Effervescent Fentanyl Subdues Cancer Pain

BY ROXANNE NELSON
Contributing Writer

SAN ANTONIO — A new rapidly acting effervescent formulation of fentanyl appears to be safe and effective when used to treat breakthrough pain in cancer patients.

Results of preliminary research show that fentanyl effervescent buccal tablets (FEBT) may provide rapid-onset analgesia in patients with cancer-related breakthrough pain, which is usually treated with a short-acting opioid.

"This formulation is designed to enhance the rate and efficiency of fentanyl absorption through the buccal mucosa," Dr. Donald Taylor reported at the annual meeting of the American Pain Society.

Dr. Taylor, medical director of a group practice specializing in pain care in Marietta, Ga., and his colleagues evaluated the efficacy and tolerability of FEBT in 123 opioid-tolerant patients with chronic pain associated with cancer, in a double-blind, randomized, placebo-controlled study.

The Sum of Pain Intensity Difference (SPID), an outcome measure that summarizes treatment response, was evaluated during the first 30 minutes as the primary efficacy measure. The researchers also assessed pain at 45 and 60 minutes after delivery of the drug, evaluated patients' self-reported pain relief, and tracked the number of times patients required rescue medication.

Clinically significant decreases in pain intensity (33% or more) were observed in 13% of episodes at 15 minutes and in 48% of episodes by 30 minutes after drug delivery. At all end points, the percentage of episodes showing a decrease in pain intensity greater than 33% was significantly greater with FEBT than with placebo. After 30 minutes, pain intensity decreased by 50% or more with FEBT in 24% of episodes.

"We looked at about 500 breakthrough pain episodes and about half were relieved at 30 minutes, if you consider 'greater than 33%' to be relief," Dr. Taylor said. In all measurements, the analgesic effect of FEBT exceeded that of placebo.

In summary, FEBT produced a rapid onset of action and was superior to placebo. It was reasonably well tolerated and appears to be a relatively effective treatment for breakthrough pain in patients with cancer, he said. ■

Opioid Prescribing Rates Vary Widely by State

BY TIMOTHY F. KIRN
Sacramento Bureau

SEATTLE — The rate of opioid use varies considerably from state to state, with some of the highest rates found in Indiana and Maine, and the lowest in California and Minnesota, federal prescription claims data show.

That variation is inexplicable medically, and suggests that opioids are being used too liberally in some states, not enough in others, or both, Dr. Judy T. Zerzan said in a poster presentation at the annual research meeting of Academy Health.

Medicare and Medicaid prescribing figures from the start of 1996 to the end of 2002 show a steep national increase in opioid prescribing. The increase coincides with efforts to improve treatment of pain, noted Dr. Zerzan of the division of general internal medicine at the University of Washington, Seattle.

Over the 7 years of the study, opioid prescribing nationally increased a mean of 24% per year. In contrast, there was a mean annual increase of 12% for an index known as the "market basket" that reflects general prescribing.

But only two-thirds of the states had an increase in the opioid prescribing . And some had a greater relative increase than others, Dr. Zerzan said.

The 10 states with the highest rates of opioid prescribing were Alaska, Indiana, Louisiana, Maine, Maryland, Missouri, Mississippi, Montana, North Carolina, and West Virginia, with rates of 87-200 defined daily doses per 1,000 Medicaid beneficiaries.

The eight states with the lowest rates were California, Minnesota, New Jersey, New Mexico, New York, Pennsylvania, Tennessee, and Vermont, with rates of 0 to 39 defined daily doses per 1,000 Medicaid beneficiaries.

One possible explanation for the variation in opioid use is differing state prescription benefit policies. Other potential explanations include that marketing of the drugs has been different in different regions, and that physician attitudes toward opioids vary by region, Dr. Zerzan said. ■

THE EFFECTIVE PHYSICIAN

Parkinson's Disease

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

The American Academy of Neurology quality standards subcommittee has recently published a series of evidence-based guidelines on Parkinson's disease.

Conclusions

Parkinson's disease (PD) is a common progressive neurodegenerative disorder. Cardinal symptoms are bradykinesia, rigidity, resting tremor, and abnormalities of gait and balance. Clinical diagnosis can be challenging; up to 20% of patients have an alternative diagnosis at autopsy.

The presence of more than one of the following features early in the disease suggests a diagnosis other than PD: frequent falls, poor response to levodopa, symmetrical symptoms, lack of tremor, rapid symptom progression, or autonomic dysfunction (urinary retention or incontinence, fecal incontinence, erectile dysfunction, or orthostatic hypotension).

Patients with newly diagnosed PD at older ages and rigidity/hypokinesia as predominant symptoms are more likely to have rapid progression of motor dysfunction and earlier development of cognitive decline. Those with tremor at the onset of disease are likely to have a more benign course and receive longer benefit from levodopa treatment.

Motor fluctuations, such as "off time" and dyskinesia, occur eventually in most patients with PD treated with dopaminergic agents.

Deep brain stimulation has largely replaced ablative surgical procedures for intractable PD. Levodopa response, younger age, and shorter duration of disease predict positive outcomes from surgery.

Nonmotor symptoms such as depression, psychosis, and dementia are common in PD. Evidence suggests that behavioral symptoms may be pathophysiologically different in PD than they are in the general public.

Implementation

Levodopa or apomorphine challenge should be considered in patients in whom the diagnosis of PD is in question after clinical evaluation. Testing of olfaction can help distinguish PD from similar neurologic syndromes.

There is insufficient evidence to support the use of MRI, PET, or brain single-photon emission CT to distinguish PD from similar neurologic syndromes.

Levodopa should be considered for initial treatment of PD; it is safe and does not accelerate disease progression.

Vitamin E is not effective for symptomatic treatment or neuroprotection. There is insufficient evidence to support the use of coenzyme Q10, amantadine, levodopa, or other medical, nutraceutical, or herbal agents to delay or prevent progression of PD.

Exercise therapy may improve motor function in PD, but current literature suggests that the functional improvements are modest. Speech therapy can improve speech volume in patients with PD complicated by dysarthria.

Entacapone and rasagiline are effective in reducing off time in PD patients receiving dopaminergic therapy. Pramipexole, ropinirole, tolcapone, and pergolide also may be considered for this indication. Tolcapone and pergolide should be used with caution because of the potential adverse effects of hepatotoxicity (tolcapone) and cardiac valvular fibrosis (pergolide).

Sustained-release levodopa and bromocriptine have not been shown to reduce off time in clinical trials.

Amantadine may reduce dyskinesia in patients with PD and motor fluctuations.

Deep brain stimulation (DBS) of the subthalamic nucleus may be considered in patients with PD who are neuropsychologically intact and who have intractable tremor, dyskinesia, or motor fluctuations. Response to levodopa should be assessed prior to surgical treatment of PD. There is insufficient evidence to make recommendations regarding DBS of other nuclei in the treatment of PD.

Amitriptyline has the best evidence base in the treatment of depression in PD patients. There is insufficient evidence concerning nontricyclic antidepressants in patients with PD to make recommendations about the use of these drugs.

Clozapine has the best evidence for treatment of patients with PD and psychosis, but patients on this agent must be monitored closely for agranulocytosis. Quetiapine may be an alternative agent. Olanzapine should not routinely be considered for psychosis in patients with PD.

Donepezil or rivastigmine should be considered for the treatment of dementia in patients with PD.

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