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Cold intolerance after brachial plexus nerve injury

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Abstract
Background The purpose of this study was to evaluate cold intolerance symptoms in patients with brachial plexus nerve injury. We hypothesized that higher levels of cold intolerance would be associated with more pain, greater disability, and unemployment.
Methods Following research ethics board approval and patient consent, we included English-speaking adults more than 6 months following brachial plexus nerve injury. Patient questionnaires included Cold Intolerance Severity Scale (CISS), McGill Pain Questionnaire, SF-36, DASH, pain catastrophizing scale, and Post-traumatic Stress Disorder Checklist. Statistical analyses evaluated the relationships among the questionnaires and the independent variables. Multivariable linear regression evaluated the factors associated with the CISS.
Results There were 61 patients, 20 women and 41 men (mean age 40±17 years). The mean questionnaire scores indicated high scores in the CISS, DASH, and pain intensity. The CISS was significantly higher in women. The final regression model with CISS as the dependent variable included the following independent variables: McGill pain rating index, DASH score, and time since injury. Neither pain catastrophizing nor post-traumatic stress scores were retained in the final model.
Conclusions Patients with brachial plexus nerve injury reported substantial cold intolerance which was associated with the McGill pain rating index, upper extremity disability, and time since injury.

Keywords Nerve injury · Pain · Cold intolerance · Brachial plexus

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Introduction

Cold intolerance has been defined as an abnormal response with exposure to cold which may follow a traumatic upper extremity injury, and it is often associated with poor outcome. The symptoms may include pain, sensory disturbances, stiffness, and/or color changes [5, 9, 10, 16, 19, 21, 22, 34, 38, 40]. Persistent cold intolerance is common following traumatic upper extremity nerve injuries and is more severe in patients with replantation injuries or digital amputations [1, 5, 6, 9–11, 16, 19, 22, 23, 28, 30, 34, 35, 37, 38]. Previous studies have evaluated cold

intolerance in upper extremity peripheral nerve injury and trauma patients, but no study has evaluated these symptoms specifically in patients with more proximal brachial plexus nerve injuries. The purpose of this study was to assess the presence of symptoms of cold intolerance in patients with long-standing brachial plexus nerve injury and to evaluate the factors associated with cold intolerance as measured by the Cold Intolerance Severity Scale (CISS). We hypothesized that higher levels of cold intolerance as measured by the CISS would be associated with more pain, greater disability, and unemployment.

Material and Methods

Subjects

After institutional and hospital research ethics board approval, patients were invited to participate in this study. Inclusion criteria were: adult, English-speaking patients, and at least 6 months after a brachial plexus nerve injury. Exclusion criteria were: amputation injury, previous upper motor neuron lesion, or inability to understand the questionnaires. Patient recruitment occurred at two locations (Toronto Western Hospital Hand Program, Toronto, ON, Canada, n=24, and Division of Plastic and Reconstructive Surgery, Washington University School of Medicine, St. Louis, MO, USA, n=37) when the study coordinator was present between October 2007 and August 2009. Following signed informed consent, patients were asked to complete the following questionnaires: CISS [7, 19, 37]; short form McGill Pain Questionnaire (sfMPQ) [15, 25, 26]; SF-36 [4, 13, 20, 24, 44], Disabilities of the Arm, Shoulder and Hand (DASH) [2, 12, 17, 18, 39]; pain catastrophizing scale (PCS) [8, 14, 31, 32, 43]; and Post-traumatic Stress Disorder Checklist (PCL-C) [3, 33, 36].

Measures

Cold Intolerance

Cold intolerance was assessed using the CISS which evaluates frequency, duration, severity, and impact of cold intolerance with activities [19, 37]. Item scores were summed for a total score ranging from 0 to 100 with higher scores indicative of greater cold intolerance. Good validity and reliability have been reported for the CISS in patients with upper extremity injury [7, 19, 37]. Missing data for the CISS were imputed using linear trend regression analysis for each item [29].

Disability

The DASH includes 30 items and was designed to assess disability. The patient was asked to rank each item on a 5-point scale. A total score was calculated (range 0 to 100) with higher scores indicative of greater levels of disability. Very good reliability and validity have been reported using the DASH questionnaire [2, 12, 17, 18, 39].

Pain

The sfMPQ was used to assess pain quality and intensity [15, 25, 26]. There are 15 pain descriptors (11 sensory, four affective), and each descriptor was ranked on a scale from none (0) to severe (3). The summation of scores on the 15 items was used to derive the total pain rating index. Pain intensity was indicated by the patient on a 10-cm visual analog scale (VAS) from 0 (no pain) to 10 (worst possible pain).

Health Status

Health status was assessed using the SF-36v2 questionnaire. Validity and reliability have been established [4, 13, 20, 24, 44]. Normalized composite scores for the physical and mental components were calculated. A lower score indicated a lower health status.

Post-traumatic Stress Symptoms

The PCL-C was used to assess symptoms of post-traumatic stress. It is a 17-item questionnaire, and each item was ranked on a scale of 1 (not at all) to 5 (extremely). Higher scores indicate more symptoms of post-traumatic stress. Validity and reliability have been presented for this measure of post-traumatic stress symptoms [3, 33, 36].

Pain Catastrophizing

The PCS was used to assess pain catastrophizing (exaggerated negative thinking relative to the pain experience) [41]. This is a 13-item questionnaire, and each item was ranked on a scale from 0 (not at all) to 4 (all the time) as to how the patient feels about each thought or feeling when they experience pain [41]. A higher score indicated higher levels of pain catastrophizing. Good validity and reliability have been reported for the PCS [8, 14, 31, 32, 43].

Statistical Analysis

Means and standard deviations were calculated for the continuous variables and frequencies for the categorical variables. Correlations were used to assess the relationships among the CISS, DASH, VAS pain intensity, pain rating index, SF-36 domains, PCS, PCL-C, age, and time since injury. T tests or analysis of variance was used to compare the outcome scores (CISS, DASH, pain disability, pain

intensity, DASH) between the following independent variables: workers' compensation or litigation involvement (yes vs. no), gender (male vs. female), dominant hand affected (yes vs. no), work status (employed, unemployed, other), and geographic location (Toronto vs. St. Louis).

Multivariable linear regression (with manual backward elimination) was used to evaluate the variables that predicted cold intolerance as assessed by the CISS. The bivariate correlation analyses were used to determine the variables to be included in the preliminary regression model. Those relationships with a p value of 0.2 or smaller were included in the preliminary model. Using the beta coefficient p value (0.1 or greater to remove a variable), manual backward elimination was used to derive the regression models. The final model included those independent variables with a p value of 0.1 or less.

Results

Sixty-one patients (41 men, 20 women) were included in this study. All had brachial plexus nerve injuries with incomplete recovery, and none had complete avulsion injuries (Table 1). The mean age was 40 years (SD 17 years), and the median time from injury was 14 months (range 6 to 145 months). Eighteen patients reported involvement of either workers' compensation or litigation.

The mean±SD questionnaire scores were: CISS 34±26, DASH 52±19, PCS 15±14, PCL-C 36±15, pain intensity 4.4±3.2, McGill pain rating index 14±11, and SF-36 composite scores physical (42±9) and mental (46±12). There was a high internal consistency found with the CISS in patients with brachial plexus injury (standardized item alpha=0.95). The CISS scores were significantly higher in women than in men ($p<0.05$, Table 2). There was no statistical difference in CISS scores between patients with workers' compensation or litigation vs. no workers' compensation or litigation ($p=0.31$) or among the different work status categories ($p=0.83$). There were significant correlation coefficients between CISS scores and the DASH, VAS pain intensity, McGill pain rating index, PCL-C, and PCS (Table 3), but not age ($r=0.14$, $p=0.30$), time since injury ($r=0.12$, $p=0.34$), SF-36 physical or SF-36 mental (Table 3).

Table 1 Patient demographics

	Number of patients (%)
Gender	
Male	41 (67)
Female	20 (33)
Dominant hand affected	36 (59)
Workers' compensation or litigation involvement	18 (30)
Work status	
Working (full or part time)	18 (30)
Unemployed	32 (52)
Homemaker, student, retired	11 (18)

Table 2 Bivariate analyses between cold sensitivity scores and independent variables

	Cold sensitivity score (mean±SD)	p value
Gender		
Female	43±24	0.05
Male	29±26	
Workers' compensation or litigation		
Yes	39±26	0.31
No	32±25	
Dominant hand injured		
Yes	34±27	0.92
No	33±24	
Work status		
Working (full or part time)	31±21	0.83
Unemployed	34±27	
Homemaker, retired or student	37±30	
Geographic location		
St. Louis	32±23	0.59
Toronto	36±30	

Based upon the above bivariate analyses, the initial regression model to predict the CISS scores included the following independent variables: gender, and scores from the DASH, PCL-C, PCS, McGill pain rating index, and VAS pain intensity. Because all patients had not achieved full recovery at the time of assessment, we chose to include time since injury in the regression model. However, the distribution of time from injury was skewed positively (skewness=2.8). The nonnormal distribution was corrected with a log10 transformation, and these data were used in the regression analysis [29]. The final model accounted for 33% of the variance and included these variables: McGill pain rating index, DASH score, and time since injury (Table 4). The scores from the PCS and the PCL-C were not retained in the final regression model. The strongest predictor of CISS scores was the McGill pain rating index.

Discussion

Cold intolerance symptoms were reported by a substantial number of patients with brachial plexus nerve injury. The final regression model showed that the cold intolerance scores were associated with a higher McGill pain rating index, greater disability as measured by the DASH, and

Table 3 Correlational relationship between the CISS scores and other questionnaires correlation coefficient (p value)

	CISS	DASH	VAS pain	McGill PRI	PCL-C	PCS	SF-36 physical	SF-36 mental
CISS	1							
DASH	0.329 (0.01)	1						
VAS pain	0.467 (0.00)	0.385 (0.002)	1					
McGill PRI	0.500 (0.00)	0.385 (0.002)	0.690 (0.00)	1				
PCL-C	0.258 (0.04)	0.277 (0.03)	0.375 (0.003)	0.490 (0.00)	1			
PCS	0.274 (0.03)	0.274 (0.03)	0.569 (0.00)	0.639 (0.00)	0.644 (0.00)	1		
SF-36 physical	−0.150 (0.25)	−0.604 (0.00)	−0.296 (−0.02)	−0.330 (−0.01)	−0.091 (0.48)	−0.159 (0.22)	1	
SF-36 mental	−0.173 (0.18)	−0.193 (0.14)	−0.334 (0.01)	−0.492 (0.00)	−0.732 (0.00)	−0.617 (0.00)	−0.059 (0.65)	1

CISS cold intolerance severity scale; *DASH* Disabilities of the Arm, Shoulder and Hand; *VAS* visual analog scale; *PRI* pain rating index; *PCL-C* post-traumatic stress disorder checklist civilian version; *PCS* pain catastrophizing scale

longer time since injury. The strongest factor in the regression model was the McGill pain rating index. The pain catastrophizing scores, post-traumatic stress symptom scores and geographic location (Toronto vs. St. Louis) were not retained in the final regression model, suggesting that these factors were not significantly related to the reporting of cold intolerance as measured by the CISS.

Previous studies have reported a relationship between cold-related symptoms and pain. In 176 patients with hand injuries, Campbell and Kay found that 73% reported symptoms related to cold exposure and most of these symptoms were related to pain [5]. Graham and Schofield reviewed patients who were more than 2 years following a hand injury and with a response rate of 34%, there were 90% who reported symptoms of cold intolerance and only 9% had an improvement in symptoms over time [16]. Nancarrow et al. reported 69% of patients following hand injury had cold intolerance and 97% continued to report these symptoms 5 years after injury [28]. Collins et al. reviewed patients who were at least 5 years following nerve injury and reported ongoing cold intolerance in 76% of these patients [9]. Meyer-Rosberg et al. evaluated patients with neuropathic pain from a variety of etiologies and found that the most intense pain was reported with cold provocation [27]. In our study of patients with brachial plexus nerve injury, the CISS scores were strongly associated with the McGill pain rating index, pain intensity, and the DASH score. Other studies have shown moderate correlation with the CISS scores and patient-reported outcomes [7, 40]. Stokvis et al. reported significant correlations with cold intolerance and pain intensity (r=0.443, p=0.01) and the DASH (r=0.438, p=0.01) [40]. In patients following hand trauma, Carlsson et al. reported a strong correlation (r=0.73) between the cold intolerance and disability as measured by the DASH [7]. Our study of patients with brachial plexus nerve injuries supports these studies regarding the negative relationship between outcome and cold intolerance and a strong relationship between pain and cold intolerance.

A number of patient self-report questionnaires and objective assessment tools have been described to assess cold intolerance [7, 9, 10, 16, 19, 23, 37, 42]. Typically objective tests have included cold water immersion and measurement of digital temperature or arterial pressures during the rewarming period. While these are objective measures of the vascular response, they do not provide subjective data regarding the pain and/or cold symptoms [1, 30, 34, 35, 42]. The CISS questionnaire includes patient-reported symptoms with cold exposure and the frequency of symptoms and impact on daily activities [19]. Irwin et al. showed that patients with a complete median or ulnar nerve injury and a vascular injury had more severe cold intolerance [19]. In healthy uninjured subjects, Ruijs et al.

Table 4 Final multivariable regression model (dependent variable, CISS scores)

Model	R^2	Predictor variables	Unstandardized coefficients beta	Standardized coefficients beta	t value	Level of significance
Final	0.33	Constant			−1.423	0.160
		McGill pain rating index	0.925	0.460	3.413	0.001
		DASH	0.361	0.268	2.107	0.04
		Time since injury	20.095	0.268	2.285	0.026

DASH Disabilities of the Arm, Shoulder and Hand

found that neither gender nor age was associated with symptoms of cold intolerance [37]. Traynor and MacDermid compared cold water immersion assessment and patient-reported questionnaires in healthy uninjured subjects [42]. There was good test–retest reliability with both the physical assessment and subjective questionnaire scores. However, there were no significant correlations between the questionnaire scores and the cold water immersion assessments. Although these evaluations were performed on healthy subjects and not individuals who have cold intolerance, it highlights the differences in subjective and objective assessments of cold intolerance. We found good internal consistency with the CISS which supports the use of this measure in patients with a brachial plexus nerve injury.

In this study we evaluated factors related to cold intolerance as measured by the CISS and included the factors that we hypothesized a priori were important. The factors related to the specific anatomy injured within the brachial plexus and treatment were not included in the analysis and merit future investigation in a longitudinal study to evaluate cold intolerance in the context of management interventions and recovery. The patient sample in this study represents a select group of patients who were at least 6 months following a brachial plexus nerve injury and who had sought medical assessment and/or treatment. As such this may represent unique patients who remain with morbidity from a brachial plexus nerve injury and therefore may report higher levels of cold intolerance and pain. This sample may not be representative of all patients with a brachial plexus nerve injury. However, this study of patients with a traumatic nerve injury at the level of the brachial plexus does highlight the presence of substantial cold intolerance in patients with incomplete recovery and continued morbidity.

In our study, patients with a brachial plexus nerve injury reported substantial cold intolerance which was associated with the McGill pain rating index, upper extremity disability, and time since injury. Future studies to evaluate treatment interventions to minimize cold intolerance may help to decrease pain and minimize disability associated with cold intolerance.

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