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Evidence-based recommendations for the management of neuropathic pain (review of the literature)

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ABSTRACT

Objective: To synthesize, through a review of the literature, the current recommendations in the management of neuropathic pain.

Methodology: Thematic review based on a highly sensitive literature search for the identification of clinical practice guidelines and systematic reviews, focused on diagnosis and management of neuropathic pain, from 2012 to 2017. From the references included, information related to definitions, relevant considerations, indications and treatment objectives, both pharmacological and non-pharmacological, and remission criteria was obtained.

Results: 34 relevant clinical practice guidelines for the management of neuropathic pain were included. The synthesis of relevant aspects focused on: 1) the screening tools available for identification and classification of neuropathic pain; 2) diagnosis and follow-up of confirmation tests; 3) pain management principles, as well as pharmacological and non-pharmacological management as first, second and third line, according to the location of lesions; and 4) follow-up. The most commonly recommended first-line treatments include tricyclic antidepressants, α2δ-ligands (pregabalin and gabapentin), and selective serotonin/noradrenaline reuptake inhibitors.

Conclusion: Neuropathic pain is a common condition in clinical practice, where the non-pain specialist will perform the diagnosis based on a detailed clinical history and directed physical examination. The treatment must be multidisciplinary and begin early with first-line drugs.

Key words: Pain management, neuralgia (MeSH), therapeutics (MeSH), clinical practice guidelines as topic (MeSH), somatosensory system.

RESUMEN

Objetivo: Sintetizar, mediante una revisión de la literatura, las recomendaciones actuales en el manejo del dolor neuropático.

Metodología: Revisión temática basada en una búsqueda de literatura altamente sensible para la identificación de guías de práctica clínica y revisiones sistémicas de la literatura enfocadas en diagnóstico y manejo del dolor neuropático, desde 2012 a 2017. De las referencias incluidas, se obtuvo información relacionada con definiciones, consideraciones relevantes, indicaciones y objetivos del tratamiento, tanto farmacológico como no farmacológico y criterios de remisión.

Resultados: Se incluyeron 34 guías de práctica clínica relevantes para el manejo del dolor neuropático. Se realizó una síntesis de aspectos relevantes enfocados en: 1) las herramientas de tamización disponibles para la identificación y clasificación del dolor neuropático; 2) el diagnóstico y seguimiento de las pruebas de confirmación; 3) principios del manejo del dolor, así como el manejo farmacológico y no farmacológico de primera, segunda y tercera línea, de acuerdo con la localización de las lesiones; y 4) seguimiento. Los tratamientos de primera línea más comúnmente recomendados influyen los antidepresivos tricíclicos, α2δ-ligandos (pregabalina y gabapentina) y los inhibidores selectivos de la recaptación de serotonina/noradrenalina.

Conclusión: El dolor neuropático es una condición común en la práctica clínica, donde el médico no especialista en dolor realizará el diagnóstico basado en una historia clínica detallada y examen físico dirigido. El tratamiento debe ser multidisciplinario e iniciarse precozmente con fármacos de primera línea.

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Palabras clave: Manejo del dolor, neuralgia (DeCS), terapéutica (DeCS), guías de práctica clínica como asunto (DeCS), sistema somatosensorial.

INTRODUCTION

Pain is currently considered a disease and not a symptom (World Health Organization, 2010), a condition of heterogeneous causality and presentation. The burden of the disease and health care costs are high for people affected by this condition (1-4). Mainly in non-specialized contexts, underdiagnosis is common(5,6). The estimated prevalence of pain with neuropathic characteristics in the general population is 7-10% (3,7), however it may vary widely according to definitions, diagnostic criteria, evaluation methods and patient selection (1,2,8). According to the Latin American Federation of Associations for the Study of Pain, the most common cause of pain in Latin America was low back pain with neuropathic component (34% of patients) (9).

Problems associated with suboptimal identification, diagnostic inaccuracies and neuropathic pain management have been researched in various contexts. 39% of patients diagnosed with pain receive treatment prescribed by their physician (10). The major problems identified include inappropriate use of nonsteroidal anti-inflammatory drugs (NSAIDs), widespread use of opioids as first-line treatment, and late referrals to specialized management with a multidisciplinary approach (1,11).

Most patients with possible neuropathic pain will be assessed at least initially by a primary care physician (12), and that is where pain assessment and management is initiated, considering that pharmacotherapy with first-line agents is simple and suitable for non-specialist physicians(6). The purpose of this document is to synthesize, through a review of the literature, the current recommendations in the management of neuropathic pain in order to guide health professionals in the timely identification of this pathology and contribute to the process of informed clinical decision-making.

METHODOLOGY

Thematic review based on a highly sensitive literature search for the identification of clinical practice guidelines and systematic reviews of the literature for the management of neuropathic pain. This search was completed in August 2017 at the American Academy of Neurology, Canadian Pain Society, EFNS (European Federation of Neurological Societies), NICE (National Institute for Health and Clinical Excellence), RLDN (Latin-American network for the study and treatment of the neuropathic pain), and other expert recommendations based on evidence review. Search terms such as "pain management" AND "neuralgia" were used, including studies in English and Spanish, and full publications between 2012 and 2017.

From the references included, information related to definitions, relevant considerations, indications and treatment objectives, both pharmacological and non-pharmacological, and remission criteria was obtained.

RESULTS AND DISCUSSION

The search initially yielded 45 potentially relevant studies, after the elimination of duplicates. In reviewing the title and summary of these articles, 34 clinical practice guidelines for the management of neuropathic pain were finally included. The most relevant aspects of the information evidenced in this review are presented below.

The International Association for the Study of Pain (IASP 2011) defines neuropathic pain as "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (10) and is currently recognized as "pain caused by an injury or disease of the sensory-somatic nervous system"(1,5).

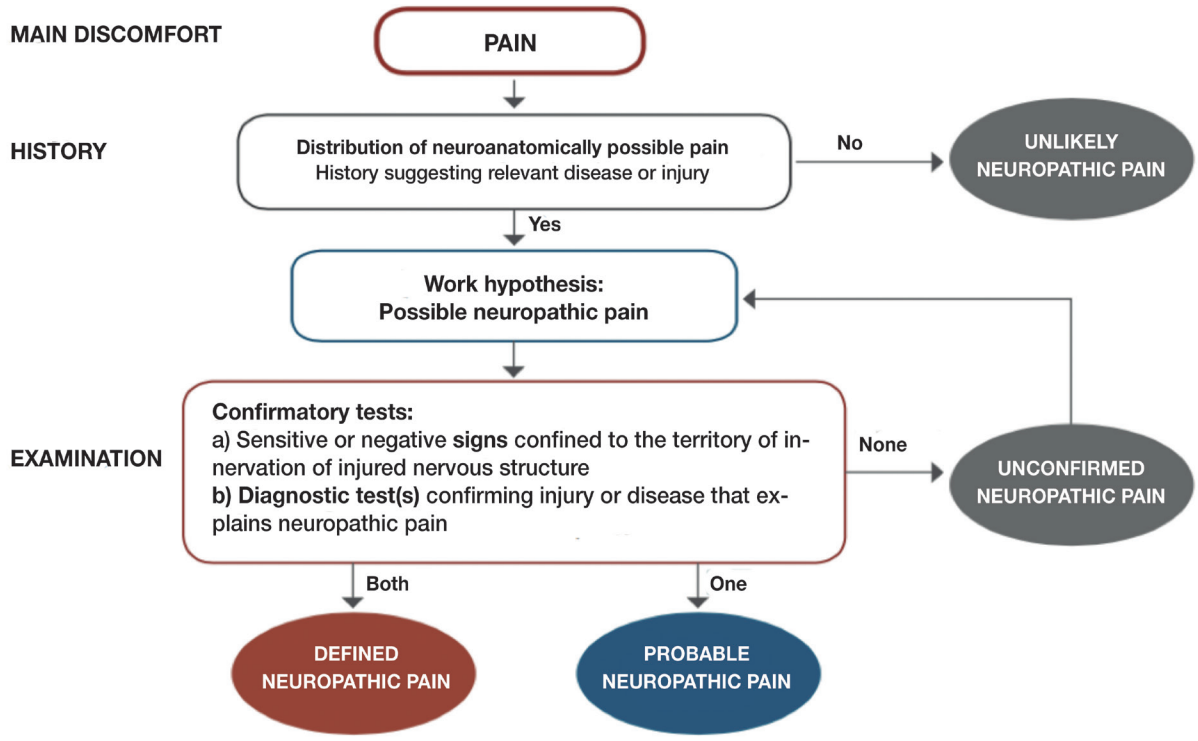
There are two components that are integrated for the final perception of pain: 1) nociceptive or sensory, which constitutes the painful sensation and is a consequence of the transmission of stimuli through the nerve pathways to the cerebral cortex. Most available painkillers act on this component; and 2) affective or reactive, which determines the so-called "pain-related suffering" that varies widely depending on the cause, time, and experience of the patient, and is related to psychological factors(10).

The most commonly used neuropathic pain classifications are based on the anatomy of injuries, aetiology, and related diseases(10). It is located and distributed in three areas especially: 1) *Central:* when the main damage or disorder is located in the central nervous system; 2) *Peripheral:* if the main damage is located in the peripheral nervous system; and 3) *Localized:* well-defined and consistent area of maximum pain (6,13), equal to or less than that of a letter-sized page (21.6 x 27.9 cm) (14,15).

The assessment of neuropathic pain is based on clinical judgment and confirmatory diagnostic tests of abnormalities in sensory-somatic pathway function, however, neuropathic pain is primarily a clinical diagnosis. A simple diagnostic guidance algorithm grades the likelihood of neuropathic pain (Figure 1).

Diagnosis of Neuropathic Pain

Diagnosing neuropathic pain involves 3 aspects: patient history, physical examination of the patient, and follow-up



Source: Correa-Illanes G. Dolor neuropático, clasificación y estrategias de manejo para médicos generales. Rev Médica Clínica Las Condes 2014;25(2):189-99. Originally adapted from: Treede RD, Jensen TS, Campbell JN, Cruccu G, Dostrovsky JO, Griffin JW, et al. Neuropathic pain: redefinition and a grading system for clinical and research purposes. Neurology 2008;70(18):1630-5.

Fig. 1. Flowchart for grading system for neuropathic pain.

of confirmation tests. One of these relevant aspects is the assessment of sensory signs, in which the patient describes the sensation after applying a precise and reproducible stimulus (touch, puncture, pressure, cold, heat, vibration), and their responses are classified as normal, decreased or increased, according to the evaluation of a loss (negative sensory signs) or a gain (positive sensory signs) of the sensory-somatic function (3).

In common practice, a history with suspicion of neuropathic pain and tests with confirmatory signs of sensory-somatic disturbance (compatible with neuropathic pain characteristics) make up a probable case of neuropathic pain. The "likely" level is usually sufficient to initiate treatment according to neuropathic pain guidelines. The "defined" level, by confirmatory tests compatible with the location and nature of the injury or disease, is useful in specialized contexts and when a causal treatment of the underlying injury or disease is an option. (16)

Careful clinical examination is essential in the assessment of neuropathic pain. Presentation characteristics include (10):

– Neuropathic pain can be intermittent/paroxysmal or constant, spontaneous (i.e. occurs without apparent stimulation) or caused.
– Typical descriptions to describe painful and unpleasant sensations (dysesthesia) or altered sensations (paraesthesia) include: shots, like an electric shock, burning, tingling, squeezing, numbness, itching, throbbing and a prickling sensation(1,5).
– Other symptoms that manifest between 15-50% (17) include allodynia (pain caused by a stimulus that normally does not cause pain such as breeze, skin contact with clothing, temperature changes), hyperalgesia (an increased response to a stimulus that is usually painful), painful anaesthesia (pain felt in an anaesthetic area or region), and sensory gain or loss (IASP 2011) (1,5). They are named after the physical stimulus that causes them: heat, cold, pressure, for example allodynia to cold or heat or mechanical.

Screening Tools

There are several standardized screening tools to assist in the identification and classification of neuropathic pain,

based on the patient's reported pain classification. Diagnostic accuracy is variable within and between patient populations, however, they are appropriate to increase patient identification due to the generally higher sensitivity (versus specificity) (12).

There are scales that differentiate neuropathic pain from a nociceptive pain, and others that allow characterizing symptoms. It is recommended to use those of self-administered neuropathic pain, validated in Spanish, to assist in early identification, prioritizing those that are simple to use and that can be quickly executed (Tables I)(1,12). Questionnaire DN4 is widely accepted as easy, simple and has the greatest specificity and sensitivity (10).

There are also different imaging techniques that can be used for the study of pain from the metabolic, functional and anatomical point of view (10):

- Metabolic study: Positron Emission Tomography (PET), Single Photon Emission Computed Tomography (SPECT) and magnetic resonance imaging. They allow the analysis of metabolic changes, including those related to neuronal integrity, excitability and inhibitory neurotransmitters, as well as agents involved in energy processing.
- Functional study: functional magnetic resonance imaging (detects changes in blood oxygenation, reflections of changes in blood flow and variations in deoxyhaemoglobin levels), and nerve-conduction and electromyography (allow diagnosis of peripheral nerve injury or its entrapment, severity and prognosis) (18).
- Structural or anatomical: anatomical magnetic resonance imaging to check that chronic pain is associated with certain structural changes in the brain.

Another simple examination-based way to identify peripheral neuropathy and differentiate it from nociceptive pain is the "3L" approach: *Listen* (listen to the verbal description of pain), *Locate* (locate the pain region and the document with a drawing of the pain, made by the patient or the physician), and *Look* (perform a simple examination of sensory-somatic functions, including sensitivity to touch, cold, heat, and pain) (1).

Principles of Neuropathic Pain Management

The main objective in most cases is to make the pain "bearable" or "tolerable", that is, on an analogous visual scale: set from 0 to 10, zero as no pain and 10 as the most unbearable pain, the objective would be 4/10. This setting of objectives can make a considerable difference in patient satisfaction when instituting pharmacological treatments (19). There are three essential aspects in the management of neuropathic pain, as described in Table II.

Pharmacological Management of Pain

Peripheral Neuropathic Pain

- First-line analgesics: options for first-line monotherapy (except trigeminal neuralgia)(1,3,5,10,19):
  - Tricyclic antidepressants (low dose amitriptyline 25 mg or other tricyclic antidepressants such as imipramine).
  - A2δ ligands (pregabalin or gabapentin) (20).
  - Serotonin-noradrenaline reuptake inhibitors (duloxetine or venlafaxine). Of choice for when there are sleep or mood disorders.
  - As a special consideration, consideration should be given to the use of tramadol (atypical opioid) for the management of acute rescue therapy or incidental pain in combination with first-line drugs (5).

  Patients should be assessed 2 to 4 weeks after starting the treatment to determine the response:
  - If the response is good, treatment should be maintained and if the response is maintained for 3 months, a slower titration can be attempted. If symptoms return, treatment should be titrated again at an effective dose.
  - If a partial response is observed within 2-4 weeks, consider increasing the dose of the current agent.
  - If the response is poor, or the drug is not tolerated, move to second-line approaches.
- Second-line analgesics: if the initial treatment is not effective or is not tolerated, monotherapy should be changed or different classes of agent combined. The monotherapy change should be for one of the remaining drugs indicated in the first line (amitriptyline, duloxetine, gabapentin, or pregabalin) and consider changing again if the second and third drugs tested are not effective or are not tolerated (5,9).

  Combined management considerations:
  - Combined therapy may offer additional analgesic benefits and benefits over the related symptoms, but the potential advantages should be weighed against the possibility of additional adverse effects, drug interactions, increased cost and reduced adherence to a more complex treatment regimen.
  - When treatment is withdrawn or changed, the decrease in drugs should be slow and progressive (5,6).
  - The combination of ≥ 2 analgesic agents in the treatment of neuropathic pain can improve analgesic efficacy and has the potential to reduce the profile of side effects if synergistic effects reduce the dose of combination drugs (9,19).

  Combined treatment options (3,5):
  - Pregabalin or gabapentin with a serotonin-noradrenaline reuptake inhibitor.

TABLE I
VALIDATED DETECTION TOOLS FOR NEUROPATHIC PAIN

Scales	*Description*	*Common items*									
		I1	*I2*	*I3*	*I4*	*I5*	*I6*	*I7*	*I8*	*I9*	*I10*
Leeds Assessment of Neuropath Symptoms and Signs (LANSS)	– Patient self-assessment – Physical examination: Checks the alteration of the threshold of a puncture and the presence of evoked tactile allodynia by rubbing with a cotton swab – Sensitivity 82% and specificity 80%	Yes	Yes	Yes	-	Yes	-	Yes	Yes	-	Yes
Douleur Neuropathique in 4 Questions (DN4)	– Patient self-assessment – Physical examination of sensory dysfunction – A total score of 4 or more suggests neuropathic pain. – Sensitivity 89.9 % and specificity 82.9 %	Yes	Yes	Yes	Yes	-	Yes	-	Yes	Yes	Yes
Neuropathic Pain Questionnaire (NPQ)	– Seven sensory items, three items of exacerbating factors, two items describing pain and emotional impact – Allows to discriminate neuro-pathic pain (positive score) from non-neuropathic pain (negative score) – There is a reduced version that includes only 3 questions with a predictive value similar to that of the full questionnaire – Sensitivity 66.6 % and specifici-ty 71.4 %	Yes	Yes	Yes	Yes	Yes	Yes	-	-	-	-
Pain Detect Questionnaire (PDQ)	– Prevalence of any neuropathic pain component in patients with low back pain – Six items of symptoms, two items related to spatial (radiant pain) and temporal characteristics – Sensitivity 85%, specificity 80%, positive predictive value 83%	Yes	Yes	Yes	Yes	Yes	-	-	-	-	-
Diagnostic tool	– Specific for diagnosis of local-ized neuropathic pain – Identifies neuropathic pain as confirmed, probable (with high suspicion) or possible (with low suspicion) pain – 4 items exploring patient histo-ry to suspect nerve disease or injury – Needs more extensive physical examination, greater sensitivity and specificity for the identifica-tion of low back pain of a neuro-pathic nature (85-90 %)	Yes	Yes	Yes	Yes	Yes	-	-	-	-	-

I1: throbbing, tingling. I2: electric shock, shot. I3: hot, burning. I4: numbness. I5: pain evoked by soft touch. I6: cold, painful, freezing pain. I7: autonomic changes. I8: allodynia brushing. I9: threshold increased to soft touch. I10: threshold increased to puncture.
Sources: Adapted from Colloca L, et al. and Sociedad Española de Médicos de Atención Primaria (SEMERGEN), 2017. (3,10) / Adapted from Bennet MJ et al. Pain 2007

TABLE II
FUNDAMENTAL ASPECTS IN THE MANAGEMENT OF NEUROPATHIC PAIN

Aspects	*Considerations*
Decide treatment (5,19,20)	– Considerations for treatment – Pain treatment should begin at the time of diagnosis – The cause of pain should be studied simultaneously with treatment – The comorbidities of the patient should be considered, such as cardiovascular pathology, liver failure, renal failure, cognitive impairment, depression, anxiety or sleep disorders, as well as the concomitant medication that he/she may be receiving for these or other pathologies – Begin treatment with a first-choice drug, with the appropriate dose increase required to reach an acceptable response or until adverse effects occur – Taking medication by schedule, not as needed – Patient response to previous treatment – Availability, route of administration, access and cost
Agree the treatment plan with the patient (5) "Patient education is a vital aspect of managing neuropathic pain(6)"	The information discussed should include: – Severity of pain and impact on lifestyle (disturbance of sleep and mood, for example) – The underlying cause of pain and pain mechanisms – Reasons for treatment selection and treatment objectives – Treatment expectations. Treatment will not be curative, but symptomatic and gradual in effect, considering a pain reduction of approximately 50% acceptable. – Possible adverse effects of pharmacological treatments, interactions with other drugs and contraindications – The importance of dosing, the risks of drug misuse and abuse – Warn the patient that drugs used for neuropathic pain have other indications (such as epilepsy and depression) – Non-pharmacological treatments: recommend or manage access to physical treatments, psychological therapies, as well as the importance of stress reduction and good sleep hygiene (1)
Define the need to refer the patient to a specialized service	Refer the patient to a specialist pain service and/or to a specific underlying condition service at any stage, including at initial presentation and examinations, if any of the following occur (6): – Severe pain or pain significantly limiting quality of life (including sleep and mood disorders) – Deterioration of the underlying health condition – Complex medical comorbidities; both cardiovascular, renal and metabolic that hinder drug treatment – Diagnosis not clear; no categorical neuropathic elements or with added elements suggesting another pathology – High potential for abuse of opioid-derived substances – Polypharmacy – Refractoriness to multiple pain therapies, both pharmacological and non-pharmacological

Source: authorship based on references (1,5,6,19,20)

- Pregabalin or gabapentin with amitriptyline (9).
- Pregabalin or gabapentin with tramadol.

Although tricyclic antidepressants and serotonin-noradrenaline reuptake inhibitors are different classes of antidepressants, they target the same mechanism, so a combination of serotonin-noradrenaline reuptake inhibitors and tricyclic antidepressants is not recommended (5), and the combination of tricyclic antidepressants with tramadol should be avoided.

– Third-line analgesics: if the patient does not respond to drug change or combination therapy, the use of strong opioids is recommended; those most closely related to the management of neuropathic pain are: tapentadol, oxycodone, methadone and buprenorphine (21), since it is a partial, and not pure, agonist (22). As well as combinations of strong opioids with dual antidepressants or with pregabalin or gabapentin, with the exception of dual analgesia: tapentadol, which is suggested to be combined with dual antidepressants(23).
– Other analgesic options: There are weak, negative, or inconclusive recommendations for the use of all other pharmacological treatments for general neuropathic pain, although some agents are likely to be effective in subgroups of patients (3). The following should not be taken to treat neuropathic pain in non-specialized places unless directed by a specialist: lacosamide, lamotrigine, morphine, oxcarbazepine, topiramate, or venlafaxine (5).

Localized Neuropathic Pain

Localized neuropathic pain is a form of peripheral neuropathic pain. Topical treatments, the basis of localized neuropathic pain management, are especially useful to reduce the consumption of oral drugs due to low performance, low tolerance or polypharmacy. Similarly, they have been associated with satisfactory efficacy, improved performance and fewer systemic side effects and drug interactions (24). The application of topical agents has demonstrated good results in peripheral neuropathic pain, safety, tolerance and continuous efficacy throughout long-term treatment. Topical modalities may also be used in combination with other medications and analgesics with limited pharmacological interactions (25,26).

Lidocaine patches (5%) have demonstrated efficacy safety and tolerability in postherpetic neuralgia(24,27). Several international guides, including the 2009 Latin American guide, place topical lidocaine as the first line in peripheral neuropathy(1). Botulinum toxin type A has shown efficacy and safety in small clinical trials with subcutaneous administration in peripheral neuropathic pain (24,28), with a recommended dose of 50-200 units to the painful area every 3 months.

The management of localized neuropathic pain is based on topical therapy starting with lidocaine patches (5%), the first line being for its management (1,21), as other treatment options, especially for the management of refractory localized neuropathic pain, the use of botulinum toxin and the combined treatment described above is recommended, if there is no response to topical treatment.

The quality of evidence on the use of capsaicin patches (8%) is high (although they are not available in Colombia). NeuPSIG guidelines on neuropathic pain assessment proposed capsaicin patches as a second line of treatment for peripheral neuropathy when trying to avoid oral treatments or if these are not tolerated (16). However, the magnitude of the effect is less than lidocaine, more likely to produce topical side effects such as pain, erythema, pruritus, and mild to moderate transient burns in the area of application (24). The recommendation is to apply them in the area of pain every 6 hours with gloves, for 8 weeks.

The following have been described for the management of postherpetic neuralgia:

– As the first line, topical management with lidocaine patches (5%) is preferred (1,21).
– As the second line, gabapentin or amitriptyline and recall the use of tramadol (atypical opioid) for the management of acute rescue therapy or incidental pain in combination with first-line drugs (5).
– As a third line of treatment combine drugs of different classes that include strong opioids.

The following have been identified for the management of trigeminal neuralgia:

– Carbamazepine (200-1,200 mg/day) as the drug of choice, however, its efficacy may be compromised by low tolerability and pharmacokinetic interactions (1,5,29).
– If the initial treatment with carbamazepine is ineffective, not tolerated or contraindicated, a specialist's advice and early referral to a specialized pain service or condition-specific service should be considered (5).

Central Neuropathic Pain

Central neuropathic pain appears to respond to the same pharmacological treatments as peripheral neuropathic pain, although patients generally have a less robust response.

– First-line analgesics:
  • Amitriptyline should be the preferred option recommended by experts.
  • Pregabalin and gabapentin. Based on scientific evidence and the added benefit in the treatment of comorbidities (depression, insomnia, anxiety), pregabalin should be the preferred option for patients aged over 65, with a better risk/benefit ratio compared to tricyclic antidepressants, and with less contraindications.
– Second and third line analgesics:
  • Switch to another first-line agent or combine medications if treatment fails.
  • Tramadol followed by stronger opioids: tramadol, tapentadol, oxycodone, methadone and buprenorphine, due to their partial agonism and antineuropathic mechanism.

– Other analgesic options:
  • Cannabinoids are suggested in multiple sclerosis if other treatments fail (30).
  • There is some mixed evidence of lamotrigine in spinal cord injury and post-stroke pain (1,30).

Pharmacological Management of Neuropathic Pain

Complementary treatments such as psychotherapy (particularly cognitive behavioural therapy) and physiotherapy-physical means for pain (31) should be administered as part of a multidisciplinary approach(1,8,9). Interventional treatments are considered for patients with refractory neuropathic pain, who have not responded adequately to standard pharmacological treatments used alone or in combination with non-pharmacological treatments (8,19).

Interventional treatments for the management of neuropathic pain should ideally be offered in clinical and research environments that collect and report data on patient outcomes (8). Only qualified professionals with extensive experience should perform these interventional procedures (5).

Specific recommendations:

– Sympathetic blocks and spinal cord stimulation in cases of pain that cannot be managed by pharmacological and complementary treatments (3) and are not candidates for corrective surgery (failed back surgery syndrome, permanent chronic postoperative pain and complex regional pain syndrome, traumatic neuropathy and brachial plexopathy) (8,32).
– Stimulation of the peripheral nerve or dorsal root ganglion is recommended in chronic neuropathic pain, including occipital neuralgia and postherpetic neuralgia. Dorsal root ganglion stimulation provided a response rate with a pain reduction of up to 60% (3).
– Epidural and transcranial cortical neurostimulation as treatment options for patients with chronic refractory neuropathic pain (3).
– Bisphosphonates: have recommendation A in complex regional pain syndrome (33), can produce long-term benefits (> 1 month) in patients who have not responded adequately to less invasive options (3,32,33).

Recommendations for epidural injections (3,32):

– Lumbar radiculopathy: short-term relief up to three months with lumbar epidural steroid injections in patients with lumbar radiculopathy who did not respond adequately to a conservative treatment.
– There is no evidence on the long-term effectiveness of epidural injections.

Follow-up of Neuropathic Pain

Patients should be assessed 2 to 4 weeks after starting the treatment to determine the response. The tools and scales used for diagnosis may be useful for clinical monitoring (although not all are validated for this use) to establish a baseline and assess the patient's response.

Monitoring of possible drug interactions, adverse events, comorbidities, need for dose assessment, etc., should be part of the follow-up plan. If a patient does not show a satisfactory therapeutic response, he/she should be referred to a pain centre.

Each follow-up should include assessment of: pain management, lifestyle impact, daily activities (including sleep disorders), physical and psychological well-being, adverse effects, and continued need for treatment.

CONCLUSIONS

Neuropathic pain is a common in health care services, where the non-pain specialist can perform the diagnosis based on the clinical history and directed physical examination. The treatment must be multidisciplinary and begin early with first-line drugs. The first-line treatments recommended by most guides are tricyclic antidepressants, α2δ-ligands (pregabalin and gabapentin), with selective serotonin-noradrenaline reuptake inhibitors sometimes included as first-line and sometimes as second-line. In localized neuropathic pain, the recommended first line is lidocaine patches (5%).

All guides recommend reserving tramadol for second-line use in stronger opioid rescue therapy and analgesics for later use, and only after non-response to another monotherapy or combination therapy with first-line agents. Evidence in central neuropathic pain is less consistent than for peripheral neuropathic pain, but first-line recommendations are amitriptyline and gabapentin or pregabalin.

Complementary therapies (psychotherapies and physiotherapy) are recommended to accompany drug management. The evidence for most interventionist treatments is weak, limited or insufficient, some evidence supports these recommendations under selected conditions of neuropathic pain.

The dissemination of risk and benefit evidence of available therapeutic options is necessary for shared decision-making and informed consent (32), as well as to ensure that persons requiring evaluation and specialized interventions are referred in a timely manner to a specialized pain management service and/or other specific services (5).

CONFLICT OF INTERESTS

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