

# Zolmitriptan Spray Effective as Migraine Tx

BY DEBBIE LERMAN  
Contributing Writer

PHILADELPHIA — For the first time, the triptan, zolmitriptan nasal spray has been found to be effective in the short-term treatment of migraines in adolescents, Paul Winner, D.O., reported at the annual meeting of the American Headache Society.

Seven triptans are currently approved for adult migraine treatment, but none of them are approved for use in adolescents, noted Dr. Winner, director of the Palm Beach (Fla.) Headache Center.

He reported on a multicenter, randomized, double-blind, placebo-controlled trial that used a novel design in which 248 adolescents were initially enrolled, and then 171 were selected for the intent-to-treat group based on lack of response to zolmitriptan in a single-blind placebo challenge (see box).

The study was supported by AstraZeneca, the maker of zolmitriptan

nasal spray (Zomig). Dr. Winner has served as a researcher, speaker, and consultant to the company.

In the 171 adolescents (mean age 14.1 years), who were treated for a total of 275 migraine attacks, zolmitriptan nasal spray produced significantly higher headache response rates than placebo at 1 hour post dose (58% vs. 43%), with an onset of action as early as 15 minutes.

At 1 hour after treatment, 28% of the adolescents in the zolmitriptan group were pain free, compared with 10% of those in the placebo group.

Also, 51% of those in the zolmitriptan group were able to resume normal activities vs. 38% of those in the placebo group. At 2 hours after treatment, 54% of those in the zolmitriptan group were pain free, vs. 36% of those in the placebo group.

There were no serious adverse events, and no one withdrew from the study because of adverse events.

“We found that the treatment was ef-

fective, fast, and well tolerated,” Dr. Winner told this newspaper.

“Hopefully, this will begin the process of getting some of these medications [triptans] approved for adolescents, a group that can clearly benefit from them,” he noted.

Triptans should not be used in all adolescents with migraine, he added, but there is a definite need for such treatment in those who do not respond to over-the-counter medications and have migraine-related disability that prevents them from normal functioning. ■

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## Study Excluded Placebo Responders

In previous studies on triptans in adolescents, placebo response rates that were significantly higher than those in adult patients with migraine prevented primary end points from reaching statistical significance, Dr. Winner said.

So he and his associates used a novel design that excluded patients who responded to placebo.

The study initially enrolled 248 adolescents and treated all of their migraine attacks with placebo nasal spray. In this single-blind phase of the study, patients who responded within 15 minutes were excluded, leaving only 171 placebo nonresponders in the intent-to-treat group.

In the double-blind phase, placebo response rates were similar to those in adult studies, Dr. Winner said.

The use of a placebo challenge to

screen out placebo responders “needs to be the standard of design moving forward,” he said. “Old designs just don’t work.”

The study design yielded an interesting finding, he added: “Once a placebo nonresponder, not always a placebo nonresponder.”

The Food and Drug Administration, which initially approved the placebo challenge design, requested an analysis that included all 248 patients. This analysis assumed that all patients in the placebo-response group (none of whom actually received subsequent treatment) would have responded to placebo and not responded to treatment, had they been included in the double-blind part of the study. In this worst-case scenario, no significant results were obtained.

## Comorbid Conduct Disorder Secondary to Depression

BY ROBERT FINN  
San Francisco Bureau

SANTA FE, N.M. — A study of children’s autonomic responses to reward and negative mood induction suggests that when conduct disorder and depression are comorbid, depression is the primary disorder.

In a poster presentation at the annual meeting of the Society for Psychophysiological Research, Hilary K. Mead, a graduate student working in the Child and Adolescent Adjustment Project at the University of Washington (Seattle), noted that previous studies have suggested that comorbidity rates for the two conditions may be as high as 82%, but that it’s unclear whether conduct disorder (CD) arises from depression or whether depression arises from CD.

A third possibility is that neither condition is primary and that both are driven by a common etiological substrate, with each representing an alternative manifestation of a single biological disposition. This hypothesis found no support in the experimental results, Ms. Mead noted.

The experiment involved 116 children, aged 8-12 years. Eighteen of those children had conduct disorder and/or oppositional defiant disorder, 15 had depression and/or dysthymia, 37 had comorbid depression and conduct disorder, and 46 had no psychiatric condition.

All children had their electrodermal re-

sponses (EDR), their respiratory sinus arrhythmia (RSA), and their cardiac pre-ejection period (PEP) measured during three successive experimental conditions: a 5-minute baseline, a monetary incentive task, and negative mood induction via an emotionally evocative film clip.

If CD were the primary disorder, groups with CD alone and with comorbid CD and depression would be expected to have a similar pattern of autonomic responses.

On the other hand, if depression were primary, groups with depression alone and comorbid CD and depression would show similar autonomic responses. If neither condition were primary, all three groups of children with psychiatric disorders would be expected to be similar, Ms. Mead said in her poster.

As it turned out, children with CD had a pattern of autonomic responses that differed significantly from the other groups. The EDR of children with CD did not change across trials of the reward incentive task, while all other groups showed decreases in EDR. During negative mood induction, children with CD had decreasing PEP and increasing RSA, while the other groups showed no change from baseline.

The investigators concluded that depression is the primary disorder in children with comorbid internalizing and externalizing psychopathologic symptoms.

The National Institutes of Health funded the study. ■

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