responsive to a variety of antidepressant medications, was begun on vilazodone, initially 20 mg and gradually increased to 60 mg a day. On 60 mg a day he noticed severe cravings for sweets, which he had never experienced prior to starting vilazodone. He found he had increased consumption, craving sweet foods including cookies and candy. For instance, in a typical day, he would eat eight Oreos, chocolate-covered graham crackers, one pint of ice cream a day, and he would crave sweets even after feeling satiated after consuming a meal. Along with this increased eating, he gained 20 pounds over the 3 months while on the vilazodone. Upon discontinuing the vilazodone, although the weight didn't change, the sweet cravings resolved.

Results. Abnormalities on: Neurological examination: Mental status examination: Immediate recall: able to remember 6 digits forwards and 3 digits backwards. Motor examination: Drift testing: right inward drift. Gait examination: unstable tandem gait. Neuropsychiatric examination: Go-No-Go test: 6/6 (normal). Animal Fluency Test: 22 (normal).

Discussion. There are myriad mechanisms whereby vilazodone may have induced glycolimia. Possibly due to its antidepressant effects, it increased hedonics, generating appetitive behaviors, including enhanced socialization, sexual, and other consumptive behaviors, including eating. Peradventure it may have enhanced motivation and socialization. Along with socialization, there is escalation in social intercourse, with accompanying commensalism. Along with such consumptive behaviors, we could anticipate glycolimia. As a 5-HT1A receptor agonist, possibly vilazodone may have acted on the arcuate pro-opiomelanocortin neurons associated with hyperphagia, with modulation of energy homeostasis in the serotonin pathway. Alternatively, vilazodone may have triggered an enhanced insulin response with secondary reduction in blood sugar, leading to a homeostatic behavioral response of increased glucose intake. In those who are treated with vilazodone, query as to glycolimia is warranted and warning as to potential manifestations of hyperglycemia should be entertained.

Funding. No Funding

Population Pharmacokinetic-Pharmacodynamic Modeling of Variable Wear Times for a Dextroamphetamine Transdermal System

Mariacristina Castelli, PhD[1], Marina Komaroff, DrPH[1], Suzanne Meeves, PharmD, MBA[1], Kanan Balakrishnan, PharmD[1], Kyle T. Baron, PharmD, PhD[2], John T. Mondick, PhD[2], Stephen V. Faraone, PhD[3] and Gregory W. Mattingly, MD[4]

[1]Product Development, Noven Pharmaceuticals, Inc., Jersey City, NJ, USA, [2]Metrum Research Group, Tariffville, CT, USA, [3]Departments of Psychiatry and of Neuroscience and Physiology, SUNY Upstate Medical University, Syracuse, NY, USA and [4]Washington University School of Medicine, Midwest Research Group, St. Louis, MO, USA

Abstract

Introduction. The Dextroamphetamine Transdermal System (d-ATS) was developed as an alternative to oral amphetamine (AMP) formulations for ADHD. In a pivotal study, d-ATS met primary and secondary efficacy endpoints for ADHD in children and adolescents. Study subjects wore d-ATS for 9 hours, and an improvement in Swanson, Kotkin, Agler, M-Flynn, and Pelham scale (SKAMP) total score was observed from 2 through 12 hours after application. Patients with ADHD may need varying durations of treatment for symptoms from day to day. This analysis describes the exposure-response (E-R) relationship for d-ATS and explores possible outcomes for wear times ≤9 hours under varying assumptions.

Methods. A population pharmacokinetic (PK) model was developed to describe AMP disposition following d-ATS administration. This model was used to construct a population pharmacokinetic/pharmacodynamic (PK/PD) model from SKAMP total score data from two pediatric clinical studies to characterize onset and duration of effect after d-ATS administration. The integrated PK/PD model was used to describe the d-ATS E-R relationship and simulate the potential onset and duration of effect of d-ATS in response to various removal times (when <9 hours) by utilizing SKAMP scores as the efficacy measure. Subject-level AMP PK and SKAMP profiles were simulated for d-ATS removal at 4–9 hours post-application under different assumptions for AMP absorption after early patch removal. Modifications were made to the original population PK model to simulate patch removal.

Results. Data from 81 children and 41 adolescents, 6–17 years old, were included. The model provided a reasonable description of the SKAMP score over time, showing an initial decline ~2 hours after patch application. In approximately 50% of children and adolescents, the maximum decline in SKAMP scores was observed within the first 4 hours after patch application. Earlier simulated d-ATS removal times were associated with reduced systemic exposure and earlier return to near-baseline scores across the range of assumptions tested.

Under different assumptions, the graphs changed modestly but not dramatically. For example, with moderate/conservative assumptions, following a 9-hour wear time, SKAMP scores returned to within 90% of baseline value in ~49% of subjects by 12 hours and ~80% of subjects by 16 hours. Following a 4-hour wear time, percentages were ~74% by 12 hours and ~95% by 16 hours.

Conclusions. Simulation results suggest that the duration of d-ATS efficacy may be related to wear time, which can be adjusted according to treatment needs, consistent with published observations for another transdermal stimulant. The d-ATS patch provides the ability to control medication exposure by shortening wear time, allowing treatment duration to be individualized and optimized in ADHD patients who have varying schedules and needs.

Funding. Noven Pharmaceuticals, Inc.

https://doi.org/10.1017/S1092852923001827 Published online by Cambridge University Press