

# Nonpharmacological interventions and outcomes in the management of complications of human T-cell lymphotropic virus type 1-related myelopathy/tropical spastic paraparesis: A systematic review

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**Background:** Human T-cell lymphotropic virus type 1 (HTLV-1)-related myelopathy/tropical spastic paraparesis (TSP) is a progressive inflammatory process affecting the spinal cord that occurs as a result of HTLV 1. The use of nonpharmacological approaches has always been one of the treatment strategies in these patients, but disagreement about these interventions and their results has led to their limited use. Therefore, this study aimed to identify nonpharmacological interventions and their consequences in these patients. **Materials and Methods:** We followed the Cochrane Handbook for systematic reviews of interventions. The present report is organized according to the preferred reporting items for systematic reviews and meta-analyses. This study was conducted at PubMed, Cochrane Library, Web of Science, and Scopus, among all published studies by December 30, 2021. Keywords were: HTLV-1, Human T-lymphotropic virus 1, HTLV-1-associated myelopathy, HAM/TSP, tropical spastic paraparesis, nonpharmacological intervention, nonpharmacological treatment, massage, physiotherapy, acupuncture, acupressure, and exercise. The quality of the studies was assessed using JADAD. **Results:** Of 288 articles, 11 were eligible for data extraction published between 2014 and 2021. 90/9% of studies were randomized clinical trials. 81/8% of articles were of high quality. The total sample size was 253 people, of which 137 (54/15%) were women. Approaches such as exercise and motion therapy, electrotherapy, behavioral therapy, and virtual reality can be used for these patients. With these interventions, results such as improved mobility and balance, physical condition, pain, quality of life, muscle spasticity, maximum inspiratory pressure, and urinary symptoms can be achieved. **Conclusion:** The most common physical therapy method used in studies was active and passive body movements, which are associated with positive results for patients. Due to the small sample size in this group of studies, it is necessary to conduct more clinical trials for more accurate conclusions. Furthermore, due to the limited number of studies that have used electrical stimulation or combined intervention packages, it is not possible to say with certainty what effect these methods have on patients. It is necessary to conduct more clinical trials.

**Key words:** Human T-cell lymphotropic virus type 1, human T-cell lymphotropic virus type 1-related myelopathy, systematic review, tropical spastic myelopathy

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## INTRODUCTION

Human T-cell lymphotropic virus type 1 (HTLV-1) is a retrovirus that is transmitted during sexual intercourse,

contact with infected blood and tissues, and from mother to child. It is clear that some countries have a higher prevalence of HTLV-1 infection based on population size.<sup>[1]</sup> There are foci in South America, especially in parts of Colombia and French Guyana, some areas

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of intertropical Africa, and in the Middle East (such as the Mashhad region in Iran), and rarely isolated clusters in Australia and Melanesia.<sup>[2]</sup> This infection can lead to a diverse clinical picture and tends to become chronic.<sup>[3]</sup> Overall, 3%–5% of people infected with HTLV-1 develop tropical spastic paraparesis (TSP) (HTLV-I-associated myelopathy [HAM]/TSP) (HTLV-I-related myelopathy/TSP) in the fourth decade of life.<sup>[4]</sup> HAM/TSP is a chronic, degenerative, and progressive inflammatory process that affects the spinal cord, and causes demyelination and decreased sensory capacity.<sup>[5]</sup> The most common symptoms of lower extremity muscle weakness are hyperreflexia, hypertension, pelvic floor dysfunction, and moderate-to-severe pain.<sup>[6]</sup> To be able to continue long-term or lifelong treatments, it is necessary to start treatment approaches as soon as possible, safely, and at a low cost.<sup>[7]</sup> Nonpharmacological methods may play an important role in the management of symptoms in people. Over the past few years, the use of nonpharmacological methods to manage the problems and physical symptoms of these patients has been considered and several articles have examined the effects of such interventions.<sup>[5]</sup> However, there is little evidence of the effectiveness of nonpharmacological approaches in patients with this disease.<sup>[7]</sup> Therefore, the current systematic review has two key objectives: first, to identify nonpharmacological approaches that can be used in these patients, and second, to identify the results of applying these approaches to patients.

## MATERIALS AND METHODS

### Study protocol

We followed the Cochrane Handbook for Systematic Reviews of Interventions.<sup>[8]</sup> The present report is organized according to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statements.<sup>[9]</sup> PICO was; (P) Patients with HAM/TSP, (I) Nonpharmacological interventions, (C) Routine care or standard care, (O) Psycho-physical. Hence, the search strategy was based on the following research question: What are nonpharmacological interventions in patients with myelopathy and what effect do it have on the psychophysical complications of patients?

### Search methods

The search was conducted in Web of Knowledge (ISI), PubMed, Scopus, and Cochrane Library by Mesh and nonMesh terms in the title, abstract, or full text of journal articles published until December 30, 2021. The search strategy included the following keywords: HTLV-1, Human T-lymph tropic virus 1, HTLV-1-associated myelopathy, HAM/TSP, Tropical Spastic Paraparesis, nonpharmacological intervention, nonpharmacological treatment, massage, physiotherapy, acupuncture, acupressure, and exercise. In addition, other references

from original articles and related reviews were searched and reviewed in these databases. Duplicate studies and reports based on screening titles and abstracts were removed. The full text of all remaining papers was reviewed for eligibility assessment. Electronic databases were searched manually in seminars, conferences, congresses and congresses, references and journals, and the WHO Clinical Trial Registration System. If you find a study abstract related to the title of the present study, the full text of the article was requested through correspondence with the responsible author. To access the grey resources, numerous searches were made in scientific databases. These searches did not yield any results.

### Eligibility criteria

Inclusion criteria included major English-language articles evaluating the effect of nonpharmacological interventions on psychological, physical, or both complications in HAM/TSP patients.

Pilot studies were omitted due to different sample sizes from the original research studies. Furthermore, if an article was published in multiple sources, the article published in the source with less validity was removed from the review. Studies whose full text could not be found despite correspondence with the authors were also excluded from the study.

### Study selection

The steps of study selection included the removal of duplicate records, the examination of titles/abstracts for possibly relevant studies, the examination of full texts for eligibility criteria, cross-checking between researchers to reach a consensus on study selection, quality assessment of select studies, and data extraction. Two authors independently examined the retrieved papers for the eligibility criteria. Disagreements were resolved by conservation. Furthermore, we manually screened the reference lists of the relevant studies to find possibly missing papers from the electronic search.

### Quality assessment

The quality of the articles was assessed using the JADAD scale. The scale also known as the Oxford quality scoring system has 7 items with a maximum score of 5 and a minimum score of 0. For the purpose of this review, studies with JADAD scores <3 were rated as low quality while those with scores ≥3 were rated as high-quality studies.<sup>[10]</sup>

### Data extraction

The data were gathered from the selected articles by two authors independently. They included authors' names, publication year, sample size, type of intervention, and findings.

## RESULTS

### Search outcome

In this study, all research conducted in English based on four stages of PRISMA was systematically reviewed. Initially, 279 studies were identified. After removing duplicate articles, abstracts and titles of 216 studies were evaluated. At this point, another 61 studies were excluded. Of the remaining 155 studies, 144 studies were excluded from the review due to the inadequacy of the full text of the articles. Finally, 11 studies were evaluated [Figure 1].

### Features of the study

A full description of the reviewed studies is provided in Table 1. Of 288 retrieved articles, 11 were eligible for data extraction, representing data on the final volume of 266 patients published between 2014<sup>[11-14]</sup> and 2021.<sup>[15]</sup> The study place is in all articles in Brazil, which is one of the endemic regions of the virus in the world, so the studies have a desirable and valid scientific background that strengthens the accuracy and robustness of the findings.

### Assessing the quality of trial methodology

Of the 11 studies extracted, 1 was a quasi-experimental study,<sup>[16]</sup> 5 were a randomized clinical trial,<sup>[14,17-20]</sup> and 5 were a randomized crossover clinical trial.<sup>[11-13,15,21]</sup> Furthermore, 18/18% of articles (2 cases) were of low quality<sup>[16,17]</sup> and 81/81% of articles (9 cases) were of high quality<sup>[11-15,18-21]</sup> [Table 2].

### Nonpharmacological interventions and consequences

In these studies, the main intervention approaches are physiotherapy, which includes exercise therapy,<sup>[11,19,20]</sup>

specialized physiotherapy movement,<sup>[12,16,18]</sup> and electrotherapy.<sup>[14]</sup> One study also used combination interventions in the form of behavioral therapy, physical exercise, and electrotherapy.<sup>[17]</sup> The use of virtual reality games<sup>[13,15,21]</sup> was another intervention used for these patients.

### Physiotherapy Exercise therapy

In two studies, the home exercise protocol was used.<sup>[19,20]</sup> Mota *et al.* used a home exercise program supervised by a physiotherapist, twice a week for 12 weeks. Each exercise therapy session lasted 50 min.<sup>[20]</sup> Macêdo *et al.* also used 45–50 min exercise sessions at home that were held twice a week for 12 weeks.<sup>[19]</sup> Borges *et al.* also considered Pilates as their intervention program, during which 1-h sessions were performed twice a week for 15 weeks.<sup>[11]</sup>

### Consequences

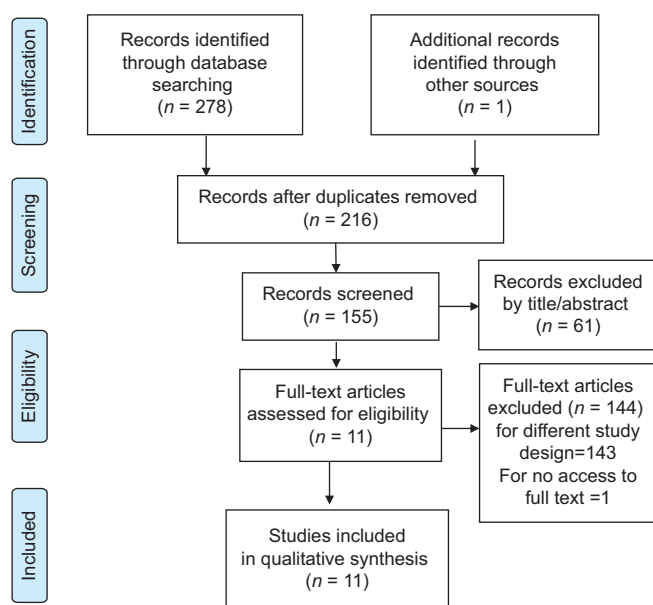
Three studies examined the effects of exercise therapy. In two studies, Mota *et al.* and Macêdo *et al.*, the home exercise program has been able to improve body angles, clinical mobility, patients' gait parameters, pain, and quality of life in terms of functional capacity.<sup>[19,20]</sup> In a study using a 15-week Pilate's program, patients' pain intensity and all aspects of their quality of life, except the functional dimension, had a significant improvement in the emotional role.<sup>[11]</sup>

### Specialized physiotherapy movement

In three studies, specialized physiotherapy movement<sup>[12,16,18]</sup> was selected as an intervention. In the study of Dias *et al.*, oral ventilation cycles with the help of a linear resistance device were considered physiotherapy exercises. Each 45-min cycle was considered three times a week for 5 weeks.<sup>[18]</sup> In a study comparing two movement therapy approaches, subjects in the experimental group practiced for 12 weeks and twice a week for 1 hour under the supervision of a physiotherapist to facilitate the movements of rolling, sitting, standing, walking and climbing stairs. In the control group, a 2-meter elastic tube was used to facilitate the same operation.<sup>[12]</sup> The study by Dosrodrigues *et al.* also benefited from twenty 50 to 60-min exercise sessions per week. This treatment program was designed by a physiotherapist with the aim of improving gait, balance, flexibility, and muscle strength.<sup>[16]</sup>

### Consequences

A study by Britto *et al.* showed that the use of deep sensory facilitation physiotherapy with the help of a physiotherapist can have a positive effect on low back pain intensity, functional independence, and Timed Up and Go test results. In this study, subjects in the control group who performed movements using a 2-m elastic tube, parallel bars, and without



**Figure 1:** Study selection process diagram (For more information, visit [www.prisma-statement.org](http://www.prisma-statement.org).)

**Table 1: Reviewed studies and their characteristics**

Reviewed studies and their characteristics	
Attributes	Status in the study
<b>1. Andrade 2016</b>	
Type	RCCT
<i>n</i>	
Control	0
Trial	21
Age (year), mean±SD	54±12
Gender	
Male	7
Female	14
Intervention	Behavior therapy + movement therapy + stimulation
Instrument	The score of the symptoms of overactive bladder + the Oxford score/PERFECT + King's Health Questionnaire
Outcome	Improvement in symptoms of urinary urgency, frequent urination, incontinence, enuresis, and feeling of incomplete emptying A decreased score of hyperactive bladder symptoms and increased perineal muscle strength Improved urodynamic parameters Reduction in the number of detrusor hyperactivity, detrusor-sphincter dyssynergia, detrusor contraction Improve the quality of life
<b>2. Borges 2014</b>	
Type	RCCT
<i>n</i>	
Control-pilates	10
Pilates-control	11
Age (year), mean±SD	48.73±10.07
Gender	
Male	6
Female	16
Body mass index	25.18±4.07
Intervention	Pilates exercises versus daily activities
Instrument	SF-36 + Visual Analog Scale
Outcome	Improvement in pain intensity Improving physical function, physical function, physical pain, vitality, general health perceptions, social role function, and mental health Lack of effect on emotional role function
<b>3. de Brito 2014</b>	
Type	RCT
<i>n</i>	
Group 1	7
Group 2	7
Age (year), mean±SD	
Group 1	47.7±14.
Group 2	50.4±12.4
Gender	
Male	7
Female	7
Average disease duration in group (year)	
Group 1	5.9±5.5
Group 2	6.1±4.2
Difficulty in walking (%)	73
Difficulty getting on the bus (%)	21
Falls (%)	7
Lower limb weakness (%)	93
Walking aids without support (%)	
Control	57

Contd...

**Table 1: Contd...**

<b>Reviewed studies and their characteristics</b>	
<b>Attributes</b>	<b>Status in the study</b>
<b>3. de Britto 2014</b>	
Trial	43
Help with a crutch (%)	
Group 1	29
Group 2	28
Help with two crutches (%)	
Group 1	14
Group 2	29
Intervention	Training to facilitate rolling, sitting, standing, walking, and climbing stairs versus using a 2-m water elastic pipe to facilitate similar functions
Instrument	Low-back pain of the patients was assessed using a yes/no question - modified Ashworth scale - Hip and knee segments (flexion and extension) were assessed, and both sides were compared- daily living activity scale - timed up and go test
Outcome	Reduction in low back pain in both groups Functional independence in the second group Improving the results of standing and walking tests in the first group Decreased right leg muscle tone in Group 2
<b>4. Dias 2020</b>	
Type	RCT
<i>n</i>	6
Age (year), mean±SD	60±0
Gender	
Male	1
Female	5
Bachelor	2
Married	3
Widower	1
Likely HAM/TSP	1
Definitive HAM/TSP	2
No HAM/TSP+tuberculosis	2
Intervention	Respiratory muscle training
Instrument	MIP using the GlobalMed® digital manovacuometer
Outcome	Increase in maximum inspiratory pressure
<b>5. Rodrigues 2015</b>	
Type	Semi-experimental
<i>n</i>	
Control	0
Trial	9
Age (year), mean±SD	51.6±0
Gender	
Male	3
Female	6
Intervention	Passive stretching (for the hip adductors, knee flexors, and ankle plantar flexors) + strength exercises were used for the upper and lower limbs and abdominal region, along with four specific PNF techniques
Instrument	Modified Ashworth Scale
Outcome	Reduction of quadriceps spasticity
<b>6. Fonseca 2021</b>	
Type	RCCT
<i>n</i>	
Early therapy	14
Late therapy	15
Age (year), mean±SD	51.02±9.83
Early therapy	46.89±11.43
Late therapy	52.27±7.95

Contd...

**Table 1: Contd...**

<b>Reviewed studies and their characteristics</b>	
<b>Attributes</b>	<b>Status in the study</b>
<b>6. Fonseca 2021</b>	
Gender	
Male	
Early therapy	5
Late therapy	8
Female	
Early therapy	9
Late therapy	7
Use of walking aid (%)	
Early therapy	8 (55.6)
Late therapy	7 (45.5)
Intervention	Sensory-motor exercises using video games
Instrument	Berg balance scale - Timed Up and Go Test - GoPro HERO 3.0® camera and analyzed with CvMob software - demographic questionnaire and provided a history of falls in the past 3 months
Outcome	Improvement in balance, standing and walking test time and walking speed
<b>7. Macêdo 2019</b>	
Type	RCT
<i>n</i>	
Supervised group	18
Unsupervised group	16
Control group	15
Age (year), mean±SD	
Supervised group	55.4±10.5
Unsupervised group	53.3±13.1
Control group	49.7±8.7
Gender	
Female	
Supervised group	12
Unsupervised group	11
Control group	9
Male	
Supervised group	6
Unsupervised group	5
Control group	6
Do not use	7
Supervised group	5
Unsupervised group	5
Control group	
Drug; reduce pain	5
Supervised group	6
Unsupervised group	3
Control group	
Drug; muscle relaxant/reduce urinary	
Supervised group	6
Unsupervised group	4
Control group	7
Drug; symptoms immunomodulatory	
Supervised group	0
Unsupervised group	1
Control group	0
Driving device; does not use	
Supervised group	7
Unsupervised group	4
Control group	8

Contd...

**Table 1: Contd...**

<b>Reviewed studies and their characteristics</b>	
<b>Attributes</b>	<b>Status in the study</b>
<b>7. Macêdo 2019</b>	
Driving device; uses	
Supervised group	11
Unsupervised group	12
Control group	8
Physiotherapy: Yes	
Supervised group	10
Unsupervised group	7
Control group	7
Physiotherapy: No	
Supervised group	8
Unsupervised group	9
Control group	8
Disease duration (year)	
Supervised group	10 (6–15)
Unsupervised group	11 (5.5–13)
Control group	8 (6–13)
Body mass index	
Supervised group	23.5±5.0
Unsupervised group	24.1±3.6
Control group	25.5±3.9
Intervention	Exercise training under the supervision of a physiotherapist versus the same exercise at home
Instrument	SF-36 health survey - the brief pain inventory - Omni scale
Outcome	Relative reduction of mean pain in both groups Improving the quality of functional life in treatment groups
<b>8. Mota 2020</b>	
Type	RCT
<i>n</i>	
Supervised group	18
Without-supervision group	16
Control group	15
Age (year), mean±SD	
Supervised group	55.4±10.5
Without-supervision group	53.3±13.1
Control group	49.7±8.7
Gender	
Female	
Supervised group	12
Without-supervision group	11
Control group	9
Male	
Supervised group	6
Without-supervision group	5
Control group	6
Intervention	Training under the supervision of a physiotherapist, performing supervised movements, and continuing exercises at home versus the same program individually according to the order of the physiotherapist exclusively in the first session versus routine care
Instrument	Timed Up and Go Test - GoProHeron2 camera- Postural Assessment Software
Outcome	Improved functional angles and mobility Positive effects on gait parameters The supervised group showed better responses than the unsupervised group, but both showed better responses than the control group
<b>9. Oliveira Arnau 2014</b>	
Type	RCCT
<i>n</i>	

Contd...

**Table 1: Contd...**

<b>Reviewed studies and their characteristics</b>	
<b>Attributes</b>	<b>Status in the study</b>
<b>9. Oliveira Arnau 2014</b>	
Control	5
Trial	4
Age (year), mean±SD	
Control	60.33±7.42
Trial	55.83±6.73
Gender	
Female	
Control	2
Trial	5
Male	
Control	2
Trial	0
Intervention	Exercises with virtual reality and exercises under the guidance of a physiotherapist versus exercises without virtual reality and under the supervision of a physiotherapist
Instrument	Sf-36 - Visual Analog Scale of pain - Berg Scale
Outcome	Improvements in balance, functional capacity Improvements in emotional aspects in the intra-group and intergroup analysis No effect on pain intensity
<b>10. Patricio 2020</b>	
Type	RCCT
<i>n</i>	
Control	13
Trial	13
Age (year), mean±SD	
Control	52.1±7.5
Trial	49.1±11.8
Gender	
Male	
Control	6
Trial	3
Female	
Control	7
Trial	10
Physiotherapy (%)	
Control	12 (92.3)
Trial	10 (76.9)
Body mass index	
Control	21.7±7.3
Trial	25.7±6.1
Intervention	Sensory-motor exercises through a virtual game versus routine care
Instrument	Baropodometry (by Footwork® system), cinemetry (angle of the body, hip and ankle alignment in the lateral view), the CVMob system, brief pain inventory, WHOQoL
Outcome	An increase in postural fluctuations in the control-test group Reduction of the occurrence of landslides Improving the quality of life in the test-control group Lack of effect on pain and balance in both groups
<b>11. Souto 2014</b>	
Type	RCT
<i>n</i>	
Control	10
Trial	10
Age (year), mean±SD	
Control	56.1±14.0
Trial	47.8±11.6

Contd...



**Table 1: Contd...**

Reviewed studies and their characteristics	
Attributes	Status in the study
Gender	
Female	
Control	7
Trial	8
Male	
Control	3
Trial	2
Use of walking device (%)	
Control	4 (40%)
Trial	5 (50)
Type of pain: Neuropathic(%)	
Control	7 (70)
Trial	6 (60)
Type of pain: Nociceptive (%)	
Control	3 (30)
Trial	4 (40)
Pain location: Lower back (%)	
Control	8 (80)
Trial	9 (90)
Pain location: Lower limbs (%)	
Control	2 (20)
Trial	1 (10)
Intervention	Electro-stimulator
Instrument	Visual analog scale, pain components description, pressure pain threshold, timed up and go test
Outcome	No significant difference between the two groups in terms of pain intensity, pressure pain, total SF-MPQ score, timed up and go

SF-36=Short Form-36; SD=Standard deviation; RCT=Randomized controlled trial; MIP=Maximal inspiratory pressure; HTLV-1=Human T-lymph tropic virus 1; HAM=HTLV-1 associated myelopathy; TSP=Tropical spastic paraparesis; PNF=Proprioceptive neuromuscular facilitation; WHOQoL=World Health Organization Quality of life; RCCT=Randomized concentration-controlled trial; SF-MPQ=short-form McGill Pain Questionnaire

the accompaniment of a physiotherapist, had less right leg muscle tone compared to the experimental group. However, based on the statistical analysis of the results of the muscle tone of the patients, there was no statistically significant difference between the two groups.<sup>[12]</sup> The study, which was conducted with the main purpose of using the International Scale of Function, Disability, and Health, showed that after using a treatment program aimed at improving gait, balance, flexibility and muscle strength, quadriceps spasticity there will be a significant reduction.<sup>[16]</sup> Furthermore, using respiratory muscle training, a significant increase in maximal tail pressure in these patients can be achieved.<sup>[18]</sup>

### Electrotherapy

In the study of Souto *et al.*, the use of electrotherapy was the intervention of choice for patients. In electrotherapy, stimulation was performed in the transcranial region. This intervention was performed with 2 mA and 25 m<sup>3</sup> electrodes for 20 min for 5 consecutive days.<sup>[14]</sup>

### Consequences

According to the findings of Souto *et al.*, transcranial electrotherapy is able to relieve patients' pain, but there was no significant difference between the two groups in

terms of pain intensity, Pressure Pain, Total SF-MPQ score, and Timed Up and Go threshold after the intervention.<sup>[14]</sup>

### Physiotherapy with other interventions

A study used a combined physiotherapy approach consisting of intra-anal or vaginal electrotherapy, behavioral therapy, pelvic floor muscle exercises, and movement therapy to change patients' posture. This combination program was used twice a week for 60 min for 10 to a maximum of 40 sessions.<sup>[17]</sup>

### Consequences

Concomitant use of behavioral therapy, pelvic floor muscle exercises, and electrotherapy can be effective in improving neurogenic genital symptoms. This combination intervention is able to reduce the urgency of defecation, incontinence, and enuresis, the feeling of incomplete emptying of the bladder. The score of hyperactive bladder symptoms decreased and the perineal muscle strength increased. Urodynamic parameters improved. The number of patients with detrusor hyperactivity, detrusor sphincter dyssynergia, low detrusor contraction, and detector areflexia decreased and finally, the quality of life of patients increased.<sup>[17]</sup>

Table 2: Quality of studies

Pointing to being random	Proper randomization			A blind investigation			Proper blinding (single-blind=0/5 double blind=1)			Refers to trial interruptions and crashes		Refer to the inclusion and exclusion criteria		Reference to the method of investigating and unwanted side effects		Reference to the statistical analysis method		Total points/ quality level	Type of study
	Yes	No	Not mentioned	Yes	No	Not mentioned	Yes	No	Not mentioned	Yes	No	Yes	No	Yes	No	Yes	No		
*	*			*			*			*		*		*		*		2	RCCT
*	*			*	0/5		*		*		*		*		*		*	L	RCCT
*	*			*	0/5		*		*		*		*		*		*	H	RCT
*	*			*		*	*		*		*		*		*		*	H	RCT
*	*			*		*	*		*		*		*		*		*	3	RCT
*	*			*		*	*		*		*		*		*		*	H	RCT
*	*			*		*	*		*		*		*		*		*	2	Que-experimental
*	*			*	0/5		*		*		*		*		*		*	L	RCCT
*	*			*	0/5		*		*		*		*		*		*	H	RCT
*	*			*	0/5		*		*		*		*		*		*	H	RCT
*	*			*	*		*		*		*		*		*		*	7/5	RCCT
*	*			*		*	*		*		*		*		*		*	H	RCCT
*	*			*		*	*		*		*		*		*		*	4	RCCT
*	*			*		*	*		*		*		*		*		*	H	RCT
*	*			*		*	*		*		*		*		*		*	6	RCT
																		H	

\*= The status of the desired study in terms of that particular feature; RCT=Randomized controlled trial; RCCT=randomized concentration-controlled trial

### Virtual reality games

In three studies, physical exercises in the form of virtual reality games were provided to participants.<sup>[13,15,21]</sup> In Patrício *et al.*'s study, which was a randomized cross-sectional clinical trial, in the experimental–control group, first, sensorimotor exercises through virtual reality, twice a week, each session for 20 min and 10 weeks, for patients. In the experimental-control group, the intervention protocol was started after 10 weeks from the beginning of the study.<sup>[21]</sup> In the study of Oliveira Arnau, *et al.* in the experimental group, exercise was applied using virtual reality and under the supervision of a physiotherapist. While in the control group, exercise was performed without supervision and the use of virtual reality. The intervention was performed twice a week with an average time of 30 min for 8 weeks.<sup>[13]</sup> Fonseca *et al.* also studied the therapeutic effects of virtual reality video games on patients' mobility and balance in their cross-sectional randomized clinical trial. In their study, sensorimotor exercises were performed using video games for 20 min, twice a week for 10 consecutive weeks in the test–control group. In the control-experimental group, after 10 weeks, the intervention was applied.<sup>[15]</sup>

### Consequences

In three studies, the effects of virtual reality games were examined. In this regard, based on the results of the study of Patrício *et al.*, Oliveira Arnau *et al.*, and Fonseca *et al.*, virtual reality is able to reduce the frequency of falls, the quality of physical and mental life,<sup>[21]</sup> improves emotional, functional capacity,<sup>[13]</sup> patient walking and sitting, and standing speed.<sup>[15]</sup> However, this intervention approach has not been able to relieve patients' pain.<sup>[13,21]</sup>

### Different and contradictory findings

Although two studies showed that the use of virtual reality therapy can improve patient's balance,<sup>[13,15]</sup> one study showed that virtual reality games did not have a significant effect on patients' balance.<sup>[21]</sup> Furthermore, based on the findings of the study, virtual reality can increase the quality of life scores of patients in the physical and psychological dimensions,<sup>[21]</sup> while the study of Oliveira Arnau *et al.*, the effectiveness of virtual reality therapy only in aspects Emotional showed the quality of life.<sup>[13]</sup> In a study by Borges *et al.*, participating in an exercise program based on Pilate's exercises was not able to improve patients' emotional role performance.<sup>[11]</sup> However, according to the findings of Macêdo *et al.*, after the implementation of the exercise program at home, only the functional capacity of patients is improved.<sup>[19]</sup>

## DISCUSSION

Due to the need to use low-cost and low-complication

treatments, using nonpharmacological approaches can improve the physical and mental results in HAM/TSP.

When myelopathy is present, the pain is chronic,<sup>[22]</sup> reduces functional capacity,<sup>[23]</sup> and increases the likelihood of developing psychological symptoms.<sup>[22]</sup> It is also associated with a negative impact on quality of life and individual independence.<sup>[22]</sup> Patients may present with a heterogeneous range of neurological problems.<sup>[24]</sup> In addition, morphological and functional changes in the respiratory system due to an inflammatory process caused by the virus can lead to bronchiectasis, thickening of the pleura, and pulmonary scars.<sup>[25]</sup> Psychiatric disorders appear to be common in patients with HAM/TSP.<sup>[26]</sup> There is no proven treatment regimen for this disorder.<sup>[27]</sup> This systematic review showed that some nonpharmacological approaches alone or in combination with other medical interventions can have promising results in improving the signs and symptoms experienced by patients. According to the findings, exercise therapy relieves back pain,<sup>[11]</sup> and improves posture angles, mobility, and walking speed<sup>[20]</sup> of patients. It is also able to improve all aspects of patients' quality of life, except the emotional role function dimension,<sup>[11]</sup> and functional capacity<sup>[19]</sup> in them.<sup>[11]</sup> The development and implementation of an exercise therapy protocol under the supervision of health-care professionals can somewhat minimize the weakness caused by the lack of evidence-based clinical studies. Furthermore, a home-based exercise program can be an alternative strategy to increase long-term adherence to a rehabilitation program.<sup>[28]</sup> Since this review is the first systematic review in HAM/TSP patients, the results were compared with systematic reviews in other neurological disorders; several studies have examined the effectiveness of exercise programs in patients with neuromuscular disorders, myelopathy, and spinal cord injuries. These studies have also shown that exercise protocols have a significant positive effect on patients' mobility,<sup>[29,30]</sup> pain,<sup>[31,32]</sup> performance,<sup>[29,32]</sup> muscle strength,<sup>[33,34]</sup> gait, posture, and balance parameters.<sup>[34]</sup> However, contrary to the results of this study, some review studies have not confirmed the effectiveness of these exercises and programs in patients with neurological disorders.<sup>[33,35]</sup> This difference in findings can be related to the heterogeneity of exercise programs and protocols and muscles involved, duration and intensity of training, sample characteristics, effectiveness criteria, type and degree of disability of target group patients, and disease progression in them.

The use of specialized physiotherapy approaches such as deep sensory facilitation or specialized physiotherapy movement can improve pain, functional independence, standing and walking, pain, body tone, and spasm. In addition, the use of a physiotherapy intervention package,

which is a combination of behavior and motion therapy and electrical stimulation, can be effective in managing neurogenic bladder symptoms. Furthermore, respiratory physiotherapy exercises can be used prophylactically to strengthen the respiratory muscles of patients. Consistent with the findings of this review, some review studies suggest deep sensory facilitation to improve gait parameters,<sup>[36,37]</sup> pain,<sup>[38,39]</sup> disability,<sup>[37,39]</sup> performance,<sup>[38,39]</sup> and spasticity,<sup>[40]</sup> is suitable in some neurological disorders. Some other review studies confirm that noninvasive stimulation of the brain and spinal cord is effective in controlling pain;<sup>[41,42]</sup> the test score for standing and walking<sup>[43]</sup> and patients' quality of life are effective.<sup>[41]</sup> Ayeleke *et al.* (2013) showed that physical therapy techniques such as electrical stimulation of sacral and peripheral nerves, penetrating electrical stimulation, electrical acupuncture, combination therapy, pelvic floor muscle support exercises and radiofrequency bipolar are associated with positive outcomes for neurogenic bladder and quality of life.<sup>[44]</sup> Another study showed that specific pulmonary physiotherapy interventions are effective in improving respiratory outcome measures.<sup>[45]</sup> However, some review evidence is also inconsistent with this section of the present review results.<sup>[38,40]</sup> Differences in pathological processes, quantity, and quality of physiotherapy techniques used along with individual, cultural, and social characteristics that affect some problems such as the pain experienced in patients, can explain the difference in findings.

According to another part of the findings, the use of virtual reality can be effective in improving the frequency of falls, quality of life, mobility, and functional capacity and has no significant effect on patient pain. Despite achieving a similar result in the effectiveness of virtual reality on patient's balance in the Arno and Fonseca study, the Patrio study showed that the use of the virtual reality approach could not improve patients' balance. Because the quality score of the study by Arnau *et al.* (2014)<sup>[13]</sup> and Fonseca *et al.*'s study (2021)<sup>[15]</sup> is higher than Patrício *et al.*'s (2020)<sup>[21]</sup>, so we can be more confident in the results of their study and conclude that virtual reality is able to improve balance. Although virtual reality-based intervention is a new treatment that is mostly used in the treatment and rehabilitation of neurological diseases<sup>[46]</sup> to date, several published studies have examined the effect of virtual reality-based intervention on various health and disease outcomes in neurologic patients, and show that virtual reality is a practical and effective tool in the treatment of neurological disorders.<sup>[47,48]</sup>

However, the results of this review contradict some systematic reviews.<sup>[49,50]</sup> One of the reasons for the discrepancy between the results obtained in this study and the results of some similar review studies is the difference in the nature of some signs and symptoms such

as pain. The nature of pain in these studies is acute, while the pain experienced in patients with myelopathy due to the HTLV-1 virus is chronic neuronal pain, and disease progression and physical condition can complicate it. This requires pain relief in these patients requires a multifaceted approach. Therefore, there is insufficient evidence to support the soothing effect of virtual reality on patients' pain. Furthermore, variables such as balance and mobility can be caused by various pathological processes, and the combination of other changes, such as visual disturbances and psychological changes, can aggravate this condition. Therefore, the results have been reported differently in different studies. On the other hand, the quality of life variable can be affected by the diversity of demographic and socio-cultural characteristics of target groups, and therefore, the consequences of using nonpharmacological approaches in different studies are inconsistent with the findings of this review.

## CONCLUSION

Although nonpharmacological approaches cannot directly affect the pathological aspects of the infection, they can make a significant contribution to the care of these patients because of the favorable clinical outcomes in improving functional status, reducing symptoms, and positively affecting the quality of life. However, there is not enough strong data to conclude which nonpharmacological approach can be most effective and with the fewest side effects. The insufficient sample size is one of the most important reasons for the low reliability of evidence. Hence, the findings of this review should be considered in light of the following limitations: the first is that the searches were conducted only in English; the second is that the articles found were studies conducted in Brazil, and therefore, there is a lack of cultural, social, and health diversity. Third, despite extensive searches in numerous databases, there may be grey and unpublished sources that researchers have not found in their studies, also, due to heterogeneity between studies, a meta-analysis was not possible.

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## Conflicts of interest

There are no conflicts of interest.

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