

# Diagnosis and Management of Neuropathic Pain: A Balanced Approach to Treatment

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## PURPOSE

To provide nurse practitioners with a conceptual framework from which to diagnose and manage chronic neuropathic pain, specifically postherpetic neuralgia (PHN). A current review of the available treatment options for the management of neuropathic pain and PHN is provided.

## DATA SOURCES

A comprehensive literature review was conducted. Clinical articles, meta-analyses, and reviews were selected for their relevance to the diagnosis and management of chronic neuropathic pain and PHN.

## CONCLUSIONS

Managing patients with chronic neuropathic pain is a common clinical challenge due to variability in individual symptoms, mechanisms, and treatment responses. In patients with PHN, a balanced treatment approach focusing on efficacy, safety, and tolerability is recommended. With appropriate treatment, most patients are able to achieve clinically significant relief from neuropathic pain.

## IMPLICATIONS FOR PRACTICE

Diagnosis and management of neuropathic pain syndromes is challenging. Because of the complexity of chronic pain, successful long-term treatment can be especially difficult (Nicholson, 2003b). While most acute pain is nociceptive (i.e., a response to noxious stimuli), chronic pain can be nociceptive, neuropathic, or of mixed origin. PHN is a chronic pain syndrome that can last for years, causing physical and social disability and psychological distress (Kanazi, 2000). Despite major recent advances in the treatment of PHN, many patients remain refractory to current therapy (Dworkin, 2003). For practicing clinicians, including nurse practitioners, viewing pain as a disease rather than a symptom is the first step towards its successful management.

Understanding the pathophysiology of chronic pain and emerging treatment paradigms for the management of neuropathic pain and PHN is critical to optimal care.

## KEY WORDS

Postherpetic neuralgia; neuropathic pain; chronic pain; gabapentin; tricyclic antidepressants; pain management.

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## INTRODUCTION

Diagnosis and management of neuropathic pain syndromes are challenging tasks. Because of the complexity of chronic pain, successful long-term treatment can be especially difficult (Nicholson, 2003b). While most acute pain is nociceptive (i.e., a response to noxious stimuli), chronic pain can be nociceptive, neuropathic, or of mixed origin. Postherpetic neuralgia (PHN) is a chronic pain syndrome that can last for years, causing physical and social disability and psychological distress (Kanazi, 2000). As the pain of PHN may become intractable over a period of months to years, PHN can significantly affect quality of life and overburden health care resources (Schmader, 1998). Despite major recent advances in the treatment of PHN, many patients remain refractory to current therapy (Dworkin & Schmader, 2003). For practicing clinicians, including nurse practitioners, viewing pain as a disease rather than a symptom is the first step towards its successful management. In this paper, the pathophysiology of chronic pain will be reviewed and emerging treatment paradigms for the management of neuropathic pain and PHN will be discussed.

## TOWARDS A DEFINITION OF PAIN

The International Association for the Study of Pain (IASP) defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage" (Merskey & Bogduk, 1994). Using this definition, the IASP was the first to propose that pain be treated from the perspective that it is a disease and not just a symptom.

## NOCICEPTIVE VS NEUROPATHIC PAIN

Pain can be categorized as nociceptive or neuropathic (Figure 1) (Nicholson, 2003a). Nociceptive pain results from activation of nociceptive sensory axons by noxious stimuli and is typically finite and localized and subsides when the stimuli are no longer present (Chong & Bajwa, 2003). Neuropathic pain is "initiated or caused by a primary lesion or dysfunction in the nervous system," according to IASP (Merskey & Bogduk, 1994). That is, when a nerve is damaged, changes within the neural pathways can result in chronic pain even in the absence of a stimulus (Chong & Bajwa, 2003).

While chronic pain is less well characterized than acute pain, it is typically described as persistent pain for more than 3 months, according to IASP. If pain alters normal function, it may be considered persistent and in that progression may be called chronic pain (Nicholson, 2003a). Common conditions categorized as neuropathic pain include diabetic neuropathy, chronic radicular pain, trigeminal neuralgia, complex regional pain syndrome, central poststroke syndrome, and PHN.

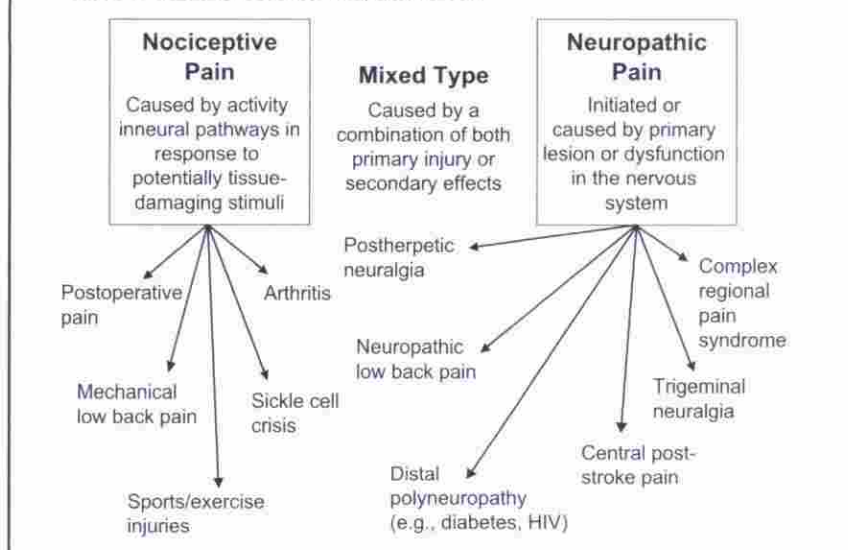
## POSTHERPETIC NEURALGIA

PHN is a neuropathic pain syndrome that can be highly debilitating and elusive to effective treatment. A complication of herpes zoster (commonly known as "shingles"), PHN is commonly defined as pain persisting or recurring in the region of a shingles eruption at least 1 month after the onset of acute rash. Shingles and subsequent PHN result from reactivation of the varicella-zoster virus acquired during the primary varicella infection, or chickenpox. While varicella is generally a childhood disease, herpes zoster and PHN become more common with increasing age (Stankus, 2000). In fact, among herpes zoster patients over 60 years of age, estimates of occurrence range from 27% to 68% (Schmader K, 1998). In addition, a patient's risk may increase through factors that decrease immune function (e.g., human immunodeficiency virus infection, chemotherapy, malignancies, and chronic corticosteroid use) (Stankus, 2000).

## PREVALENCE OF NEUROPATHIC PAIN, PHN

The prevalence of neuropathic pain is imprecise. In the United States, an estimated 3.8 million individuals suffer neuropathic pain, including

Figure 1. Nociceptive Versus Neuropathic Pain



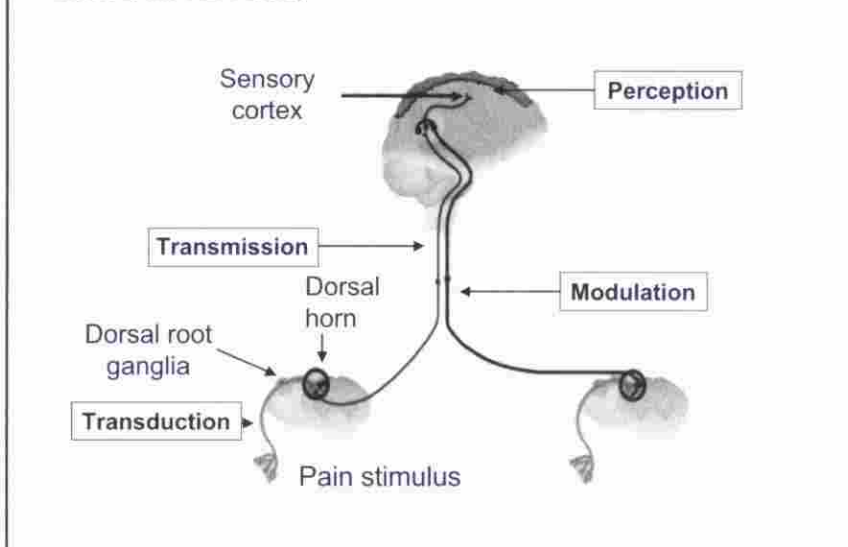
neuropathic low back pain (Bennett, et al., 1997). In the United Kingdom, neuropathic pain affects an estimated 1% of the general population, with as many as 1 million persons experiencing PHN (Bowsher,

1999; Bowsher, 1991). PHN is estimated to affect about 20% of patients with herpes zoster (Stankus, 2000) and accounts for as much as 15% of all referrals to pain clinics (Bowsher, 1997).

Table 1. Difference in Acute Versus Chronic Pain

Characteristic	Acute pain	Chronic pain
Cause	Generally known	Often unknown
Duration of pain	Short, well characterized	Persists after healing ≥ 3 months
Treatment approach	Underlying disease	Underlying disease and pain disorder

Figure 2. The Pain Pathway



## PATHOPHYSIOLOGY OF PAIN

In disease states such as diabetes or hypertension, the abnormal pathophysiology is known. In diabetes, the alteration in pancreatic islet cell sensitivity is the result of a whole host of endocrinologic phenomena. Studies have shown where interference with endocrinologic mechanism or pathways can prevent or treat hyperglycemia or hypoglycemia. Currently, the mechanisms responsible for acute and chronic pain are not clearly understood (Table 1). In acute pain, treatment has an effect on the peripheral stimulus (i.e., where the tissue was injured) with resolution of tissue injury and restoration of normal tissue structure and thus pain relief. In chronic pain, like that experienced by patients with PHN, the infection is no longer present but the patient continues to experience pain.

The mechanisms responsible for the persistent pain are multifaceted. The development of neuropathic pain involves a series of changes, including primary and secondary hyperalgesia, peripheral and central sensitization, and wind-up phenomena, with neurotransmitters playing a critical role (Nicholson, 2000).

By definition, a disease process alters the way a system or organ system responds to different types of homeostatic processes within the body. In disease states such as diabetes or hypertension, there are alterations in the endocrinologic or cardiovascular systems. Similarly, in persistent pain caused by nerve injury from herpes zoster infection or diabetes, there are alterations in nerve function at the spinal cord level. At the level of the spinal cord, cells in the dorsal horn transmit stimuli that are normally not interpreted as painful but because of nerve cell injury become painful (Figure 2).

Changes in gene function or changes at the levels of transformation, transduction, or modulation due to nerve injury may result in persistent pain (Nicholson, 2003a). In neuropathic pain and in chronic, inflammatory-type pain, there are reversible and irreversible changes in how the nervous system responds. In some cases, if the stimulus is eliminated, the system may revert back to normal. However, in patients with PHN, normal nerve fibers are often destroyed because of the intensity of the inflammation caused by the infection. These damaged nerve fibers permanently and negatively affect the function of other nerve fibers, thus resulting in chronic pain (Nicholson, 2003a).

## ASSESSMENT OF NEUROPATHIC PAIN

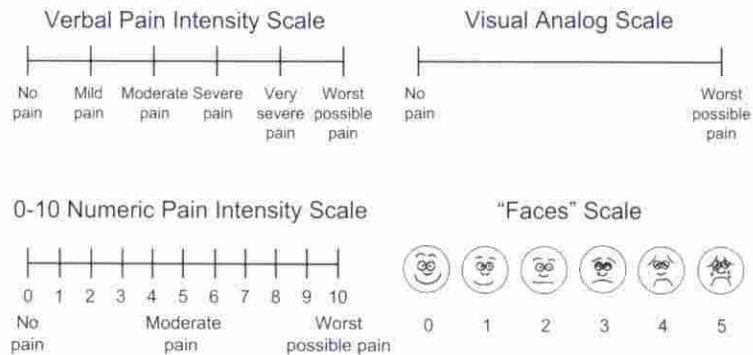
An initial objective evaluation of neuropathic pain should include the use of pain assessment scales. Consistent use of the pain assessment scale is important to develop a baseline understanding of the intensity of a patient's pain, how the pain is affecting his or her quality of life, and how comorbid-related conditions are tied into the intensity of pain. Typically, pain scales use a 0-to-10 scale or 0-to-100-mm visual analog scale, with 0 being the least amount of pain and 10 or 100 being the worst pain ever experienced (Figure 3). Data also show that increasing pain intensity is correlated with functional response. The presence of pain and increasing pain intensity are significantly ( $P < .0001$ ) associated with greater impairment in functional ability as measured by the Brief Pain Functional Interference Index in patients with human immunodeficiency virus (Figure 4) (Breitbart, et al., 1996). This finding may be applied to other groups of patients suffering with chronic pain.

The McGill Pain Questionnaire is a frequently used tool that assesses sensory, affective, and evaluative measures of pain in patients with neuropathic pain (Melzack, 1975). The Neuropathic Pain Scale is a relatively new tool addressing different qualities and common descriptors of neuropathic pain that may assist the clinician in individualizing treatment based on patient symptoms (Galer & Jensen, 1997). Other tools in development include the Leeds Assessment of Neuropathic Symptoms and the Signs Pain Scale (Bennett, 2001). By periodically reassessing a patient's response to treatment using objective assessments, clinicians may gain a better understanding of pain, its treatment, and progression over time (Nicholson, 2003a).

## DIAGNOSING NEUROPATHIC PAIN

In diagnosing pain, first and foremost is determining whether the patient is suffering from neuropathic pain or from pain due to another cause (Nicholson, 2003a). Using the traditional medical model allows the clinician to assess the pain more systematically (Nicholson, 2003a). The diagnostic workup in patients with suspected neuropathic pain should include a detailed medical history, review of systems, and comprehensive medical and neurologic examinations (Chong & Bajwa, 2003). Assessing the onset, location, quality, intensity, and duration of the pain affords the clinician more information useful in mak-

Figure 3. Pain Assessment Scales



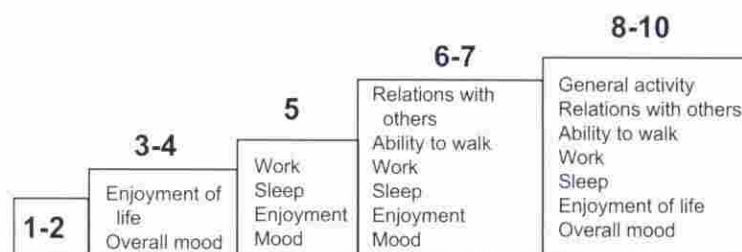
Portenoy R.K., Kanner R.M., eds. (1996). *Pain Management: Theory and Practice*. Philadelphia, Pa: Davis.  
Wong D.L. (1997). *Whaley and Wong's Essentials of Pediatric Nursing*, 5th ed. St. Louis, Mo: Mosby Inc.  
McCaffery M., Pasero C. (1999). *Pain: Clinical Manual*. St. Louis, Mo: Mosby, Inc.

ing an accurate diagnosis and designing a treatment regimen to specifically address a patient's pain (Nicholson, 2003a).

The diagnosis of neuropathic pain is made clinically. Laboratory studies are not diagnostic but help determine whether a patient has a treatable lesion (i.e., nerve root compression). Electromyography and other nerve conduction studies evaluate large nerve fibers, rather than the small sensory nerve fibers that are responsible for neuropathic pain. Quantitative sensory testing may provide additional information (Dworkin, 2002); however, the clinical examination is key to making the diagnosis of neuropathic pain (Nicholson, 2003a).

Examination of a patient, which can be done in the office within 5 to 7 minutes, is necessary to determine a diagnosis of neuropathic pain (Nicholson, 2003a). Patients may report tingling or numbness over a particular area, which suggests that an alteration or loss of normal neurologic function has occurred. Symptoms of neuropathic pain may be classified as either spontaneous pain or stimulus-evoked pain (Dworkin, 2002; Nicholson, 2003a). Spontaneous pain-type symptoms include burning, throbbing, electric, stabbing, or shooting pains, which may be continuous or intermittent in affected patients (Dworkin, 2002). Stimulus-evoked pain includes allodynia, which is a painful

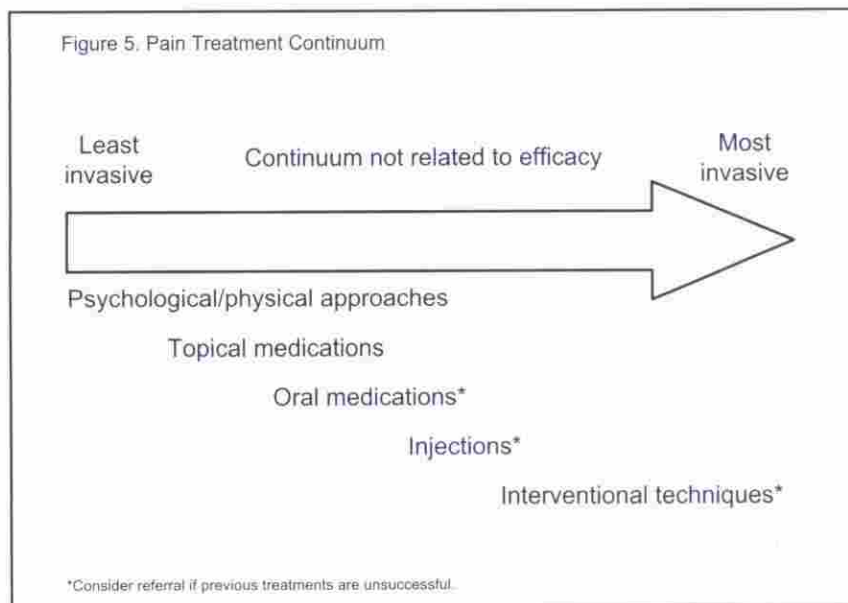
Figure 4. Pain Intensity and Functional Interference



Functional Impact Is Significantly Correlated with Pain Severity ( $P < .0001$ ).

Breitbart, W., McDonald, M.V., Rosenfeld, B., et al. (1996). *Pain*, 66, 315-321.

Figure 5. Pain Treatment Continuum



response to a normally nonpainful stimulus, and hyperalgesia, which is increased pain to a normally painful stimulus (Merskey & Bogduk, 1994).

A tuning fork, a piece of gauze, a pin, and a paperclip are simple tools that can be used to discern the presence of allodynia and provide key information pertaining to a diagnosis of neuropathic pain. Often, a patient with PHN or neuropathic pain describes an intensely uncomfortable and/or burning sensation when a cool or cold object (e.g., tuning fork) touches the affected area. Patients with allodynia describe an intense pain when a piece of gauze or light cloth is drawn across the

area, indicating that the nervous system has been disrupted. The slight pressure exerted from the gauze activates A $\beta$ -fiber mechanoreceptors, which are normally activated by nonpainful mechanical stimuli but are now interpreted as painful when the stimulus is transmitted from the periphery to the spinal cord to the brain (Dworkin, 2002; Nicholson, 2003a). Patients with neuropathic pain also report abnormal sensations, including dysesthesias (unpleasant abnormal sensations) and paresthesias (abnormal sensations that are not unpleasant), which may include itching, numbness, tingling, pricking, and pins and needles sensations (Dworkin, 2002).

Typically, allodynia combined with tingling and numbness are hallmark symptoms of neuropathic pain (Nicholson, 2003a). Concomitant conditions that may be present in patients with chronic neuropathic pain include anxiety, sleep disturbances, and depression (Nicholson, 2003a).

## TREATMENT OF NEUROPATHIC PAIN

From the perspective that neuropathic pain is a disease rather than a symptom, it is important to treat patients based on his or her pain intensity and a continuum of treatment, from least invasive to most invasive (Figure 5) (Nicholson, 2003a). A balanced approach to treatment that considers both efficacy and safety is important because a number of commonly used medications are not necessarily indicated for use in patients with neuropathic pain (Nicholson, 2003a). In most cases, polypharmacy may be necessary. The majority of patients with neuropathic pain are effectively treated with a combination of cognitive, behavioral, and pharmacologic therapies (Table 2) (Nicholson, 2003a).

Recent major advances in the treatment of PHN are based on results of randomized controlled trials, which show that gabapentin, the lidocaine patch 5%, and opioid analgesics are efficacious in the treatment of PHN, and that nortriptyline and amitriptyline provide equivalent analgesic benefits for patients (Dworkin, 2003).

**Anticonvulsants.** Both neuropathic pain and epilepsy result from injury to the nervous system. Thus, it is not surprising that anticonvulsant therapy is a viable treatment option for patients with neuropathic pain (Nicholson, 2003a).

First-generation agents, such as phenytoin and carbamazepine, and second-generation agents, such as gabapentin, lamotrigine, and oxcarbazepine, have been effective in randomized, controlled clinical trials in patients with neuropathic pain (Backonja, 2003; Collins, et al., 2000; Nicholson, 2003a; Tremont-Lukats, et al., 2000).

Anecdotal reports or case series have been reported with other anticonvulsant agents (Chong & Libretto, 2003). In general, the anticonvulsants appear equally effective, but lack of response with one agent does not necessarily predict outcome with other anticonvulsants. Doses for analgesia are typically less than those used to treat epilepsy. Adverse effects associated with anticonvulsants, specifically phenytoin and carbamazepine, include sedation, memory disturbances, electrolyte imbalances, liver

Table 2. Management of Chronic Neuropathic Pain

### Pharmacologic Therapy

- Topical agents
- Aspirin/nonsteroidal preparations
- Capsaicin
- EMLA (eutectic mixture of local anesthetics) cream
- Topical lidocaine patch 5%
- Oral agents
- Anticonvulsants
- Carbamazepine
- Gabapentin

### Cognitive Therapy

- Psychosocial therapy

### Behavioral/Alternative Therapies

- Acupuncture
- Biofeedback
- Hypnosis

- Antidepressants
- Amitriptyline
- Nortriptyline
- Imipramine
- Desipramine
- Opiates
- $\alpha$ -adrenergic agents
- Nerve blocks
- Corticosteroids
- Local anesthetics

### Interventional Therapy

- SCS
- Intrathecal opiates
- Neuro-lesioning
- Transcutaneous electric nerve stimulation (TENS)

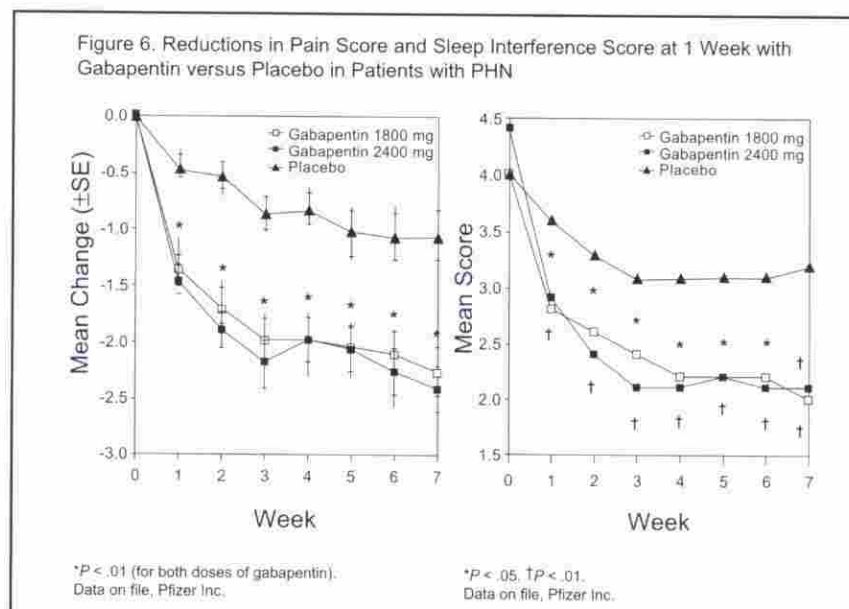
dysfunction, anemia, and/or thrombocytopenia (Stankus, et al., 2000).

**Gabapentin.** Gabapentin is a second-generation anticonvulsant that provided significant benefit over placebo in the 2 largest controlled clinical trials involving PHN (Backonja & Glanzman, 2003; Rice & Maton, 2001; Rowbotham, et al., 1998). These studies clearly demonstrate significant improvement in pain with gabapentin over placebo at 1 week and at 8 weeks (Nicholson, 2003a). Significantly more patients rated themselves as moderately or much improved with gabapentin compared with placebo (43% vs 12%;  $P < .001$ ) (Nicholson, 2003a). Gabapentin 1800 mg to 3600 mg/day significantly reduced daily pain ratings and improved sleep, mood, and quality of life (Figure 6).

Gabapentin has an excellent safety and tolerability profile and does not interfere with P450 CYP isoenzymes, so it has no significant drug-drug interactions. Somnolence, dizziness, and mild peripheral edema are the most commonly reported adverse effects, but dose adjustment typically allows the patient to continue therapy. Gabapentin is largely eliminated by the kidney and dosage adjustment may be necessary in patients with renal insufficiency. To reduce adverse effects and increase patient compliance with treatment, gabapentin should be initiated at 300 mg in a single dose taken at bedtime and then titrated by 300 mg per day to an initial dose of 300 mg t.i.d., as tolerated. Many patients experience at least partial pain relief at a dosage of 1800 mg/day, and titration can be continued to 3600 mg/day (1200 mg 3 times per day), as tolerated. Because gabapentin is absorbed with some variability across patient populations, dosage titration should be based on pain relief and tolerability (Dworkin & Schmader, 2003).

**Lidocaine patch.** Lidocaine 5% patch is indicated for the treatment of PHN and specifically for the treatment of allodynia related to PHN (Nicholson, 2003a). Lidocaine patch 5% has an excellent safety and tolerability profile. The most common adverse effects involve mild skin reactions and/or sensitivity at the application site. Systemic adverse effects are uncommon because the topical delivery system largely bypasses the systemic circulation. Although systemic absorption is minimal, the lidocaine patch should be used with caution in patients receiving class I antiarrhythmic drugs.

The lidocaine patch was effective for the treatment of PHN in randomized con-



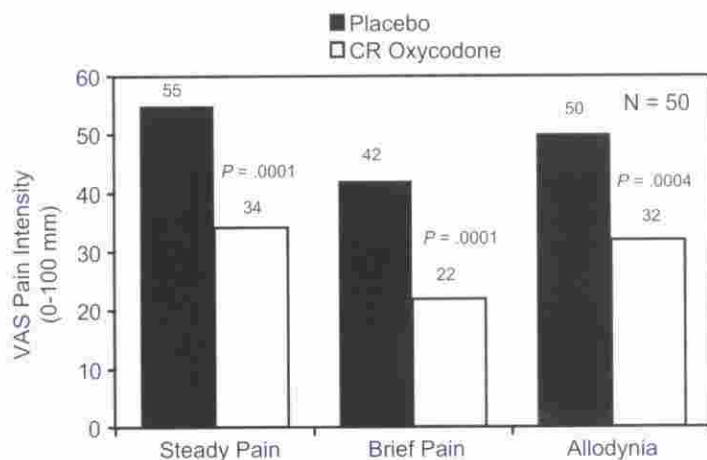
trolled trials (Galer, et al., 1999; Rowbotham, et al., 1996). In patients with PHN and allodynia, pain relief was significantly better with lidocaine patch 5% compared with vehicle-control patches (Galer, et al., 1999; Rowbotham, et al., 1996). A recent open-label trial demonstrated significant reductions in the interference of pain with daily activities with lidocaine patch 5% treatment (Katz, et al., 2002). Up to 3 patches may be applied once daily over the affected site. It is recommended that the patch be worn for 12 hours with a 12-hour patch-free period (Nicholson, 2003a). Recently reported data suggest that up to 4 patches may be worn safely for a 24-hour period (Nicholson, 2003a). Patients with open lesions should not use lidocaine patch 5% because the available formulation is not sterile (Dworkin & Schmader, 2003).

**Opioids.** Opioids have been studied in patients with nonmalignant neuropathic pain (fentanyl), PHN (morphine, controlled-release oxycodone), diabetic neuropathy (controlled-release oxycodone, tramadol), painful polyneuropathy (tramadol) and phantom limb pain (oral morphine) (Gimbel, et al., 2003; Harati, et al., 1998; Nicholson, 2003a; Raja, et al., 2002; Rowbotham, et al., 1991; Sindrup, et al., 1999a; Sindrup, et al., 1999b; Reder, 2001; Watson & Babul, 1998). However, controversy exists regarding their use in neuropathic pain and other pain syndromes, particularly in regard to appropriate prescribing and understanding addiction, physical dependency, and tolerance (Nicholson, 2003a; Nicholson, 2003b).

In patients with PHN, intravenous morphine was shown to be superior to placebo in a double-blind trial. This study demonstrated that pain associated with PHN may be responsive to opioid analgesics and suggested that longer-term oral treatment might be effective (Rowbotham, et al., 1991). Subsequently, 2 double-blind, placebo-controlled, randomized trials of oral opioid analgesics in patients with PHN were conducted (Watson & Babul, 1998; Raja, et al., 2002). Compared with placebo, controlled-release oxycodone (maximum dosage of 60 mg daily) resulted in statistically significant improvements in pain, disability, and allodynia (Figure 7) (Watson & Babul, 1998). In a 3-period crossover trial, controlled-release morphine, TCAs, and placebo were compared in 50 patients with PHN (Raja, et al., 2002). Controlled-release morphine (maximum dose of 240 mg daily) resulted in statistically significant improvements in pain and sleep but not physical functioning or mood (Raja, et al., 2002). Patients preferred treatment with opioid analgesics over treatment with TCAs or placebo despite an increased incidence of adverse effects during opioid treatment (Raja, et al., 2002). Common opioid-associated adverse effects are constipation, sedation, and nausea. Opioid analgesics may cause cognitive impairment and impaired mobility in elderly patients.

Reductions in analgesic benefit over time (i.e., tolerance) may develop in patients treated with opioid analgesics, but stable dosing regimens are achievable. Physical dependence or withdrawal symptoms occur in all opioid-treated patients with

Figure 7. Improvements in Pain and Allodynia Visual Analog Scale Scores with Controlled-Release Oxycodone versus Placebo in Patients with PHN



Adapted from Watson C.P., Babul N. (1998). *Neurology*, 50, 1837-1841.

abrupt discontinuation or rapid dose reduction. Patients should be advised against abrupt drug discontinuation. The risk of addiction in patients with no history of substance abuse is very low and may not justify refraining from the use of opiates in patients with neuropathic pain (Nicholson, 2003a). Opioid analgesics must be used cautiously, as accidental death or suicide can occur in association with overdose. Fixed-dose regimens (i.e., around-the-clock dosing) with controlled-release opioids are preferred over as-needed PRN dosing (Nicholson, 2003a). Initial treatment may consist of a short-acting medication at morphine oral equi-analgesic dosages of 5 mg to 15 mg every 4 hours, as needed. After 1 to 2 weeks of treatment, the patient's total daily dose can be converted to an equi-analgesic dosage of a long-acting opioid analgesic (i.e., controlled-release morphine, controlled-release oxycodone, transdermal fentanyl, levorphanol, or methadone) with the short-acting medication taken as needed (Dworkin & Schmadier, 2003). Use of stool softeners may proactively minimize any constipation, particularly in older patients. The use of opioid written-care agreements, documented treatment plans, and patient pain-management contracts are strongly recommended when initiating opioid therapy. After a reasonable trial period of approximately 3 months, if pain is not reduced or function improved, opioid therapy should be discontinued (Nicholson, 2003a).

**Antidepressants.** Several classes of antidepressants have been used in the treatment of neuropathic pain. Tricyclic antidepressants

(TCAs), most commonly the tertiary and secondary amines, have long been used in patients with PHN or diabetic neuropathy (Nicholson, 2003a). Randomized, controlled trials and meta-analyses demonstrate the benefit of TCAs, particularly amitriptyline, nortriptyline, imipramine, and desipramine in the treatment of neuropathic pain (Bowsler, 1992; Collins, et al., 2000; Kingery, et al., 1997; Nicholson, 2003a; O'Malley, et al., 1999; McQuay, et al., 1996; Sindrup & Jensen, 1999). The selective serotonin reuptake inhibitors have shown inconsistent benefits in the treatment of diabetic neuropathy (Goodnick, 2001; Jung, et al., 1997; Nicholson, 2003a).

The analgesic effect of the TCAs appears to be independent of their antidepressant effect (Dworkin & Schmadier, 2003; Nicholson, 2003a). Amitriptyline is the most widely prescribed TCA because it is the most extensively studied in patients with postherpetic neuropathy and other neuropathic pain syndromes (Aparasu & Sitzman, 1999; Mort & Aparasu, 2002; Max, 1995). However, in elderly patients, amitriptyline is poorly tolerated (Ahmad & Goucke, 2002). In a randomized, double-blind trial, nortriptyline demonstrated equivalent efficacy with amitriptyline, but nortriptyline was better tolerated (Watson, et al., 1998). Based on this finding, nortriptyline is the preferred TCA when used in elderly patients with neuropathic pain. Desipramine may also be used, particularly for patients who experience excessive sedation with nortriptyline (Dworkin & Schmadier, 2003).

Despite their efficacy, TCAs possess a significant side-effect profile and may result in a number of drug-drug interactions, particularly in older patients (Collins, et al., 2000). Nortriptyline and desipramine have fewer adverse effects than imipramine, doxepin, or amitriptyline (Nicholson, 2003a). Interestingly, nortriptyline and desipramine are active metabolites of amitriptyline and imipramine, respectively, and may account for the differences in observed adverse effects in elderly patients. Dry mouth is the most common side effect, occurring in up to 40% of patients treated with amitriptyline and 25% of patients treated with nortriptyline. Constipation, sweating, dizziness, disturbed vision, and drowsiness are reported by as many as 20% to 30% of patients treated with amitriptyline and 5% to 15% of those treated with nortriptyline. All TCAs must be used very cautiously by patients with a history of cardiovascular disease, glaucoma, urinary retention, autonomic neuropathy, and substance abuse. Balance problems and cognitive impairment are common in elderly patients taking TCAs. To minimize adverse effects, TCA treatment should be initiated at low dosages (i.e., 10 mg per week) in a single dose taken at bedtime and slowly titrated up to maximum doses of 100 mg daily, as tolerated. Because of variability in treatment response, if patients do not respond within 2 weeks, titration to higher doses, up to 100 mg daily, as tolerated, may be necessary. Dividing the dose may reduce the occurrence of adverse effects (Nicholson, 2003a). Appropriate monitoring at these higher dosages includes periodic evaluation of serum TCA concentrations and electrocardiograms (Dworkin & Schmadier, 2003). Frequently, patients have a partial response and use of polypharmacy may be needed (Nicholson, 2003a). Currently, the American Geriatric Society considers TCAs as second-line therapy for patients over the age of 65 years because of the significant cognitive and anticholinergic side effects they produce (Nicholson, 2003a).

## OTHER TREATMENT OPTIONS

**Capsaicin.** Capsaicin, an extract from hot chili peppers, is used topically for the treatment of neuropathic pain (Nicholson, 2003a). In order for analgesia to occur via depletion of substance P, capsaicin must be applied 4 to 5 times a day for a minimum of 4 weeks. However, owing to the significant burning sensation, the tolerability of this agent is markedly reduced (Stankus, et al., 2000). Patients should be informed that

temporary increases in pain may occur during the initial days (5-7 days) of capsaicin treatment and that thorough hand-washing after treatment application is necessary. Clinical studies indicate that capsaicin is more effective than placebo and similar to other conventional treatments (Stankus et al., 2000; MacFarlane et al., 1997). Capsaicin is an effective treatment for neuropathic pain but often causes significant distress for patients and is not well tolerated (Nicholson, 2003a).

## CONCLUSION

Chronic neuropathic pain is a complex phenomenon because of the variability in patient symptoms, underlying mechanisms of pain, and treatment response. When neuropathic pain is managed as a disease rather than a symptom, a more objective and systematic approach to individual patient management can be achieved. Anticonvulsant therapy is a treatment of choice for patients with neuropathic pain. The goal of therapy is to minimize and control pain and improve quality of life. Selection of a particular agent should be based on proven efficacy, safety, and tolerability in patients with neuropathic pain.

In patients with PHN, first-line agents include topical lidocaine patch 5% or gabapentin, with TCAs or opioid analgesics useful as second-line agents. Overall, many patients experience clinically significant pain relief with a balanced treatment approach that may include multiple pharmacologic and nonpharmacologic therapies (Nicholson, 2003a). □

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