Drug Monitor

Inhaled Insulin vs. Dual Oral Therapy

"Surprisingly effective despite its short duration of action"—that's the verdict on inhaled insulin, according to researchers who conducted a 12-week study involving 309 patients with type 2 diabetes at 48 outpatient centers in the United States and Canada.

The patients, whose diabetes was ineffectively controlled by dual oral therapy consisting of an insulin secretagogue and an insulin sensitizer, were randomly assigned to one of three treatments: premeal inhaled insulin plus the existing, stable dual oral therapy; premeal inhaled insulin alone; or continued oral therapy alone. Patients administered inhaled insulin within 10 minutes before meals and self-monitored blood glucose levels at least four times daily.

At week 12, reductions in mean glycosylated hemoglobin (HbA_{1C}) levels were significantly greater in both inhaled insulin groups, compared to the dual oral therapy group. The most dramatic reductions, however, were seen in patients taking inhaled insulin along with dual oral therapy. In this group, HbA_{1C} dropped 1.9 percentage points (from 9.2% to 7.3%), compared to 1.4 percentage points (from 9.3% to 7.9%) with inhaled insulin monotherapy and 0.2 percentage points (from 9.3% to 9.1%) with oral therapy alone.

Inhaled insulin also reduced fasting plasma glucose concentrations, which suggests that its glucose lowering effects extend beyond the postprandial period. This type of effect has been observed in other studies, the researchers say, though the reason is unknown.

Inhaled insulin was well tolerated by participants, with no patients discontinuing therapy due to treatment-related adverse events. Pulmonary function was similar between the treatment groups, despite an increase in mild cough observed with inhaled insulin therapy. Other adverse effects associated with inhaled insulin were mild weight gain (which is consistent with all forms of insulin therapy) and an increase in hypoglycemic events.

Source: *Ann Intern Med.* 2005;143:549–558.

Pindolol for Fibromyalgia

Early research offers new hope for patients who experience the pain, stiffness, and restless sleep of fibromyalgia (FM). Hypothesizing that the moderately lipophilic nature of pindolol, a mixed $serotonin_{1A}$ presynaptic autoreceptor/beta-adrenergic receptor antagonist, might allow the drug to penetrate the central nervous system better than selective serotonin reuptake inhibitors (SSRIs) in order to exert its antiadrenergic and proserotonergic effects, researchers from Louisiana State University tested the drug in an open-label trial involving 20 female patients with FM.

Participants began treatment with pindolol 2.5 mg three times daily and were titrated to a maximum dosage of 5 mg three times daily over the 90-day study period. Researchers administered the Tender Point Count (TPC) and Tender Point Score (TPS) instruments, which test the presence of tenderness to light palpation at 18 discrete locations, at the initial screening visit and all subsequent visits. Participants also completed the Fibromyalgia Impact Questionnaire (FIQ)—a 19-item, self-report instrument widely used to evaluate FM severity and treatment efficacy—at each visit and the Fibromyalgia Symptom Inventory—a currently unvalidated self-report instrument developed by the researchers to monitor a broad spectrum of FM symptoms—at screening and at the end of weeks four, eight, and 12.

Of the 15 women who completed the study, 12 were titrated up to and maintained the maximum dosage, two remained at the starting dosage, and one was stabilized at a single bedtime dose of 5 mg. In general, the drug was well tolerated, with minimal adverse effects that were consistent with the drug's labeling (such as increased dreaming, perspiration, fatigue, and headache).

The group as a whole demonstrated significant improvement in primary outcome measures, including TPC, TPS, and FIQ scores. In addition to relieving the cardinal FM symptoms, pindolol treatment helped improve such secondary symptoms as dizziness, cold sensitivity, and headache. Results did not differ significantly between patients who were taking an SSRI at the time of enrollment and those who were not.

Findings from this preliminary study—which the researchers say is the first to test an adrenergic antagonist in FM—appear to support the hypothesis that sympathetic hyperactivity plays a role in the development and maintenance of this condition. The fact that FM pain has not been linked to peripheral pathology, the researchers note, has led many to suspect hypersensitivity within nociceptive pathways, a form of so-called central sensitization, which amplifies sensory processing. By reducing sympathetic tone, pindolol may reduce the adrenergic component of muscle tension and, thus, the signal available for amplification. ●

Source: *Ann Pharmacother.* 2005;39:1812–1816.