

Anticonvulsant Warning Led to Decreased Use

BY ROXANNA
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SAVANNAH, GA. — Black box warnings on antipsychotics led to a decrease in their use to treat patients with dementia, without a commensurate increase in use of antianxiety or other psychotropic agents but with a rise in the use of anticonvulsant therapies, some of which appear to be riskier than the antipsychotics in older patients.

In fact, valproate appears to have a higher mortality than the antipsychotics studied, Dr. Helen C. Kales and Kara

Zivin, Ph.D., of the University of Michigan and the VA Healthcare System in Ann Arbor, said in reporting the preliminary findings from an ongoing National Institutes of Health–funded study at the annual meeting of the American Association for Geriatric Psychiatry.

Antipsychotics once were widely prescribed as an off-label treatment for dementia, but in 2005, the Food and Drug Administration issued a black box warn-

ing that the use of atypical antipsychotics in the treatment of behavioral disorders in elderly patients with dementia was associated with increased mortality. A similar warning for conventional antipsychotics was issued in 2008.

To see how the warnings affected practice patterns, Dr. Kales and Dr. Zivin looked at national data from 254,564 Department of Veterans Affairs outpatients with dementia.

They found that a decline in use of atypical antipsychotics began in 2003, coinciding with the release of data from randomized, controlled trials about cerebrovascular events. The decline accelerated after the black box warning.

For conventional antipsychotics, the major decline in use came during the 1990s with the introduction of atypical antipsychotics. After 2003, the rates of conventional antipsychotic use among

VITALS **Major Finding:** After 2003, rates of conventional antipsychotic use among outpatients with dementia were less than 2%.
Data Source: National data from the Department of Veterans Affairs on 254,564 outpatients with dementia.
Disclosures: Neither Dr. Kales nor Dr. Zivin disclosed any conflicts.

Memantine ER Seems Safe and Well Tolerated

SAVANNAH, GA. — An extended release formulation of memantine 28 mg taken once daily was safe and well-tolerated in patients with moderate to severe Alzheimer's disease in a 52-week, open-label, fixed-dose study.

Dr. Barnett Meyers of Weill Medical College, White Plains, N.Y., and his colleagues presented their findings in a poster at the annual meeting of the American Association for Geriatric Psychiatry.

Memantine (Namenda) is administered in twice-daily, immediate-release doses of 10 mg each. A previous 24-week trial indicated that a once-daily 28-mg dose of memantine ER was safe and effective for patients with moderate to severe AD on cholinesterase inhibitors (Alzheimer's Dement. 2008;4[suppl. 1]:T793).

A total of 164 outpatients aged 50 or older with probable AD were either titrated to the target dose of memantine ER 28 mg daily over 4 weeks or were switched from twice-daily, immediate-release memantine 10 mg.

Overall, 150 patients reported adverse events, and 8 (5%) had events related to the study medication; 44 patients (27%) had a serious adverse event, but none of the 12 deaths were considered related to treatment. Dr. Meyers and his colleagues concluded that patients taking the 10-mg twice-daily dose can safely switch to memantine ER without a titration period.

—Roxanna Guilford-Blake

Disclosures: The study was funded by Forest Laboratories. Dr. Meyers reported having no conflicts; two of his coauthors are employees of Forest Research Institute.

People who have had chicken pox are at risk for shingles and postherpetic neuralgia (PHN) pain^{1,2}
This year, ~1 million Americans will develop shingles.^{1,2}
1 in 5 of them will go on to develop PHN pain¹



Indication

LIDODERM (lidocaine patch 5%) is indicated for relief of pain associated with post-herpetic neuralgia. Apply only to **intact skin**.

Important Safety Information

LIDODERM is contraindicated in patients with a history of sensitivity to local anesthetics (amide type) or any product component.

Even a *used* LIDODERM patch contains a large amount of lidocaine (at least 665 mg). The potential exists for a small child or a pet to suffer serious adverse effects from chewing or ingesting a new or used LIDODERM patch, although the risk with this formulation has not been evaluated. It is important to **store and dispose of LIDODERM out of the reach of children, pets, and others**.

Excessive dosing, such as applying LIDODERM to larger areas or for longer than the recommended wearing time, could result in increased absorption of lidocaine and high blood concentrations leading to serious adverse effects.

Avoid contact of LIDODERM with the eye. If contact occurs, immediately wash the eye with water or saline and protect it until sensation returns.

Avoid the use of external heat sources as this has not been evaluated and may increase plasma lidocaine levels.

Patients with severe hepatic disease are at greater risk of developing toxic blood concentrations of lidocaine, because of their inability to metabolize lidocaine normally. LIDODERM should be used with caution in patients receiving Class I antiarrhythmic drugs (such as tocainide and mexiletine) since the toxic effects are additive and potentially synergistic. LIDODERM should also be used with caution in pregnant (including labor and delivery) or nursing mothers.

Allergic reactions, although rare, can occur.

During or immediately after LIDODERM treatment, the skin at the site of application may develop blisters, bruising, burning sensation, depigmentation, dermatitis, discoloration, edema, erythema, exfoliation, irritation, papules, petechia, pruritus, vesicles, or may be the locus of abnormal sensation. These reactions are generally mild and transient, resolving spontaneously within a few minutes to hours. Other reactions may include dizziness, headache, and nausea.

When LIDODERM is used concomitantly with local anesthetic products, the amount absorbed from all formulations must be considered.

outpatients with dementia were less than 2%.

No significant compensatory increase was found in the use of antianxiety or antidepressant agents, Dr. Zivin said. In an interview, Dr. Kales speculated that possibly those drugs are not viewed as substitute therapies for the types of behaviors for which antipsychotics are prescribed.

The research did turn up a small but statistically significant increase in anticonvulsant use among outpatients with dementia.

The researchers also examined mor-

tality for 13,857 elderly patients with any diagnosis and 3,954 patients with dementia who had been prescribed individual antipsychotics (haloperidol, olanzapine, quetiapine, and risperidone) and individual anticonvulsants (valproate and carbamazepine).

The researchers examined records for elderly patients in general as well as for those with dementia. As in prior studies, they found that haloperidol was associated with higher mortality than were the atypicals.

What was unexpected was the finding that valproate was associated with high-

er mortality than all of the antipsychotics, including haloperidol.

The populations of older patients receiving haloperidol and valproate differed somewhat from those receiving atypicals. The haloperidol cohort included more African Americans, and more subjects with schizophrenia and medical comorbidities. The valproate cohort was younger and a lower proportion had dementia. Neither accounting for selection bias nor excluding for bipolar disorders changed the results, Dr. Kales reported.

More research on the association be-

tween mortality and antipsychotics is needed, Dr. Kales said in an interview. "Is it a direct medication effect or related to the pathophysiology underlying the need for use?" She plans to use an electronic medical record search engine to look for other variables in such studies, including the severity of cognitive impairment and the type of behavioral disturbance. ■

Disclosures: The study was funded by the National Institutes of Health. Neither Dr. Kales nor Dr. Zivin disclosed any relevant conflicts of interest.

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^a A randomized, double-blind, placebo-controlled, 4-way crossover trial ($N=35$) assessed safety and efficacy of LIDODERM. Patients were allodynic with a mean age of 75 years and mean PHN duration of 48 months. Pain intensity measured with horizontal 100-mm Visual Analogue Scale: 0=no pain and 100=worst pain imaginable. Measurements were recorded before patch application, at 30 minutes, and hours 1, 2, 4, 6, 9, and 12. Least-squares means were used as the best unbiased estimate of patients' mean values.

^b Demonstrated over 14 days in a post hoc analysis of a randomized, enriched-enrollment, double-blind, placebo-controlled, crossover trial. Patients enrolled in the study had been using LIDODERM for ≥ 1 month (ie, enriched enrollment); mean age of 77.4 years and mean PHN duration of 7.3 years. Pain relief measured using 6-item verbal scale: 0 (worse), 1 (no relief), 2 (slight relief), 3 (moderate relief), 4 (a lot of relief), and 5 (complete relief). Patients exited the study if their verbal pain relief rating decreased more than 2 categories for any 2 consecutive days from baseline.

^c Results of enriched-enrollment studies can't be generalized to the entire population; subjects in such studies may be able to distinguish the active drug from placebo based on nontherapeutic features of the treatments.

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