Assessing Gender Differences in Neuropathic Pain Management: Findings from a Real-Life Clinical Cross-Sectional Observational Study

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Background
Neuropathic pain is defined as pain induced by a lesion or disease of the somatosensory nervous system. Pharmacological and non-pharmacological treatments are frequently employed. In the current clinical investigation, we assessed the effects of sex on the safety and effectiveness of medications used to treat neuropathic pain.

Methods
We conducted a prospective analysis between 1 February 2021 and 20 April 2024, involving patients with neuropathic pain referred to the Ambulatory of Pain Medicine of "Renato Dulbecco" University Hospital in Catanzaro (Calabria, Italy). Patients over 18 years old with signs of neuropathic pain (Douleur Neuropathique en 4 questionnaire ≥ 4) were included. Exclusion criteria comprised patients with Alzheimer's disease; patients with nociplastic or nociceptive pain; and patients with neoplasms.
Patients with fewer than two accesses to ambulatory care were excluded, as were those who did not sign the informed consent. Clinical data were collected from each enrolled patient and subsequently analyzed, considering clinical outcomes. Sex and gender differences in efficacy were estimated using multivariate linear modeling and propensity-score matching.

Results
During the study, 531 patients were screened, and 174 were enrolled (33.5%, mean age 61.5 — During the study, 531 patients were screened, and 174 were enrolled (33.5%, mean age 61.5 ± 13.1; 64 males and 110 females, mean age 60.6 ± 13.4 and 61.96 ± 13.0) in accordance with the inclusion and exclusion criteria. Only minor differences in treatment prescription were observed based on age, body mass index, and comorbidities. Smoking, sex, educational level, and body mass index did not induce a significant change in pain perception. Males required slightly higher, though not significantly (except for oxycodone), doses of drugs for pain control than females. The treatment was not significantly more effective for females than for males. Females exhibit a lower number of adverse drug reactions compared to men, without reaching statistical significance.

Conclusion
The current study found that there are no appreciable differences between the sexes when it comes to the treatment of neuropathic pain.

Efficacy and safety main results

Table Pain evaluation in males and females. NRS: numerical rating scale.

	Admission	End of the Study	*p*
	NRS		
Males	8.0 (2.8)	5.0 (4.0)	<0.01
Females	8.0 (2.0)	5.0 (4.0)	<0.01
	$p > 0.05$	$p > 0.05$	

Table Linear modeling of NRS-change score. Estimated by the multiple linear regression model. R-squared: 0.17. Linearity, homoscedasticity, and normality of residuals were verified.

Delta NRS	Coefficient	[95% Conf. Interval]		*p*
Sex	0.37	−0.34	1.09	0.301
DN4	0.28	0.04	0.52	0.023
Cardiovascular comorbidities	0.50	−0.20	1.20	0.163
Psychiatric comorbidities	0.82	−0.10	1.73	0.081
Buprenorphine	1.53	0.32	2.75	0.014
Codeine	0.69	−0.07	1.45	0.075
Tramadol	0.94	0.10	1.79	0.029
Oxygen-ozone therapy	−1.14	−1.88	−0.40	0.003
NRS first access	−0.37	−0.62	−0.12	0.004

Table Types of adverse drug reactions (ADRs) recorded in treated patients (males 13 (20.3%), females 19 (17.3%)) for the management of neuropathic pain. * Same patient with more ADRs during polytherapy. Females' groups *a, *b, *c, *d, *e, *f, represent six patients (a–f) that developed more than one ADR.

	Males (n: 13)			Females (n: 19)			*p*
	Number	%	Type	Number	%	Type	
Oxycodone	1	7.7	Stypsis (1)	1	5.3	Drowsiness (1) *a	1.000
oxycodone/naloxone	2	15.4	stypsis (1) *; confusion (1)	1	5.3	stypsis (1) *f	1.000
buprenorphine	1	7.7	blood hypertension (1)	2	10.5	stypsis (1); skin rash (1) *a	1.000
Codeine	1	7.7	Stypsis (1)	1	5.3	stypsis (1) *b	1.000
Tramadol	0	0.0		2	10.5	blood hypertension (1), (1) *c	0.535
Tapentadol	0	0.0		0	0.0		N.C.
Fentanyl	1	7.7	Stypsis (1)	0	0.0		0.364
amitriptyline	2	15.4	confusion (1); drowsiness (1)	1	5.3	Confusion	0.299
Duloxetine	1	7.7	Confusion (1)	3	15.8	confusion (1); drowsiness (2)	1.000
Pregabalin	2	15.4	confusion (1) *; drowsiness (1)	6	31.6	Drowsiness (3), (1) *d, (1) *e, (1) *f	0.712
cyclobenzaprine	4	30.8	drowsiness (3), (1) *	4	21.1	Drowsiness (1), (1) *b; (1) *d; skin rash (1) *e	1.000
Nutrients	0	0.0		3	15.8	blood hypertension (1) *c; bowel dysfunction (1), (1) *f	0.555
oxygen-ozone therapy	0	0.0		2	10.5	pain in the site of administration (2)	0.535

N.C.: It's "not calculable" since no side effects were observed with tapentadol.

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