duloxetine Indications

- **Major Depressive Disorder** (MDD) (≥18 years of age)
- **Generalized Anxiety Disorder** (GAD) (≥7 years of age)
- **Diabetic Peripheral Neuropathic Pain** (DPNP) (≥18 years of age)
- **Fibromyalgia** (FM) (≥13 years of age)
- **Chronic Musculoskeletal Pain** (CMP) (≥18 years of age)

Diabetic Peripheral Neuropathic Pain (DPNP)

Case

- A 58-year-old man with 10 years history of type 2 DM ,HTN, HLP is referred for pain in his feet.
- His hemoglobin A1c is between 8% and 9%.
- He is taking insulin, metformin, losartan and atorvastatin.
- C/S - , Alcohol -

Cont..

- About 4 years ago, he noticed stabbing pains and numbness in his toes.
- There was also some gait imbalance.
- Since that time, the numbness has migrated to the middle of his shins
- The pain has progressed and become bothersome.

Cont..

- He states that when he walks he feels like he is stepping on broken glass.
- He describes burning in his feet at night.
- The stabbing pains continue in his toes and also occur in his shins

Cont..

- BP = 120/75 mm Hg
- Pulse = 78 b/min
- RR = 14/min
- Heart sound normal
- Normal dorsalis pedis pulses

Neurologic exam

- There is decreased pinprick and temperature perception to the knees bilaterally.
- The patient has absent vibratory perception in the toes.
- Proprioception is mildly reduced in the toes.

Neurologic exam

- There is no point tenderness over his heels. Reflexes are 1/4 in the arms, 1/4 at the knees, and absent at the ankles.

- Plantar responses are flexor bilaterally.

- Cranial nerve testing normal

Cont..

You diagnose = peripheral neuropathy.

This type of sensorimotor peripheral neuropathy is seen in DM.

- **Diabetic neuropathy** is the most common complication of diabetes mellitus (DM), affecting as many as **50%** of patients with type 1 and type 2 DM.
- In **type 1 DM**, distal polyneuropathy typically becomes symptomatic **after many years** of chronic prolonged hyperglycemia
- In **type 2 DM**, it may be apparent after only **a few years** of known poor glycemic control or **even at diagnosis**.
- According to American Diabetic Association, all patients with diabetes should be screened for neuropathy **at diagnosis** of **type 2 diabetes** and **five years** after diagnosis of **type 1 diabetes**

Medscape. Diabetic Neuropathy. 2020

Signs and symptoms

- **Sensory** – Negative or positive, diffuse or focal; usually insidious in onset and showing a stocking-and-glove distribution in the distal extremities

- **Motor** – Distal, proximal, or more focal weakness, sometimes occurring along with sensory neuropathy (sensorimotor neuropathy)

- **Autonomic** – Neuropathy that may involve the cardiovascular, gastrointestinal, and genitourinary systems and the sweat glands

Medscape. Diabetic Neuropathy. 2020

Sensory symptoms

- Usually is insidious in onset and shows **a stocking-and-glove distribution in the distal extremities**.
- May be **negative** or **positive**, **diffuse** or **focal**.
- **Negative** sensory symptoms include feelings of **numbness** or **deadness**, which patients may describe as being akin to wearing gloves or socks. **Loss of balance**, especially with the eyes closed, and **painless injuries** due to loss of sensation.
- **Positive** symptoms may be described as **burning**, **prickling pain**, **tingling**, **electric shock–like feelings**, **aching**, **tightness**, or **hypersensitivity to touch**.

Medscape. Diabetic Neuropathy. 2020

Motor symptoms

- May include **distal**, **proximal**, or more **focal** weakness.

- **Distal** motor symptoms may include **impaired fine hand coordination** and difficulty with tasks such as opening jars or turning keys. **Foot slapping** and **toe scuffing** or **frequent tripping** may be early symptoms of foot weakness.

- Symptoms of **proximal** limb weakness include **difficulty climbing up and down stairs**, **difficulty getting up from a seated or supine position**, **falls due to the knees giving way**, and **difficulty raising the arms above the shoulders**.

Medscape. Diabetic Neuropathy. 2020

Autonomic symptoms

- May involve the **cardiovascular**, **gastrointestinal**, **genitourinary systems** and the **sweat glands**.

- Patients with generalized autonomic neuropathies may report **ataxia**, **gait instability** and **syncope**.

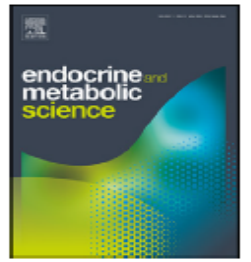
Medscape. Diabetic Neuropathy. 2020

Endocrine and Metabolic Science 1 (2020) 100053

Contents lists available at ScienceDirect

Endocrine and Metabolic Science

journal homepage: www.elsevier.com/locate/endmts



Prevalence and risk factors of diabetic peripheral neuropathy in a diabetics cohort: Register initiative "diabetes and nerves"

André Pfannkuche, Ahmad Alhajjar, Antao Ming, Isabell Walter, Claudia Piehler, Peter R. Mertens*

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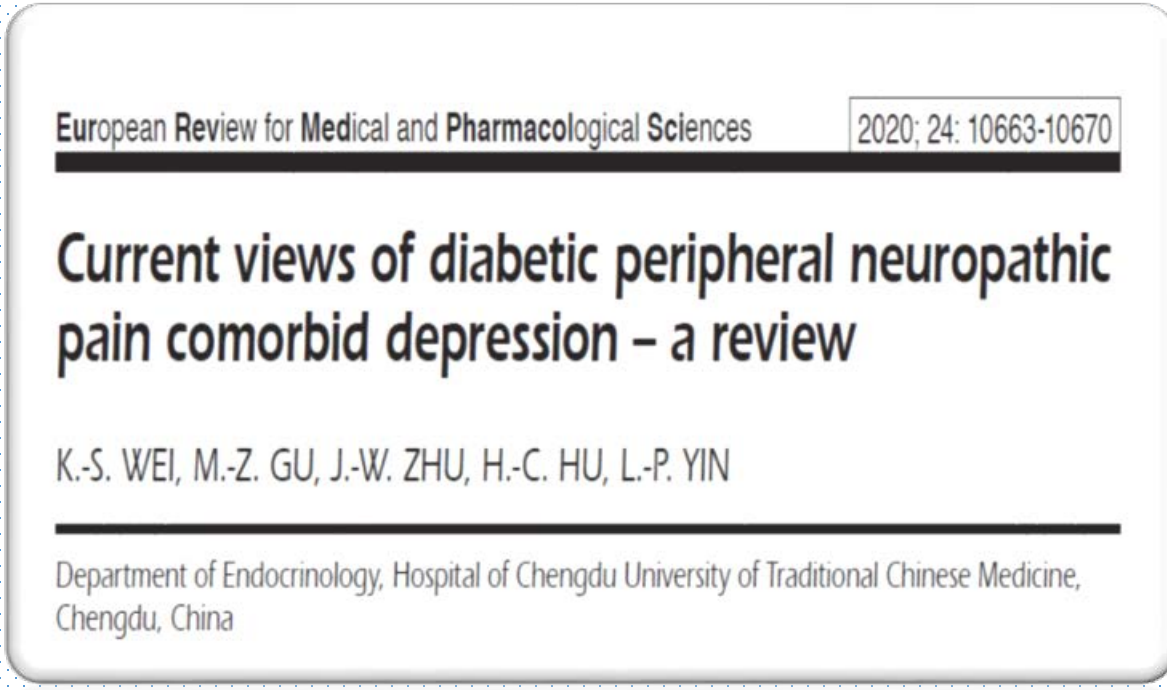
40.3% of diabetic patients (**42.2%** of patients with **type 2 diabetes** and **29.1%** patients with **type 1 diabetes**) suffer from peripheral neuropathy.

Endocrine and Metabolic Science. 2020; 1(1-2):100053.

DPNP Comorbid Depression & Anxiety

Diabetic peripheral neuropathic pain is particularly severe at night, so DPNP patients usually have sleep disorders. The fatigue due to the severe lack of sleep at night and the pain they have to suffer during the day both contribute to patients' loss of capability in everyday life, which then may cause serious **anxiety and depression**.



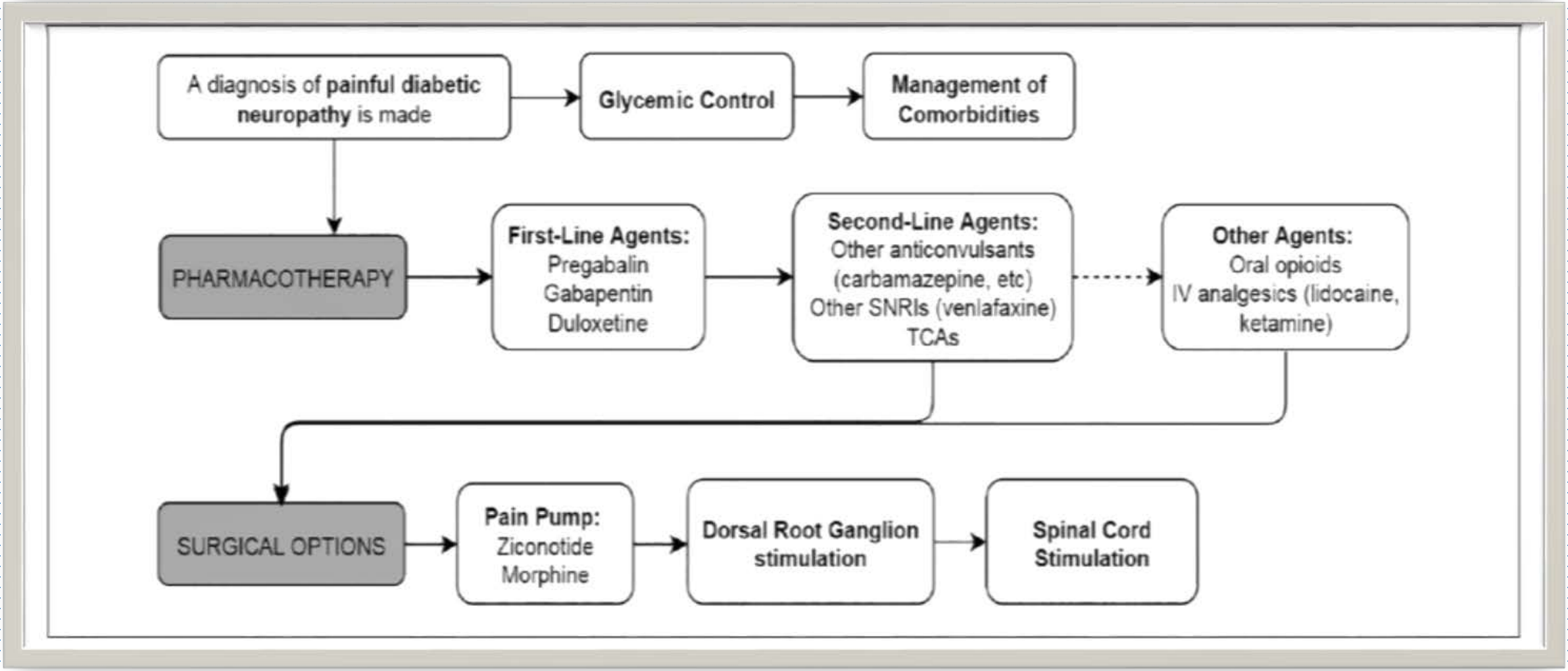
Eur Rev Med Pharmacol Sci. 2020; 24: 10663-10670.

Management

- **Foot care**, including regular follow-up, patient education, and referral as appropriate
- Tight, stable **glycemic control** (most important for slowing progression of neuropathy)
- **Pain management**

Medscape. Diabetic Neuropathy. 2020

Painful Neuropathy Management Options



Journal of Diabetes Science and Technology. 2020.; 28: 1-12

Pain Management

- **Selective Serotonin and Noradrenaline Re-uptake Inhibitors (SNRIs):** Duloxetine- Venlafaxine
- **Tricyclic Antidepressants (TCAs):** Amitriptyline
- **Anticonvulsive Drugs:** Pregabalin- Gabapentin
- **Other Medications:** Opioids (Tramadol, Tapentadol)- topical (Capsaicin and Lidocaine)

Medscape. Diabetic Neuropathy. 2020

SNRIs

- Can effectively block **5-HT** and **norepinephrine** transporters and inhibit monoamine's reuptake from synaptic cleft into the presynaptic end, and ultimately inhibit the generation of excitatory impulses and reduce pain.

- **Duloxetine** is the only SNRI that has **FDA approval for DPNP**.

- Studies on venlafaxine are relatively fewer.

Medscape. Diabetic Neuropathy. 2020

TCAs

- Are non-selective monoamine uptake inhibitor with multiple pharmacological effects, including blocking the reuptake of **5-HT** and **norepinephrine**, and **blocking sodium and calcium channels**.

- TCAs, especially **amitriptyline**, have obvious side effects, including typical **cholinergic effects** such as dry mouth, sweating, dizziness, and sedation, so the use of TCAs is often restricted in the elderly.

- The **cardiovascular status** of patients should be fully evaluated before the first use of the drug, and it should be used with caution in patients with heart disease or suspected cases.

Medscape. Diabetic Neuropathy. 2020

Anticonvulsive Drug

- Two main mechanisms of action of anticonvulsants: **blocking sodium ion channels** and **binding to calcium ion channels**.

- **Gabapentin** and **Pregabalin** work by binding to the **α-2-δ subunit of the calcium channel**, thereby reducing the release of neurotransmitters and thus decreasing peripheral excitability.

Medscape. Diabetic Neuropathy. 2020

Other Medications

- **Opioids:** very effective in treating pain of DPNP patients.

  acting on **peripheral nociceptors**, **presynaptic receptors**, **encephalin**

  interstitial and **postsynaptic receptors**, as well as **descending systems**.

➢ Opioids can enhance patients' **apathy**, **drowsiness** and other **vegetative symptoms** in depressed patients. opioid **abuse** is also a risk factor for the diagnosis of depression and is related to the severity of depressive symptoms.

- **Topical medications:** capsaicin and lidocaine

Medscape. Diabetic Neuropathy. 2020

Duloxetine mentioned as first-line therapy for DPNP in 4 major guidelines

Treatment	FDA approval for DPNP	FDA approval for MDD	ADA (2021)	NICE (2021)	AACE (2015)	EFNS (2010)
Amitriptyline	No	Yes	NM	1-2	1	1
Duloxetine	**Yes**	**Yes**	**1**	**1-2**	**1**	**1**
Pregabalin	Yes	No	1	1-2	1	1
Gabapentin	No	No	1	1-2	1	1
Venlafaxine ER	No	Yes	NM	NR	NM	1
Tramadol	No	No	3	3 (short term)	2	2-3

MDD: Major Depressive Disorder
NM: not mentioned, NR: not recommended,
NICE: National Institute of Clinical Excellence,
ADA: American Diabetes Association,
AACE: American Association of Clinical Endocrinologists,
EFNS: European Federation of Neurological Societies

Choosing a Medication

- Pain characteristics
- Patient characteristics

Pain characteristics

1. Does your pain feel like burning? (Burning pain)

2. Does your pain feel like squeezing? (Pressing pain)
2. Does your pain feel like pressure? (Pressing pain)

3. Does your pain feel like electric shocks? (Paroxysmal pain)
3. Does your pain feel like stabbing? (Paroxysmal pain)

4. Pain increased by brushing? (Evoked pain)
4. Pain increased by pressure? (Evoked pain)
4. Pain increased by cold? (Evoked pain)

5. Do you feel pins and needles? (Paresthesia/ dysesthesia)
5. Do you feel tingling? (Paresthesia/ dysesthesia)

Patient characteristics

1. Sleep disturbance

2. Low mood and depression

3. Anxiety

PAIN® 155 (2014) 2171–2179

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www.elsevier.com/locate/pain

Neuropathic pain phenotyping as a predictor of treatment response in painful diabetic neuropathy: Data from the randomized, double-blind, COMBO-DN study

Didier Bouhassira [a], Stefan Wilhelm [b,*], Alexander Schacht [c], Serge Perrot [d], Eva Kosek [e], Giorgio Cruccu [f], Rainer Freynhagen [g], Solomon Tesfaye [h], Alberto Lledó [i], Ernest Choy [j], Paolo Marchettini [k], Juan Antonio Micó [l], Michael Spaeth [m], Vladimir Skljarevski [n], Thomas Tölle [o]

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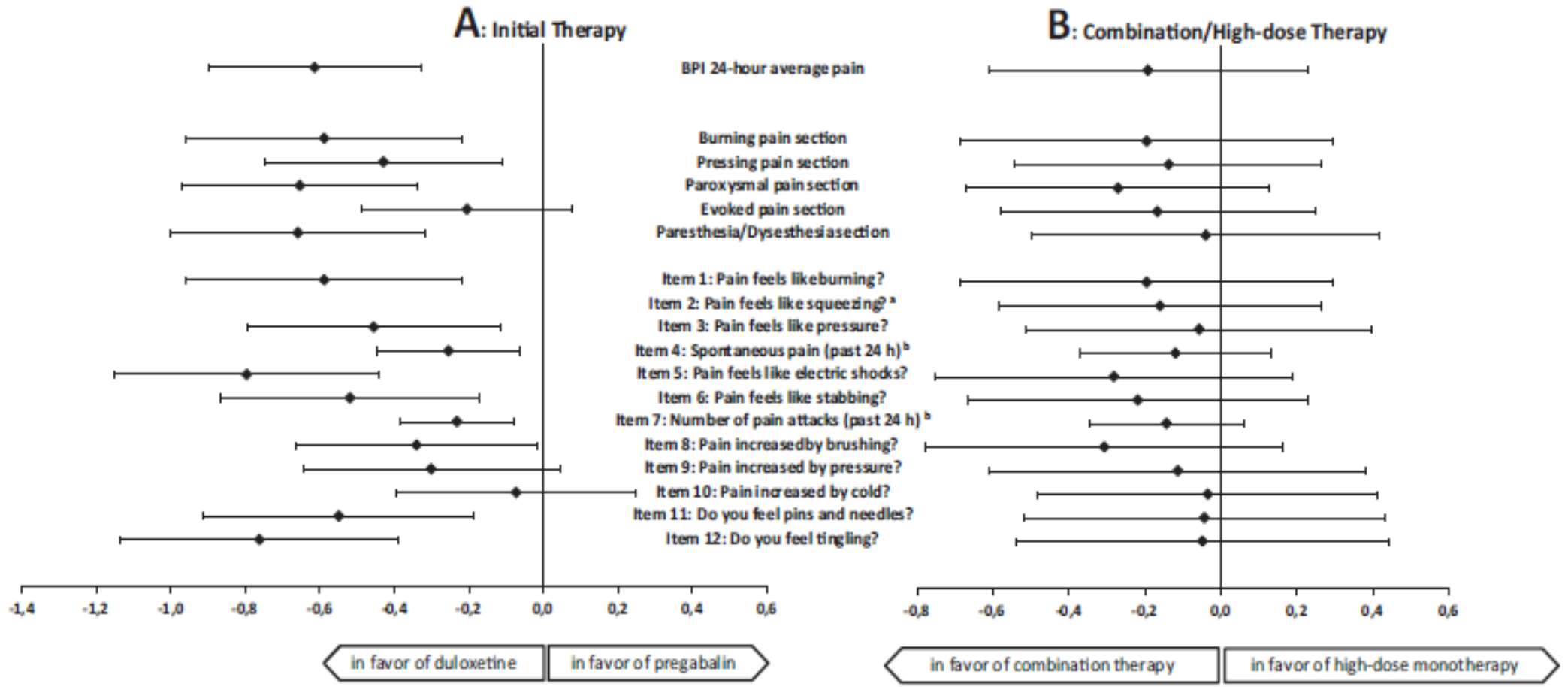
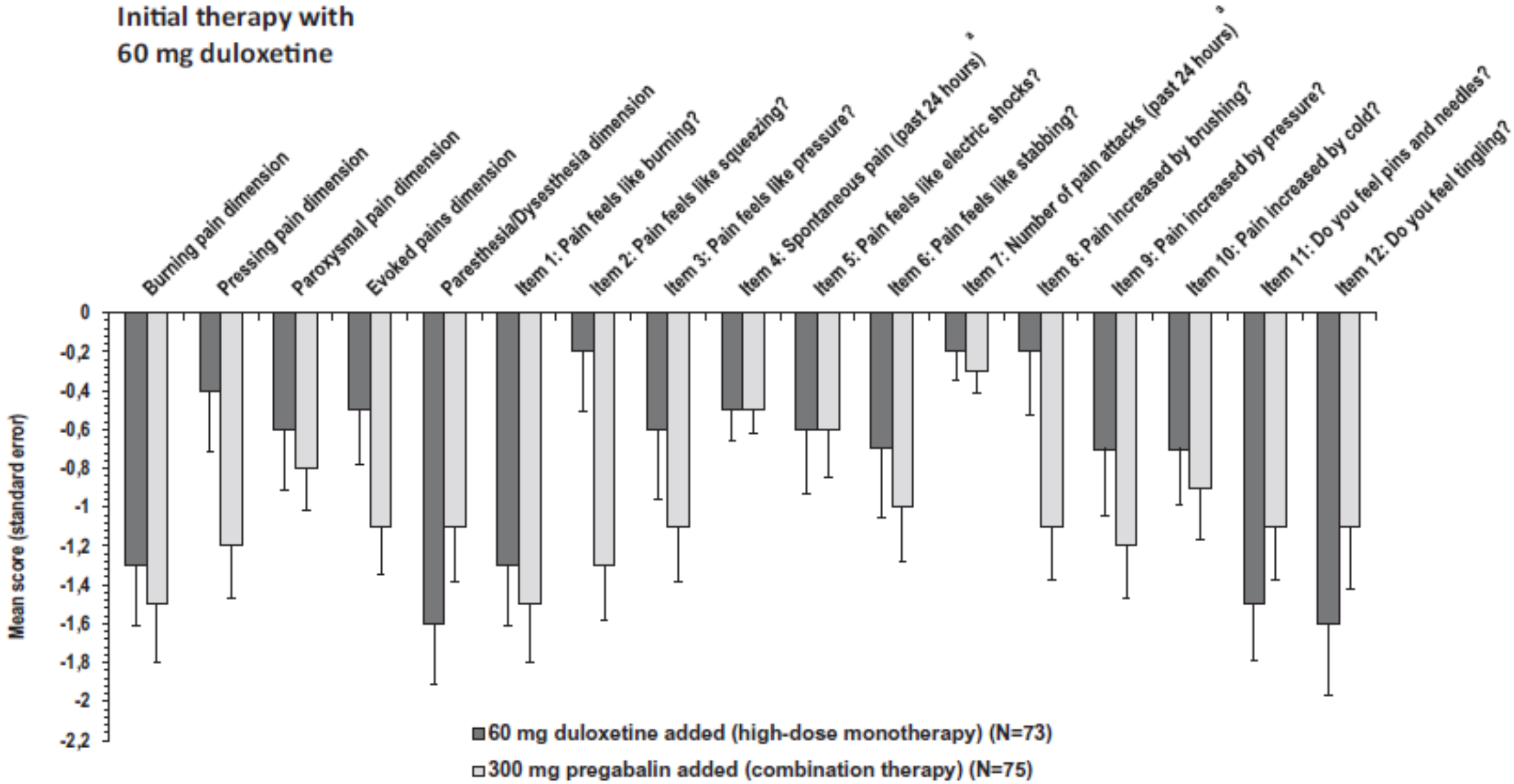
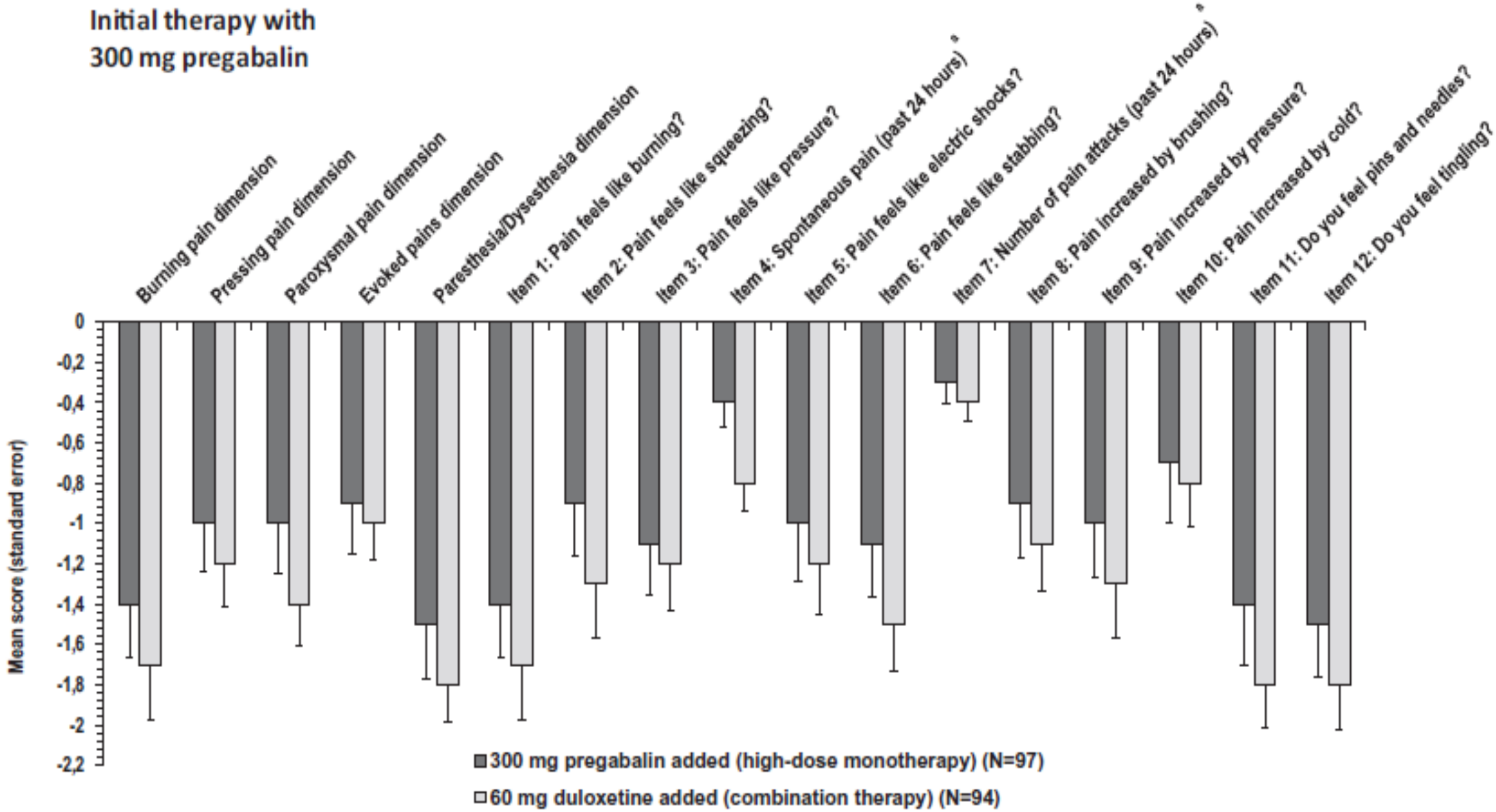


Fig. 1. Treatment effects in changes of BPI average pain and NPSI at the end of initial therapy (Visit 5) and end of combination/high-dose therapy (visit 8) cluster. (a) Algorithm did not converge for the initial treatment data due to infinite likelihood for both unstructured and autoregressive covariance matrixes. (b) Signs were reversed for consistency across all items. Note: diamond symbol denotes the least square mean for the difference between duloxetine and pregabalin in the initial therapy period and combination therapy and high-dose monotherapy in the combination/high-dose therapy period; the horizontal line denotes the associated 95% confidence interval. BPI, Brief Pain Inventory; NPSI, Neuropathic Pain Symptom Inventory.


Initial therapy with
60 mg duloxetine
Burning pain dimension
Pressing pain dimension
Paroxysmal pain dimension
Evoked pains dimension
Paresthesia/Dysesthesia dimension
Item 1: Pain feels like burning?
Item 2: Pain feels like squeezing?
Item 3: Pain feels like pressure?
Item 4: Spontaneous pain (past 24 hours) *
Item 5: Pain feels like electric shocks?
Item 6: Pain feels like stabbing?
Item 7: Number of pain attacks (past 24 hours) *
Item 8: Pain increased by brushing?
Item 9: Pain increased by pressure?
Item 10: Pain increased by cold?
Item 11: Do you feel pins and needles?
Item 12: Do you feel tingling?
Mean score (standard error)
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
-1,4
-1,6
-1,8
-2
-2,2
60 mg duloxetine added (high-dose monotherapy) (N=73)
300 mg pregabalin added (combination therapy) (N=75)


Initial therapy with
300 mg pregabalin
Burning pain dimension
Pressing pain dimension
Paroxysmal pain dimension
Evoked pains dimension
Paresthesia/Dysesthesia dimension
Item 1: Pain feels like burning?
Item 2: Pain feels like squeezing?
Item 3: Pain feels like pressure?
Item 4: Spontaneous pain (past 24 hours)*
Item 5: Pain feels like electric shocks?
Item 6: Pain feels like stabbing?
Item 7: Number of pain attacks (past 24 hours)*
Item 8: Pain increased by brushing?
Item 9: Pain increased by pressure?
Item 10: Pain increased by cold?
Item 11: Do you feel pins and needles?
Item 12: Do you feel tingling?
Mean score (standard error)
0
-0,2
-0,4
-0,6
-0,8
-1
-1,2
-1,4
-1,6
-1,8
-2
-2,2
300 mg pregabalin added (high-dose monotherapy) (N=97)
60 mg duloxetine added (combination therapy) (N=94)

Improve Patient Adherence by less Frequent Dosing

Drug Name	Dosing in pain management	Frequency of use	Available dosage forms
Gabapentin	900- 3600 mg/day	q8hr	Cap 100, 300 mg
Pregabalin	150- 600 mg/day	q12hr or q8hr	Cap 50, 75, 100, 150 mg
Duloxetine	60-120 mg/day	single daily dose or q12hr	Cap 20, 30, 60 mg

1. emc. 17 Jul, 2019. https://www.medicines.org.uk/emc/product/4636/smpc
2. emc. 26 Mar, 2021. https://www.medicines.org.uk/emc/product/7132/smpc
3. emc. 11 Jun, 2020. https://www.medicines.org.uk/emc/product/3880/smpc

BMC Neurology

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Research article

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Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain

Sibilia Quilici[1], Jeremy Chancellor*[2], Mickael Löthgren[3], Dominique Simon[4], Gérard Said[5], Trong Kim Le[6], Ana Garcia-Cebrian[7] and Brigitta Monz[8]

Background

- Few direct head-to-head comparisons have been conducted between drugs for the treatment of diabetic peripheral neuropathic pain (DPNP).
- Approved or recommended drugs in this indication include duloxetine (DLX), pregabalin (PGB), gabapentin (GBP) and amitriptyline (AMT).
- Conducted **an indirect meta-analysis** to compare the **efficacy and tolerability** of **DLX** with **PGB** and **GBP** in DPNP, **using placebo as a common comparator**.

BMC Neurology. 2009; 9:6

Methods

- Searched **PubMed**, **EMBASE**, **CENTRAL** databases and **regulatory websites** for randomized, double-blind, placebo-controlled, parallel group or crossover clinical trials (RCTs) assessing DLX, PGB, GBP and AMT in DPNP

- Study arms using **approved dosages** with assessments after **5–13 weeks** were eligible

- **Efficacy** criteria: - **Reduction in 24- hour pain severity** (24 h PS) for all three drugs
  - **Response rate (≥ 50% pain reduction)** and Patient Global Impression of Improvement/Change (PGI-I/C) for DLX and PGB only

- **Tolerability** criteria: **discontinuation**, **diarrhea**, **dizziness**, **headache**, **nausea** and **somnolence**

- **Direct comparisons versus placebo** were conducted in at least two studies of each drug

- **Indirect comparisons** were performed between DLX and each of PGB and GBP

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Results

- **Three studies of DLX**, **six of PGB**, **two of GBP** and **none of AMT** met the inclusion criteria
- **DLX, PGB and GBP, all were superior to placebo for all efficacy parameters**, with some tolerability trade-offs
- Indirect comparison of DLX with PGB found **no differences in 24 h PS**, but significant differences **in PGI-I/C, favoring PGB**, and **in dizziness, favoring DLX** were apparent
- **Comparing DLX and GBP, there were no statistically significant differences**

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Table 2: Random-effects pooled results: duloxetine vs. placebo.

Outcome	Treatment effect (θ)	95% CI for θ	U-test (p-value)	τ^2	*NNT/NNH (95% CI)*
Efficacy					
Reduction in 24-hour pain intensity	-1.128	(-1.364; -0.891)	<0.001	0	-
Response	0.856	(0.628; 1.085)	<0.001	0	5(3;7)
PGI	-0.756	(-1.004; -0.508)	<0.001	0	-
Tolerability					
Premature study discontinuation due to:					
- Lack of efficacy	-0.962	(-1.800; -0.124)	(0.024)	0	
- Adverse events	1.077	(0.663; 1.490)	<0.001	0	*11 (7; 23)*
- Other	-0.278	(-0.636; 0.079)	(0.127)	0	
Diarrhoea	0.233	(-0.436; 0.903)	(0.307)	0.307	
Dizziness	0.817	(0.398; 1.235)	<0.001	0	
Headache	0.468	(0.090; 0.845)	(0.015)	0	
Nausea	1.306	(0.942; 1.669)	0.039	0.039	
Somnolence	1.472	(1.044; 1.900)	<0.001	0	

Note:
θ is absolute difference for 24-hour pain intensity.
θ is log-odds ratio for Response, PGI and all tolerability analyses.
τ^2 is between-study heterogeneity.
NNT/NNH: Number needed to treat, number needed to harm. NNTs were calculated for response rate and NNHs were calculated for discontinuation due to adverse events.

BMC Neurology. 2009; 9:6

Table 3: Random-effects pooled results: pregabalin vs. placebo.

Outcome	Treatment effect (θ)	95% CI for θ	U-test (p-value)	τ^2	*NNT/NNH (95% CI)*
Efficacy					
Reduction in 24-hour pain intensity	-0.901	(-1.234; -0.568)	<0.001	0.147	
Response	0.840	(0. 524; 1.155)	<0.001	0.154	5(4;8)
PGI	-1.291	(-1.722; -0.860)	<0.001	0.019	
Tolerability					
Premature study discontinuation due to:					
- Lack of efficacy	0.713	(-1.205; -0.221)	(0.005)	0	
- Adverse events	0.926	(0.463; 1.389)	<0.001	0	*19 (10; 48)*
- Other	-0.209	(-0.721; 0.302)	(0.330)	0	
Diarrhoea	-0.660	(-1.734; 0.414)	0.139	0.139	
Dizziness	1.900	(1.314; 2.487)	0.028	0.028	
Headache	-0.216	(-0.823; 0.392)	0.486	0	
Somnolence	2.063	(1.361; 2.764)	<0.001	0	

Note:
θ is absolute difference for 24-hour pain intensity.
θ is log-odds ratio for Response, PGI and all tolerability analyses.
τ^2 is between-study heterogeneity.
NNT/NNH: Number needed to treat, number needed to harm. NNTs were calculated for response rate and NNHs were calculated for discontinuation due to adverse events.

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Table 4: Random-effects pooled results: gabapentin vs. placebo.

Outcome	Treatment effect (θ)	95% CI for θ	U-test (p-value)	τ^2	*NNT/NNH (95% CI)*
Efficacy					
Reduction in 24-hour pain intensity	-1.437	(-2.211; -0.663)	<0.001	0.109	*
Tolerability					
Premature study discontinuation due to:					
- Lack of efficacy	-1.066	(-2.786; 0.653)	0.224	0	
- Adverse events	0.241	(-0.786; 1.267)	0.646	0	*63 (30; ∞)*
- Other	-0.036	(-1.162; 1.090)	0.950	0	
Diarrhoea	0.393	(-0.555; 1.341)	0.416	0	
Dizziness	1.833	(0.834; 2.833)	<0.001	0	
Headache	1.146	(-0.018; 2.310)	0.054	0	
Nausea	0.595	(-0.532; 1.722)	0.301	0	
Somnolence	1.582	(0.643; 2.520)	0.001	0	

Note:
θ is absolute difference for 24-hour pain intensity.
θ is log-odds ratio for all tolerability analyses.
τ^2 is between-study heterogeneity.
NNT/NNH: Number needed to treat, number needed to harm. * NNT was not calculated, due to absence of required binary data on responder rates. NNH was calculated for discontinuation due to adverse events.

BMC Neurology. 2009; 9:6

Table 5: Indirect comparison results: duloxetine vs. pregabalin.

Outcome	Indirect treatment comparison (δ) Mean (median)	95% CI for δ	Between-study variance (τ^2) Mean (median)	95% CI for τ^2
Efficacy				
Reduction in 24-hour pain intensity	-0.248 (0.248)	(-0.667;0.162)	0.052 (0.024)	(0.001;0.252)
Response	0.033 (0.034)	(-0.393;0.451)	0.075 (0.052)	(0.001;0.287)
PGI-I/PGI-C	0.542 (0.545)	(0.016;1.060)	0.025 (0.009)	(0.001;0.151)
Tolerability				
Premature study discontinuation due to:				
- Lack of efficacy	-0.251 (-0.235)	(-1.288;0.717)	0.058 0.015)	(0.001;0.381)
- Adverse events	0.152 (0.154)	(-0.505;0.790)	0.039 (0.012)	(0.001;0.243)
- Other	-0.068 (-0.069)	(-0.735;0.589)	0.045 (0.013)	(0.001;0.281)
Diarrhoea	0.886 (0.885)	(-0.414; 2.183)	0.248 (0.050)	(0.001; 1.628)
Dizziness	-1.084 (-1.074)	(-1.903; -0.317)	0.075 (0.020)	(0.001; 0.477)
Headache	0.700 (0.704)	(-0.078; 1.458)	0.037 (0.011)	(0.001; 0.235)
Somnolence	-0.554 (-0.552)	(-1.458; 0.328)	0.052 (0.013)	(0.001; 0.347)

Note:
δ is the mean difference in treatment effect between DLX and each comparator.
τ^2 is between-study heterogeneity.

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Table 6: Indirect comparison results: duloxetine vs. gabapentin.

Outcome	Indirect treatment comparison (δ) Mean (median)	95% CI for δ	Between-study variance (τ^2) Mean (median)	95% CI for τ^2
Efficacy				
Reduction in 24-hour pain intensity	0.270 (0.266)	(-0.469; 1.022)	0.041 (0.013)	(0.001; 0.247)
Tolerability				
Premature study discontinuation due to:				
- Lack of efficacy	0.067 (0.065)	(-1.988; 2.116)	0.177 (0.028)	(0.001; 1.281)
- Adverse events	0.841 (0.835)	(-0.348; 2.065)	0.062 (0.015)	(0.001; 0.406)
- Other	-0.245 (-0.252)	(-1.527; 1.075)	0.060 (0.015)	(0.001; 0.386)
Diarrhoea	-0.244 (-0.246)	(-1.645; 1.164)	0.273 (0.051)	(0.001; 1.825)
Dizziness	-1.044 (-1.054)	(-2.258; 0.183)	0.090 (0.021)	(0.001; 0.590)
Headache	-0.689 (-0.697)	(-1.986; 0.638)	0.053 (0.013)	(0.001; 0.348)
Nausea	0.704 (0.700)	(-0.567; 2.021)	0.085 (0.022)	(0.001; 0.529)
Somnolence	-0.101 (-0.107)	(-1.249; 1.078)	0.080 (0.016)	(0.001; 0.545)

Note:
δ is the mean difference in treatment effect between DLX and each comparator.
τ^2 is between-study heterogeneity.

BMC Neurology. 2009; 9:6

Conclusion

- DLX shows comparable efficacy and tolerability to GBP and PGB in DPNP
- DLX provides an important treatment option for DPNP

BMC Neurology. 2009; 9:6

Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

- **Venlafaxine (Effexor XR)** (serotonin: norepinephrine ratio= 30:1)
- **Duloxetine (Cymbalta)** (10:1)
- **Desvenlafaxine (Pristiq)** (not available in Iran) (10:1)
- **Milnacipran (Savella)** (not available in Iran) (1:3)
- **Levomilnacipran (Fetzima)** (not available in Iran) (1:2)

Pharmacokinetics and Safety

Clinical pharmacology:

- Well absorbed orally
- In 6 hours reaches the C max
- Food not affect the C max, but delays the time to reach peak concentration from 6 to 10 hours, and decreases the extent of absorption (AUC) by about 10%
- $t_{1/2}$ about 12 hours (in plasma)
- Protein binding >90% (may cause free concentration of the other drug)
- Metabolized by CYP2D6 and 1A2 (co-administration with CYP2D6 and 1A2 inhibitors may cause drug interaction)

  - Moderate inhibitor of 2D6
  - No induction of CYP isoenzymes

Pharmacokinetics and Safety

- **Discontinuing:** Gradually reduce dosage to avoid discontinuation symptoms
- **Hepatic Impairment:** Avoid use in patients with chronic liver disease or cirrhosis
- **Renal Impairment:** Avoid use in patients with severe renal impairment, GFR <30 mL/min

Common Duloxetine Side effects

- Nausea (23%)
- Headache (14%)
- Dry mouth (13%)
- Somnolence (10%)
- Constipation (9%)
- Fatigue (9%)
- Dizziness (9%)
- Insomnia (9%)
- Diarrhea (9%)
- Decreased appetite (7%)
- Hyperhidrosis (6%)
- Abdominal pain (5%)

Key Facts

- Duloxetine normally takes **2 to 4 weeks** to work. It may take longer if you're taking it for nerve pain.

- **Side effects** are usually mild and **go away after a couple of weeks**.

- For taking off duloxetine, **reduce the dose gradually** to help prevent extra side effects.

Pregnancy

- Pregnancy Category: C

- Data from published literature and from a post-marketing retrospective cohort study have not identified a clear drug-associated risk of major birth defects or other adverse developmental outcomes

- There's no firm evidence that duloxetine is harmful to an unborn baby. But for safety, pregnant women are usually advised to only take it if the benefits of the medicine outweigh the potential risks.

Lactation

- Duloxetine passes into breast milk in **very small amounts**, but it's not known if it's harmful to the baby.

- Infants exposed to duloxetine should be monitored for **sedation**, **poor feeding** and **poor weight gain**

Dosing and Titration

Indication	Starting Dose	Target Dose	Maximum Dose
MDD	40- 60 mg/day	**Acute Treatment:** 40 mg/day (20 mg twice daily) to 60 mg/day (once daily or as 30 mg twice daily); **Maintenance Treatment:** 60 mg/day	120 mg/day
GAD			
Adults	60 mg/day	60 mg/day (once daily)	120 mg/day
Elderly	30 mg/day	60 mg/day (once daily)	120 mg/day
Children and Adolescents (7 to 17 years of age)	30 mg/day	30 to 60 mg/day (once daily)	120 mg/day
DPNP	**60 mg/day**	**60 mg/day (once daily)**	**60 mg/day**
FM	30 mg/day	60 mg/day (once daily)	60 mg/day
CMP	30 mg/day	60 mg/day (once daily)	60 mg/day

Conclusion

Duloxetine is the only antidepressant approved by FDA for neuropathic pain