NEW DRUG

Levodopa Combination for Parkinson’s Disease

The U.S. Food and Drug Administration (FDA) has approved Stalevo™ (carbidopa, levodopa, and entacapone) tablets for the treatment of patients with idiopathic Parkinson’s disease who experience diminished benefits as the effects of levodopa wear off. Novartis plans to market the drug, and Orion Pharma will manufacture it in the U.S.

Parkinson’s disease affects more than 1% of people over age 65. Its cause is unknown, but symptoms result primarily from the degeneration of neurons in a part of the brain that controls movement. Patients experience Trembling limbs, slowness of movement, stiffness and rigidity of the limbs, and gait or balance problems.

Levodopa is currently the most widely used agent for treating Parkinson’s disease. Carbidopa reduces the side effects of levodopa, and entacapone optimizes its benefits, providing patients with an improved ability to perform everyday tasks and a reduction in disease-related symptoms.

Within one to two years, almost 50% of patients receiving levodopa therapy begin to notice that the effect lasts for shorter periods of time. In 15% to 20% of patients, the wearing-off effect becomes extreme and disabling. It is anticipated that Stalevo™ will be able to provide levodopa to the brain for a longer time.


DRUG NEWS

Anticholinergics Effective for Overactive Bladder?

Anticholinergic agents are the first-line drug treatment for overactive bladder, but do they work that much better than placebo? To find out, researchers from the University of Ontago in New Zealand, reviewed 32 trials that included 6,800 participants.

Overall, the anticholinergics did alleviate symptoms of urgency, frequency, and nocturia as well as improve patients’ reported quality of life. Most of the patients experienced great relief with the drugs, but this was true of the placebo groups as well, the researchers explain. The differences between the groups, although statistically significant, were not clinically significant.

(Source: BMJ 2003;326:841–844.)

Insomnia in Children

Sleep disturbances in infants, children, and adolescents are among the most common and challenging complaints in pediatric practice. Although the effectiveness of behavioral treatments for sleep disorders has been studied, pharmacological treatment is inadequately researched. According to one study, no medications have been labeled by the FDA for sleep disturbances in children.

The use of both prescription and nonprescription medications for pediatric insomnia seemed to fall into two general patterns: short-term situational use of nonprescription medications (e.g., for travel, acute pain, or stress) and longer-term use of prescription drugs in children with special needs, such as mental retardation, attention-deficit/hyperactivity disorder (ADHD), and autism.

The number of children with significant sleep problems seen in a six-month period was greatest in infants and toddlers and decreased with age. Over-the-counter antihistamines were the most commonly recommended of all medications in all age groups, and alpha-agonists were the most frequently prescribed sleep medications. About 15% of the respondents recommended melatonin or herbal remedies.

For more information on pediatric drug testing, see Dr. Goldenberg’s article in the June 2003 issue of P&T.


Treating Infections in Cancer Patients

Should infections in cancer patients be treated? A study of 255 patients with advanced cancer suggests that antimicrobials may relieve symptoms but do not alter rates of survival.

Researchers from the Walther Cancer Research Center at the University of Notre Dame discussed antimicrobial options with patients who entered a community-based hospice and palliative-care program. Most of the patients (79%) chose not to receive antimicrobial agents, or they used them for symptom control only. The antimicrobials were most effective in controlling urinary symptoms but less successful in treating the other infections. Patients showed improvement when their symptoms responded to the antimicrobials.

Survival was not affected by the use of antimicrobials or by the prevalence of infections. Thus, symptom control might be the major indication for antimicrobial use in hospice care.

(Source: J Pain Symptom Manage 2003; 25:438–443.)

SSRIs Safe for Nursing Mothers

Nursing women can safely take selective serotonin reuptake inhibitors (SSRIs), according to Norwegian investigators. This is good news for women who are at risk for postpartum depression, say the researchers, whose findings were reported at the 156th annual meeting of the American Psychiatric Association in San Francisco.

Five different SSRIs were tested in 23...
nursing women and their infants: citalopram (Celexa® TM, Forest), sertraline (Zolof®, Pfizer), paroxetine ( Paxil®, GlaxoSmithKline), venlafaxine (Effexor®, Wyeth-Ayerst), and fluoxetine (e.g., Prozac®, Eli Lilly, Distal). Although the women took doses of 20 to 130 mg/day and their serum drug levels were in the therapeutic range, the drugs did not enter the mothers’ milk in significant amounts. Drug levels in the infants ranged from 0 to 10% of those in the mother’s blood.


Tamoxifen and Depression: A Long-Term Side Effect?

Even if women have been taking tamoxifen citrate (Nolvadex®, AstraZeneca) for months, they should be observed for symptoms of depression, according to researchers who presented their findings at the American Psychiatric Association’s annual meeting in May 2003.

Tamoxifen interferes with estrogen activity and is often prescribed for women with advanced and early breast cancer and as additional therapy after primary treatment for early-stage breast cancer. In a study of nearly 3,000 women, depression appeared an average of eight months after tamoxifen therapy was begun.


Diuretics and End-Stage Renal Disease

Diuretics may lead to end-stage renal disease (ESRD) in some patients, according to a study reported at the American Society of Hypertension’s 18th annual meeting in New York. Researchers found a direct relationship between annual changes in the prescription diuretic supply and annual variability in the incidence of ESRD. From 1990 to 2001, changes in the supply and use of diuretics were directly associated with changes in the incidence of ESRD two years later.


Which Drug for Pneumonia?

It’s about a hundred times more expensive, but it may be the better choice any way. In phase III studies for the treatment of gram-positive hospital-acquired (nosocomial) pneumonia, Linezolid (ZyvoxTM, Pharmacia & Upjohn) was superior to vancomycin (Vancocin® HCL, Eli Lilly), report researchers from Methodist University Hospital. Their findings were presented at an American Thoracic Society meeting in Seattle in May 2003.

Linezolid was particularly efficacious in treating methicillin-resistant Staphylococcus aureus (MRSA) pneumonia, and patients receiving linezolid were twice as likely to survive as patients who received vancomycin. The researchers explained that vancomycin is associated with renal toxicity, and patients at risk for renal problems might therefore be receiving underdoses. Linezolid is not associated with renal toxicity, and it seems to offer greater lung penetration.

Linezolid, which was approved in 2000, is the first FDA-approved oxazolidinone, a new class of antibiotics.


Brief Therapy for Lyme Disease

How long should antibiotic treatment last for early Lyme disease? Researchers from Westchester Medical Center in Valhalla, New York, say treatment rarely fails and that doubling doxycycline (Vibramycin® Calcium, Pfizer) treatment from 10 to 20 days or adding one dose of ceftriaxone (Rocephin®, Roche) to the beginning of a 10-day course of doxycycline does not add any benefit. At all time points—20 days, 3 months, 12 months, and 30 months—the complete response rate was similar for all treatment groups. At 30 months, 84% of patients in the 20-day doxycycline group, 90% in the 10-day group, and 86% in the combination group showed a complete response.

(Source: Ann Intern Med 2003;138: 697–704.)

Two-Drug Combination for Blood Pressure and Cognition

Aggressively treating high blood pressure can reduce the risk of dementia and cognitive decline associated with recurrent stroke, according to findings from the Perindopril Protection against Recurrent Stroke Study (PROGRESS). The long-term study compared the effects of active treatment, consisting of perindopril erbumine (Aceon®, Solvay) and indapamide (Mylan, Par, Watson) with those of placebo in 6,105 patients with a previous stroke or a transient ischemic attack.

Active treatment reduced the risk of dementia by 12% and the risk of dementia with recurrent stroke by 34%. Therapy also reduced risk of cognitive decline by 19% and the risk of cognitive decline with recurrent stroke by 45%.

(Source: Arch Intern Med 2003;163: 1069–1075.)

Switching Antibiotics Can Save Lives

Cutting back on third-generation cephalosporins might reduce the num-
When Are Statins Risky?

When Are Statins Risky?

Statins, which are often prescribed to reduce high cholesterol levels, have proved safe, effective, and well tolerated; however, interactions with other drugs may be putting some patients at higher risk for myopathy (muscle disease).

Myopathy is traditionally defined as a creatine kinase level greater than 10 times the upper limits of normal. Symptoms include generalized myalgia, fatigue, and weakness. Elevated creatine kinase levels are biochemical markers of the muscle damage.

Myopathy occurs in approximately 0.1% of patients receiving statin monotherapy. In studies with lovastatin (Mevalcor®, Merck), those numbers rose to 2% in patients receiving concomitant niacin (vitamin B3), 5% when niacin was given in patients receiving concomitant niacin or other severe illnesses. Because myopathy can impair liver function, patients at risk for liver problems should not take statin–fibrate therapy. Patients taking statin–niacin combination therapy should be monitored for liver transaminase levels and for any symptoms of myopathy.

Although no clinical data from thousands of patients have suggested that the concomitant use of calcium-channel antagonists, such as diltiazem (Cardizem®, Biovail) and verapamil (Covera-HS™, Searle; Isoptin®, Abbott; Verelan®, Schwarz Pharma), increases the risk of simvastatin-associated myopathy, two cases of rhabdomyolysis have been reported. Even so, the researchers advise, it is essential to weigh the risks against the tremendous benefits of statins and statin-combination treatments.

Despite the risk with statin–cyclosporine interactions, for example, it is crucial to treat dyslipidemia in patients after transplantation because cardiovascular disease accounts for nearly 50% of all deaths in transplant recipients. Similarly, mixed hyperlipidemia, which is common in diabetic patients, can rarely be treated successfully with a single drug; for those patients, statin–fibrate combination therapy might offer an advantage.

If patients report unexplained generalized muscle pain, tenderness, or weakness, statin therapy should be discontinued and serum creatine kinase levels should be monitored.

(Source: Arch Intern Med 2003;163:553–564.)

Cholesterol Drug Combination Produces a One-Two Punch

Taking two different types of cholesterol-lowering drugs appears to reduce serum cholesterol levels more effectively than taking either drug alone.

People who took both atorvastatin (Lipitor®, Pfizer) and ezetimibe (Zetia™, Schering-Plough/Merck) showed larger declines in cholesterol than patients taking either drug by itself and had no additional side effects.

In the study, 628 patients with high cholesterol levels were offered one of four treatments: ezetimibe alone, atorvastatin alone, ezetimibe plus atorvastatin, or a placebo. After 12 weeks of therapy, the subjects taking the combination of the two drugs experienced a larger reduction in cholesterol than those taking either treatment alone.

Patients receiving the drug combination showed a 12% larger drop in levels of “bad” low-density lipoprotein-cholesterol (LDL-C) than patients taking atorvastatin alone. This treatment also reduced levels of triglycerides and C-reactive protein more successfully than did atorvastatin alone. A 10-mg dose of ezetimibe appeared to reduce cholesterol equally well when combined with a 10-mg or an 80-mg dose of atorvastatin.

(Source: Reuters Health, May 1, 2003; Circulation 2003;107 (April 28), electronic, rapid-access edition.)

Interferons and Psychosis

Interferon alfa (IFN-α) therapy can have adverse psychiatric effects. Although symptoms, such as hallucinations, usually improve shortly after the drug is stopped, they may occasionally persist. Turkish researchers who treated a man with chronic hepatitis B advise monitoring the mental status of patients receiving IFN-α during all stages of therapy.

**New Drugs**

**Prices of HIV/AIDS Drugs Reduced for Developing World**

GlaxoSmithKline has announced that it has further reduced the not-for-profit prices of its medicines used for patients with human immunodeficiency virus or acquired immunodeficiency syndrome (HIV/AIDS) in the world’s poorest countries by up to 47%. The latest reduction lowers the cost of amivudine/zidovudine (Combivir®) to 90 cents per day. The company has also reduced the not-for-profit price of many of its other HIV/AIDS medicines. 3TC (Epivir®) is now available at 35 cents per day, and AZT (azidothymide, zidovudine, Retrovir®) is priced at 75 cents per day, for reductions of 45% and 38%, respectively. (Source: PR Newswire–First Call, April 28, 2003.)

**Colonoscopy More Cost-Effective Than New Drugs**

A new study gives Americans over age 50 one more reason not to put off having a colonoscopy to check for colon cancer and its forerunners. The screening technique not only is excellent at detecting problems but also appears to be far more cost-effective for most people than new cancer-preventing drugs will probably ever be.

Researchers at the University of California, San Francisco, and the University of Michigan Health System used a computer model to compare the cost-effectiveness of colonoscopy and other screening procedures for colon cancer with that of COX-2 inhibitors, a class of drugs used to treat arthritis but also considered promising in preventing colon cancer.

The data suggest that the drugs are unlikely to be as effective—as colonoscopy in cutting cancer death risk for those with average colon cancer risk. Screening plus drugs was most effective but was even more costly.

Two other studies reportedly found that even aspirin had only a modest effect on preventing colon polyps and predicted that aspirin’s effectiveness in reducing colorectal cancer risk would never be superior to the life-saving effect of colonoscopy.

For an average-risk person, it would cost $20,200 to save one life-year through colonoscopy screening but $233,300 to save the same life-year through COX-2 inhibitors. Even for a person with a higher risk of colon cancer, a colonoscopy once every five years would still cost less and save more years of life than a daily drug. But the difference was smaller: $3,900 per life-year saved through screening every 10 years or $6,200 for screening every five years, versus $80,300 for drug therapy. (Source: Am J Med 2003;114:7.)

**Minocycline for Acne**

The FDA has approved a new dosage form of the drug minocycline HCl (Dynacin®, Medicis) for the adjunctive treatment of severe acne. Par Pharmaceutical, a wholly owned subsidiary of Pharmaceutical Resources, Inc., is scheduled to manufacture tablets in strengths of 50, 75, and 100 mg for Medicis pursuant to an exclusive manufacturing and supply agreement. (Source: Business Wire, April 16, 2003.)

**Side Effects Worse with Newer Epilepsy Drugs**

Two commonly prescribed epilepsy drugs have varied cognitive side effects on patients, report doctors from Georgetown University Medical Center in Washington, DC.

In a double-blind, randomized study, researchers looked at two drugs, valproate (released in 1978) and topiramate (approved in 1996). Each drug was added to carbamazepine, a standard epilepsy treatment, and then given to patients with epilepsy. The cognitive effects on the patients taking topiramate were slightly, although noticeably, worse than those taking the older valproate for a subset of patients. (Source: Neurology 2003;60:1483–1488.)

**Hormone Patches or Pills?**

There may be important differences in how women respond to various routes of hormone delivery in terms of the quality of their sexual lives and renin substrate levels.

A study examined differences between oral conjugated estrogens/methoxyprogesterone acetate tablets (Prempro™, Wyeth) and the norethindrone acetate transdermal system CombiPatch®, Novogynenovartis/Noven), an estrogen–progestin combination patch. Findings were presented at the 51st annual meeting of the American College of Obstetricians and Gynecologists, April 26–30, 2003, in New Orleans.

Postmenopausal women using the patch experienced improved libido nearly twice as often as those using Prempro™. Plasma renin substrate levels, which have been associated with increased blood pressure, decreased in patients using the patch but increased in patients receiving Prempro™. In a similar study, postmenopausal women using estrogen patches had a lower risk of heart disease than those taking estrogen pills.

The patch contains natural hormones, derived from plants. Prempro™ is composed of conjugated equine estrogens, derived from the urine of pregnant mares, and medroxyprogesterone acetate, a synthetic progestin.

(Source: ACOG meeting, April 2003; www.noven.com; www.novartis.com.)

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