ONSITEINSIGHT®

ON ISSUES IN THE MANAGEMENT OF PERSISTENT PAIN • MAY 2009

Novel Treatments for Neuropathic Pain Syndromes

Several posters assessed novel therapies for neuropathic pain. Campbell et al presented efficacy data of the novel topical clonidine gel, ARC-4558†, among 166 subjects with painful diabetic neuropathy (PDN) who were randomized to clonidine gel 650 µl (0.1%) or 500 µl (0.2%), or placebo gel (per dose, per foot). Treatments were applied to the feet bid until Week 2 and tid for 6 weeks; use of concomitant pain medications was allowed. Pain was assessed using an 11-point Numerical Pain Rating Scale (NPRS).

Significantly greater pain reduction was noted among subjects receiving 0.1% clonidine gel vs placebo (P=0.015). Pain reduction among those treated with clonidine gel 0.2% did not differ from the placebo

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Safety, Efficacy of Diclofenac Sodium 1% Gel Assessed for Osteoarthritis

Osteoarthritis (OA) is a highly prevalent and often disabling joint disease that occurs most frequently in the knee or hand. Increased OA prevalence is often seen in older populations. Altman et al assessed the safety and efficacy of topical diclofenac sodium 1% gel (DSG) among ambulatory men and women aged ≥35 years with mild-to-moderate symptomatic OA (>6 months). After a 7-day washout of analgesics, subjects were randomized to DSG (4 g; n=208) or its vehicle[a] (n=212), applied to one or both knees 4 times/day for 12 weeks. Primary outcomes: WOMAC pain and physical function subscales, and global rating of benefit (GRB) in the more symptomatic knee.

Results at Week 12:

- Significantly greater improvements in WOMAC pain (52.6% vs 43.1%; P=0.008) and physical function (49.7% vs 39.4%; P=0.004) scores were seen for DSG vs vehicle relative to baseline
- Nonsignificantly lower GBR (mean [SD]) with DSG vs vehicle (24.1 [24.9] mm vs 28.8 [26.7] mm, respectively)
- In subjects treated in contralateral knees (n=277), WOMAC scores were numerically but not statistically significant; may be due to milder pain in contralateral knee at baseline
- Rate of treatment-related adverse events was low: 7.7% DSG vs 4.2% vehicle

SD=standard deviation; [a]Identical in composition except for absence of diclofenac sodium
WOMAC=Western Ontario and McMaster Universities Osteoarthritis Index

Oxymorphone ER Assessed for Chronic Neuropathic Pain

Neuropathic pain (NP) is a complex condition that often requires combination therapy, which can increase adverse events and negatively affect quality of life. Nalamachu et al examined the safety and efficacy of a single treatment, oxymorphone ER†, for chronic NP among 30 subjects (opioid tolerant; aged 18–75 years) with pain secondary to diabetic neuropathy ≥6 months.

Participants were converted from current opioid treatment to closest lowest dose of oxymorphone ER (titrated over 2 wks). Adjuvant neuropathic and breakthrough pain medications, excluding long-acting opioids, were continued at existing doses. Primary endpoint: mean change in Brief Pain Inventory (BPI) average pain intensity from baseline to Week 12. Results:

- Statistically significant changes in BPI average pain score (P=0.047) and BPI worse pain score (P=0.008) were noted
- Improved pain scores were seen within 2 weeks and persisted throughout the study
- Among subjects with most severe pain at screening (n=14), 43% reported a >75% decrease, and 21% a 33–50% decrease, in average daily pain
- No serious adverse events were reported

†Investigational formulation; not yet FDA approved
ER=extended release

The data reported in this issue of *OnsiteInsight*® were presented during the 28th Annual Scientific Meeting of the American Pain Society (APS), May 7–9, 2009, in San Diego, California.

INSTRUCTIONS FOR PARTICIPATION:
OnsiteInsight® readers can receive instant, free CME credit by reading this newsletter in its entirety, and completing the accompanying posttest and evaluation form at **http://www.painknowledge.org/newsletter**.

LEARNING OBJECTIVES:
After reading articles in this issue of *OnsiteInsight*®, participants should be able to:

- Relate findings from clinical trials on the management and treatment of persistent pain, and apply to clinical practice as appropriate
- Discuss new and emerging therapeutic strategies for treating older patients with pain and improving functionality and quality of life
- Describe comorbidities and treatment barriers associated with persistent pain

TARGET AUDIENCE:
Neurologists, family physicians, general practitioners, internal medicine specialists, rheumatologists, physical medicine and rehabilitation specialists, and other healthcare professionals who treat patients with persistent pain

RELEASE/VALID THROUGH DATES:
05/14/2009–05/13/2010

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PPS STAFF DISCLOSURES: Managing Editor Melanie Visalli has indicated that her spouse is a salaried employee of Hoffmann-La Roche Inc. Program Director Lisa Cariaga, Executive Editor/Director of Online Content Danielle Gabriel, and Vice President Program Management Steven Rifkind have no relevant financial relationships to disclose.

FACULTY: Penny Tenzer, MD, Associate Professor of Clinical Family Medicine, University of Miami Miller School of Medicine, Department of Family Medicine, Miami, Florida, has indicated that she is a member of the speakers bureau for Abbott Laboratories.

This activity is not part of the official APS Scientific Meeting 2009.

Aging and Pain: A New Subfield in Pain Research

A series of presentations focused on the phenomenon of pain with aging. An overview:

- Robert Yezierski, PhD, said that aging and pain is an emerging subfield in pain research—one that bears significantly on quality-of-life issues. He cited data showing that 40% of community-dwelling older patients report some pain affecting their lives, while 27–83% of those living in institutions report pain. Despite these statistics, 40–80% of community-dwelling older patients and 16–27% of those in an institutional setting don't receive pain treatment.
- Dr Yezierski also discussed the effects of age on pain sensitivity, noting that results from human and animal studies are similar in terms of pain. He said there is an increased thermal sensitivity with advancing age demonstrated in rat studies, similar to that seen in humans.
- Suzanne Leveille, PhD, RN, discussed data from the MOBILIZE Boston Study, in which 765 women and men aged ≥70 years were followed for 2 years to assess pain as a risk factor for falls. Pain commonly occurred in multiple joint sites. When specific joint sites were considered, >80% of subjects with hand/wrist pain had multisite pain (≥1 other pain site), and >40% with hip pain had pain at ≥3 other sites. There was a marked increase in mobility difficulty, which increased with pain at multiple joint sites.

Odds ratios for mobility difficulty

Pain Measure	Odds ratio (95% confidence interval)
Pain Map: 0 sites	1.0
1 site	1.8 (1.0–3.2)
2–3 sites	2.7 (1.6–4.5)
4–6 sites	2.8 (1.6–5.0)
≥7 sites	4.2 (2.1–8.4)

- Monique Cherrier, PhD, reviewed data on cognitive effects of chronic pain in older adults, citing studies showing that increased pain can decrease cognition. She noted that cognition can be affected by multiple factors; involves memory, attention, and executive functions; and is not universal among all patients. She also cited studies showing that cognition can improve with effective pain management.

MOBILIZE Boston=Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly of Boston

Short-Acting Opioids for Breakthrough Pain: Improvements in QOL?

Luu et al assessed whether short-acting opioids for breakthrough pain (BTP) improve pain scores and functional status among subjects with chronic pain. Data from medical records of subjects at the Duke Pain Clinic taking chronic opioid therapy were reviewed, and subjects were designated as part of a control group (n=51; stable dose of long-acting opioid for >3 months) or BTP group (n=41; long-acting opioid >3 months plus short-acting opioid for BTP as needed).

Improvement in pain scores and functional status was assessed using visual analog and BPI scores. No statistical between-group differences were seen with either assessment (range: P=0.42 to P=0.9). BTP subjects used more total oral morphine/day (BTP 114 mg vs control 79.7 mg; P<0.0002) and had longer duration of care in the pain clinic (BTP 72 months vs control 67 months; P=0.42).

BPI=Brief Pain Inventory; BTP=breakthrough pain; prn=as needed

Emerging Therapies for Chronic Low Back Pain

Numerous posters explored emerging treatments for low back pain (LBP). In a Phase III trial, Buynak and colleagues assessed the safety and efficacy of tapentadol ER over 15 weeks for treating chronic moderate-to-severe LBP†. The study included a 3-week titration period and a 12-week maintenance period. Subjects were randomized to tapentadol ER (100–250 mg bid), oxycodone CR (20–50 mg bid), or placebo bid. Primary efficacy endpoint: change from baseline in average pain intensity at Week 12. Results:

- Significant decrease in pain intensity with tapentadol ER (mean, -2.9; SD 2.66; P<0.001) and oxycodone CR (mean, -2.9; SD, 2.52; P<0.001) vs placebo (mean, -2.1, SD; 2.33)
- Treatment-emergent AEs: placebo 59.6%, tapentadol ER 75.5%, and oxycodone CR 84.8%
- Increased number of patients in oxycodone group discontinued treatment due to AEs during double-blind (32.3%) and titration (26.5%) periods vs those receiving tapentadol ER (16.7% and 10.7%, respectively) or placebo (4.7% and 2.5%, respectively)

Steiner et al evaluated the novel Buprenorphine Transdermal System (BTDS)† among 660 subjects with moderate-to-severe LBP. Subjects were randomized to BTDS 20 (N=219), BTDS 5 (N=221), oxymorphone (OxyIR®) 40 mg qd (N=220; active comparator), or matching placebos. Significant differences in average pain over last 24 hours at Wks 4, 8, and 12 were seen for BTDS 20 vs BTDS 5, and for BTDS 5 vs OxyIR (P<0.001 for both). A total of 49% of subjects in the BTDS 20 group and 35% in the BTDS 5 group had a 30% improvement in pain (P=0.004 for BTDS 20 vs BTDS 5)

†Investigational agent and/or delivery system; not yet FDA approved
AEs=adverse events; CR=controlled release; ER=extended release; SD=standard deviation

Novel Treatments CONTINUED FROM COVER

group, although a trend was observed (P=0.054). Among responders, 47.2% in both clonidine groups had ≥30% pain relief vs 29.3% in the placebo group (P=0.026).

Irving et al assessed data from four studies of the novel high-concentration capsaicin dermal patch (8% w/w), NGX-4010†, for postherpetic neuralgia. Participants received a single 60-minute application of NGX-4010 (n=597) or control (low-concentration capsaicin patch; N=530) for 30, 60, or 90 mins. Lidocaine 4% was applied to the painful site prior to application of study medication. Primary efficacy endpoint: percent change in NPRS score from baseline during Weeks 2 to 8. At baseline, ~50% of participants were taking concomitant pain medications.

NPRS scores over Weeks 2-8 among subjects receiving a single 60-minute NGX-4010 application were significantly decreased vs controls whether concomitant neuropathic pain medications were used (-26.1% vs -18.1%; P=0.0011) or not used (-36.5% vs -26.2%; P=0.0002). More NGX-4010 subjects achieved a ≥30% decrease in pain vs controls regardless of concomitant pain medication use.

†Investigational agent; not yet FDA approved

Opioid Rotation: Considerations for Subpopulations

Opioid switching or conversion is frequently necessary to achieve a more favorable therapeutic response and/or adverse event profile. Few data are available regarding switching certain subpopulations to oxymorphone ER. Rauck et al assessed the effectiveness of titration, efficacy, and safety of oxymorphone ER among subjects with moderate-to-severe chronic low back pain (LBP). Data presented were from a subanalysis of the open-label titration phase of a previously published controlled, randomized-withdrawal trial of oxymorphone ER vs placebo among subjects using oxycodone at study outset.[1] The subanalysis evaluated only subjects converting from oxymorphone ER; data included were from the titration period.

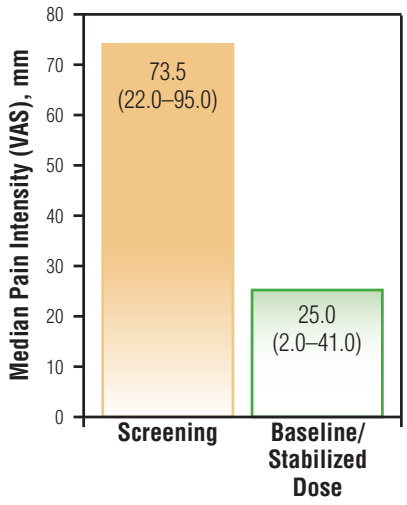
Doses of oxymorphone ER were titrated in 10-mg increments q 12 h every 3–7 days until a stable, well-tolerated dose was achieved. Use of oxymorphone IR (5 mg every 4–6 hrs) was allowed during titration. Titration was successful when a stabilized dose of oxymorphone ER reduced average pain intensity to ≤40 mm on a 100-mm VAS (0=no pain; 100=worst pain imaginable). Findings:

- Of 79 subjects using oxycodone, 45.6% successfully titrated to oxymorphone, and 54.4% discontinued during titration
- 72% achieved dose stabilization ≤28 days
- Titration success was higher in men vs women (56.4% vs 35.0%) and for younger vs older subjects (aged <65 years, 47.8% vs ≥65 years, 33.3%)
- Median (range) VAS score decreased by 66% between screening and dose stabilization (*See Figure*)
- 27.8% of subjects reported mild, 22.8% moderate, and 11.4% severe AEs. AEs were typical for use of opioids.

1. Hale ME, et al. *J Pain*. 2007;8(2):175-184.

AEs=adverse effects; ER=extended release; IR=immediate release; VAS=visual analog scale

VAS SCORE SCREENING VS BASELINE STABLE DOSE



Individual Differences in Pain Responses

A plenary session, moderated by Roger Fillingim, PhD, focused on individual differences in pain responses. Key messages:

- Robust individual differences in pain exist: the same painful event in different people elicits vastly different pain results. Many individual differences are also seen in response to various pain treatments.
- Individual differences aid in explaining the poor correspondence between tissue damage and pain.
- Many factors contribute to these differences. Ethnic and gender disparities have been observed independent of pain severity; data suggest that many women are at greater risk for clinical pain conditions. Heritability accounts for 35–60% of pain conditions, and candidate genes have been associated with pain sensitivity.
- Individual differences can also help to identify those at risk for chronic pain. Dr Fillingim noted that the ongoing OPPERA study will identify risk factors for development of orofacial pain.
- Dr Fillingim concluded that identification of genetic markers associated with drug response can facilitate individualized pain treatment.

OPPERA=Orofacial Pain: Prospective Evaluation and Risk Assessment

Reviving Interdisciplinary Pain Management Programs

The number of IPM programs in the US has decreased substantially over the past decade despite high-quality empirical evidence validating their efficacy. A three-part symposium explored the value of IPMs, barriers to use, and future strategies.

- Steven Stanos, DO, reviewed literature evaluating interdisciplinary treatments, noting that evidence supports the use of multi- and interdisciplinary management. Dr Stanos remarked that the recently published LBP guidelines[1] include interdisciplinary rehabilitation as a justifiable up-front treatment of LBP—not as a "last resort." Today, many patients referred to interdisciplinary programs are considered "treatment failures." Even a modest reduction in pain can be extremely helpful to patients, and evidence shows a benefit to IPMs.
- Robert Gatchel, PhD, ABPP, attributed lack of IPM use to improper interpretation of guidelines, interspecialty competition, and no true means of enforcement. He also cited tertiary gains, insurance issues, and politics as impediments.
- Michael Schatman, PhD, provided strategies for resurrecting IPMs, including engaging insurance companies, hospitals, and specialty medical groups. He noted that insurance companies can be the best allies for advocating this type of treatment. Presentations to individual healthcare insurance plans should emphasize cost savings, include outcomes data of interest to the company, and list admission criteria for ensuring that only the "best-fit" patients will be considered.

In a related poster session, Barrett et al assessed the effect of interdisciplinary treatment (IDT) on chronic pain. Subjects (N=69) took part in an intensive (5 days/week) or modified (1–2 half days/week) outpatient program involving individual and/or group appointments for pain psychology, physical and occupational therapy, relaxation training, and medical management. Before IDT, mean pain intensity was 5.77 and, after graduation, was significantly reduced to 4.5. Other significant decreases were shown in pain-related anxiety and depression. Significant increases were reported for acceptance of pain and cognitive coping.

IPM=interdisciplinary pain management; LBP=low back pain

1. Chou R et al. *Spine*. 2009;34(10):1066-1077

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ON ISSUES IN THE MANAGEMENT OF PERSISTENT PAIN • MAY 2009

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The 28th Annual Scientific Meeting of the American Pain Society (APS) in San Diego featured clinical insights, lectures, plenary sessions, and poster presentations, focusing on a variety of approaches toward neuropathic pain and low back pain (LBP), as well as ongoing studies of opioid usage in chronic noncancer pain (CNCP).

Interdisciplinary Pain Management

Although the concept of interdisciplinary pain management has been promoted in the literature and is supported by high-quality empirical evidence, its utilization in pain management programs in the United States has continued to decline substantially. Various programs were presented at the meeting reviewing the history, literature, usage, and proposed future of interdisciplinary pain care.

In his review of the literature, Steven Stanos, DO, noted evidence supporting the use of multi- and interdisciplinary programs for pain management, noting that the newer LBP guidelines (Chou R et al. *Spine*. 2009;34[10]:1066-1077.) include interdisciplinary rehabilitation as an initial treatment. Michael Schatman, PhD, suggested techniques for interdisciplinary care, including partnering with insurance companies, hospitals, and specialty medical groups, and Barrett et al presented data from a study of 69 subjects who participated in an intensive (5 days/week) or modified (1–2 half days/week) outpatient program involving individual and/or group appointments for pain psychology, physical and occupational therapy, relaxation training, and medical management. Using this model, patients displayed significant improvement in pain intensity, as well as pain-related anxiety and depression, with improved pain acceptance and coping.

While treating pain and its comorbidities can be complex and time consuming, these sessions remind us to think inter- and multidisciplinary care early in our management of pain patients. In addition, we can create individual versions of the interdisciplinary model in our own practices. This can be done by involving our patients, their support system (family), their spiritual beliefs, therapeutic modalities (eg, physical, occupational, and cognitive therapies), pharmacists, allied healthcare professionals, office support staff, specialists, and other members of the team as deemed appropriate. By doing so, we mold our own teams and models to fit the needs of our individual patients and practices. Involving the patient and providing tools that they can use to manage their pain is enlightening and empowering. Functioning as part of a team can improve communication between patients and healthcare providers, as well as improve various pain outcome measures and patient and provider satisfaction.

OPUS: The Opioid Utilization Study

The Opioid Utilization Study (OPUS) is an ongoing multicenter, prospective, observational cohort study involving >1,600 subjects with CNCP. The main objective of the study is to characterize the use of opioid therapy in patients with CNCP. Other outcomes being assessed include clinical and quality of life (QOL) measures, as well as economic and healthcare resource utilization. The study is due to close in March 2010. A variety of data regarding patient gender, economic, comorbidities, and function measures were reviewed at the APS meeting.

Preliminary data from the trial presented at the APS meeting included results from Yanni et al, who assessed OPUS patients' (N=1,668) baseline mood data. Results suggested that these patients had mild-to-moderate anxiety and depression while overall maintaining a moderately positive outlook. Subsets showed that women had higher anxiety and depression scores with no differential in positive outlook. Argoff et al, utilizing part of the Brief Pain Inventory (BPI), assessed baseline pain levels and pain interference in OPUS patients (N=1,570), comparing those with CNCP for ≤1 year vs >1 year. Subsets of this population with LBP or osteoarthritis (OA) for ≤1 year experienced more interference with general activities and sleep, as well as more severe pain, than patients with LBP for >1 year. These results may indicate that patients with OA or LBP for <1 year may not have found adequate pain management therapy. In addition, perhaps pain improves for patients with OA and LBP with longer duration of opioid therapy; less interference with general activities may also result from longer-term opioid therapy.

It is anticipated that the data from this large cohort study will provide useful information regarding key outcomes in

pain management, including the impact of treatment on function, QOL, and common pain comorbidities. In addition, we may find demographic markers and predictors of pain and pain response over time. Stay tuned until next March for more!

Novel Treatments for Neuropathic Pain Syndromes

Neuropathic pain syndromes are a commonly seen problem, yet they are often difficult to adequately manage. Several newer treatments and modalities for neuropathic pain were presented at the 2009 APS meeting. A poster by Campbell et al presented the efficacy data of topical 0.1% and 0.2% clonidine gel† for the treatment of painful diabetic neuropathy (PDN) of the feet. There was a significantly greater pain reduction in patients on 0.1% cloinidine gel vs placebo. Although results for patients treated with clonidine gel 0.2% did not statistically differ from the placebo, trends showing improvement were noted. Among responders, 47.2% in both clonidine groups had 30% pain relief vs 29.3% in the placebo group (P=0.026).

Four double-blind, controlled studies by Irving et al involving high-concentration capsaicin dermal patch (8%)† usage in postherpetic neuralgia were presented. Results from these studies demonstrated that the capsaicin patch was associated with greater improvement in NPRS (Numeric Pain Rating Scale) scores compared with the control, when used either alone or with other neuropathic pain medications. The most common adverse event (AE) reported from the patch was local transient application-site reactions.

An additional poster by Altman et al assessed the safety and efficacy of diclofenac sodium 1% gel for the treatment of OA. At 12 Weeks, patients showed significantly greater reductions in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scores on the diclofenac gel with a relatively low rate of adverse events (7.7% vs 4.2% vehicle).

These newer pain medications, as well as modes of delivery for medication, show promise as additional tools we may use as we manage complex pain syndromes such as neuropathic pain. We use the term "rational polypharmacy" when we discuss chronic pain management to describe the use of various low-dose medications, which may work synergistically to treat the various proposed pathways and mechanisms of such pain when individual medications alone may not be effective. Elderly patients in particular are prone to adverse drug reactions. Having a variety of vehicles to deliver pain treatment with less noted AEs may be particularly helpful in this population. In addition, some elderly patients may prefer a topical treatment to place on the site of the pain as opposed to another pill.

Other Updates of Interest

Data on two newer medications, tapendatol ER* and the Buprenorphine Transdermal Delivery System (BTDS)†, as treatment for chronic LBP were reviewed. A significant decrease in the pain intensity score was noted in tapendatol ER compared with placebo. A total of 49% of patients in the BTDS 20 dosage and 35% of the BTDS 5 dosage groups showed a 30% improvement in pain.

A series of presentations focused on the subject of pain with aging. As our geriatric population continues to grow, we anticipate seeing more of our elderly patients present with pain complaints. Robert Yezierski, PhD, cited data showing that 40% of elderly patients in the community report pain affecting their lives. An even broader statistic showed 27–83% of those living in institutions report pain. This range may be due to the fact that it is difficult to assess pain in this population because of issues with communication and cognitive impairment, among others. Yet 40–80% of community-dwelling older patients and 16%–27% of those in an institutional setting don't receive pain treatment. This gives us all food for thought and an opportunity for improvement.

Suzanne Leveille, PhD, RN, discussed data from the MOBILIZE Boston Study (Maintenance of Balance, Independent Living, Intellect, and Zest in the Elderly of Boston), in which 765 women and men aged ≥70 years were followed for 2 years to assess pain as a risk factor for falls. The study revealed that in this population, pain often occurred in multiple joints. The majority of patients (>80%) had hand/wrist pain, and >40% of patients with hip pain had pain in ≥3 other sites. These data are significant not only in regard to their implications in pain management, but also because they demonstrate a significant increase in difficulty with mobility. Patients with pain in one site had an odds ratio average for mobility difficulty of 1.8 vs those patients with pain in ≥7 sites, who displayed an odds ratio average of 4.2%. In addition, the risk of falls with mobility problems in this population is extremely concerning. Falls in this population can significantly change the lives and function of our elderly patients. These data remind us of the importance of prevention and encouraging all our patients (particularly our elderly ones) to include proper nutrition, as well as regular physical and mental activity, in treatment plans.

†Investigational agent; not FDA approved
*Not FDA approved for this indication

Opioid Pain Management:
Baseline Findings From OPUS

Several posters featured data from the ongoing OPUS trial, a multicenter, prospective observational cohort study assessing the clinical, economic, and QOL impact of opioid therapy after 12 months among 1,668 subjects with CNCP. The study is scheduled to close in March 2010.

- Irving et al analyzed baseline data of OPUS participants (N=1,236) as reported on the SF-12. Mental and physical functioning scores were significantly lower among study subjects vs the general US population ($P<0.001$ for both). No baseline differences in mean SF-12 scores were observed when duration of chronic pain and race was assessed, nor did physical functioning vary with sex or income. However, a higher mean mental functioning score was significantly associated with higher income (41.7 for income <$20,000 vs 45.5 for income >$60,000; $P\leq0.04$); mean mental functioning scores were significantly lower in women vs men (42.0 vs 46.0; $P<0.001$).
- Yanni et al examined OPUS patients' (N=1,668) baseline mood data as reported on the DAPOS scale. Subjects had mild-to-moderate depression and anxiety (mean 2.0 [SD 1.0] and 2.0 [1.1], respectively), and a moderately positive outlook (3.4 [1.0]). Subset results showed that women had higher depression and anxiety vs men (2.1 [1.0] vs 1.8 [0.09], $P<0.001$ and 2.1 [1.1] vs 1.8 [1.0], $P<0.001$, respectively); there were no gender-related differences in positive outlook.
- Using responses to 3 questions on the BPI, Argoff et al assessed baseline pain levels and pain interference in OPUS patients (N=1,570), comparing those with CNCP for ≤1 year vs >1 year. Although no significant differences were observed between the ≤1-year duration of pain group vs >1-year group in pain on average, worst pain, or interference with daily activity, significant differences were reported in subgroup analyses. Among subjects with OA or LBP, average pain was significantly higher for those having pain for≤1 year vs >1 year ($P<0.05$); subjects with LBP ≤1 year experienced more severe interference with general activities or sleep vs those with >1-year duration of pain ($P<0.05$).

BPI=Brief Pain Inventory; CNCP=chronic noncancer pain; DAPOS=Depression, Anxiety, and Positive Outlook Scale; LBP=low back pain; OA=osteoarthritis; OPUS=Opioid Utilization Study; QOL=quality of life; SD=standard deviation; SF-12=Short Form-12 Health Survey®

Concurrent Opioid Dosing for CNCP:
Fewer Adverse Events?

Chronic noncancer pain (CNCP) is a common problem among US adults, and undertreatment is associated with significant direct and indirect costs. Richards et al examined the safety and efficacy of 2 ratios of morphine + oxycodone† vs morphine alone in subjects with CNCP in 2 randomized, double-blind, 2-period crossover studies (Study A [N=21] and Study B [N=23]). Subjects were randomized to morphine + oxycodone or morphine alone q 4 h for 3–7 days, and were then crossed over to receive the other treatment for 3–7 days. The ratio for morphine and oxycodone was 3:2 in Study A and 1:2 in Study B. Primary efficacy endpoint: patient-assessed pain level on a 10-cm VAS (0=no pain; 10=worst imaginable pain). Total daily steady state of treatment drug was also assessed. Results:

- Study A: no significant differences in pretreatment VAS vs steady-state VAS for morphine ($P=0.19$) or 3:2 morphine + oxycodone ($P=0.64$)
- Study B: pretreatment and steady-state VAS were similar for morphine and 1:2 morphine + oxycodone
- Mean steady-state morphine-equivalent doses for morphine + oxycodone were lower vs those for morphine alone in both studies
- Increase in morphine-equivalent dose for equianalgesic effects of morphine + oxycodone: 61.6% in Study A ($P<0.006$), 46.8% in Study B ($P=0.0026$)
- Morphine + oxycodone q 4 h for up to 7 days did not result in unusual adverse events

†Investigational combination; not yet FDA approved
VAS=visual analog scale

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