship with the number of interventions.

Several studies have mentioned the importance of evaluating flexibility (and interventions related to this) by means of strategies based on stretching the lower limbs through sitting and reaching, and sustained stretching in ankle dorsiflexion (2,3). This study was aimed at maintaining age-adjusted mobility ranges and regarding each child's clinical condition by means of overall activities through play, showing that retractions had been maintained or become reduced in most children.

Strength is important regarding a child's overall physical state and motor performance; studies found in the pertinent literature endorsed training concerning lower and upper limb strength for performing tasks regarding execution and displacement, without including abdominal strength training tests (2,5,6). Gowers' test was used in the present research and abdominal resistance for identifying muscular response regarding actions such as changes in position and recreational and basic daily activities. Important alterations were found concerning this quality in the whole population, meaning that the present study's results represent clinically significant findings as this determinant's level was maintained, thereby ensuring that physical condition did not become affected.

A study by Wright et al., (12) used the GMFM seated and biped modules and showed that children suffering ALL obtained poorer scores (compared to a control group), even though being able to carry out the tests. However, though such alterations may not imply disability, they do have a negative influence on self-esteem, physical condition and being able to enjoy recreational, educational and social activities (5,12). Gross motor skills in the present study (evaluated by GMFM) showed that such condition contributed towards performance, regardless of a school-aged child's basic daily activities, significant changes being found for both the seated and biped modules and no regression regarding scores.

An item which lacked optimal development in the study by Wright et al., (12) was managing to stand on one leg for 10 seconds; this agreed with the proprioceptive performance results observed in the children participating in the present programme, since they had difficulty in performing such test, with or without visual feedback. This response changed following the PE programme, better scores being obtained. However, no material was found in the pertinent literature sustaining such results, as proprioceptive capacity has not been included in physical condition rehabilitation programmes involving this population.

Even though the effect of drugs such as vincristine have been described (3) causing peripheral neuropathies and thereby limiting activities, the range of articular movement and muscular strength, their effect on proprioceptive performance has not

been analysed. The present study's findings led to highlight the importance of including this quality in PE programmes directed toward the child population being studied, depending on the number of interventions and showing an important change between evaluations.

Few studies in the literature describe play-based intervention programmes targeting infant ALL patients, as most studies base their interventions on individual or home-based activities. The study by Gohar et al., (6) involved game-based activities with friends in the home-based sessions, thereby posing the need for including therapeutic strategies facilitating adherence to PE programmes.

The present study's limitations involved difficulties regarding patient follow-up as the children were only treated when they were hospitalised; however, their parents were given recommendations regarding the importance of regular and supervised PE. Another limiting factor concerned to the participation in the programme, this subjected to the children's clinical conditions and days' hospitalisation, hereby negatively influencing the number of days the intervention lasted.

## Conclusion

A PE programme should be engaged in following evaluation of children's physical condition, thereby establishing safe levels for prescribing PE which have been adapted to each child's possibilities. Game-based PE is useful for managing PDS in 5-12 year-old children suffering from ALL and encourages new forms of physiotherapeutic intervention.

Children should be included in PE programmes using the concept of "physical condition" and not chemotherapeutic treatment phase, including all the determinants of such condition, better results thus being obtained compared to each quality's intervention independently.

There must be continuity regarding physiotherapeutic intervention, once the beneficial effect of PE has been identified, including home-based activities supervised by parents or caregivers, meaning that educating the family is fundamental to such type of programme. Further studies are needed which involve a larger population and longer intervention time thereby facilitating new findings in the area.

## Conflict of interest

The authors expressly state that they have no conflicts of interest.

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