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Longitudinal Comparison of Duloxetine and Mirogabalin in Chemotherapy-Induced Peripheral Neuropathy

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Introduction

Chemotherapy induced peripheral neuropathy (CIPN) is a common neurotoxic complication of chemotherapy that can cause pain, sensory disturbances, and functional impairment, thereby affecting quality of life. Duloxetine has the most established evidence for symptom control in CIPN; however, various agents, including gabapentinoids, are used in practice. Mirogabalin has potential clinical utility for neuropathic pain management, but comparative evidence against duloxetine in patients with CIPN remains limited. Accordingly, we compared the treatment effects of mirogabalin and duloxetine in patients with CIPN and analyzed clinical factors associated with treatment response.

Methods

We conducted a single-center, open-label, randomized controlled trial including 62 patients with clinical features of CIPN. Participants were randomly assigned to receive duloxetine (n=32) or mirogabalin (n=30), with no additional neurotoxic chemotherapy administered during the study period. The interval from the last exposure to neurotoxic chemotherapy to initiation of CIPN medication was recorded and dichotomized at 6 months. Baseline comparability between groups, including chemotherapy type and adverse events, was evaluated using independent t-tests and chi-square or Fisher's exact tests. Treatment response was assessed at T0 (baseline), T1 (2 weeks), and T2 (4 weeks) using validated instruments for CIPN assessment, including pain severity and interference (BPI-SF), neuropathy grading (NCI-CTCAE), quality of life (EORTC QLQ-CIPN20), and neuropathic pain characteristics (KNPQ). The primary analysis was performed using a linear mixed model (LMM) to compare longitudinal changes in the primary outcome (BPI-SF) and secondary outcomes (NCI-CTCAE, EORTC QLQ-CIPN20 and KNPQ) between groups.

Results

Baseline characteristics, including exposure to neurotoxic chemotherapy, were comparable between groups and adverse event related discontinuation rates were similar (Table 1). In LMM analyses, no significant time-by-group interaction was observed for most outcomes, indicating comparable longitudinal treatment effects between the two groups. However, a significant interaction was found in the CIPN20 sensory domain (p=0.028) (Table 2). A significant main effect of time was observed for most variables, reflecting consistent symptom relief over the study period. In duration based subgroup analyses, a significant time-by-group interaction was observed only for the CIPN20 motor domain in the duloxetine group (p=0.002), suggesting greater improvement in patients who initiated duloxetine within 6 months after chemotherapy (Table 3).

Table 1. Baseline demographic, characteristics and adverse event related discontinuation

Variables	Categories	Duloxetine group (n=32)	Mirogabalin group (n=30)	p-value
Age, years (mean ± SD)		63.3 ± 9.5	64.8 ± 9.0	0.504º
Sex, n (%)	Male	19 (59.4)	16 (53.3)	0.632†
	Female	13 (40.6)	14 (46.7)	
Group, n (%)	≤ 6 month	19 (59.4)	15 (50.0)	0.459†
	> 6 month	13 (40.6)	15 (50.0)	
Neurotoxic chemotherapy type, n (%)	Oxaliplatin	20 (62.5)	23 (76.7)	0.277‡
	Docetaxel	8 (25.0)	8 (26.7)	1.000‡
	Paclitaxel	3 (9.4)	0 (0.0)	0.238‡
	Cisplatin	1 (3.1)	2 (6.7)	0.607‡
Any adverse event leading to drop out, n (%)	Total	3 (9.4)	2 (6.7)	1.000‡
	Nausea	1 (3.1)	1 (3.3)	
	Nausea + chills	0 (0.0)	1 (3.3)	
	Dizziness	1 (3.1)	0(0.0)	
	Irritability	1 (3.1)	0(0.0)	

† p-values for sex and group are Pearson chi-square p-values, ‡ p-values for chemotherapy exposure are two-sided Fisher's exact test p-values (exposed vs. not exposed by group).
º age p-value estimated from group summary statistics using t-test.

Table 2. Linear mixed model analysis comparing duloxetine and mirogabalin. Convariates included age, sex, and chemotherapy type.

Outcome	Effect	F (p-value)
BPI-SF severity	Time	21.300 (0.000*)
	Time × Treatment	0.062 (0.939)
BPI-SF interference	Time	27.952 (0.001*)
	Time × Treatment	0.065 (0.938)
NCI-CTCAE	Time	7.603 (0.001*)
	Time × Treatment	1.263 (0.288)
EORTC QLQ-CIPN20 sensory	Time	5.331 (0.006*)
	Time × Treatment	3.726 (0.028*)
EORTC QLQ-CIPN20 motor	Time	13.008 (0.000*)
	Time × Treatment	0.707 (0.496)
EORTC QLQ-CIPN20 autonomic	Time	2.941 (0.057)
	Time × Treatment	0.567 (0.569)
EORTC QLQ-CIPN20 total	Time	10.243 (0.000*)
	Time × Treatment	2.301 (0.106)
KNPQ	Time	21.765 (0.000*)
	Time × Treatment	0.145 (0.865)

BPI-SF; brief pain inventory-short form, NCI-CTCAE; national cancer institute c ommon terminology criteria for adverse events, EORTC QLQ-CIPN20; European organization for research and treatment of cancer quality of life-chemotherapy induced peripheral neuropathy questionnaire, KNPQ; Korean neuropathic pain questionnaire, Asterisk means statistically significant (p<0.05).

Table 3. Linear mixed model analysis results for Time and Time × Group Effects. Group defined by interval from the last exposure to neurotoxic chemotherapy to initiation of CIPN medication: ≤6 months vs >6 months). Convariates included age, sex, chemotherapy type.

Outcome	Effect	Duloxetine F (p)	Mirogabalin F (p)
BPI-SF severity	Time	9.581 (<0.001*)	11.586 (<0.001*)
	Time × Group	1.215 (0.306)	0.304 (0.739)
BPI-SF interference	Time	13.806 (<0.001*)	14.234 (<0.001*)
	Time × Group	1.376 (0.263)	1.108 (0.338)
NCI-CTCAE	Time	2.227 (0.120)	6.317 (0.004*)
	Time × Group	1.584 (0.217)	0.809 (0.452)
EORTC QLQ-CIPN20 sensory	Time	6.154 (0.005*)	2.076 (0.136)
	Time × Group	0.457 (0.636)	0.789 (0.460)
EORTC QLQ-CIPN20 motor	Time	8.510 (<0.001*)	5.807 (0.006*)
	Time × Group	7.373 (0.002*)	0.914 (0.408)
EORTC QLQ-CIPN20 autonomic	Time	1.570 (0.221)	1.647 (0.203)
	Time × Group	0.300 (0.742)	0.370 (0.692)
EORTC QLQ-CIPN20 total	Time	6.398 (0.004*)	5.496 (0.007*)
	Time × Group	1.730 (0.191)	1.626 (0.208)
KNPQ	Time	11.610 (<0.001*)	10.230 (<0.001*)
	Time × Group	2.457 (0.098)	1.029 (0.365)

BPI-SF; brief pain inventory-short form, NCI-CTCAE; national cancer institute common terminology criteria for adverse events, EORTC QLQ-CIPN20; European organization for research and treatment of cancer quality of Lif e-chemotherapy induced peripheral neuropathy questionnaire, KNPQ; Korean neuropathic pain questionnaire, Asterisk means statistically significant (p<0.05).

Conclusion

Mirogabalin was associated with significant longitudinal improvement in CIPN symptoms over 4 weeks. Early initiation of duloxetine resulted in greater clinical improvement in CIPN motor symptoms compared to late initiation. Both the mirogabalin and duloxetine groups showed significant longitudinal improvement in symptoms over time.

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