A Longitudinal Study of Changes Observed in the 6-Min Walk Test Over a 4-Month Period in Healthy 6 to 12-Year-Old Children

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Abstract

Simpler and less expensive field tests, such as the 6-min walk test, have been employed to evaluate exercise tolerance in chronic paediatric conditions. However, patterns of longitudinal change for outcome measures could show initial gains attributable to normal growth and development in children. We aimed to verify the effect of growth on the distance achieved in 6-min walk test in children 6 to 12 years of age over a 4-month period. Healthy children from 6–12 years of age were recruited. Two trials of the 6-min walk test were performed on the same day and after a 4-month period. We employed the intraclass correlation coefficient to assess test-retest reliability when the 6-min walk test was applied with a 4-month time interval. 59 children (28 boys and 31 girls) were assessed. The distance covered in the 6-min walk test and anthropometric variables showed a statistically significant increase after 4 months. After 4 months, we established a 12% change from the initial measurement (79.69 m) as the minimal detectable change for a 90% confidence level, while a 15% change (94.66 m) was determined as the minimal detectable change for a 95% confidence level.

Conclusions: The distance covered in the 6-min walk test improved as the children's height increased, establishing a 12% change in the score of at least 79.69 m as the most appropriate value in interpreting longitudinal functional performance data when assessing exercise tolerance in healthy children aged 6 to 12 years.

Introduction

Exercise tolerance can be determined by maximal exercise tests involving bulky and high-cost laboratory equipment, such as a cycle ergometer and treadmill, which are considered the gold standard [1]. However, such equipment might not be widely available and might need to be modified for young patients. Children rarely engage in sustained, heavy exercise, suggesting that classical maximal exercise tests might not provide a realistic simulation of a young person's physical capacity [2].

Simpler and less expensive field tests, such as the 6-min walk test (6MWT), have been employed for assessing exercise tolerance in chronic paediatric conditions [3, 4]. The 6MWT represents a submaximal exercise test capable of reflecting the limitations of children with neuromuscular diseases [5], cystic fibrosis [6], cardiovascular diseases [7], acquired brain injury [8], obesity [9], idiopathic arthritis [10], end-stage renal disease [11], among others. The test is easy to administer, better tolerated, and more reflective of activities of daily living than the other walk tests [12], providing valuable clinical information on factors that limit activity performance on a day-to-day basis [13]. In fact, the 6MWT provides a more realistic approximation of the realities of daily life activities using exercise patterns actually encountered in children's lives [4].

One of the challenges in interpreting the longitudinal functional performance data from children and adolescents is the background of normal childhood growth and development. Patterns of longitudinal change for outcome measures such as 6MWT could show initial gains attributable to normal growth and development in children. A major premise of this commentary is that patients might reach a functional gain phase in the context of interventional trials, followed by an overt and clinically appreciable increase in functional performance where changes in the patients' abilities might be clearly identical to changes in their healthy peers. Research in this field has focused on cross-sectional studies that have found a significantly positive correlation between children's anthropometric characteristics (age and height) and the 6-min walk distance (6MWD) [14–19], mainly in the 5–8-year age group [20]. Even boys up to the age of 7 years with Duchenne muscular dystrophy achieve similar distances during the test to those of their normally developing peers [21, 22]. To date, however, there have been no longitudinal studies that have evaluated the medium-term repercussions of maturation on a submaximal exertion test in school-age children.

Evaluating the medium-term repercussions of growth on the 6MWT in healthy children appears to be relevant in evaluating functional capacity in epidemiological studies, the monitoring of intervention effectiveness, and especially as a parameter for the response to rehabilitation programs and the follow-up of physiotherapeutic protocols in paediatric conditions. The purpose of the present longitudinal study was to establish the spectrum and magnitude of changes in the 6MWT observed in children 6 to 12 years of age over a 4-month period to verify the effect of growth on the distance achieved.

Methods

This was an observational, descriptive and longitudinal design study approved by the a local Research Ethics Committee and it was conducted in accordance with the Declaration of Helsinki. Data were collected at two primary schools between January 2019 and March 2020. Written informed consent was obtained from all the children and from their parents or legal guardians.

Participants

A convenience sample of children of both sexes from 6 to 12 years of age was recruited. All children willingly agreed to perform the 6MWT and had to be able to understand and fully comply with the assessments. Children who were taking medication, had chronic or acute disease (cardiac, respiratory, neurological) or musculoskeletal disorders that affected their ability to walk were excluded.

6-min walk test

The 6MWT was performed following the European Respiratory Society/American Thoracic Society recommendations [23]. The children were asked to walk as far as possible from one end of a 30-m flat covered corridor to the other for 6 min. Two tests were performed on the same day, separated by 30 min of rest to prevent participant fatigue and learning bias [23], and after a 4-month period. Perceived exertion at the start and end of the tests was assessed using the EPInfant rating scale for the paediatric population [24]. The results are presented as the distance covered (in m) in 6 min (6MWD).

Physical activity questionnaire

The short version of the Minnesota Leisure Time Physical Activity Questionnaire was used to measure physical activity using metabolic equivalents of tasks [25]. Participants were given a list of suggested activities (e.g., walking, aerobic conditioning exercise, water activities) and asked to mark those performed during the week.

Study procedures

Before the start of the 6MWT, the children's weight and height were measured. The children sat quietly on a chair for 10 min while the baseline measurements were recorded. Blood pressure was measured at the start and end of each test using an electronic sphygmomanometer (AM-08A, AMIS Medical, Jiangsu, China). The children's heart rate was monitored before, during and after the tests using a pulsometer (FT1, Polar Electro Oy, Kempele, Finland). During the 30-min rest period between tests, the physical activity questionnaire was administered.

Sample size

We estimated the sample size using the method described by Walter et al. [26] which is recommended for estimating sample sizes based on the intraclass correlation coefficient (ICC). We employed Power Analysis and Sample Size software (PASS 15) to calculate the sample size. According to the criteria of numerous clinical investigations [27], we established an ICC value of 0.6 (p_0) as the minimal acceptable ICC. In addition, we chose an expected ICC value of 0.8 (p_1), along with a power of 90% and a significance level of 5%. Thus, taking into account that 2 replications were performed per participant and assuming a 10% loss due to the study's longitudinal nature, we determined a minimum sample size of 60 participants.

Data analysis

We performed the statistical analysis using SPSS statistical software (Statistical Package for the Social Sciences 25, SPSS Inc., Chicago, IL USA), and all statistical tests were interpreted using a 5% significance level ($P < .05$). We employed Student's t-test to detect differences in anthropometric variables, as well as in the level of physical activity, between the initial measurement (baseline) and the measurement taken after 4 months. We also determined the effect sizes according to the criteria proposed by Cohen (small, 0.20–0.49, medium, 0.50–0.79, large, ≥0.8) [28]. In addition, a linear mixed effects model was applied to analyse whether the variables age, sex, and change in height, weight and level of physical activity over the 4-month period significantly influenced the change in the 6MWD walked by the children. Finally, a multiple linear regression analysis was performed to estimate the percentage of variance explained by the variables potentially predictive of the change in the 6MWD walked by the children after 4 months. For this purpose, it was used a stepwise selection method. The entry and removal of the variables from the regression model was determined according to significance levels of 0.05 and 0.15, respectively.

We employed the $ICC_{2,1}$ to assess test-retest reliability when the 6MWT was applied with a 4-month time interval (baseline of the 6MWT vs. the value read at 4 months) in healthy children aged 6–12 years. We established the reliability levels according to the following classification: excellent reliability (ICC ≥0.90), good reliability (0.90 > ICC ≥0.70), fair reliability (0.70 > ICC ≥0.40) and poor reliability (ICC < 0.40) [29]. We measured the precision of the reliability results using the standard error of measurement (SEM), which was calculated as *Standard Deviation of difference score/√2* [30]. Following the same criteria as a previous study [31], we calculated the minimal detectable change (MDC) for a 90% and 95% confidence level in both absolute and relative values. Lastly, the reliability of the within-session test-retest (measurement 1 and 2 at baseline and at 4 months) was provided, as well as the SEM and the MDC, to have a reference for the effect of the time factor (4 months between measurements) on all of these parameters.

Results

A total of 64 participants were initially recruited, however, 4 of them were excluded for not having performed all of the tests and 1 was excluded for not having completed the physical activity questionnaire. The final sample therefore consisted of 59 healthy children: 28 boys (47.5%) and 31 girls (52.5%). The participants' age range was 6–12 years, with a mean age of 9.08 ± 1.8 years at baseline. None of the participants reported adverse effects during the study, and the 6MWT measurements were performed as usual. **Table 1** lists the distances covered in the two 6MWT attempts at baseline and at 4 months, as well as the physiological variables and subjective variables of dyspnoea and fatigue.

Table 2 shows the comparisons between the measurements at baseline and at 4 months for age, physical activity levels, anthropometric variables and distance covered in the 6MWT, all of which showed a statistically significant increase, except for the physical activity level. It should be noted, however, that the magnitude of the change was small, given that the effect sizes ranged from 0.12 to 0.25. Regarding the results obtained from the mixed-effect linear model, it was identified that the change in distance covered in the 6MWT by the children was significantly influenced by the growth in their height ($t = 4.704$, $P < .001$, but not by their age, gender, nor by the change in their weight or level of physical activity ($P < .05$). In the multivariate linear regression analysis, the best-fit and most efficient models established that 46.0% of the variation in the change in the 6MWD walked by the children could be explained only by its growth in height (see **Table 3**).

Test-retest reliability

The test-retest reliability observed between the initial measurement and that performed at 4 months was fair-good (**Table 4**). After 4 months, we established a 12% change from the initial measurement (79.69 m in this particular study) as the MDC_{90}, while a 15% change (94.66 m in this particular case) was determined as the MDC_{95}.

The variability of the within-session measurements (at baseline and at 4 months) was less than that observed in the inter-session measurements. In particular, the within-session test-retest reliability was good-excellent, requiring a smaller percentage change to detect real differences (MDC_{90}, 10%, MDC_{95}, 12%). **Table 4** shows the descriptive statistics, ICCs and associated 95% CIs, SEMs, MDC_{90} and MDC_{95} for the within-session and inter-session agreement.

Discussion

The present study investigated the influence of maturation and growth on distance covered in the 6MWT in the medium term and reported the test-retest reliability and MDC for healthy children aged 6–12 years. As far as we know, the present study is the first to address the influence of anthropometric variables longitudinally, within a 4-month time frame, on the 6MWD for healthy children. Our findings demonstrated that the anthropometric values and the 6MWD showed a statistically significant increase after the 4-month period. The test-retest reliability obtained between the initial measurement and the one at 4 months was fair-good, obtaining a MDC_{90} and MDC_{95} of 79.69 m (12% change) and 94.66 m (15% change), respectively. This study therefore confirms the medium-term repercussion of growth on the 6MWD in healthy children. These data contribute to evaluating the effectiveness of interventions based on functional capacity, by defining the magnitude of change attributable to the intervention and the extent to which this change is due to the individual's growth and maturation.

In the current study, the mean distance walked at baseline and after 4 months was 632.98 ± 78.54 m and 650.05 ± 77.47 m, respectively, with a statistically significant increase of 17.07 m between the measurements. In line with our results, studies conducted on healthy children have reported reference values with the range of 470 ± 59 m to 677 ± 62.2 m [17, 32]. Thus, both of the measured distances travelled by the children in this study were within the expected values for their age. The wide range reported in the literature for the reference values for the 6MWD might be due to differences in group size, the methodology employed, racial diversity, socioeconomic differences and differences in the distribution of groups by age range. In addition, cognitive and behavioural factors, such as understanding the test procedure and attention levels, can lead to variations in scores, especially among very young children.

To our knowledge, there have been no published values for the 6MWT in the medium term for healthy children with which to compare our data. However, our findings reflect a change in the 6MWD walked by the children, which we assume is attributed exclusively to the 4 months elapsed during their participation in the study. In children, the factors that can determine the distance walked are diverse, but the most important are age, weight, and height [16, 17, 19]. Predictably, the participants' age, weight and height experienced a statistically significant increase after the 4-month period. Although 4 months might seem like a short period, a motor development maturation stage occurs in young children [33] that can positively affect their walking patterns by increasing the ability to walk longer distances. Numerous authors point to age as a strong predictor of distance covered in children and adolescents [14–19]. In addition to age, height has been indicated as one of the variables that most influences the 6MWD [14–19]. It is to be expected that taller individuals have longer legs and, consequently, greater strides that enable them to cover greater distances in shorter times. Supporting this theory and in line with our results, several studies have shown an improvement in functional test scores in healthy children as their height increases [34, 35]. In terms of increases in weight, this age group is associated with a growth in muscular mass, which enables a greater walking cadence and speed. In a study of Mexican children, Blanco et al. [36] indicated that for every kilogram that the children's weight increased, the 6MWD increased by 7.78 m.

Physical activity significantly influences the 6MWD [15, 37]. In our study population, however, physical activity (measured in metabolic equivalents of tasks) did not experience a statistically significant increase. The increase in the 6MWD was therefore not related to the positive adaptations in aerobic capacity, the increase in strength or the endurance associated with greater physical activity of our population, which reinforces the validity of our findings. For all of the above reasons, we believe that the growth and maturation process that occurred during the 4-month study period can, by itself, explain the increase of 17.07 m in the 6MWD, however, we must point out that height is, of all the potentially predictive variables, the most significant and relevant factor to consider, since it alone explains 46% of the increase in distance covered. In the implementation of a clinical trial, understanding the functional changes during growth is essential because the effect of the intervention can be more difficult to detect or present more variability than expected, depending on the individual's state of maturation.

The 6MWT has proven to be a reliable and reproducible tool, showing good-excellent within-session test-retest reliability (ICC of 0.87 at baseline; ICC of 0.88 at 4 months) and a fair-good inter-session measurement reliability (ICC of 0.79; baseline compared with 4 months). The reduction in reliability is due to the time elapsed between the measurements, given that an optimum period of no more than 7 days has been established between assessments for the analysis of test-retest reliability [38] and that long periods between measurements can affect the ICC [39]. However, the 6MWT continued to demonstrate its reliability and validity, even in the 4-month time interval employed in this study, which could be defined as long. Numerous studies have also shown the reliability of the 6MWT in healthy children [8, 18, 40] and those with paediatric conditions [41, 42].

According to the MDC established in the present study, healthy children aged 6–12 years require a difference of at least 79.69 m in the 6MWD in the medium term to consider it a significant change (MDC_{90} of 79.69 m and MDC_{95} of 94.66 m). As expected, the MDC value established between the sessions was significantly higher than that determined when the 6MWT was applied on the same day (approximately 25 m). This increase could easily be explained by the fact that maturation and growth alone represent a significant increase in the 6MWD. Therefore, the reduced accuracy in the reliability and MDC between the sessions could be explained by the variability in anthropometric measurements inherent in the child's growth. In contrast to our results on MDC established within-session, Goemans et al. [40] reported an MDC of less than 57.4 m for healthy children with a test–retest interval of 12 days. As mentioned above, the reference values have a wide range due to various factors such as methodology used, age, and socioeconomic level, which might explain the differences between the two studies. However, the real reason for these findings is unclear. On the other hand, the MDC established inter-session could not be compared with that of previous studies, given that to our knowledge, such values do not exist. However, interventions aimed at improving exercise tolerance in children and adults require at least 6–8 weeks to generate adaptations. We therefore recommend assessing the magnitude of change attributable to an intervention using the MDC established in this study and not those of previous studies, because our MDC does not ignore the fact that any treatment develops in parallel in the context of the typical anthropometric changes of childhood. Thus, the assumption of real change using MDCs established from two sessions spaced less than 2 weeks apart could result in an overestimation of an intervention's effect.

Lasty, we would like to note the importance of expressing changes as a percentage (not as an absolute value) in tests that evaluate functional performance in children and adolescents, a common feature of respiratory function assessments [43, 44]. Given that the changes produced by a treatment or disease occur in the context of changes produced by maturation and growth, there is the risk of interpreting as normal those values that a young child presents but nonetheless reflect a significant deterioration in an older child, as can occur in the assessment. An example of this is the inverted U-shaped development typical of Duchenne muscular dystrophy, where a functional plateau occurs at the age of 7 years, at which time the initial gains attributable to growth are outweighed by the deterioration caused by the disease progression [21].

The present study has a number of limitations. First, in the absence of previous studies that report the 6MWD in the medium term in other populations and ethnicities, it was not possible to determine the relevance of these factors in the established data. Additionally, the assessments might have been affected by differences in factors such as encouragement and enthusiasm, especially in younger boys. However, this variability was reduced as much as possible because the evaluators were trained and supervised by a physiotherapist with extensive experience in evaluating functional tests in children and strictly followed a standardized protocol established by the European Respiratory Society/American Thoracic Society [23].

Conclusion

In conclusion, this study provides evidence of the influence of growth and development in the medium term on the 6MWD in healthy children aged 6 to 12 years. The 6MWD improved as the children's height increased, establishing a 12% change in the score of at least 79.69 m (MDC_{90}) as the most appropriate value in interpreting longitudinal functional performance data when assessing children's tolerance to exercise after an intervention.

Abbreviations

6-min walk test (6MWT), 6-min walk distance (6MWD), intraclass correlation coefficient (ICC), standard error of measurement (SEM), minimal detectable change (MDC)

Declarations

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Conflicts of interest/Competing interests: No potential conflict of interest was reported by the authors

Availability of data and material: The data that support the findings of this study are available from the corresponding author [PGF] upon reasonable request.

Code availability: Not applicable

Authors' contributions: Profs ILUV and TDC designed the study. JTC, GRP, PTL and NSM collection data. Prof ILUV analyzed the data. Profs ILUV, PGF and TDC interpreted the data. JTC, GRP, PTL, NSM, TDC and PGF did the literature search. All authors prepared the figures, tables and wrote the first draft of the manuscript. All authors critically reviewed and edited the manuscript.

Ethics approval: The study was approved by the local ethics committee of La Salle University Center for Advanced Studies (Madrid, Spain) (registration number: CSEULS-PI-211/2018) and the institutional boards of the participating schools and was conducted in accordance with the Declaration of Helsinki.

Consent to participate: Written informed consent was obtained from all the children and from their parents or legal guardians.

Consent for publication: All authors consent to publication of this manuscript.

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Tables

Table 1**.** Distances covered in the two 6-min walk test attempts, physiological variables and subjective variables of dyspnoea and fatigue at baseline and at 4 months.

		Baseline		4 months	
		Trial 1	**Trial 2**	**Trial 1**	**Trial 2**
6MWT (m)	**Mean ± SD**	613.53 ± 72.44	623.49 ± 82.11	633.38 ± 77.83	638.98 ± 79.99
	(min-max)	(448.5 – 744)	(489.3 – 800)	(474 – 795)	(486.5 – 784)
HR (bpm)	**Mean ± SD**	150.59 ± 28.53	152.95 ± 26.47	154.75 ± 23.9	154.97 ± 25.57
	(min-max)	(100 – 208)	(100 – 205)	(102 – 197)	(100 – 194)
Systolic BP (mmHg)	**Mean ± SD**	119.85 ± 10.64	119.78 ± 11.26	122.95 ± 11.52	121.97 ± 12.04
	(min-max)	(93 – 144)	(99 – 149)	(97 – 140)	(99 – 146)
Diastolic BP (mmHg)	**Mean ± SD**	71.19 ± 7.04	69.36 ± 7.15	69.37 ± 6.44	69.44 ± 6.22
	(min-max)	(55 – 89)	(56 – 88)	(58 – 83)	(58 – 82)
Dyspnoea (EPInfant)	**Mean ± SD**	5.64 ± 1.74	6.37 ± 2.3	6.17 ± 2.24	6.63 ± 2.55
	(min-max)	(2 – 10)	(1 – 10)	(1 – 10)	(0 – 10)
LL-Fatigue (EPInfant)	**Mean ± SD**	5 ± 2.5	5.32 ± 2.59	5.32 ± 2.72	5.19 ± 2.94
	(min-max)	(0 – 10)	(0 – 10)	(0 – 10)	(0 – 10)

Abbreviations: SD, standard deviation, 6MWT, six-minute walk test, HR, heart rate, BP, blood pressure, LL, lower limbs.

Table 2**.** Descriptive data and the comparisons between the measurements at baseline and at 4-months for age, physical activity levels, anthropometric variables, and distance covered in the 6-min walk test.

	Mean ± SD		Mean difference (95% CI), Effect size *(d)*
	Baseline	4 months	
Age (years)	9.08 ± 1.8	9.29 ± 1.8	-0.2 (-0.31 to -0.1)**, *d*= 0.12
Weight (Kg)	35.13 ± 8.92	37.14 ± 9.16	-2.01 (-2.25 to -1.78)**, *d*= 0.22
Height (cm)	136.77 ± 12.28	139.81 ± 11.98	-3.04 (-3.53 to -2.55)**, *d*= 0.25
Physical activity level (METs)	7272.88 ± 6937.48	8797.21 ± 8048.3	-1524.33 (-3549.38 to 500.73), *d*= 0.20
6MWD (m)	632.98 ± 78.54	650.05 ± 77.47	-17.07 (-29.65 to -4.48)**, *d*= 0.22

Abbreviations: 6MWD, six-minute walk test distance, CI, confidence interval, METs, metabolic equivalent of task.

Table 3. Regression model for change in 6MWD walked by healthy children after 4 months.

Criterion variable: Change in 6MWD after 4 months				
R^2 = 0.460 SEE = 35.786 F = 48.650 P < .001 Durbin-Watson = 1.769				
	Regression coefficient (B)	**Standardized coefficient (β)**	**P-value**	**VIF**
Predictor variables				
height	17.338	0.679	<.001	1.00
Excluded variables				
Age	-	-0.069	0.482	1.000
Sex	-	-0.103	0.298	1.009
eight	-	0.064	0.621	1.701
METs	-	0.002	0.983	1.033

Abbreviations: 6MWD, six-minute walk test distance, SEE, standard error of the estimate, VIF, variance inflation factor, METs, metabolic equivalent of task.

Table 4. Descriptive statistics and the test-retest reliability observed within and between the initial measurement and that performed at 4 months for the 6-min walk test.

Inter-sessions Test-retest Reliability for the 6MWT (Baseline vs 4 months)					
Mean ± SD	**ICC (95% CI)**	**SEM**	**MDC$_{90}$**	**MDC$_{95}$**	**4 months**
Baseline					
632.98 ± 78.54	650.05 ± 77.47	0.79 (0.66 to 0.88)	34.15 m	79.69 m, 12%	94.66 m, 15%
Within-session Test-retest Reliability for the 6MWT					
Mean ± SD		**ICC (95% CI)**	**SEM**	**MDC$_{90}$**	**MDC$_{95}$**
Baseline Trial 1	**Baseline Trial 2**				
613.53 ± 72.44	623.49 ± 82.11	0.87 (0.79 to 0.92)	27.51 m	64.19 m, 10%	76.25 m, 12%
Mean ± SD		**ICC (95% CI)**	**SEM**	**MDC$_{90}$**	**MDC$_{95}$**
4 months Trial 1	**4 months Trial 2**				
633.38 ± 77.83	638.98 ± 79.99	0.88 (0.81 to 0.93)	26.93 m	62.84 m, 10%	74.65 m, 12%

Abbreviations: 6MWT, six-minute walk test, SD, standard deviation, ICC, intraclass correlation coefficient, CI, confidence interval, SEM, standard error of measurement, MDC, minimal detectable change.