

Weight Gain on Valproate May Be Normal Growth

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LOS ANGELES — Children taking sodium valproate for epilepsy may not be as vulnerable as adults to the significant weight gain associated with the medication, said Cia M. Sharpe, M.D.

In an effort to uncover possible clinical predictors of weight gain associated with valproate in the treatment of epilepsy, Dr. Sharpe and colleagues at the University of

California, San Diego, conducted a chart review of 109 patients aged 2-20 years with valproate-treated epilepsy.

The investigators assessed body mass index (BMI) changes in the treated population by computing z slopes representing mean changes in BMI percentile for age at each available visit for each patient.

Using univariate analysis, they looked at the relationship between the z slopes and predictors of weight gain, including pretreatment BMI percentile for age, average

valproate dose, average serum valproate level, standard or extended release formulation, age at onset of epilepsy, duration of valproate treatment, seizure disorder type, concurrent use of other medication, gender, and ethnicity—none of which proved to be useful predictors, Dr. Sharpe reported in a moderated poster session at the annual meeting of the Child Neurology Society.


Over the 2-year period, “there were no significant correlations between potential

predictors of [weight gain] and z slope,” Dr. Sharpe said. Additionally, “the mean z slopes were less than expected, at -0.006 per year, and only 25 of the 109 patients had sufficient BMI changes to increase their z score by 0.5 or more.”

While seemingly significant gains in weight have been reported with valproate therapy in children, “the increases may prove to be normal growth when change in BMI percentile for age is calculated,” Dr. Sharpe concluded. ■

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Important Safety Information

Most frequent adverse events

In clinical trials, the most frequent adverse events with RAZADYNE ER were similar to those with RAZADYNE (formerly REMINYL).

The most frequent adverse events that occurred with RAZADYNE were nausea, vomiting, diarrhea, anorexia, and weight loss.

Anesthesia

Cholinesterase inhibitors, such as galantamine HBr, are likely to exaggerate the neuromuscular blocking effects of succinylcholine-type and similar neuromuscular blocking agents during anesthesia.

Cardiovascular events

Because of their pharmacological action, cholinesterase inhibitors have vagotonic effects on the sinoatrial and atrioventricular (AV) nodes, leading to bradycardia and AV block. These actions may be particularly important to patients with supraventricular cardiac conduction disorders or to patients taking other drugs concomitantly that significantly slow heart rate. In clinical trials, galantamine HBr was associated with more frequent reports of bradycardia and syncope vs placebo.

Gastrointestinal

Cholinesterase inhibitors may increase gastric acid secretion. Patients should be monitored closely for symptoms of active or occult gastrointestinal bleeding, especially those with an increased risk of developing ulcers, eg, those with a history of ulcer disease or patients using concurrent nonsteroidal anti-inflammatory drugs.

Genitourinary

Cholinesterase inhibitors may cause bladder outflow obstruction.

Neurological conditions

Cholinesterase inhibitors are believed to have some potential to cause generalized convulsions. In clinical trials, there was no increase in the incidence of convulsions with galantamine HBr compared with placebo.

Pulmonary conditions

Cholinesterase inhibitors should be prescribed with care to patients with a history of asthma or obstructive pulmonary disease.

Deaths in subjects with mild cognitive impairment (MCI)

In controlled trials of elderly subjects with MCI, 13 subjects on RAZADYNE (n=1026) and 1 subject on placebo (n=1022) died of various causes. About half of the RAZADYNE deaths appeared to result from various vascular causes (myocardial infarction, stroke, and sudden death). RAZADYNE and RAZADYNE ER are not indicated for the treatment of MCI.

Hepatic or renal impairment

In patients with moderately impaired hepatic or renal function, dose titration should proceed cautiously. The use of RAZADYNE or RAZADYNE ER in patients with severe hepatic impairment or severely impaired renal function ($CL_{Cr} < 9$ mL/min) is not recommended.

Reference: 1. Brodaty H, Corey-Bloom J, Potocnik FCV, Truyen L, Gold M, Damaraju CRV. Galantamine prolonged-release formulation in the treatment of mild to moderate Alzheimer's disease. *Dement Geriatr Cogn Disord.* 2005;20:120-132.

*As measured by the ADCS-ADL inventory.

[†]Results shown are from a 6-month, randomized, double-blind, parallel-group, placebo-controlled, flexible dose study comparing the safety, tolerability, and efficacy of RAZADYNE ER with that of placebo in patients with mild to moderate dementia of the Alzheimer's type.

“Activities of daily living” include eating, walking, using the restroom, bathing, grooming, dressing, physical performance, using common household appliances, conversation, tending to the home, managing personal belongings, travel, shopping, knowledge of current events, reading, and writing.

Please see the adjacent brief summary of the Prescribing Information for RAZADYNE ER.