

Task-specific walking training improves walking ability in an individual with vitamin B12 deficiency peripheral neuropathy: a case report

Treino específico da tarefa melhora a capacidade de marcha em um indivíduo com neuropatia periférica por deficiência de vitamina B12: relato de caso

El entrenamiento específico para tareas mejora la capacidad de marcha en un individuo con neuropatía periférica por deficiencia de vitamina B12: um estudio de caso

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Resumo

Introdução. Homem de 32 anos, com neuropatia periférica induzida por deficiência de vitamina B12, diagnosticado por meio de parâmetros laboratoriais e eletroneuromiografia. Apresentava história de 3 meses de fraqueza leve de ambos os membros inferiores, associada a distúrbios da marcha, histórico de quedas e fadiga. **Método.** Após a avaliação pré-tratamento, iniciou o programa de treino específico da tarefa. Para elucidar os efeitos terapêuticos do programa de terapia, o TUG, 10MWT e 6MWT foi realizado para avaliar o risco de queda, velocidade da marcha, resistência da marcha e capacidade de caminhar longas distâncias e funcionalidade na linha de base pré-tratamento, 90 dias e 180 dias de programa de treino específico da tarefa de marcha. **Resultados.** Após 180 dias de intervenção, apresentou melhora no teste TUG, totalizando uma melhora de 31% em relação ao tempo basal (5,1 segundos mais rápido). No 10MWT, a melhora da velocidade da marcha apresentou um aumento de 50% em relação à velocidade inicial. Na última avaliação da distância percorrida, aos 180 dias de intervenção, o participante também apresentou melhora da resistência, chegando a 284 metros em 6 minutos de caminhada confortável. **Conclusão.** O treino específico da tarefa de marcha descrito para este paciente resultou em melhora da capacidade de caminhada após 180 dias de intervenção, incluindo velocidade da marcha, resistência da marcha, capacidade de caminhar por longas distâncias e risco de queda.

Unitermos. Neuropatia periférica; vitamina B12; reabilitação; fisioterapia

Abstract

Introduction. A 32-year-old man, diagnosed with vitamin B12 deficiency neuropathy by means of laboratory parameters and electroneuromiography, and presented 3 month history of mild weakness of both lower limbs, associated with gait disturbances, fall history and fatigue. **Method.** After the pre-treatment evaluate, he started the exercise therapy program. To elucidate the therapeutic effects of exercise therapy program, the TUG, 10MWT and 6MWT was performed to evaluate the fall risk, gait speed, gait endurance and ability to walk over longer distances and functionality at the pre-treatment baseline, 90 days and 180 days

of exercise therapy program. **Results.** After 180-days of intervention, he showed an improvement on TUG test, totalizing an improvement of 31% when compared to the baseline time (5.1 seconds faster). On the 10MWT, the gait speed improvement presented an increased of 50% compared to the baseline speed. On the last walking distance assessment, at 180-days of intervention, the participant also showed an improvement of endurance, reaching 284 meters in 6 minutes of comfortable walking. **Conclusion.** The described exercise therapy program for this patient resulted in improved walk ability after 180-days of intervention, including gait speed, gait endurance, ability to walk over longer distances and fall risk.

Keywords. Peripheral neuropathy; vitamin B12; rehabilitation; physical therapy

Resumen

Introducción. Hombre de 32 años con neuropatía periférica inducida por déficit de vitamina B12, diagnosticada mediante parámetros de laboratorio y electroneuromiografía. Presentaba debilidad leve en ambos miembros inferiores de 3 meses de evolución, asociada a alteraciones de la marcha, antecedentes de caídas y fatiga. **Método.** Después de la evaluación previa al tratamiento, se inició el programa de entrenamiento específico de la tarea. Para dilucidar los efectos terapéuticos del programa de terapia, se realizaron TUG, 10MWT y 6MWT para evaluar el riesgo de caídas, la velocidad de la marcha, la resistencia a la marcha y la capacidad para caminar largas distancias y la funcionalidad al inicio del pretratamiento, 90 días y 180 días de tratamiento específico. programa de entrenamiento para el retraso de la marcha. **Resultados.** Después de 180 días de intervención, mostró mejoría en la prueba TUG, totalizando una mejora del 31% en relación al tiempo basal (5,1 segundos más rápido). A las 10MWT, la mejora en la velocidad de la marcha mostró un aumento del 50% con relación a la velocidad inicial. En la última valoración de la distancia recorrida, a los 180 días de intervención, la participante también mostró mejoría en la resistencia, alcanzando los 284 metros en 6 minutos de marcha cómoda. **Conclusión.** El entrenamiento específico para retrasar la marcha descrito para este paciente dio como resultado una mejora en la capacidad para caminar después de 180 días de intervención, incluida la velocidad de la marcha, la resistencia de la marcha, la capacidad para caminar largas distancias y el riesgo de caídas.

Palabras clave. Neuropatía periférica; vitamina b12; rehabilitación; fisioterapia

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INTRODUCTION

Vitamin deficiencies is a common nutritional disorder and, unless severe, they are often clinically unrecognized. Vitamin B12 is an essential micronutrient required for normal cell function as it participates in a variety of critical processes including DNA, fatty acids and myelin synthesis^{1,2}. The exact prevalence of vitamin B12 deficiency in the general population is unknown and the actual data is

devived from a small survey, however, it may be a public health problem that could affects millions globally in both developing and developed countries³⁻⁵. The main causes of B12 deficiency are inadequate dietary intake, the animal source foods are the only natural source of this vitamin, so deficiency is prevalent when intake of these foods is low due to their high cost, lack of availability, or cultural or religious beliefs^{1,4}. Another frequent cause of B12 hypovitaminosis is caused by the food-cobalamin malabsorption syndrome. Further causes of hypovitaminosis are gastric surgery, drugs, genetic mutations., parasitic infection, medications (proton pump inhibitors)^{1,4,6}.

Vitamin B12 deficiency is a condition associated with haematological and central nervous system manifestation¹. However, there is an accumulating body of evidence indicating that B12 deficiency leads to peripheral nervous system abnormalities, such as sensory deficits, muscle weakness, increased fadigability and pain, but differently to the common form of neuropathies, B12 deficiency neuropathy are sometimes asymmetrical, or have a non-length-dependent distribution^{1-3,7}. Therefore, diagnosing B12 deficiency as a cause of peripheral neuropathy remains challenging, mostly because of the poor sensitivity of methods of determination for B12 levels as well as the numerous other causes of neuropathies^{6,8,9}.

The current management of peripheral neuropathy is mostly symptomatic and a large number of medications

have been proposed for the management symptoms, which may not rehabilitate the neuromuscular function that has been affected by the neuropathy¹⁰. On the other hand, the exercise therapy was discussed in a Cochrane review in 2004, the primary aim was to examine its effect on functional ability in the treatment of people with peripheral neuropathy and also, as a secondary aim, it was verified the outcomes of muscle strength, endurance, broader measures of health and wellbeing. The included trials did not show that strengthening and endurance exercise programs improve functional ability or reduce disability in people with peripheral neuropathy. However, there is some evidence that strengthening exercise programs were moderately effective in increasing the strength of tested muscles¹¹. Therefore, exercise therapy with the aim of developing strength and endurance, should be integrated into the routine management of neuropathies and may serve as a prioritised approach in rehabilitation.

In the present report, we describe a rare case of a young adult patient who was diagnosed with vitamin B12 deficiency neuropathy by means of laboratory parameters and electroneuromyography, who manifested an asymmetrical weakness in the lower limbs, gait deficit, fall reporting and increased fatigability, which all combine to contribute considerably to impair his functionality. Furthermore, the purpose of our study was to discuss and evaluate an exercise therapy program based on strengthening

exercises plus task-specific walking training four times per week over 180 days as propose to improve its functionality.

METHOD

Study Design and case presentation

This study was characterized as a case report and carried out from November 2021 to June 2022. This study was approved by the Human Research Ethics Committee (CAAE: 51338221.5.0000.5378). The case participant was a 32-year-old male man, diagnosed with vitamin B12 deficiency neuropathy by means of laboratory parameters and electroneuromiography, and presented 3 month history of mild weakness of both lower limbs, mainly in the right side which was associated with gait disturbances, fall history and fatigue. There were urinary symptoms and constipation but non symptoms related to sensitive system. There was no history of Human Immuno deficiency Virus (HIV) infection, diabetes, thyroid disease, syphilis, liver disease, renal disease, diphtheria, spinal cord injury or exposure to heavy metals. The participant was in use of cytidine-uridine-hydroxicobalamine complex, twice daily by oral administration, and it continued througout the duration of the intervention.

At the time of the study, the participant required assistance with activities of daily living, but was able to walk short distances with the aid of a Lofstrand crutch (Canadian crutch) and slowly climb the stairs one leg at a time using the handrail to provide stabilitiby and support.

The complete blood exams and electroneuromyography was presented to the physical therapist at pre-treatment baseline to confirm hematological alterations and the vitamin B12 deficiency peripheral neuropathy by means of vitamin B12 parameters and electroneuromyography pattern (Table 1 and 2). The blood test and the electroneuromyography was performed at the same week of the beginning of exercise therapy program.

Exercise therapy program

The physiotherapy evaluation and treatment was performed in a Center of Physical Rehabilitation from a non-profit non-governmental organization named ABAVIN, in Barretos, São Paulo, Brazil. The proposed exercise therapy program was based on strengthening exercises and task-specific walking training, which consisted of 1 hour session, four times per week over 180 days. The strengthening exercises for lower limbs and task-specific walking training was conducted in an interspersed way.

For the strengthening program the participant was instructed to perform three sets of 10 repetitions for each exercise. The following lower limb muscular groups were trained during sessions: hip flexors and extensors; knee flexors and extensors; ankle dorsiflexors and plantarflexors. The progression of the strengthening exercises was focused on increase the range of motion and, once resistance was

introduced, the progression was made by increasing the weight machines.

Table 1. Complete laboratory parameters presented in the initial evaluation.

	Results	Units	Reference interval
RBC	3.29	million/mm ³	4.5 – 6
Hemoglobin	11.7	g/dL	13 – 18
Hematocrit	34.5	%	36 – 54
MCH	35.6	Pg	27 – 31
MCV	104.9	fL	82 – 94
MCHC	33.9	g/dL	32 – 36
RDW	14.1	%	11 – 14
WBC	4180	cell/mm ³	5000 – 10000
Neutrophils	50.3	%	50 – 70
Eosinophils	3.8	%	1 – 4
Basophils	0.2	%	0 – 1
Lymphocytes	38.8	%	20 – 45
Monocytes	6.9	%	4 – 8
Platelets	263,000	cell/mm ³	150,000 – 440,000
Magnesium	2.1	mg/dL	1.6 – 2.6
Potassium	3.8	mEq/L	3.5 – 5.0
Sodium	139	mEq/L	136 – 145
Total cholesterol	170	mg/dL	< 200
Triglycerides	147	mg/dL	< 150
TSH	1.35	microUI/mL	0.38 – 5.85
Vitamin B12	50	pg/mL	211 – 911

Table 2. Values of motor and sensory nerve conduction presented in the initial evaluation.

Nerve	Latency ¹ (ms)		Amplitude ²		Velocity (m/s)	
	left	right	left	right	left	right
Motor						
Posterior tibial	5.74	6.23	5.57	5.45	40.47	44.75
Common fibular	4.52	3.78	3.91	4.88	44.71	40.48
F-wave	57.37	58.11	-	-	-	-
Sensitive						
Sural	4.15	4,52	1.95	4.33	35.71	36.88
H-reflex	34.18	33.81	-	-	-	-

¹ Peak latencies of all sensory nerves, onset latencies of all motor nerves; ² Amplitudes are measured in millivolt (mV, motor) and in microvolt (μ V, sensory). All amplitudes were determined based on the base-to-peak value.

The task-specific walking training consisted in a program which incorporate the practice of functional movements in a real situation with an objective to help patients to gain optimal control strategies for improving motor control. The following activities were used in the program: step up and down on a block; lateral step up and down on a block; lateral walking; backward walking; walking on a straight line; one leg plantarflexion; normal squat. The progression of the task-specific walking training was focused on reduce hand support and increase speed of the activities.

Gait-related measures

The gait assessment was performed at the pre-treatment baseline to verify the walking ability before the proposed intervention, and was assessed at 90 and 180

days of intervention by means of the Timed Up & Go (TUG) test¹², the 10-meter walk test (10MWT)¹³, and the 6-minute walk test (6MWT)¹⁴. All the tests were performed in an outdoor 15-meter-long corridor in our Center of Physical Rehabilitation, completely free of traffic, with a flat floor and marked at 1 meter intervals. The delimitation of the circuit was indicated with traffic cones. Participant wore comfortable clothing and shoes, and was allowed to use his usual walking aids, if necessary. Immediately before starting each test, the patient received guidance.

Timed Up & Go test

To perform the TUG test, the participant was asked to stand up from a 45cm-high-chair, walk 3 meters as quickly and safely as possible, turn around in a traffic cone, return to the chair and sit down, at the initial position. The required time to perform this activity was measured (in seconds). A total of three measurements were performed with an interval of 3 minutes between measurements, with the best performance being considered for data analysis.

The TUG test was used to determine his performance of multiple tasks, including sit-to-stand transfers, gait speed, and postural stability. The time required for a subject to stand up from a chair, walk 3 meters, return to the chair and sit down has been used as an indicator of patients who are at risk of falling.

10-Meter Walk Test

The participant was asked to walk for a 15-meter-long corridor at a comfortable speed. To eliminate the acceleration and deceleration component of the gait, the initial and the final 2.5 meters were discarded of the measurement, therefore, only the central 10 meters of the corridor was used as outcome. The time required to perform this activity was measured (in seconds) and the gait speed is defined as the distance walked per unit time (meters per second). Three measurements were performed and the best performance was used for data analysis. The participant also had 3 minute to rest, between measurements.

The gait speed were calculated and converted into percentage of improvement, which is the ratio of positive change, expressed by a percentage. The improvement percentage of the participant is relative to the baseline walking speed and these data was converted into functional ambulation classes according as follows: <0.15m/s - physiological; 0.15–0.4m/s - household; 0.4–0.8m/s - limited community; and >0.8m/s - full community¹⁵.

6-Minute Walk Test

To execute the 6MWT, the participant was asked to walk for a 15-meter-long corridor during 6 minutes, at a comfortable speed. Standardized verbal encouragement was provide at minute intervals ("You are doing well",

"Good job, continue!" And "Keep up the good work"). The 6MWT was used to determine gait endurance and ability to walk over longer distances. The participant walked for 6 minutes at comfortable speed and could rest when they felt unable to continue.

Outcomes analysis

The participant was assessed at the pre-treatment baseline and 90 and 180 days of the exercise therapy program. All collected data were entered into a Microsoft Excel spreadsheet. Tables and graphs were used to make comparisons among different periods of gait assessment in order to verify the effectivity of the exercise therapy program. For the TUG and 10MWT test, three measurements were performed and the best performance was used for data analysis.

RESULTS

Laboratory parameter

A review of her laboratory parameters at the pre-treatment baseline showed lower values in hemoglobin (11.7g/dL) and hematocrit levels (34.5%) compared to normative values, which was an indicative of a mild anemia. There was also a decrease in Vitamin B12 level, proving a severe hypovitaminosis. The participant presented 50pg/mL of B12, while the normative value for vitamin B12 is between 211 and 911pg/mL, as shown in Table 1.

Electroneuromyography parameters

The assessment of sural, superficial fibular, posterior tibial and common fibular nerve was performed by means of electroneuromyography. The analysis showed a reduction of motor and sensitive conduction velocity, with decreased amplitude of motor and sensory action potentials. The H-reflex and F-wave of posterior tibial nerve showed prolonged latencies with preserved amplitudes, suggestive of demyelinating sensorimotor neuropathy of all analyzed nerves, as shown in Table 2.

Gait parameters

The measurements of the TUG, 10WMT and 6MWT from pre-treatment baseline, 90 and 180-days of proposed intervention are compiled, as shown in Table 3.

The assessment of walking ability at the pre-treatment baseline showed that the time required on TUG test was 16.22 seconds, however, after 90-days of intervention the measurement showed an improvement in 20% of the initial time, reaching 12.97 seconds to perform the activity (3.25 seconds faster). After 180-days of intervention, the measurement also showed an improvement of the time, reaching 11.12 seconds to complete the activity, totalizing an improvement of 31% when compared to the initial time (5.1 seconds faster).

Table 3. Measured values of gait parameters at the pre-treatment baseline, 90 days and 180 days of exercise therapy program.

Gait tests	Pre-treatment baseline	90-days	180-days	Units
TUG (time)	16.22	12.97	11.12	seg
10MWT (time)	13.52	10.87	8.93	seg
10MWT (speed)	0.74	0.92	1.12	m/seg
6MWT (distance)	135	254	284	meters
6MWT (speed)	0.37	0.70	0.78	m/seg

At baseline, the gait speed measured on the 10MWT was 0.74m/seg, which means the participant completed the activity in 13.52 seconds. The analysis of the data showed an improvement in 90 and 180-days of intervention, reaching 0.92 and 1.12m/seg, respectively, and completed the activity in 10.87 and 8.93 seconds, showing an improvement in all tested period. The percentage of gait speed on the 10MWT increased approximately 25% at 90-days of the proposed intervention. Moreover, at 180-days of intervention the percentage of gait speed improvement presented an increased of 50% compared to the baseline speed, indicating an important functional improvement.

The walking distance on the 6MWT was 135 meters at the pre-treatment baseline, whereas at 90-days of intervention the analysis showed that the walking distance was 254 meters. On the last walking distance assessment,

at 180-days of intervention, the participant also showed an improvement of endurance, reaching 284 meters in 6 minutes of comfortable walking. The gait speed measured on the 6MWT was 0.37m/seg at the pretreatment baseline and, 0.70 and 0.78m/seg at 90 and 180-days of intervention, respectively.

DISCUSSION

In the present study, we addressed the possibility to discuss an exercise therapy program based on strengthening exercises plus task-specific walking training four times per week over 180 days as proposed to improve functionality and walk ability. We observed that the findings of the current study are in accordance with previous reports that vitamin-B12 deficiency produces important long-lasting effects on functionality, manifested by an asymmetrical weakness in the lower limbs, gait deficit, fall reporting and increased fatigability. The therapeutic effects of the exercise therapy program were determined based on the results of the TUG, 10MWT and 6MWT that were performed to evaluate the fall risk, gait speed, gait endurance and ability to walk over longer distances and, besides that, it was possible to establish the walk ability classification at the pre-treatment baseline, 90 days and 180 days of exercise therapy program.

Vitamin B12 deficiency with haematological and neurological manifestations is uncommon in young adults, however, it was observed in this reported case with

alterations in laboratory and electroneuromyography parameters. Compared to normative values, a lower value of hemoglobin, hematocrit and Vitamin B12 was observed in the laboratory parameters, which was an indicative of a mild anemia and a severe hypovitaminosis. Evidence of demyelinating neuropathy was also observed with a reduced conduction velocity and a decreased action potential amplitude of motor and sensory nerve, registered by means of electroneuromyography.

Globally, the vitamin B12 deficiency is particularly more frequent in elderly and it is generally higher in women than in men. Its deficiency is most likely due to the low consumption of animal-source foods, high incidence of atrophic gastritis or difficulty in absorbing vitamin B12 from animal-source foods caused by absence of intrinsic factor^{1,4,9}. The vitamin B12 deficiency affects <3% of those aged 20–39 years³ and it indicates that this report presents a rare case of vitamin B12 deficiency with hematological and neurological manifestation in a young adult. Besides that, only a very few reports have been documented cases about gait disturbances in patients with vitamin B12 deficiency peripheral neuropathy or reports aiming to verify the effectivity of the exercise therapy program which increase the importance of this report.

Gait abnormalities negatively impact daily life activities, participation at home and/or in the community, and affect the quality of life of people with disabilities, thus, an effective approach aiming to reduce gait alterations is

essential. Many interventions have been designed to improve walking function, however, an accumulating body of evidence reveals that task-specific training is effective in improving lower limb activities in general and walking outcomes specifically¹⁶⁻¹⁹. In this therapy the patients practice context-specific motor tasks and focus on improvement of performance in functional tasks through goal-directed practice and repetition¹⁶. However, “task-specific training” is an generic term used to describe several approaches including task-orientated training and repetitive task training^{16,18,19}.

The results shown here are consistent with our hypothesis that strengthening exercises plus task-specific walking training may act improving the patient functionality against the gait alterations in a young adult patient who was diagnosed with vitamin B12 deficiency neuropathy. So far, there is plenty of evidence indicating that the brain is able to reorganize itself in response to change in behavioural demands through neuroplasticity^{16,20}, therefore, the task-specific training can restore function by using non-affected or supplementary parts of the brain (for detail review²¹). Studies reveal that task-specific training shows effective results in diferents neurological conditions, as stroke, traumatic brain injury, Parkinson’s disease, spinal cord injury and brachial plexus injury, however, to the best of our knowledge, the tast-specific training have never been used to analyze the therapeutic effects on gait ability in vitamin B12 deficiency peripheral neuropathy. More

studies need to be performed in order to establish the effectiveness of task-specific walking training in peripheral neuropathy.

The gait speed was measured in two types of tests and, the data obtained on the 6MWT showed a lower speed compared to that results on the 10MWT. Thus, using the gait speed data obtained on the 10MWT, the individual was classified as limited community ambulator at the baseline assessment and, at the end of the exercise program he was classified as full community ambulator. On the other hand, using the gait speed data collected on the 6MWT, the individual was classified as household ambulator at the baseline assessment and limited community ambulator at the end of the exercise program¹⁵. Suggesting that 10MWT and the 6MWT may measure different aspects of walking function in patients with peripheral neuropathy.

CONCLUSION

The results presented here suggests that a strengthening exercises plus task-specific walking training could be an effective form of exercise therapy program for improving mobility in patients with peripheral neuropathy. This program significantly improved walk ability, including gait speed, gait endurance, ability to walk over longer distances and fall risk.

Due to the case report design of the present study, we could not compare the effect of this particular exercise therapy program to a control group. Further research with

larger sample sizes is required before recommendations for practice can be made, hence, a randomized controlled trial is warranted.

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