Pain Management Review Part 3

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Objectives

- Study the impact of transdermal fentanyl on quality of life in rheumatoid arthritis.
- Evaluate intradiscal etanercept in patients with chronic discogenic low back pain or lumbosacral radiculopathy.
- Discuss a case study looking at the effectiveness of deep dry needling for the management of hypertonia.
- Discuss the efficacy of electrical nerve stimulation for chronic musculoskeletal pain.
- Assess whether patients can accurately identify their headaches as migraine at onset, and evaluate cues that patients use to correctly identify migraine attacks.
- Discuss the problem of the appropriateness of terminal sedation in the presence of nonphysical symptoms.
- Study the pain-relieving effect of short-course pulse prednisolone in managing frozen shoulder.
- Study the impact of acute herpes zoster pain and discomfort on functional status and quality of life in older adults.
- Study the use of sumatriptan/naproxen sodium for migraine, its efficacy, health related quality of life, and satisfaction outcomes.
- Discuss the altered blood flow in terminal vessels after local application of ropivacaine and prolocaine.

Impact of transdermal fentanyl on quality of life in rheumatoid arthritis.

Berliner MN et al

Journal: Clin J Pain 23(6):530-534, 2007. 22 References
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Faculty Disclosure: Abstracted by T. Newitt, who has nothing to disclose.

Because the level of analgesia that can be achieved with NSAIDS is not satisfactory in all patients with

rheumatoid arthritis (RA), stronger analgesics are often indicated. The current prospective, open-label study was conducted to investigate the effectiveness and tolerability of transdermal fentanyl in a treatment regimen in patients with RA under daily routine conditions. Data of 226 patients (171 women) were documented in this study. Patients diagnosed with RA as defined by the criteria of the American College of Rheumatology were eligible after exclusions.

Transdermal fentanyl is a patch that releases the active ingredient continuously over a period of 72 hours. The treatment should be initiated with the smallest dose (25 µg/hr) and could be increased every 72 hours by steps of 25 µg/hr, if needed.

The initial study duration was 30 days. After being familiarized with the protocols, patients rated their average pain of the last 24 hours using a 0 (no pain) to 10, using a numerical rating scale (NRS). Using the same scale, patients individually defined a pain level that would be long-term tolerable (treatment goal). Sleep, pain-related impairment of daily activities, and treatment satisfaction were rated using a 5-point verbal rating scale (VRS). The Marburg questionnaire was administered at the beginning and at the end of the study. This questionnaire assesses general well-being; higher values correspond with better well-being.

To investigate if the short-term improvements of a treatment with transdermal fentanyl could be maintained during a long-term treatment, patients were contacted for follow-up at 6 months and at 12 months. Any adverse events that occurred were reported throughout the observation period.

Prior opioid treatment was terminated before initiation of a treatment with transdermal fentanyl, which was started at 25 µg/hr in 192 patients (85%), 33 patients were started at low initial dose of 50 µg/hr, and one patient was started at 75 µg/hr.

Forty-six of the 226 patients (20%) discontinued the treatment with transdermal fentanyl prematurely. Forty-two of these (91%) had been started with 25 µg/hr and 4 (9%) with 50 µg/hr. Twenty-one patients terminated prematurely because of adverse events. Four patients terminated prematurely because of lack of efficacy. For 3 of these, lack of compliance was given as a second reason for early termination. In 17 patients, treatment was terminated because the analgesic effect at 25 µg/hr was already considered too strong.

One hundred and eighty patients finished the study according to protocol. Of these, 95 (53%) remained at their starting dose and 85 needed a dose increase. The mean pain intensity dropped from 8.0 to 4.0 by the end of the study. In 75% of study participants, the pain intensity dropped to or below their individually defined treatment goal. The mean quality of nighttime sleep and activities of daily living and social activities improved significantly during the study. In 85.4% of the patients, treatment satisfaction improved by at least 1 unit on the 5-point VRS.

For each item in The Marburg Questionnaire on general well-being, there was a significant improvement of approximately 1.5 units, respectively. Consistently, treatment satisfaction remained high throughout the follow-up period of 12 months.

During the course of the study, a total of 75 adverse events were recorded in 39 patients, most of which were considered to be related to the study medication. In 85% of cases, the symptoms had disappeared by the end of the study. In 40% of adverse events, a symptomatic treatment was required. Nausea was the most frequently reported adverse event.

In summary, the addition of transdermal fentanyl to a treatment regimen in patients with RA seemed to be efficient in combination with a well-known safety and tolerability profile. Patients reported less pain and demonstrated better function, sleep, and well-being, which resulted in an overall high treatment satisfaction. In a subgroup, these benefits remained stable over a time period of 12 months. Therefore, transdermal fentanyl is a valuable treatment option for patients with chronic pain due to RA

A double-blind, placebo-controlled, dose-response pilot study evaluating intradiscal etanercept in patients with chronic discogenic low back pain or lumbosacral radiculopathy.

Cohen SP et al

Journal: Anesthesiology 107(1):99-105, 2007. 36 References
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Faculty Disclosure: Abstracted by T. Newitt, who has nothing to disclose.

In recent years, compelling evidence has emerged implicating the inflammatory cytokinin tumor necrosis factor alpha (TNF-α) as a major cause of radiculopathy, and to and a lesser extent, discogenic low back pain (LBP). In *in vitro* bovine discs, the application of low levels of TNF-α to nucleus pulposus induces protean degenerative changes comparable to that found in internal disc destruction.

Etanercept is a soluble p75 TNF-α receptor genetically fused with the Fc portion of immunoglobulin G. When etanercept binds to TNF with a longer half-life than the native receptor, it blocks its interaction with cell surface receptors. In an effort to reduce side effects, improve efficacy, and establish safety data for future studies, the authors undertook a double-blind, placebo-controlled, dose-response study evaluating escalating doses of intradiscal etanercept in the treatment of chronic radicular and discogenic LBP.

All discographies were done as screening procedures for intradiscal electrothermal therapy, percutaneous disk decompression, or open surgery. No discographies were done exclusively for etanercept study. Inclusion criteria included chronic low back pain and/or leg pain of more than 6 months' duration, lack of response to conservative therapy, age 60 years or younger, disk height greater than 50% of normal, body mass index less than 30, and one or more discs with evidence of degenerative changes including loss of

disk height, disc dessications, and endplate signal changes. In addition to other exclusion criteria, all study patients had to have a normal complete blood cell count and negative antinuclear antibody and double-stranded DNA on prescreening laboratory testing.

Patients were randomized into 6 groups of 6 patients each, 5 receiving etanercept in a specific dosage and one to receive only saline solution. Both patients and physicians were blinded to the contents of the injectate. In Group 1, 0.1 mg etanercept was the active ingredient. In groups 2 through 6, etanercept increased to 0.25 mg, 0.5 mg, 0.75 mg, 1.0 mg, and 1.5 mg respectively. All injectate volumes were 0.5 ml. Under sedation with midazolam and fentanyl, if necessary, discs were injected based on abnormal imaging studies and physical examination. Twenty-two gauge, 7-inch spinal needles were inserted into the center of the nucleus pulposus using oblique, anteroposterior, and lateral fluoroscopic views.

The primary outcome measure was the visual analogue scale (VAS) pain score. Secondary outcome measures included Oswestry Disability Index (ODI, reduction in analgesic medications), and global perceived effect. Data were analyzed from 36 patients.

The results of this small pilot study do not support a one-time, low-dose intradiscal injection of etanercept as a treatment for either chronic discogenic LBP or sciatica. Despite neutral findings, the long-term safety data of intradiscal etanercept remains unknown.

A case study looking at the effectiveness of deep dry needling for the management of hypertonia.

Gallego PH, del Moral OM

Journal: J Musculoskel Pain 15(2):55-60, 2007. 19 References
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Faculty Disclosure: Abstracted by T. Newitt, who has nothing to disclose.

The resistance felt when moving a limb passively, or the resistance to passive movement (RTPM), is called hypertonia. Hypertonia in patients with upper motor neuron (UMN) lesions results from a combination of spasticity, thixotropy, and changes in the viscoelastic properties of muscle, which may ultimately lead to the development of fixed muscle contractures. It is now accepted that the exaggerated stretch reflex in a muscle is only partly responsible for hypertonia and that other positive features of the UMN syndrome and biomechanical changes contribute significantly to RTPM.

Pediatric physiotherapists who work with profoundly impaired children often realize that one of the most important difficulties for parents managing their children is the increase of RTPM.

The current methods of treatment for muscle spasticity include systemic antispasticity drugs such as baclofen, dantrolene, tizanidine, diazepam, clorazepate dipotassium, clonazepam, or clonidine, which are nonselective in their action and may cause functional loss. Paradoxically, in some patients, some of these

drugs reduce force in the normal muscles without having an effect on muscle spasticity.

Tolerance develops after a few months of treatment, and incremental increases in dosage are often required to maintain the initial clinical response. These lead to added adverse effects. Focal injection of botulinum type A (BTX-A) has been demonstrated to be the elective treatment for spasticity, although the review of current evidence suggests the lack of general consensus among clinicians about the dose, site of injection, injection technique, etc. BTX-A inhibits the release of acetylcholine into the synaptic cleft, and it also seems to have a remote effect, which could be explained by indirect central effect.

For about 30 years, dry needling has been used as a pain-relieving procedure. In this study, the effectiveness and efficiency of deep dry needling (DDN) of trigger points (TrPs) was investigated based on the widely reported success of DDN on neuropathic pain. When comparing BTX-A treatment with DDN, the authors state that the affect of BTX-A is produced in the same place as DDN, the motor endplate zone. However, the way they act is different; while BTX-A acts in a chemical way, DDN acts in a mechanical way.

The hypothetical action mechanism of DDN in TrP treatment is the mechanical destruction of dysfunctional motor endplates in which, according to hypothesis, there are contraction knots (active loci), which lead to palpable findings of TrPs and taut bands.

The present case concerns a 4-year-old child. Medical diagnosis at birth was severe hypoxic-ischemic encephalopathy caused by perinatal fetal distress, which appears clinically as spastic tetraparesia with axial hypertonia, with severe impairment of the right upper limb. His only means of communicating is by smiling or crying to express happiness or pain.

Passive range of movement (PROM) was assessed in the elbow, wrist, and finger joints. With the hand in the patient's resting position the following positions were used: the thumb fully flexed and unopposed, one-quarter open, one-half open, three-quarters open, and fully extended with passive muscle stretch. On initial assessment, the patient's thumb could only be passively stretched to one-half open.

Spasticity was assessed with the Modified Ashworth Scale (MAS) before and after treatment. Muscles treated were the thenar muscles, the wrist flexors, and the elbow flexors. Intervention consisted of 9 sessions for the thenar muscles. From the fifth to the ninth session, elbow and wrist flexor muscles were also treated. Intervention was performed twice a week for the first 4 sessions and once a week for the remaining 5.

The treatment with DDN decreased RTPM in the treatment session and throughout the sessions in spastic muscles located in this patient's upper limb. It is difficult to determine whether decreased RTPM measured with the MAS is due to changes in viscoelastic properties or to decreased spasticity. Since the authors treat

TrPs, it is possible that improvement in MAS scores could be more due to changes in the viscoelastic properties than in spasticity.

Efficacy of electrical nerve stimulation for chronic musculoskeletal pain: a meta-analysis of randomized controlled trials.

Johnson M, Martinson M

Journal: Pain 130(1-2):157-165, 2007. 28 References
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Faculty Disclosure: Abstracted by T. Newitt, who has nothing to disclose.

Transcutaneous and percutaneous electrical nerve stimulation (TENS and PENS; collectively, ENS) are the application of electrical energy in various waveforms, amplitudes, and frequencies to peripheral nerves through electrodes. ENS has been widely used for the treatment of acute and chronic pain.

The most common stimulation modes are high frequency, low frequency, variable-frequency, and acupuncture-like, which employs very low frequency, high-amplitude stimulation. The mechanism of action for pain relief has been elucidated by two theories: the gate control theory and stimulation-induced release of endogenous endorphins.

The results of existing studies, including randomized controlled trials (RCTs), have been inconclusive, with some showing a benefit of ENS and others showing none. It is likely the majority of these studies were underpowered. The primary objective of this meta-analysis was to determine whether ENS reduces chronic musculoskeletal pain more effectively than placebo. The secondary objectives were to determine whether therapy parameters including ENS frequency, duration of therapy, type of ENS electrode, improvements in design, and scientific rigor of the study affecting the degree of pain relief.

Journal articles published between January 1976 and November 2006 from the Cochrane Library, EMBASE, and the National Library of Medicine database were searched using appropriate keywords. Inclusion and exclusion criteria are described in this article.

A total of 134 original research papers were reviewed; 29 papers with 38 studies met the inclusion criteria. There were a total of 1227 patients: 892 ENS patients and 753 placebo patients.

As the number of available pharmacological options for the management of chronic pain has decreased due to recently appreciated side affects, the need to provide scientifically sound evidence regarding the efficacy of ENS therapy is as pressing as ever. Conclusions reached in this article, combined with the fact that the present analysis shows that ENS therapy provides significant pain relief on its own, indicate that ENS is a viable treatment of chronic pain.

Can migraineurs accurately identify their headaches as "migraine" at attack onset?

Ng-Mak DS et al

Journal: Headache 47(5):645-653, 2007. 24 References
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Faculty Disclosure: This study was funded by Merck & Company, Inc. Co-authors Dr Ng-Mak, Dr Chen, Dr Hu and Mr Ma are employees of Merck & Company, Inc.

Abstracted by T. Newitt, who has nothing to disclose.

The notion of treating early migraine with triptans while the headache is mild is not new. In one study, patients taking sumatriptan 50 mg without waiting for headache pain progressing to moderate or severe intensity had a significantly higher pain-free rate at 4 hours after dosing. However, the potential benefits should be balanced against the potential risks of medication or overuse and/or misuse. Migraine patients should treat early only if they are capable of reliably self-identifying a headache as a migraine at onset.

The aims of this study are two-fold: (1) to evaluate the extent to which self-identification of a headache as a migraine at onset is consistent with self-identification of a headache as a migraine at peak; and (2) to assess headache cues/factors that are used by migraine patients to identify a headache as a migraine.

Migraine patients were recruited from 14 headache clinics in the United States during the first half of 2005. Participants were provided with a hand-held electronic diary and were asked to record their headache experiences daily over the course of 1 month. They were encouraged to treat as they normally would. Patients were either prescribed with or given samples of an oral triptan medication for acute migraine attacks.

Patients completed a baseline questionnaire that captured demographic characteristics, migraine history, migraine frequency and severity, impact of migraine attacks, treatment decisions in the last 3 months, general beliefs about migraine and migraine treatment, and use of medications.

Subjects were asked to keep their electronic diary daily over 30 consecutive days, each diary day capturing the occurrences of 1 headache episode if applicable. Whenever a headache episode occurred, information regarding the headache onset and headache at peak times, severity and patient-classification of headache, symptoms associated with the headache, medications used, reasons for and against taking medications, pain relief strategy, disability due to headache, and patient satisfaction were documented. Further, patients provided answers to 2 identical sets of questions regarding certainty of migraine, headache-associated symptoms: headache severity at onset and peak were recorded per headache episode.

For the measurement of pain severity, patients rated their headache on a 4-point Likert scale (0 = no pain). Headache-associated symptoms were chosen from a list that included loss of appetite, nausea, vomiting,

sensitivity to light, sensitivity to odors, sensitivity to noise, dizziness, sparkling/flashing/colored lights, blurred or double vision, and aura. At the baseline, patients checked if they also suffered from tension-type headache in addition to migraine.

The vast majority of migraine patients in tertiary care settings are capable of self-identifying a headache as a migraine by evaluating their migraine-associated symptoms at onset (sensitivity to light, nausea, and visual disturbances), headache severity at onset, and ruling out tension-type type headache at onset. For migraine patients who can identify a headache as a migraine at an early phase of an attack, they would benefit by treating early while the pain is mild for their acute migraine attacks.

To sedate or not to sedate?

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Journal: J Pain Symptom Manage 34(1):105-107, 2007. 9 References
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"Existential" is a philosophy developed by the French philosopher John-Paul Sartre and focuses on the human experience of "being," the notion that humans should be able to create for themselves a meaning or purpose, to find a sense in life.

The authors present the case of Mrs. D., an 84-year-old woman, who was admitted in 2004 with an aggressive left parietal glioblastoma. She refused diagnostic craniotomy, surgery, radiation therapy, and chemotherapy. She was treated symptomatically with corticosteroids and sent home. Two months later she was admitted with marked asthenia, anorexia, anxiety, and right-side weakness.

Since she had no immediate family or other surrogates, she was willing to make her own decisions about end-of-life care and asked to write advance directives according to a specific legislation. Her concerns about physical symptoms were discussed in detail, but psychosocial problems such as loss of self-esteem, loss of intellectual and social functions, anxiety and agitation were apparently not included. Her final document included refusal for admission to the ICU and refusal of attempts to be resuscitated, but allowed symptom alleviation even if unconscious, and sedation in case of intractable symptoms.

One month later, her cognitive functions progressively deteriorated, and she became increasingly anxious and agitated. She was dysphasic, and existential distress related to communication impairment was prominent. Modifications of her body image and general functioning, together with increased dependency, added to her distress. Finally, hopelessness and the perceived meaninglessness of her present condition were increasing her concerns about death. Somatic causes or chemical reasons for delirium were not found.

The introduction of palliative sedation for this patient was discussed by a multidisciplinary team, including nurses, residence, and the consulting psychiatrist. It was decided not to introduce sedation, although distress was recognized, because the patient's condition was assessed as too good. Thus, the existential distress was not considered as a refractory symptom. The clinical situation was, therefore, not modified, and no improvements were seen over the few next days. One week later she developed probable pneumonia and died.

The appropriateness of terminal sedation in the presence of nonphysical symptoms remains controversial, and further research is needed to establish standard therapy for existential distress of terminally ill patients, in particular when patients cannot communicate. Palliative care specialists are among the few clinicians capable of establishing existential suffering at the same level as physical suffering. When a patient with advanced disease decides to complete advance directives, information and education about palliative sedation are crucial. A clear goal must be established with the patient, the surrogate, and the caregivers. The difference between intractable physical and nonphysical symptoms should be openly discussed, and a detailed treatment plan should be developed to include hydration and nutrition, and the depth of duration of sedation.

Pain relieving effect of short-course, pulse prednisolone in managing frozen shoulder.

Saeidian SR et al

Journal: J Pain Palliat Care Pharmacother 21(1):27-30, 2007. 26 References
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Faculty Disclosure: Abstracted by T. Newitt, who has nothing to disclose.

Although frozen shoulder (shoulder periarthritis, stiff painful shoulder, or adhesive capsulitis) is a common disorder of the gleno-humeral joint, it is poorly understood and has remained an enigma. It is characterized by a contraction and thickening of the joint capsule which causes gradual loss of joint motion, pain, and disability.

Most patients recover within 2 years after onset whether or not it is treated. To decrease this time and to improve outcomes for this condition a carefully designed treatment plan including physiotherapy, pain medication, and corticosteroid is required. Numerous studies have shown little long-term advantage in any one treatment regimen, but steroid injections may improve the patient's pain and range of motion in the early stage of this condition.

Although glucocorticoids play a significant role in the treatment of arthritic conditions, using prednisolone pulses for treating chronic frozen shoulder is not reported. This study evaluated the effect of pulse prednisolone therapy of chronic frozen shoulder by measuring patients' reported pain using a visual

analogue scale (VAS) and patients' complaints of nighttime sleep difficulties.

This study was performed on two age and sex matched groups of 30 patients suffering from painful shoulder stiffness who were referred to a musculoskeletal pain clinic during the period of January 2002 to January 2005. The mean duration of patients' awareness of their shoulder motion limitation and discomfort was 5 months. The first group of 30 patients received oral diclofenac for 10 days associated with physiotherapy including pulse ultrasound for 10 minutes, interferential therapy for another 10 minutes, and active assisted range of shoulder motion exercises for the whole 10-day treatment period.

For the second group, treatment started with 500 mg of intravenous prednisolone for 3 consecutive days added to the treatments provided to the first group. Finally, the mean reported pain scales by the 2 groups before and 2 weeks after the treatment were calculated and compared as the indicators of treatment efficacy.

The initial mean pain scale for the first group was 7.17 and for the second group was 7.1. The mean pain scale for the first group decreased to 4.9 following the treatment course and the mean pain scale for the second group decreased to 2.96 after the treatment period. The results of this study support the inclusion of pulse prednisolone therapy in patients with adhesive capsulitis.

The impact of acute herpes zoster pain and discomfort on functional status and quality of life in older adults.

Schmader KE et al

Journal: Clin J Pain 23(6):490-496, 2007. 20 References
Reprint: Durham VAMC, 182 GRECC, 508 Fulton St, Durham, NC 27705 (KE Schmader, MD)
Faculty Disclosure: Support was received from Merck & Co., Inc., Durham VAMC GRECC, and Grant K24-AI-51324 from the National Institute of Allergy and Infectious Diseases (NIAID).

Abstracted by T. Newitt, who has nothing to disclose.

Although postherpetic neuralgia has been rightly recognized as a serious complication of herpes zoster (HZ) that negatively impacts functional status and health-related quality of life (HRQL), acute herpetic pain, defined as pain within 30 days of HZ rash onset, has the potential to significantly impact functional status and HRQL in older adults.

The overall aim of this study is to describe the impact of acute HZ pain and discomfort on the functional status and HRQL in older persons. The specific objectives were (1) to describe the impact of acute pain and discomfort intensity on individual measures of interference with activities of daily living (ADL) and HRQL, and (2) to measure the association between acute pain and discomfort intensity and summary measures of ADL and HRQL.

Eligible participants had physician-diagnosed HZ, were ≥60 years of age, and could be enrolled within 14 days of HZ rash onset. Participants received usual care for HZ from their physicians.

Pain measures included Zoster Brief Pain Inventory (ZBPI) and the McGill Pain Questionnaire. The ZBPI is a zoster-specific modification of the Brief Pain Inventory (BPI). The present pain intensity (PPI) scale from the McGill Pain Questionnaire was used. The functional status measures included the ZBPI and the zoster impact questionnaire (ZIQ). The ZIQ measures interference with ADL. The HRQL measures included the standard version of the SF-12 and the EuroQoL.

Eligible, consenting study participants completed all of the above questionnaires in-person or via telephone every 2 to 3 days for the first 14 days, weekly from weeks 2 to 6, and monthly thereafter up to 182 days after rash onset, or until they reported no pain at 2 consecutive interviews. The questionnaires were all self-administered.

Over the entire time of the study, 160 patients had 2 or more assessments with complete estimates of composite pain and were retained for the multivariable analysis.

The study found that moderate to severe pain and discomfort was common during the acute rash phase of HZ. As the intensity of pain and discomfort increased, the impact on functional status and HRQL became increasingly severe, often substantial, as determined by a zoster-specific functional measure of and generic HRQL measures. ZBPI interference items such as sleep, general activity, and enjoyment of life were particularly affected, although all ZBPI interference items were also negatively affected, especially in patients with pain and discomfort of moderate and severe intensity. ZIQ interference items particularly affected after HZ rash onset were leisure activities, getting out of the house, traveling, and going shopping.

The clinical significance of these findings was that although chronic pain is difficult to endure, acute zoster pain and discomfort should also be recognized as having a substantial negative impact on the patient and be managed accordingly. Furthermore, experts theorize that acute zoster pain may contribute to the development of chronic pain via central mechanisms, and we do know that acute pain severity is a predictor of chronic pain. Therefore, the prevention and care for control of acute zoster pain takes on great importance.

Sumatriptan/Naproxen sodium for migraine: efficacy, health related quality of life, and satisfaction outcomes.

Smith T et al

Journal: Headache 47(5):683-692, 2007. 33 References
Reprint: Mercy Health Research and Ryan Headache Center, 12680 Olive Blvd, St. Louis, MO 63141 (T Smith, MD)
Faculty Disclosure: This study was sponsored by POZEN, Inc., and supported by GlaxoSmithKiline, Inc.

Abstracted by T. Newitt, who has nothing to disclose.

Triptans are the mainstay of therapy for acute treatment of migraine and their effectiveness has been well established in controlled clinical trials. Sumatriptan has been used to treat over 800 million migraine attacks worldwide. The efficacy of the concurrent use of sumatriptan and naproxen sodium for the acute treatment of migraine has recently been established in clinical trials. This article discusses the patient-reported pain assessments at 2 hours, satisfaction with treatment, and health-related quality of life (HRQOL) reported by patients over the course of a long-term safety study.

This was a phase 3, open-label, multicenter study in patients with a demonstrated history (at least 6 months,) of migraine headaches diagnosed using IHS criteria. The 12-month study consisted of a screening visit and home treatment with sumatriptan/naproxen sodium, a combination of sumatriptan 85 mg and naproxen sodium 500 mg in a unique fixed-dose, single tablet formulation.

When patients treated a moderate or severe migraine attack, they were to complete a study diary just prior to taking study medication and for the next 24 hours. A second dose of sumatriptan/naproxen sodium could be used to treat the same attack after at least 2 hours from the initial dosing if the response was unsatisfactory or incomplete. Additional rescue medication was permitted beginning 2 hours after the last dose of study medication if 1 or 2 doses of the study drug did not achieve adequate results.

Six hundred patients were recruited from 39 sites. *Pain severity* was recorded on a 4-point scale for each treated attack at baseline, at 2 hours following the first dose, and just prior to rescue medication, if taken. *Pain relief* was defined as mild or no pain at 2 hours, without rescue or a second dose prior to 2 hours. *Pain-free* was defined as no pain at 2 hours without further medication prior to 2 hours.

Patient satisfaction was captured using the Patient Perception of Migraine Questionnaire (PPMQ), using 8 attributes of migraine medication on a 7-point Likert scale. Migraine-related HRQOL was measured using the migraine specific quality of life Questionnaire (MSQ).

Of the 600 patients enrolled in the study, 94% treated at least 1 attack, 73% completed 6 months and 64% completed 12 months of treatment. Of the 24,485 attacks that were treated with sumatriptan/naproxen sodium, 81% experienced pain relief and 60% were pain-free at 2 hours. Patients treated most attacks (69%) with a single dose without additional rescue medication of any kind. Patients treated 31% of all attacks with a second dose or another medication indicating a low rate of recurrence and sustained relief over the 24-hour observation period. The treatment effects persisted over the yearlong study and there was no attenuation of effect observed: 80% experienced pain relief and 60% were pain-free at 2 hours following a single dose at 12 months.

Migraine-specific HRQOL results showed that 56%-65% of patients experienced at least a minimal clinically important improvement in each of the MSQ domains over 12 months.

During the conduct of the study, a total of 152 patients (27%) had at least 1 adverse event that was judged to be related to treatment. Treatment-related events reported by 2% or more of patients included: nausea, dyspnea, muscle tightness, dizziness, upper abdominal pain, somnolence, paresthesia, throat tightness, and chest discomfort. No deaths occurred among patients enrolled in this study.

The combination of sumatriptan and naproxen sodium in a single, fixed-dose tablet provides fast, sustained relief of migraine attacks with low-recurrence rates. Treatment effects were consistent over 12 months, resulting in improved patient satisfaction and migraine-specific quality of life--2 important outcomes of quality care

Altered blood flow in terminal vessels after local application of ropivacaine and prilocaine.

Wienzek H et al

Journal: Reg Anesth Pain Med 32(3):233-239, 2007. 27 References
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Faculty Disclosure: This study received support from AstraZeneca, Wedel, Germany.

Abstracted by T. Newitt, who has nothing to disclose.

In contrast to other local anesthetics, ropivacaine reduces blood flow when administered directly in vessels in the central nervous system or injected into the skin. Case reports have described a critical reduction in blood flow when ropivacaine was used for peripheral-nerve block or epidural anesthesia. The mechanism causing vasoconstriction is as yet unknown, nor is the relation between the degree of vasoconstriction and the concentration of ropivacaine. This article concerns a study of this topic using rat-tails.

The studies were conducted in 76 rats weighing 252 to 275 g. Under anesthesia, the artery in the tail was dissected out, and monitors for perfusion and temperature of the distal tail were applied. The capacity of different local anesthetics to produce vasoconstriction was tested by applying them directly to the tail artery. Effects on perfusion were detected by laser Doppler flowmetry and thermography scans.

The animals were randomized into 6 groups of 10 each. Ropivacaine was administered at 3 different concentrations (0.2%, 0.5%, and 0.75%). Prilocaine 0.5% was applied with and without the addition of epinephrine 1:200,000, and the control tails received a saline solution of 0.9%. An assumption was that ropivacaine in tissues supplied by end arteries causes arterial vasoconstriction and thus reduces blood perfusion. The degree of constriction was hypothesized to be directly proportional to the concentration of ropivacaine.

The application of ropivacaine at all concentrations tested caused a significant reduction in blood-flow velocity index in comparison with the control group at t = 10, 20, 30, and 40 minutes. The largest effect was noticed for ropivacaine 0.5%, with a blood-flow velocity index reduction of 64.5% after 30 minutes. For ropivacaine 0.75%, the maximum reduction in blood flow blood-flow velocity index was 53% after 30 minutes and 61% after 40 minutes.

Prilocaine 0.5% with epinephrine 1:200,000 reduced blood flow velocity index by 44.7% at t = 20 minutes with a continuous increase toward the end of the observation period. In comparison with the control group, ropivacaine 0.75% and 0.5% caused temperature to decrease at t = 20, 30, and 40 minutes. Ropivacaine 0.2% had no influence on the tail temperature in comparison with the control group. No decrease in the tail temperature occurred after the application of prilocaine in comparison with the control group. The addition of epinephrine 1:200,000 to prilocaine 0.5% decreased the temperature significantly.

This study demonstrated that ropivacaine causes a decrease in tissue blood flow when applied locally near an end artery. For prilocaine, no clear vasoactive response was observed, except when epinephrine was added. On the basis of the significant and long-lasting reduction in blood flow observed in this animal study, ropivacaine at higher concentrations cannot be recommended for peripheral-nerve block if an end artery is affected or pre-existing vascular diseases are known that might alter the blood supply to the dependent tissue.