Hospital Plató

Àrea Integral de Salut Barcelona Esquerra

IMPORTÀNCIA DE LES MESURES DE PREVENCIÓ

Neuropatia Diabètica, importància.

Dra. Neus Fabregat

IX JORNADA D'ATENCIÓ COMPARTIDA EN CIRURGIA VASCULAR DE L'AIS-BE

Sala Polivalent, Vil·la Florida, C/ Muntaner, 544

24 febrer 2017

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The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL PRACTICE

Caren G. Solomon, M.D., M.P.H., *Editor*

Diabetic Sensory and Motor Neuropathy

Aaron I. Vinik, M.D., Ph.D.

N Engl J Med 2016;374:1455-64.

KEY CLINICAL POINTS

DIABETIC SENSORY AND MOTOR NEUROPATHY

- Symptoms of distal symmetric motor and sensory polyneuropathy may be "positive" (manifested as sensations of tingling, burning, or stabbing pain) or "negative" (manifested as sensory loss, weakness, or numbness). These symptoms occur in one third of patients with type 1 or 2 diabetes.
- Decreased sensation confers a predisposition to painless foot ulcers and to amputations. Proprioceptive impairment leads to imbalance and unsteadiness in gait and to an increased likelihood of falls and serious traumatic injury.
- Laboratory testing should be used to rule out other causes of neuropathy, including vitamin B_{12} deficiency, which may occur with metformin use.
- Lifestyle interventions (diet and exercise) may restore nerve fibers, and exercises that improve strength and balance may reduce the risk of falls.
- Medications most commonly used in pain management include anticonvulsants (particularly gabapentin and pregabalin), tricyclic antidepressants, and serotonin–norepinephrine reuptake inhibitors.
- Treatment choices should take into account coexisting conditions, such as insomnia, depression, and anxiety.

I. PREVALENÇA, CLASSIFICACIÓ, PATOGÈNESI.

II. CLÍNICA I DIAGNÒSTIC.

III. TRACTAMENT.

I. PREVALENÇA, CLASSIFICACIÓ, PATOGÈNESI.

II. CLÍNICA I DIAGNÒSTIC.

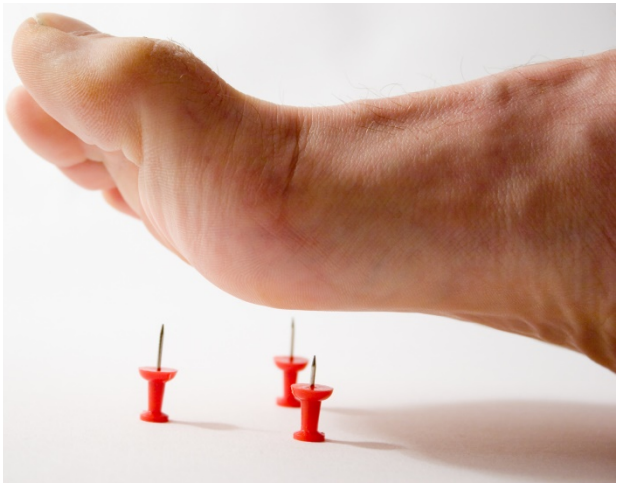
III. TRACTAMENT.

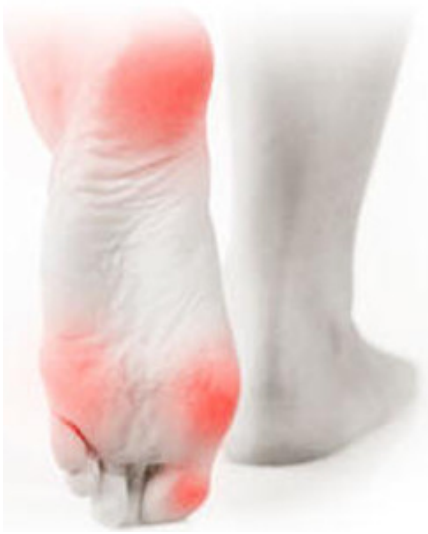
NEUROPATIA DIABÈTICA: 25-50% diabètics, 25% intolerància glucosa.

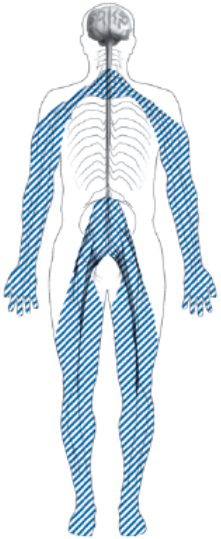
ULCERA EN PNP DIABÈTICA: 15-25%.

CLASSIFICACIÓ PNP DIABÈTICA:

- Polineuropatia simètrica distal (50% ➔ 14% transtorn marxa)
- Neuropatia autonòmica (7%)
- Poliradiculopatia, dorsal i lumbar (3%)
- Mononeuritis, perifèrica o craneal (III, VI, IV).
- Mononeuritis múltiple (25%)
- Neuropaties agudes doloroses: induïdes pel tractament, severa pèrdua de pes.







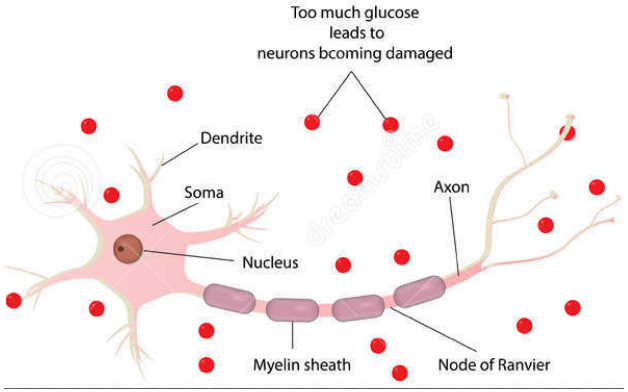
Partanen, N Engl J Med 1995;333-89
Abbot, Diabetes Care 2011; 34:2220
Dyck, Diabetes Metab Res Rev 2011;27:620
Jaiswal, Diabetes Care 2013; 36:3903
Gibbons, Brain 2015;138:43

PATOGÈNESI:

Axonopatia distal de les fibres sensitives mielíniques i amielíniques de major longitut, i autonòmiques.

Oclusions dels vasa nervorum.

- Metabòlic + vascular (disfunció endotelial) + hormonal.
- Equilibri dany-reparació fibra nerviosa.

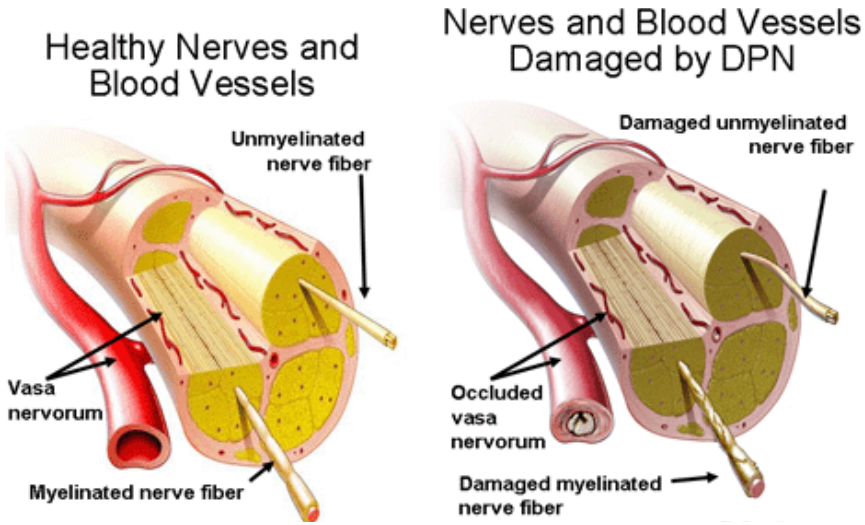


PREVENCIÓ:

Control glicèmic.

Tractament altres factors de risc vascular.

Educació del pacient.



Cameron NE, Diabetologia 2001; 44:1973
Kles KA, Curr Diabetes Rev; 2006;2:131
Callaghan BC, Lancet Neurol 2012;11:521
Callaghan BC, Cochrane Database Sys Rev 2012; CD007543

FACTORS DE RISC:

- Durada i severitat de l´hiperglicèmia.
- Dislipèmia.
- HTA.
- Tabac.
- Index massa corporal.
- Malaltia cardiovascular (x2).

Tesfaye, N Engl J Med 2005;352:341
Genuth, Endocr Pract 2006;12 Suppl 1:34
Wiggin, Diabetes 2009;58:1634
Callaghan, Curr Opin Neurol 2012;25:536
Peltier, BMJ 2014;348:g1799
Callaghan, Cochrane DatabaseSyst Rev 2012;CD00743

I. PREVALENÇA, CLASSIFICACIÓ, PATOGÈNESI.

II. CLÍNICA I DIAGNÒSTIC.

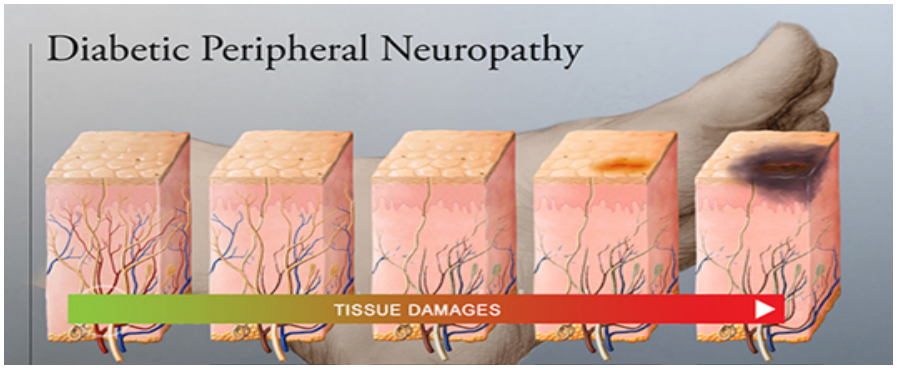
III. TRACTAMENT.

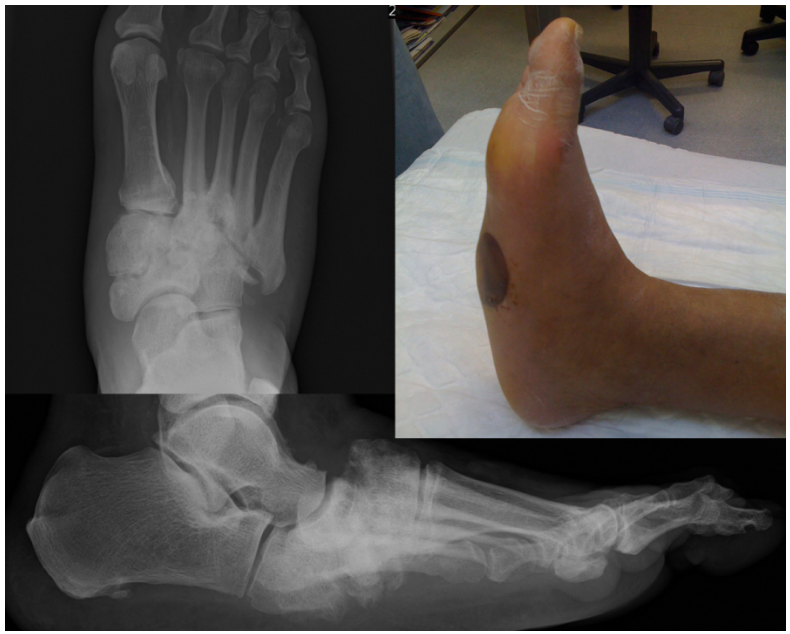
- Sensitiva, simètrica, distal, extremitats inferiors.

- Progressió gradual “mitjons-guants” i sensitivo-motora:
  pèrdua sensibilitat vibratòria, **ROTS**, tacte, temperatura i dolor, autònom, motor.

- Parestèsies, disestèsies, hipoestèsia, dolor (20%), dèficit motor (fases avançades).

- **Complicacions:** úlcera (alteracions sensibilitat, disfunció autonòmica), infeccions, transtorn marxa (propiocepció, microtraumatismes), peu de Charcot, fractures.





Davies M. Diabetes Care 2006;29:1518
England JD. Neurology 2005;64:199
Dyck PJ. Diabetes Metab Res Rev 2011;27:620
Kanji JN. JAMA 2010;303:1526E

England JD. Neurology 2005;64:119

Table 1. Approaches to the Diagnosis of Neuropathies of Large and Small Nerve Fibers.*

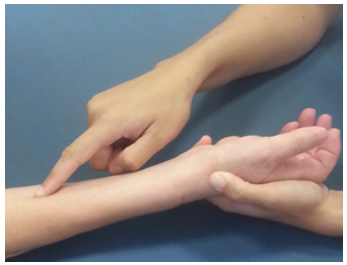
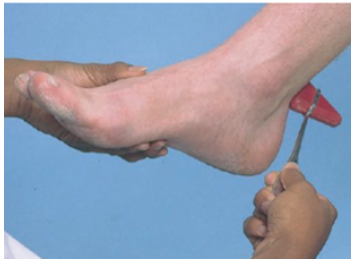
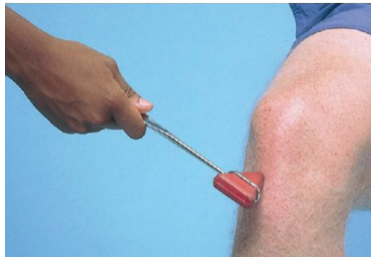
Approach	Large Myelinated A-Type α- and β-Fibers	Small Myelinated and Unmyelinated A-Type δ-Fibers and Small Unmyelinated A-Type δ-Fibers and C-Type Fibers
Assess symptoms	Numbness, tingling, deep-seated gnawing or aching pain, weakness, ataxia with poor balance, falling	Burning pain with sensation of stabbing and electric shocks, allodynia, hyperalgesia, hyperesthesia
Conduct physical examination	Impaired reflexes, loss of proprioception and perception of vibration, wasting of small muscles of hands and feet, weakness in feet	Impaired sensation of warm and cold temperatures and of pinprick; normal strength, reflexes, and nerve conduction; impaired autonomic function, with dry skin, poor blood flow, cold feet, and impaired sweating
Recognize clinical implications	Impaired sense of pressure and balance; susceptibility to falls, traumatic fractures, and Charcot's arthropathy	Impaired nociception, susceptibility to foot ulcers, increased risk of amputation
Conduct diagnostic tests	Nerve conduction: abnormal test results (e.g., median, sural, and peroneal nerves) Quantitative sensory testing to detect loss of perception of vibration	Nerve conduction: normal results despite presence of symptoms Skin biopsy to detect loss of intraepidermal nerve fibers Corneal confocal microscopy Quantitative sensory tests to detect sensitivity to hot and cold and impairment of pain perception Sudorimetry (performed with neuropad or sudoscan) to obtain objective measures of sweating
Consider differential diagnosis	Consider chronic inflammatory demyelinating polyneuropathy, monoclonal gammopathies, Guillain–Barré syndrome, and myopathies, B_{12} or folate deficiency, hypothyroidism, paraneoplastic syndromes, and effects of chemotherapy	Consider metabolic causes such as uremia, hypothyroidism, B_{12} or folate deficiency, acute intermittent porphyria, toxic alcohol, heavy metals, industrial hydrocarbons, inflammation or infection, connective-tissue diseases, vasculitis, celiac disease, sarcoidosis, Lyme disease, human immunodeficiency virus, hepatitis B or C virus, hereditary diseases, monoclonal gammopathies, paraneoplastic syndromes, and amyloidosis

N Engl J Med 2016;374:1455-64.

DIAGNÒSTIC:

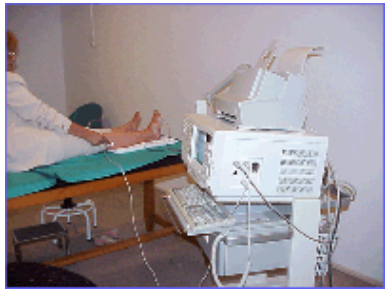
Precoç i presimptomàtic ➔ Sospitar en DM-I >5 anys, i DM-II, neuropatia dolorosa idiopàtica.

Clínic: inici distal extremitats inferiors, progressió ascendent
sensibilitat vibratòria (indicador precoç), tàctil, posicional
tèrmica i dolorosa ➔ increment risc úlcera
disminució reflexes (aquili)
dèficit motor lleu

Cal pensar en altres causes si:

- Símptomes o signes assimètrics.
- Sever dèficit motor.
- Ràpida progressió.



Estudi electrofisiològic (sensitiu, motor, autonòmic) ➔ no essencial.

Analítica.

N Engl J Med 2016;374:1455-64.

MONITORITZACIÓ:

- Tots pacients amb DM-I >5anys, i tots DM-II cal fer screening PNP.
- Mínim anualment interrogar símptomes.
- Mínim anualment cal fer seguiment funció sensitiva i reflexes: vibració, pressió, ROTS, agulla, temperatura.
- Inspecció diària dels peus pel pacient.
- Educació per a la cura del peu.
- Estar atent a presentació o evolució atípica per a descartar altrer causes: polienuropatia inflamatòria crònica idiopàtica, dèficit B12, urèmia, hipotiroidisme

Davies M. Diabetes Care 2006;29:1518
England JD. Neurology 2005;64:199
Dyck PJ. Diabetes Metab Res Rev 2011;27:620
Kanji JN. JAMA 2010;303:1526E

Patient Version

MICHIGAN NEUROPATHY SCREENING INSTRUMENT

A. History (To be completed by the person with diabetes)

Please take a few minutes to answer the following questions about the feeling in your legs and feet. Check yes or no based on how you usually feel. Thank you.

1.	Are you legs and/or feet numb?	☐ Yes	☐ No
2.	Do you ever have any burning pain in your legs and/or feet?	☐ Yes	☐ No
3.	Are your feet too sensitive to touch?	☐ Yes	☐ No
4.	Do you get muscle cramps in your legs and/or feet?	☐ Yes	☐ No
5.	Do you ever have any prickling feelings in your legs or feet?	☐ Yes	☐ No
6.	Does it hurt when the bed covers touch your skin?	☐ Yes	☐ No
7.	When you get into the tub or shower, are you able to tell the hot water from the cold water?	☐ Yes	☐ No
8.	Have you ever had an open sore on your foot?	☐ Yes	☐ No
9.	Has your doctor ever told you that you have diabetic neuropathy?	☐ Yes	☐ No
10.	Do you feel weak all over most of the time?	☐ Yes	☐ No
11.	Are your symptoms worse at night?	☐ Yes	☐ No
12.	Do your legs hurt when you walk?	☐ Yes	☐ No
13.	Are you able to sense your feet when you walk?	☐ Yes	☐ No
14.	Is the skin on your feet so dry that it cracks open?	☐ Yes	☐ No
15.	Have you ever had an amputation?	☐ Yes	☐ No

Total: _____

B. Physical Assessment (To be completed by health professional)

1. Appearance of Feet

	Right	Left
a. Normal	☐0 Yes ☐1 No	Normal ☐0 Yes ☐1 No
b. If no, check all that apply:		If no, check all that apply:
Deformities	☐	Deformities ☐
Dry skin, callus	☐	Dry skin, callus ☐
Infection	☐	Infection ☐
Fissure	☐	Fissure ☐
Other	☐	Other ☐
specify:	_____	specify: _____

		Right			Left		
		Absent		Present	Absent		Present
2.	Ulceration	☐0		☐1	☐0		☐1
		Present	Present/ Reinforcement	Absent	Present	Present/ Reinforcement	Absent
3.	Ankle Reflexes	☐0	☐0.5	☐1	☐0	☐0.5	☐1
		Present	Decreased	Absent	Present	Decreased	Absent
4.	Vibration perception at great toe	☐0	☐0.5	☐1	☐0	☐0.5	☐1
		Normal	Reduced	Absent	Normal	Reduced	Absent
5.	Monofilament	☐0	☐0.5	☐1	☐0	☐0.5	☐1

Signature:_____ Total Score _____/10 Points

Neuropathy Disability Score (NDS)			
		Right	**Left**
Vibration Perception Threshold 128-Hz tuning fork; apex of big toe: normal = can distinguish vibrating/ not vibrating	Normal = 0 Abnormal = 1		
Temperature Perception on Dorsum of the Foot Use tuning fork with beaker of ice/warm water			
Pin-Prick Apply pin proximal to big toe nail just enough to deform the skin; trial pair = sharp, blunt; normal = can distinguish sharp/not sharp			
Achilles Reflex	Present = 0 Present with reinforcement = 1 Absent = 2		
	NDS Total out of 10		

I. INTRODUCCIÓ: PREVALENÇA, CLASSIFICACIÓ, PATOGÈNESI.

II. CLÍNICA I DIAGNÒSTIC.

III. TRACTAMENT.

TRACTAMENT

I. Control glicèmic i factors de risc.
II. Cura dels peus.
III. Tractament del dolor.

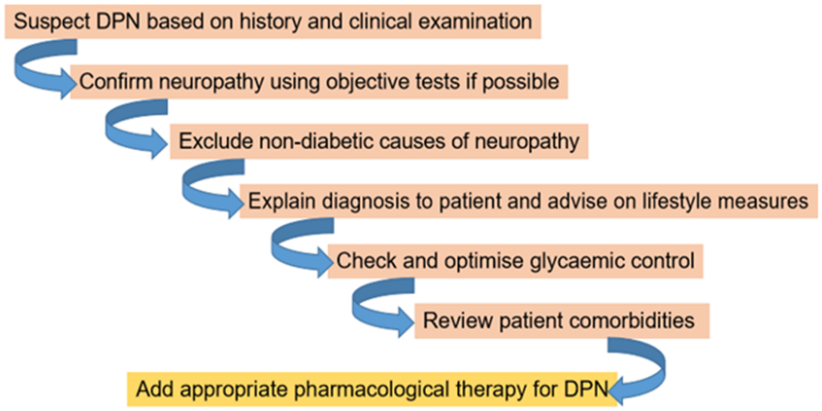
CONTROL GLICÈMIC (dieta, exercici, fàrmacs)

- Millora velocitat de conducció.
- Millora dintell percepció vibració.

- Corregir HTA, DL.
- Evitar reducció ràpida HbA1c (<1% per mes) i hipotensió.

CURA DELS PEUS

- Inspecció.
- Entrenament i fisioteràpia.



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TRACTAMENT DEL DOLOR

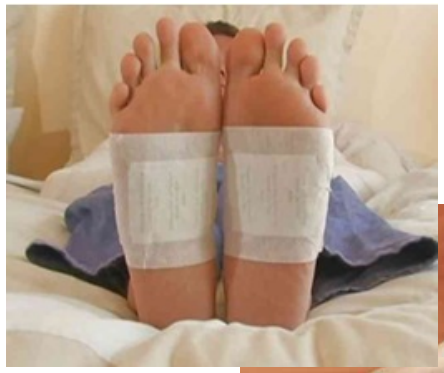
Diagnòstic diferencial.

Iniciar dosis baixes, increment en 2-4 setmanes.

Si en 1 mes no resposta, canvi o combinació.

Fàrmacs:

- **Antidepressius: amitriptilina, DULOXETINA, venlafaxina.**
- **Anticonvulsivants: gabapentina, PREGABALINA, valproat sòdic, topiramato.**
- **Capsaicina, lidocaina, TENS**
- B12 < 450 pg/ml ➔ methylcobalamina (2000 µg/dia).
- Àcid alpha lipoic 300mg/12h.
- Acupuntura.



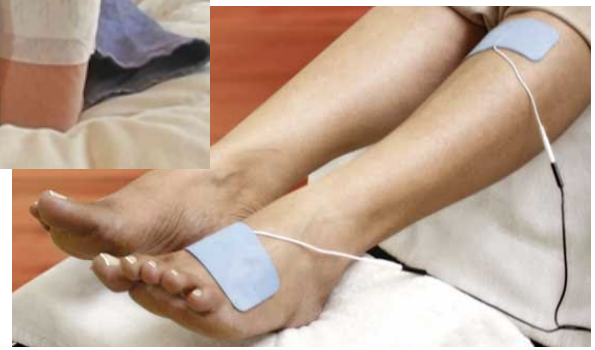


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Table 2. Pharmacologic Agents Often Used for Pain Relief in Patients with Distal Symmetric Polyneuropathy.*

Drug Class and Agent	Dose		NNT for Improvement of 50% in One Person†	Common Adverse Events‡	Serious Adverse Events§
	Initial	Effective			
Anticonvulsants					
Pregabalin (Lyrica)¶	25–75 mg, 1 to 3 times/day	300–600 mg/day	7.7 (6.5–9.4)	Somnolence, dizziness, peripheral edema, headache, ataxia, fatigue, xerostomia, weight gain	Angioedema, hepatotoxicity, rhabdomyolysis, seizures after abrupt discontinuation, suicidal thoughts and behavior, thrombocytopenia
Gabapentin (Neurontin)	100–300 mg, 1–3 times/day	900–3600 mg/day	6.3 (5.0–8.3)	Somnolence, dizziness, ataxia, fatigue, weight gain	Seizures after rapid discontinuation, Stevens–Johnson syndrome, suicidal thoughts and behavior
Topiramate (Topamax)	25 mg/day	25–100 mg/day	No estimate¶	Metabolic acidosis, paresthesia, somnolence, dizziness, anorexia, cognitive dysfunction, tremor, changes in taste	Glaucoma, hypokalemia, nephrolithiasis, osteomalacia, Stevens–Johnson syndrome, suicidality, toxic epidermal necrolysis
Antidepressants					
SNRIs					
Duloxetine (Cymbalta)‖	20–30 mg/day	60–120 mg/day	6.4 (5.2–8.4)	Nausea, somnolence, dizziness, constipation, dyspepsia, diarrhea, xerostomia, anorexia, headache, diaphoresis, insomnia, fatigue, decreased libido, shift to mania in patients with bipolar disorder	Bone fractures, cardiac arrhythmias, delirium, gastrointestinal hemorrhage, glaucoma, hepatotoxicity, hypertensive crisis, myocardial infarction, neuroleptic malignant syndrome, Stevens–Johnson syndrome, seizures, serotonin syndrome, severe hyponatremia, suicidal thoughts and behavior
Venlafaxine (Effexor)	37.5 mg/day	75–225 mg/day	4.5**	Nausea, somnolence, dizziness, constipation, dyspepsia, diarrhea, xerostomia, anorexia, headache, diaphoresis, insomnia, fatigue, decreased libido	Bone fractures, cardiac arrhythmias, delirium, gastrointestinal hemorrhage, glaucoma, hepatotoxicity, hypertensive crisis, myocardial infarction, neuroleptic malignant syndrome, Stevens–Johnson syndrome, seizures, serotonin syndrome, severe hyponatremia, suicidal thoughts and behavior
Tricyclic agents					
Amitriptyline (Elavil)	10–25 mg/day	25–150 mg/day	3.6 (2.1–4.4)	Xerostomia, somnolence, fatigue, headache, dizziness, insomnia, orthostasis with conduction block, hypotension, anorexia, nausea, urinary retention, constipation, blurred vision, accommodation disturbance, mydriasis, weight gain	Bone fractures, bone marrow suppression, fragility, hepatotoxicity, neuroleptic malignant syndrome, serotonin syndrome, severe hyponatremia, shift to mania in patients with bipolar disorder, suicidal thoughts and behavior
Nortriptyline (Pamelor)	25–50 mg at bedtime	Increase from 25–50 mg/day every 2–3 days to maximum of 150 mg/day	No estimate¶	Fewer anticholinergic effects than with amitriptyline	

Opioids					
Tapentadol (Nucynta)‡††	Immediate release, 50–100 mg, 4–6 times/day; extended release, 50 mg, 2 times/day	Immediate release, day 1, 700 mg, after day 1, 60 mg/day; extended release, 50 mg, 2 times/day	10.2 (5.3–18.5)	Somnolence, nausea, vomiting, constipation, dizziness, respiratory depression, serotonin syndrome, seizures	Hypertension, neonatal opioid-withdrawal syndrome
Tramadol (Ultram)‡	50 mg, 1–2 times/day	100–200 mg/day	4.7 (3.6–6.7)	Somnolence, nausea, vomiting, constipation, light headedness, dizziness, headache	Cardiac arrhythmias, confusion, hypersensitivity reactions, hypertension, seizures, Stevens–Johnson syndrome
Capsaicin 8.0% patch (Qutenza)	Apply for 30 min	Apply for 60 min	10.0 (7.4–19)	Burning at site of application	Damage to C-type fibers, with loss of sensation

N Engl J Med 2016;374:1455-64.

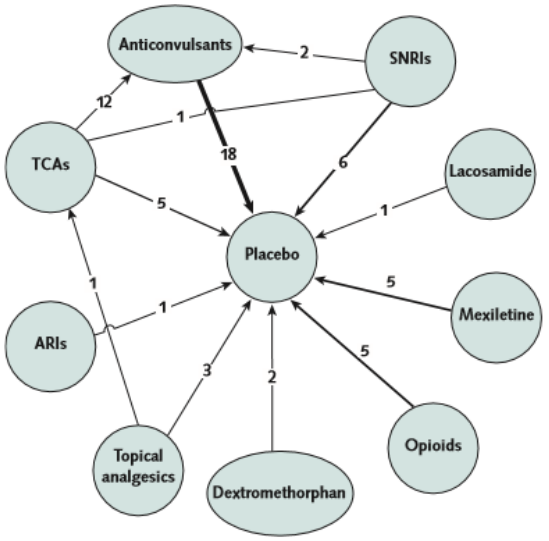
Pharmacologic Interventions for Painful Diabetic Neuropathy

An Umbrella Systematic Review and Comparative Effectiveness Network Meta-analysis

Marcio L. Griebeler, MD; Oscar L. Morey-Vargas, MD; Juan P. Brito, MD; Apostolos Tsapas, MD, PhD; Zhen Wang, PhD; Barbara G. Carranza Leon, MD; Olivia J. Phung, PharmD; Victor M. Montori, MD; and M. Hassan Murad, MD, MPH

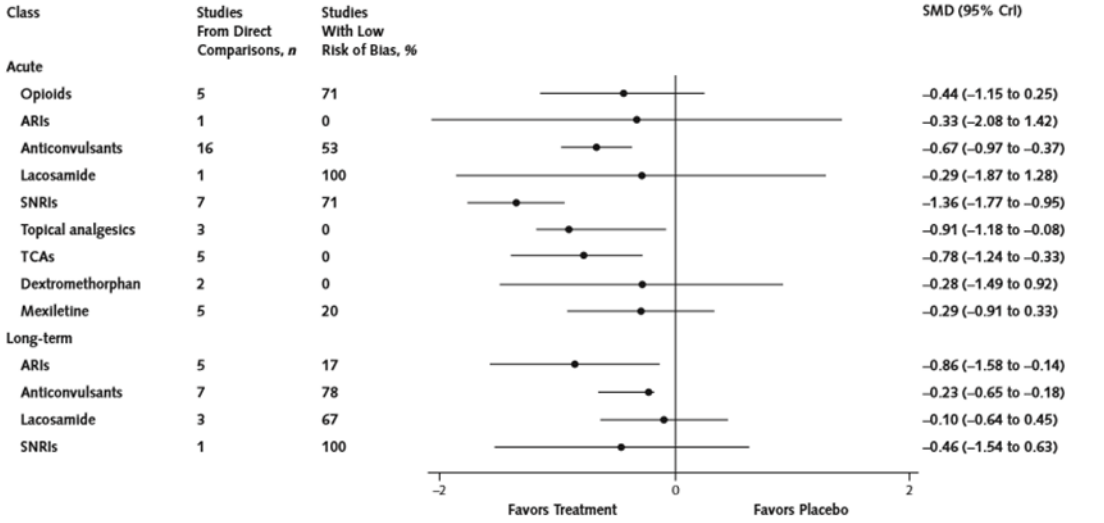
Quina monoteràpia iniciar? ➔ tractament comorbilitats (ansietat, insomni, depressió, pes)
Monoteràpia o tractament combinat? ➔ 30% no responen primer fàrmac.

Figure 1. Network of RCTs evaluating painful diabetic neuropathy within 3 mo, by drug class.



Width of the lines is proportional to the number of trials for that comparison. ARI = aldose reductase inhibitor; RCT = randomized, controlled trial; SNRI = serotonin–norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant.

Figure 2. Agents for treatment of diabetic peripheral neuropathy compared with placebo, by class.



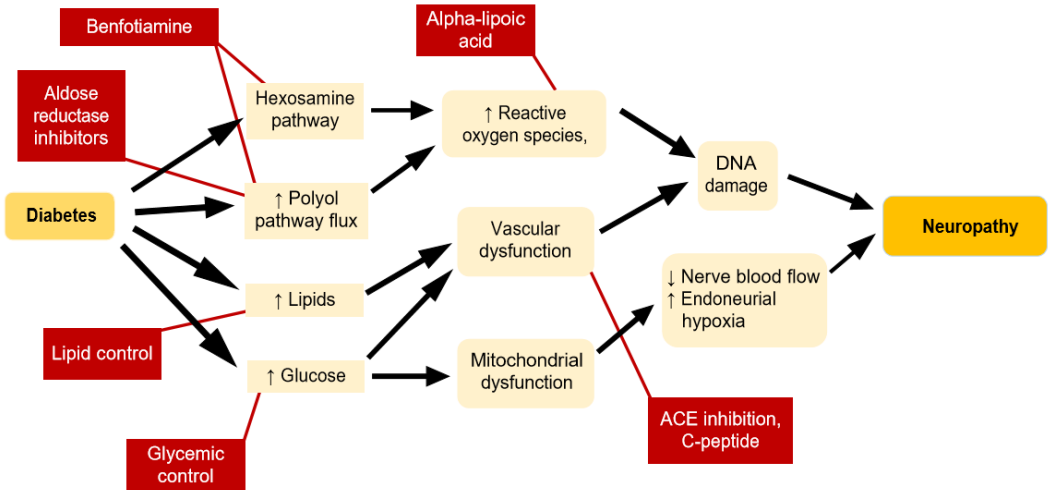
Combined direct and indirect estimates. ARI = aldose reductase inhibitor; CrI = credible interval; SMD = standardized mean difference; SNRI = serotonin–norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant.

Ann Intern Med. 2014;161:639-649.

Treating Diabetic Neuropathy: Present Strategies and Emerging Solutions

Saad Javed[1], Uazman Alam[1,2] and Rayaz A. Malik[1,3]

The Review of DIABETIC STUDIES Vol 12 No 1-2 2015



Aldosa reductasa: enzim que catalitza la conversió de glucosa a sorbitol. L´acúmul de sorbitol i la disminució de mioinositol al teixit nerviós s´ha suggerit com a factor coadjuvant al desenvolupament de PNP.

Factors neurotròfics.

15 Ametov A.S. et al. (2003): The Sensory Symptoms of Diabetic Polyneuropathy are Improved With -Lipoic Acid. Diabetes Care, vo 26, n.3
http://care.diabetesjournals.org/content/26/3/770.short

16 Lee W. Y. et al. (2009) Molecular Mechanisms of Lipoic Acid Modulation of T-Type Calcium Channels in Pain Pathway; The Journa of Neuroscience, 29(30): 9500 –9509
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3073510/

17 Yun Ho Choi et al. (2010) Lipoic acid suppresses compound 48/80-induced anaphylaxis-like reaction; Anat Cell Biol 43:317-324
http://synapse.koreamed.org/DOIx.php?id=10.5115/acb.2010.43.4.317&vmode=FULL

18 Konrad D. et al. (2001) The Antihyperglycemic Drug α-Lipoic Acid Stimulates Glucose Uptake via Both GLUT4 Translocation an GLUT4 Activation. Diabetes vol. 50
https://www.ncbi.nlm.nih.gov/pubmed/11375349

19 Jameel N.M. et al. (2006) α-lipoic acid: An inhibitor of secretory phospholipase A2 with anti-inflammatory activity. Life Sciences 80(2):146-53
https://www.researchgate.net/publication/6782502_a-lipoic_acid_An_inhibitor_of_secretory_phospholipase_A2_with_anti-inflammatory_activity

20 Ruessmann H.J. (2008) Switching from pathogenetic treatment with α-lipoic acid to gabapentin and other analgesics in painfu diabetic neuropathy: a real-world study in outpatients. Journal of Diabetes and Its Complications; 23(3):174-7.
https://www.ncbi.nlm.nih.gov/pubmed/18403218

21 Porasuphatana S et al. (2012): Glycemic and oxidative status of patients with type 2 diabetes mellitus following ora administration of alpha-lipoic acid: a randomized double-blinded-placebo controlled study. Asia Pac J Clin Nutr; 21 (1):12-21
https://www.ncbi.nlm.nih.gov/pubmed/22374556

22 Zamboni P et al. (2013): Inhibitory Effect of Natural Anti-Inflammatory Compounds on Cytokines Released by Chronic Venou Disease Patient-Derived Endothelial Cells. Mediators of Inflammation Article ID 423407
https://www.hindawi.com/journals/mi/2013/423407/

23 Román-Pintos LM et al. Diabetic Polyneuropathy in Type 2 Diabetes Mellitus: Inflammation, Oxidative Stress, and Mitochondria Function. Journal of Diabetes Research. Volume 2016 (2016), Article ID 3425617
https://www.hindawi.com/journals/jdr/2016/3425617/

24 Sharma L et al. Hyperhomocysteinemia: Impact on Neurodegenerative Diseases. Basic Clin Pharmacol Toxicol. 2015 Nov;117(5):287-96.
https://www.ncbi.nlm.nih.gov/pubmed/26036286
https://www.researchgate.net/publication/13075861_Alpha-lipoic_acid_provides_neuroprotection_from_ischemia-

25 Patel et al. A study of the use of carbamazepine, pregabalin and alpha lipoic acid in patients of diabetic neuropathy. J Diabetes Metab Disord. 2014 May 27;13:62.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4055259/

26 Çakici et al. Systematic review of treatments for diabetic peripheral neuropathy. Diabet Med. 2016 Nov;33(11):1466-1476.
https://www.ncbi.nlm.nih.gov/pubmed/26822889

27 Snedecor SJ et al. Systematic review and meta-analysis of pharmacological therapies for painful diabetic peripheral neuropathy. Pain Pract. 2014 Feb;14(2):167-84.
https://www.ncbi.nlm.nih.gov/pubmed/23534696

28 Wile DJ et al. Association of metformin, elevated homocysteine, and methylmalonic acid levels and clinically worsened diabetic peripheral neuropathy. Diabetes Care. 2010 Jan;33(1):156-61
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2797962/

EDITORIAL | Annals of Internal Medicine

Painful Diabetic Neuropathy: Many Similarly Effective Therapies With Widely Dissimilar Costs

The cost of 1 month of the typical starting dose for each of these medications ranges widely. According to Drugstore.com, pregabalin is the most expensive at $189.98 per month, followed by duloxetine at $170.99 per month. Although venlafaxine is generic, its cost remains high at $119.98 per month. In contrast, gabapentin ($18.99 per month), amitriptyline ($12.99 per month), and nortriptyline ($19.99 per month) are more affordable options. Capsaicin is available over the counter without a prescription and is another cheaper alternative ($13.99 per month). These price differences become even more striking over time, with pregabalin costing $2123.88 more than amitriptyline over the course of 1 year of treatment.

The American Academy of Neurology guidelines granted only pregabalin a level A recommendation.

Comorbid conditions and potential adverse effects are other important considerations.

Given the current price of these medications, we believe that the **most cost-effective approach is to try 1 or more TCAs as first-line medications, followed by gabapentin.**

The high-cost options of venlafaxine, duloxetine, and pregabalin should be reserved for when these other medications have failed.

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