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Examination of the psychometric properties of pediatric-modified total neuropathy score in Turkish children with cancer

Bilge Özdemir, RN, MSc, Lecturer [a,g,*], Gülçin Özalp Gerçeker, PhD, RN, Associate Professor [b], Emine Zahide Özdemir, PhD, RN, Doctor Research Assistant [b], Büşra Güliz Yıldırım, RN, MsC, PhD student [c,g], Hale Ören, MD, Professor [d], Uluç Yiş, MD, Professor [e], Çağatay Günay, MD [e], Gülten Öztürk Thomas, MD [f]

[a] Istanbul Gedik University, Gedik Vocational School, Department of Medical Services of Techniques, Anesthesia Program, Istanbul, Turkey
[b] Dokuz Eylul University, Faculty of Nursing, Department of Nursing, Izmir, Turkey
[c] Dokuz Eylul University Child Hospital, Izmir 35340, Turkey
[d] Dokuz Eylul University Children's Hospital Pediatric Hematology Department, Izmir, Turkey
[e] Dokuz Eylul University Children's Hospital Department of Pediatric Neurology, Izmir, Turkey
[f] Marmara University Pendik Training and Research Hospital, Department of Pediatric Neurology, Istanbul, Turkey
[g] Dokuz Eylul University Health Sciences Institute PhD Student, Turkey

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ABSTRACT

Background: Evaluation of chemotherapy-induced peripheral neuropathy has gained importance in symptom management of pediatric patients with cancer. This study aimed to perform the Turkish validity and reliability study of the Pediatric-Modified Total Neuropathy Score (Ped-mTNS).
Methods: A methodological, descriptive, and cross-sectional design was used in the study. Forty children aged between 5 and 18 and were treated for cancer and 40 age- and gender-matched healthy children (control group) were included in the study. The mean scores of the items on the Ped-mTNS were compared, and item-total score correlations were evaluated. Cronbach's alpha coefficient of the Ped-mTNS was calculated for internal consistency.
Findings: Cronbach's alpha value of the scale was found as 0.709. The item-total correlations of the scale items ranged from 0.260 to 0.658. The mean score of cancer patients on the Ped-mTNS was found as 4.4 ± 3.8.
Discussion: Ped-mTNS scores of children with cancer indicated more deficits than those of the control group. In the evaluation of children in the patient and control groups, a difference was found in terms of light touch sensation, which is one of the sensory symptoms in the items of the Ped-mTNS, and pin sensibility and strength, which are among the clinical symptoms.
Application to practice: The Ped-mTNS was determined to be a valid and reliable measurement tool for children with cancer aged between 5 and 18 in the Turkish population.

Introduction

With developments in cancer treatment, the five-year survival rate of patients with cancer aged 0–14 has reached 84%. This rate in patients with leukemia has increased to 87% (American Cancer Society, 2021). In Turkey, the five-year survival rate of all childhood cancers was found to be 74% (Ataseven et al., 2019). With the prolongation of life expectancy in cancer, symptoms caused by the chemotherapy agents used in the treatment and the management of these symptoms have gained importance (Arpaci & Altay, 2021). Some chemotherapy agents cause toxicity in the peripheral nervous system, resulting in chemotherapy-induced peripheral neuropathy (CIPN) (Pro et al., 2021). There needs to be more data on the prevalence of CIPN due to the lack of easy-to-use, specific, and sensitive measurement tools (Binner et al., 2011; Gilchrist & Tanner, 2013; Visovsky et al., 2007). Balance and gait disturbances, tingling, numbness, and pain in fingers and toes, and changes in temperature sensation are observed in children with cancer, similar to adult patients receiving chemotherapy in cancer treatment (Kandula et al., 2018; Smolik et al., 2018; Tofthagen et al., 2011). A comprehensive measurement tool must be used to help assess these symptoms.

Although CIPN is seen as a common side effect of cancer treatment in children, measurement tools that evaluate how prevalent and which

* Corresponding autor at: Gedik University, Gedik Vocational School, Department of Medical Services of Techniques, Anesthesia Program; Gedik Vocational School, No: 1/1 Şeyhli, 34913 Pendik, Istanbul, Turkey.
E-mail addresses: bilgeozdemir123@gmail.com (B. Özdemir), hale.oren@deu.edu.tr (H. Ören), uluc.yis@deu.edu.tr (U. Yiş), gulten@thomas.md (G.Ö. Thomas).

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dimension of the nervous system (sensory, motor, autonomic) affects more are limited (Gilchrist et al., 2014). The Total Neuropathy Score (TNS) was first developed for assessing peripheral neuropathy in adults (Cornblath et al., 1999). The Pediatric-Modified Total Neuropathy Score (ped-mTNS) was adapted from the original TNS scale to be used in oncology clinics to determine CIPN and its severity in children receiving cancer treatment (Gilchrist et al., 2009; Gilchrist & Tanner, 2013).

For health professionals to better manage the symptoms of children receiving chemotherapy, assessment tools that they can apply or that are reported by the patient should be developed (Mohrmann et al., 2017; Smith et al., 2021). Recognition and early detection of peripheral neuropathies, which are known as side effects of chemotherapy agents, are essential for hematology/oncology nurses. Assessment of CIPN should become standard in patient care during and after chemotherapy treatment (Smolik et al., 2018).

Assessment of CIPN has gained importance in the symptom management of pediatric patients with cancer. Using a standardized assessment tool will improve the quality of symptom management and prevent potential complications. However, since there is no measurement tool to evaluate CIPN in Turkey, a standard neuropathy assessment cannot be made. This study was conducted to investigate the psychometric properties of the ped-mTNS in children and adolescents with cancer aged between 5 and 18 in the Turkish population to measure CIPN. Specifically, convergent validity, construct validity, and the internal reliability of the ped-mTNS scale were analyzed to describe the symptoms of neuropathy and compare neuropathy symptoms in children with cancer and healthy children.

Method

Study design and sample

A methodological, descriptive, and cross-sectional design was employed in the study. Patients who were followed up in the pediatric hematology and oncology services and children who presented to the neurology outpatient clinics of two university hospitals composed the study population. The patients aged between 5 and 18 and received inpatient or outpatient Vincristine or Cisplatin treatment in the pediatric hematology and oncology clinic were included in the study. For construct validity, 40 children receiving cancer treatment (cases) and 40 age- and gender-matched healthy children (controls) were included in the study. The ped-mTNS consists of 8 parts. Since the sample group included in the study made up the population of children who were diagnosed with cancer and the age range was limited, applying the rule of five times the number of items was deemed adequate to determine the sample size (Sencan, 2005). Forty pediatric cancer patients were included in the study. The healthy group consisted of patients who presented to the pediatric neurology outpatient clinic due to pain. The study was conducted between September 2020 and September 2021.

Inclusion criteria for the patient group.

- Child aged between 5 and 18.
- Diagnosed with cancer (leukemia, lymphoma, solid tumor).
- Absence of relapsed or second cancer.
- On a chemotherapy protocol using vincristine and/or cisplatin.
- On chemotherapy treatment for more than two months.
- Participation of the child and his/her parents in the study voluntarily.
- Child with no physical, developmental, or psychological deficit.

Inclusion criteria for the healthy group.

- Child aged between 5 and 18.
- No diagnosis of any known disease and not receiving any treatment.
- Admission to the hospital due to pain.
- Participation of the child and his/her parents in the study voluntarily.
- Child with no physical, developmental, or psychological deficit.

Exclusion criteria for the patient group.

- Diagnosis of a tumor involving the central nervous system.
- Diagnosis of relapsed cancer or on the terminal stage.
- Unwilling to participate in the study.

Exclusion criteria for the healthy group.

- Child with developmental, mental disorders, neuromuscular disorders, lower-extremity amputation, and Diabetes Mellitus.
- Have pain with underlying pathology or trauma.

Data collection tools

The study data were collected by using a Socio-Demographic Data Form, the Pediatric-Modified Total Neuropathy Scale, and the Common Terminology Criteria for Adverse Events (CTCAE) v4.0.

The Socio-Demographic Data Form: This form was used to question pediatric hematology–oncology patients' age, gender, height, weight, diagnosis, chemotherapy protocol, chemotherapy date-dose, status of receiving radiotherapy, status of steroid, glutamine, B1 and B6 intake, status of electromyography (EMG), and detection of neuropathy according to EMG results. Age, gender, height, weight, and pain data of the healthy group were recorded.

The CTCAE Peripheral Neuropathy Grading Scale (version 4.0): This form consisted of >330 items used to record cancer treatment-induced adverse events in 26 different categories. Possible grades ranged from 0: no symptoms to 3 (severe symptoms), or if the adverse event is likely to be fatal, category 4 means life-threatening and category 5 means death. The items of the CTCAE, used as a measure of CIPN, were about peripheral sensory neuropathy and peripheral motor neuropathy. Each item scored between 0 and 5 (National Cancer Institute, 2009).

The Pediatric-Modified Total Neuropathy Score (Ped-mTNS): The Total Neuropathy Score (TNS) was developed as a clinical evaluation of peripheral neuropathy in adults and is used as a measure of CIPN in adult patients with cancer (Cornblath et al., 1999). The items of the TNS were adapted to the Ped-mTNS for use in children receiving chemotherapy. The Ped-mTNS statements of subjective symptom questions simplified to be appropriate for school-aged children. It had a specific and sensitive grading measurement for CIPN that validated in the pediatric cancer population. The Ped-mTNS consisted of three sets of questions, including sensory, functional, and autonomic symptoms, and a clinical examination by which light touch sensation, pin sensibility, vibration sensation, and strength and deep tendon reflexes checked. Medipin™ used to measure pin sensitivity (Gilchrist et al., 2009). Each question scored between 0 and 4, where 0 means no symptoms on clinical examination, 4 means advanced progression/spread of symptoms. Minimum and maximum scores on the scale ranged between 0 and 32. High scores indicated that the severity of neuropathy is worse (Gilchrist & Tanner, 2013; Smith et al., 2013).

Data collection

Responses of the participant to questions about sensory, functional, and autonomic symptoms were recorded. In Gilchrist and Tanner's study, Semmes-Weinstein monofilaments (Rolyan-Ability One, Germantown, WI, USA) were used in the evaluation of the light touch sensation (Gilchrist & Tanner, 2013). Omejec and Podnar compared cotton and Semmes-Weinstein monofilaments in the evaluation of neuropathy in their study, and they found that cotton was more sensitive (Omejec & Podnar, 2018). In our study, cotton was used to evaluate the light touch sensation because it was more accessible in the clinic.

The purpose of using cotton during the assessment of the light touch sensation was explained to the child and family, and it was demonstrated on the hand. The child was asked to close his/her eyes and then the test was applied on the index finger with the eyes closed. The stimulus was repeated three times and the child was asked to indicate it each time he/she felt it. Sometimes the child was warned when it was thought that he/she felt the cotton but did not state it. The light touch sensation was considered normal if the child was able to correctly identify the three stimuli.

The pin sensitivity was tested by using Medipin™ (Medipin Ltd., Hertfordshire, UK). Gilchrist and Tanner, who conducted validity and reliability studies of the Ped-mTNS, had also used Medipin (Gilchrist & Tanner, 2013). The purpose of using the Medipin was explained to the child and family and it was demonstrated on the hand. The child was asked to close his/her eyes, and then it was applied on the distal extremities (plantar pads of the toes and palmar pads of the fingers) with the eyes closed (Gilchrist & Tanner, 2013). Four stimuli were given with "pointy" and "not pointy" ends on each extremity, and the child was asked to distinguish between these two types of stimuli. If the child could not identify even one stimulus, the test was graded as abnormal, and then the procedure was repeated for the next proximal segment until he/she gave a 100% correct answer. The child who did not give a 100% correct answer was recorded. The scoring of the scale was as follows: 0, normal pain sensitivity; 1, decreased sensitivity in fingers and toes; 2, decreased sensitivity up to wrist/ankle; 3, decreased sensitivity up to knee and elbow; 4, decreased sensitivity up to the knee and above the elbow.

The Biothesiometer™ was used to measure vibration sensitivity during the development of the original scale. It was easier to reach the tuning fork in clinics. Another study used a 128 Hz tuning fork in the evaluation of neuropathy (Smith et al., 2013). In another study in which the validity and reliability study of the ped-mTNS was conducted, a 64 Hz tuning fork was used (Schouten et al., 2020). During the measurement of the vibration sensation in this study, a 128 Hz weighted tuning fork was utilized. The grading of the vibration was as follows: 0, normal; 1, decreased sensation in the fingers and toes; 2, decreased sensation up to the wrist/ankle; 3, decreased sensation up to the knee and elbow; 4, decreased sensation up to the knee and above the elbow. The vibration of the tuning fork was increased by tapping slightly. After the tuning fork was vibrated, it was touched the participant on the left-hand fingers and then right-hand fingers, and the child was asked if he/she felt the vibration. In the absence of sensation, the vibration was measured at the left and right wrists, and elbows, respectively. After the upper extremity was completed, the assessment procedure continued for the lower extremity. The child was asked whether he/she felt the vibration first in the left toes and then in the right toes. In cases where the participant did not feel the vibration, it was measured at the ankle, knee, and above the knee from left to right, respectively.

For the assessment of strength, the muscle strength of the great toe extensors, finger abductors, ankle dorsiflexors, and wrist extensors was evaluated. The scale scores were graded as follows: 0, normal; 1, mild weakness (MRC 4); 2, moderate weakness (MRC 3); 3, severe weakness (MRC 2); 4, paralysis (MRC1–0). Great toe extensors, finger abductors, ankle dorsiflexors, and wrist extensors were assessed on the left and right sides. The worst score obtained determined the strength assessment.

While the child was seated with lower extremities free moving, deep tendon reflexes (DTR), achilles, and patellar tendon reflexes were assessed. The scale scores were graded as follows: 0, normal; 1, decreased ankle reflex (Achilles +1); 2, no ankle reflex (Achilles 0, Patella +2); 3, no ankle reflex, others decreased (Achilles 0, Patella +1); 4, no reflexes at all (All zero).

Validity and reliability

The ped-mTNS was translated into Turkish for language validity. After the translations made by two linguists who had a good command of both languages were compared, it was finalized by the researchers. In the next step, the back-translation method was used. The ped-mTNS was found to be very similar to its original form. The original version and Turkish version of the ped-mTNS were evaluated by the Davis technique over the responses given by a group of 10 academicians (5 neurologists, 2 hemato-oncologists, 3 faculty members with Ph.D. in Child Health and Disease Nursing) for content validity (Davis, 1992). These ten experts evaluated the scale items over four options (1 = not appropriate, 2 = the item needs to be improved, 3 = appropriate but needs minor modification, 4 = very appropriate). The item and scale-level content validity index were found to be 1.0. The scale was applied to a group of 10 participants first by a pediatric neurologist, and then it was re-applied by the nurse researcher one hour later for inter-rater reliability. For the test-retest procedure, ten different participants were recruited, and the ped-mTNS was applied to each participant and then one week later, it was re-applied by the same researcher. There was no statistically significant difference between the two applications ($p > 0.05$). For the item analysis and construct validity of the scale, 40 children with cancer and 40 age- and gender-matched healthy children were recruited. The following steps were applied for the validity and reliability of the ped-mTNS.

1) Language validity: English and Turkish versions of the ped-mTNS were assessed by a group of 10 academicians. The inter-rater agreement was evaluated with the content validity index.
2) Inter-rater reliability: The ped-mTNS was administered to 10 patients first by the pediatric neurologist and then by the nurse researcher at an interval of one hour. It was evaluated by using intra-class correlation analysis.
3) Convergent Validity (Test-retest): Convergent validity was analyzed using intra-class correlations between the two measurements. The ped-mTNS was applied to 10 different patients at an interval of one week and the two measurements were compared with intra-class correlation analysis. During this period, patients did not receive any chemotherapy agent that would lead to CIPN.
4) Item analysis: The mean item scores and item-total score correlations of the ped-mTNS, which was applied to 40 children with cancer, were evaluated.
5) Internal reliability: The reliability of the scale was assessed with internal consistency. The internal consistency was considered acceptable when Cronbach's alpha was >0.70 of the ped-mTNS, which administered to 40 children with cancer.
6) Construct validity: The scores of the ped-mTNS which was applied to 40 children with cancer and 40 healthy children were compared by using the independent samples *t*-test. A pediatric hematologist/oncologist evaluated the CTCAE score of 40 children with cancer. The correlation between the CTCAE score and the ped-mTNS score was evaluated.

Analysis

Numbers, percentages, and mean values were used for the evaluation of demographic data. Test-retest and inter-rater reliability were evaluated by using intra-class correlation coefficients (>0.9 acceptable). Internal consistency was evaluated by using Cronbach's alpha (>0.7) and item-total score correlations (>0.25). The number of cases with the lowest and highest scores was evaluated. Construct validity of the ped-mTNS was evaluated by comparing patient and control groups via independent samples t-test. The relationship between items on the ped-mTNS was examined by using Spearman correlation analysis. Data of patients with cancer and the ped-mTNS total score were evaluated by using ANOVA analysis. The correlation between the mean score of the ped-mTNS applied to patient group and the CTCAE score determined by the pediatric hematologist/oncologist was evaluated. The SPSS version 23.0 software package was used for all statistics.

Ethics of the study

The approval of the Non-Interventional Research Ethics Committee of University Hospital (no: 2020/29-06), and the institutional permission of two university hospitals was obtained. Also, the permission of the author who developed the scale was obtained via e-mail for its Turkish validity and reliability study. Verbal and written informed consent of the participants and their parents was obtained.

Results

Descriptive data

The study consisted of 40 children diagnosed with cancer and age- and gender-matched 40 healthy children who presented to the outpatient clinic due to pain. The diagnoses of the children with cancer and the chemotherapeutic agents that they used are given in Table 1. The mean dose of patients receiving vincristine ($n = 36$) was 11.5 ± 6.6 mg/m2 (min1.0 - max.31.2). The mean dose of patients receiving cisplatin (n = 3) was 452.0 ± 248.0 mg/m2 (min.208 - max.704). One patient was receiving both Cisplatin and Vincristine treatment.

Table 1
Descriptive Data of Participants.

Variables	Cases ($n = 40$)	Controls (n = 40)
Age	M ± SD (Min-Max)	M ± SD (Min-Max)
	9.7 ± 3.8 (5–17)	9.1 ± 3.4 (5–17)
Sex	n (%)	n (%)
Female	12 (30%)	12 (30%)
Male	28 (70%)	28 (70%)
Height (cm)	137.2 ± 21.7 (105–184)	134.51 ± 17.64 (109–173)
Weight (kg)	36.0 ± 15.7 (16–76)	30.88 ± 12.06 (18–64)
Body Surface Area (m^2)	1.1 ± 0.3 (0.6–1.9)	1.15 ± 0.33 (0.68–1.91)
Pain Area		n (%)
Head		15 (37.5%)
Abdomen		14 (35%)
Back		1 (2.5%)
Chest		4 (10%)
Waist		6 (15%)
Cancer Diagnosis	n (%)	
ALL	27 (67.5%)	
Ewing Sarcoma	6 (15%)	
Non Hodgkin Lymphoma	3 (7.5%)	
Osteosarcoma	3 (7.5%)	
Wilms Tumor	1 (2.5%)	
Received Chemotherapy	n (%)	
Vincristine	36 (90%)	
Cisplatin	3 (7.5%)	
Vincristine+Cisplatin	1 (2.5%)	
Last Received Chemotherapy – Time Between Data Collection	M ± SD (Min-Max)	
Date (days)	15.3 ± 24.2 (1–90)	
Status of Receiving Radiotherapy	n (%)	
Yes/No	6 (15.0%) / 34 (85.0%)	
Status of Receiving Steroid	n (%)	
Yes/No	8 (20%) / 32 (80%)	
Status of Taking Steroids Before	n (%)	
Yes/No	27 (67.5%) / 13 (32.5%)	
Status of Taking Glutamine in Treatment	n (%)	
Yes/No	11 (27.5%) / 29 (72.5%)	
Status of Vitamin B1 and B6 Intake	n (%)	
Yes/No	6 (15%) / 34 (85%)	
Status of EMG	n (%)	
Yes/No	14 (35%) / 26 (65%)	
Detection of Neuropathy with EMG	n (%)	
Yes/No	2 (2.3%) / 38 (97.7%)	

The ped-mTNS scores of children with cancer

The mean Ped-mTNS score of the patients was 4.4 ± 3.8. Also, 45% ($n = 18$) of the patients had sensory symptoms, 50% ($n = 20$) had functional symptoms, and 47.5% ($n = 19$) had autonomic symptoms. Abnormal findings/deficits were determined in the light touch sensation of 10% ($n = 4$), pin sensitivity of 7.5% (n = 3), vibration sensitivity of 47.5% ($n = 19$), strength of 17.5% ($n = 7$), and deep tendon reflex of 35% ($n = 14$) (Table 2).

The results of the validity and reliability analysis

The inter-rater agreement was determined as 1.00 for each item and the total content validity index. The inter-rater reliability of the ped-mTNS for the item and total scale scores was found to be acceptable (ICC > 0.95) in the assessment that was performed by a pediatric neurologist and a nurse on 10 children with cancer at an interval of one hour. According to the assessment results that was performed on 10 children at an interval of one week for test-retest purposes, the Ped-mTNS total and intra-class correlation coefficients of the items ranged from 0.92 to 1.00.

Cronbach's alpha value of the total scale was determined as 0.709. When the internal consistency was evaluated, it was found that the item-total correlations of the scale items ranged from 0.260 to 0.658 (Table 3). No item was excluded from the scale.

In the *t*-test analysis that was conducted for the construct validity of the ped-mTNS, more deficits were found in the children treated for cancer than those in the control group. Children diagnosed with cancer got bad scores mostly from the functional symptoms ($n = 20$, 50%), which is one of the subjective symptoms of the ped-mTNS, and from the vibration sensitivity (n = 19, 47.5%), which is one of the clinical symptoms of the scale. Of the children in the control group included in the study, 15% ($n = 6$) had deficits in functional symptoms, while 5% ($n = 2$) had deficits in pain sensitivity and deep tendon reflex, which are among clinical symptoms. These children in the control group did not receive any diagnosis. In the evaluation of the children in the patient and control groups, a difference was found in terms of light touch sensation, which is one of the sensory symptoms in the items of the ped-mTNS, and pin sensitivity and strength, which are among the clinical symptoms ($p < 0.05$) (Table 4).

The total scale score was 32, and it was found that none of the children in the patient and control groups had this value. In the patient group, one child scored 21 and one scored 14 points, and the rest of the children had low scores. While 10% ($n = 4$) of the children in the patient group had 0 points, 65% ($n = 26$) of the children in the control group had 0 points. The highest score in the control group was 3 ($n = 3$, 7.5%).

No difference was found between the scores of the children in the patient group on the total ped-mTNS scale and their age, gender, diagnosis, chemotherapy protocol, radiotherapy protocol, use of steroids, previous steroid use, glutamine use, vitamin B1 and B6 intake, and vincristine dose ($p > 0.05$). A difference was found between their ped-mTNS total scale scores and detection of neuropathy via EMG (detection of neuropathy via EMG n = 2, M ± SD = 14.5 ± 9.1, undetected $n = 38$, M ± SD = 3.8 ± 2.7) ($p < 0.05$).

A significant positive correlation was found between the ped-mTNS total scale score of the children in the patient group and the evaluation of sensory neuropathy ($r = 0.574^{**}$) and motor neuropathy ($r = 0.645^{**}$) ($^{**}p < 0.001$) by CTCAE.

Discussion

In this study, CIPN was evaluated and the validity and reliability of the ped-mTNS were tested on a sample of Turkish pediatric hematology-oncology patients aged between 5 and 18 and an age-and gender-matched control group via the Turkish version of the ped-mTNS. Cronbach's alpha value of the ped-mTNS was found to be 0.709

Table 2
Mean Item and Item-Total Scores of the ped-mTNS.

Ped-mTNS items		n (%)
Sensory Symptoms		
"Do you have any parts of your body that are tingly, numb (can hardly feel), or hurt?"	None/ Symptoms limited to fingers or toes/ Symptoms extend to ankles or wrists/ Symptoms extend to knee or elbow	22 (55)/ 7 (17.5)/ 8(20)/ 3(7.5)
Tingly	None/ Symptoms limited to fingers or toes/ Symptoms extend to ankles or wrists	33 (82.5)/ 3 (7.5)/ 4 (10.5)
Numb	None/ Symptoms limited to fingers or toes/ Symptoms extend to ankles or wrists	33 (82.5)/ 5 (12.5)/ 2 (5)
Hurt	None/ Symptoms extend to ankles or wrists/ Symptoms extend to knee or elbow	34 (85)/ 3 (7.5)/ 3 (7.5)
Functional Symptoms	Not Difficult/ A little difficult/ Somewhat difficulty/ I need help	20 (50)/ 12 (30)/ 6 (15)/ 2 (5)
"Do you have trouble buttoning shirts or zipping zippers?"	Not Difficult	40 (100)
"Do you have trouble walking such as tripping frequently?"	Not Difficult/ A little difficult/ Somewhat difficulty/ I need help	32 (80)/ 4 (10)/ 3 (7.5)/ 1 (2.5)
"Do you have trouble going up or down stairs?"	Not Difficult/ A little difficult/ Somewhat difficulty/ I need help	21 (52.5)/ 13 (32.5)/ 4 (10)/ 2 (5)
Autonomic Symptoms	Never/ A little bit/ Sometimes/ Very much	21 (52.5)/ 7 (17.5)/ 10 (25)/ 2 (5)
"Do you feel dizzy or light-headed when you get up out of bed?"	Never/ A little bit/ Sometimes/ Very much	32 (82.5)/ 2 (5)/ 3 (7.5)/ 2 (5)
"Do your hands or feet feel hotter or colder than normal?"	Never/A little bit/ Sometimes	27 (67.5)/ 5 (12.5)/ 8 (20.0)
Light Touch Sensation	Normal/ Reduced in fingers/toes/ Reduced up to wrist-ankle/ Reduced up to elbow-knee	36 (90)/ 1 (2.5)/ 2 (5)/ 1 (2.5)
Pin Sensibility	Normal/ Reduced up to wrist/ankle	37 (92.5)/ 3 (7.5)
Vibration Sensibility	Normal/ Reduced in fingers-toes/ Reduced up to wrist-ankle/ Reduced up to elbow-knee/ Reduce to above elbow-knee	21 (52.50)/ 9 (22.5)/ 2 (5)/ 3 (7.5)/ 5 (12.5)
Strength	Normal/ Mild weakness/ Moderate weakness	33 (82.5)/ 6 (15)/ 1 (2.5)
Great Toe	Normal/ Mild weakness	38 (95)/ 2 (5)
Great Toe Region	None/ Right	38 (95)/ 2 (5)
Ankle dorsiflexion	Normal/ Mild weakness/ Moderate weakness	34 (85)/ 5 (12.5)/ 1 (2.5)
Ankle Region	None/ Right/ Left	34 (85)/ 4 (10)/ 2 (5)
Finger abduction	Normal	40 (100)
Finger Region	None	40 (100)
Wrist Extension	Normal	40 (100)
Wrist Region	None	40 (100)
Deep Tendon Reflexes	Normal/ Ankle reflex reduced (Achilles +1)/ Ankle reflex absent (Achilles 0, Patellar +2)/ Ankle reflex absent, others reduced (Achilles 0, Patellar +1)/ All reflexes absent (All 0)	26 (65)/ 10 (25)/ 2 (5)/ 1 (2.5)/ 1 (2.5)
Total		M ± SS 4.4 ± 3.8 (min:0, max: 21)

in our study, and its reliability was considered adequate. This finding is similar to the value found by Gilchrist and Tanner (2013). The validity and reliability of the ped-mTNS were also tested on a sample of North American and Dutch children (Gilchrist & Tanner, 2013; Schouten et al., 2020). Our study results can be compared with these two studies. In the study conducted by Gilchrist and Tanner (2013), in which the validity and reliability of the original scale were evaluated, 41 sick children and 41 age-and gender-matched healthy children were included. In the study conducted by Schouten et al. (2020), 56 pediatric patients and 56 children in the control group consisted the sample. Our study consisted of 40 patients and 40 age-and gender-matched children in the control group who presented to the neurology outpatient clinic with complaints of pain. When compared with other studies, our study had a similar sample size. In addition, reaching a sample of at least five times the items on the scale was considered adequate in the literature (Sencan, 2005).

For the reliability analysis in Gilchrist and Tanner's study, 10 children were evaluated by different researchers at an interval of one hour, and the inter-rater reliability was evaluated (Gilchrist & Tanner, 2013). In our study, we also evaluated the inter-rater agreement between the pediatric neurologist and the nurse researcher who applied the scale to 10 children at an interval of one hour. Schouten et al. (2020) found the inter-rater agreement as 0.63 by performing test-retest analysis at an interval of 4–16 days. The inter-rater agreement coefficient was found to be moderate (Schouten et al., 2020). Similar to Schouten's study, the ped-mTNS was applied to 10 children by the same researcher one week later in our study. For the test-retest reliability, the intra-class correlation coefficient was evaluated between the measurements taken at an interval of one week, and it was found to be >0.9, which was acceptable.

In our study, the evaluation of the ped-mTNS was performed by a nurse researcher and a pediatric neurologist. The fact that the

Table 3
Internal Consistency of the ped-mTNS.

Ped-mTNS Items	Item Total Correlation	Chronbach's alpha if Item Deleted
Sensory symptoms	0.260	0.703
Functional Symptoms	0.658	0.660
Autonomic symptoms	0.462	0.680
Light touch	0.572	0.682
Pin sensibility	0.523	0.692
Vibration sensation	0.298	0.699
Strength	0.390	0.702
Deep tendon reflexes	0.578	0.669

Table 4
Comparison of the item-total scores of the ped-mTNS in patient and control groups.

Ped-mTNS Items	Cases (n = 40)		Controls (n = 40)	
	% with deficit	Mean	% with deficit	Mean
Subjective symptoms				
Sensory symptoms	18 (45%)	0.80*	5 (12.5%)	0.13
Functional Symptoms	20 (50%)	0.75	6 (15%)	0.15
Autonomic symptoms	19 (47.5%)	0.83	3 (7.5%)	0.08
Light touch	4 (10%)	0.20**	2 (5%)	0.05
Clinical examination				
Pin sensibility	3 (7.5%)	0.15**	2 (5%)	0.05
Vibration sensation	19 (47.5%)	1.05	1 (2.5%)	0.03
Strength	7 (17.5%)	0.20*	1 (2.5%)	0.02
Deep tendon reflexes	14 (35%)	0.52	2 (5%)	0.05

* $p < 0.05$.
** $p < 0.001$.

individuals who applied the scale included a nurse and a pediatric neurologist suggested that it increased the reliability of the study. In clinics, nurses can also evaluate patients with the ped-mTNS and monitor neuropathy symptoms. Multidisciplinary care is very important for children at risk of CIPN. The impact of care depends on the evidence-based knowledge of the nurses in this team, their assessment and training of patients on CIPN, planning of child-centered care, and effective communication. Nurses can evaluate patients' risk for developing CIPN and direct the care and treatment of the patient accordingly (Kanzawa-Lee, 2020).

In the evaluation of the children in the patient and control groups, a difference was found in terms of light touch sensation, which is one of the sensory symptoms of the ped-mTNS, and pain sensitivity and strength, which are two of the clinical symptoms. In the original study, a difference was found in terms of the items on the scale compared to the control group, except for autonomic symptoms and pain sensitivity (Gilchrist & Tanner, 2013). It is seen that the results of our study and those of the study conducted with the original form of the scale were mostly similar.

Gilchrist and Tanner (2013) reported that the patient group had a significantly higher score than the healthy controls on the ped-mTNS. It was found that of the control group, 9.8% in the study of Gilchrist et al. (2014), 68% in the study of Schouten et al. (2020), and 65% in our study scored 0 on the ped-mTNS. It was thought that this difference in the control group in the study of Schouten et al. (2020) was not due to the difference in the population but due to the education level of the raters and the difference in the way the scale was evaluated. In the present study, to evaluate whether the ped-mTNS can discriminate between patients and healthy children in terms of neuropathy, children with no history of a disease who presented to the neurology outpatient clinic with only pain complaints were included in the control group. The reason for the high number of patients in the control group who scored 0 on the ped-mTNS in our study was the reduction of confounding factors. Although more deficits were detected in the control group in the study of Gilchrist and Tanner (2013), high Ped-mTNS neuropathy scores were not found in the control group of other studies as in our study (Ped-mTNS<5). A score of 5 or greater on the ped-mTNS indicates the presence of neuropathy in children and adolescents who have not been diagnosed with cancer or who have not received neurotoxic chemotherapy before. In our study, the ped-mTNS score of the control group was 3.

In the study of Schouten et al. (2020), the correlation between the ped-mTNS total score and CTCAE was found to be moderate. The patient group had significantly higher ped-mTNS scores than the control group. In our study, a positive and significant correlation was found between the ped-mTNS total score of the children in the patient group and the sensory neuropathy and motor neuropathy assessment via CTCAE ($p < 0.001$). In one study, the CIPN grades of the ped-mTNS and CTCAE v3.0 were compared, and the ped-mTNS was found to detect sensory and motor neuropathies better (Gilchrist et al., 2014). Therefore, it is recommended to use the ped-mTNS when evaluating neuropathy in pediatric patients, since it can better determine the potential development of neuropathy (National Cancer Institute, 2009).

In our study, we also evaluated the status of using vitamins B1 and B6, receiving radiotherapy, and taking glutamine. We did not find any difference between these variables and the ped-mTNS score. One third of the patient group was taking glutamine in their treatment. In a study, it was found that taking glutamine reduced the symptoms of sensory neuropathy and increased the quality of life (Sands et al., 2017). Regular use of the ped-mTNS can also guide the evaluation of the effect of supportive treatments used on neuropathy symptoms.

In our study, we found a significant relationship between the detection of neuropathy via EMG and the ped-mTNS. We observed that the Ped-mTNS scores of two patients diagnosed with neuropathy as a result of EMG were high. The regular use of the ped-mTNS in pediatric hematology-oncology patients can guide the adjustment of chemotherapy doses and the necessity of EMG in patients with high scores.

Limitations

The ped-mTNS is a valid and reliable measurement tool for evaluating CIPN in children aged between 5 and 18. The lack of an adapted measurement tool to evaluate CIPN in children under five years of age is a limitation in this population. The lack of validation in other languages made it difficult to compare our results. Also, the absence of another scale assessing neuropathy prevented us from comparing our data.

Conclusion

In conclusion, the ped-mTNS was found to be valid and reliable in children aged 5–18 years in the Turkish population in our study. The results obtained from the study will guide the evaluation of CIPN in children with cancer using measurement tools. With its use both in the clinical field and future research, the ped-mTNS will help to control neuropathy symptoms. Using the ped-mTNS in the evaluation of chemotherapy-induced peripheral neuropathy in children with cancer will set a standard in pediatric hematology and oncology clinics.

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CRediT authorship contribution statement

Bilge Özdemir: Conceptualization, Methodology, Validation, Investigation, Writing – original draft, Writing – review & editing. **Gülçin Özalp Gerçeker:** Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Writing – review & editing. **Emine Zahide Özdemir:** Investigation, Resources. **Büşra Güliz Tekin:** Investigation, Resources. **Hale Ören:** Methodology, Validation, Resources. **Uluç Yiş:** Methodology, Validation, Resources. **Çağatay Günay:** Validation, Investigation. **Gülten Öztürk Thomas:** Validation, Investigation.

Declaration of Competing Interest

No potential conflict of interest was reported by the authors.

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