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Humalog Mix75/25 vs. Lantus in Type 2 Diabetes

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Study Results Unveiled at the American Diabetes Association Annual Scientific Sessions

When people are first diagnosed with type 2 diabetes - the most common form of diabetes - they are often treated with diet and exercise and/or oral medications. Over time, as the disease progresses, patients frequently require insulin therapy.

In two separate studies comparing Humalog[®] Mix75/25[™] to Lantus, the former did a better job than the latter of helping patients with type 2 diabetes lower their blood sugar levels and achieve better diabetes control over time.

Humalog[®] Mix75/25[™] (75% insulin lispro protamine suspension, 25% insulin lispro injection [rDNA origin]) is an insulin analog mixture. Lantus (insulin glargine [rDNA origin] injection) is a basal insulin analog.

"Maintaining control of blood sugar is important for all patients with diabetes in order to prevent the onset of debilitating and sometimes fatal diabetes-related complications, such as stroke and heart disease," said James Malone, M.D., who was involved in conducting both studies and is a diabetes medical director at Eli Lilly and Company, which developed Humalog Mix75/25. "These studies indicate the benefit of a twice-daily insulin analog mixture on achieving and maintaining improved glucose control specifically in patients with type 2 diabetes."

In the studies, both of which were open label, blood sugar, or glucose, levels were measured via a glycosylated hemoglobin test (A1C), a standard test used by health care professionals when treating patients with diabetes. An A1C shows a patient's "average" blood sugar level over the previous two or three months, thereby giving an overall picture of his or her diabetes control.

Both studies compared the responses of twice-daily Humalog Mix75/25 plus metformin (a commonly-prescribed oral medication for type 2 diabetes) to once-daily Lantus plus metformin on A1C levels, post-meal blood glucose levels and overall rates of hypoglycemia (low blood sugar). Managing glucose levels, including post-meal glucose levels, is critical to diabetes control.

Study one consisted of 105 patients in the United States with type 2 diabetes who were new to insulin therapy. Participants received 32 weeks of treatment - 16 weeks with each insulin (Humalog Mix75/25 and Lantus, though not necessarily in that order) plus metformin.

According to the results, which were presented today at the annual meeting of the American Diabetes Association (ADA) Scientific Sessions in Orlando, Fla:

- A1C results were significantly improved in both groups, but the improvement was greater for Humalog Mix75/25.
 - The A1C endpoint was the primary objective of this study. The average A1C at endpoint for Humalog Mix75/25 was 7.4 percent and for Lantus 7.8 percent.
 - On average, A1C results dropped 1.3 percent when patients received Humalog Mix75/25. By comparison, when patients received Lantus, their A1C results dropped an average of 0.9 percent.
- At the study's conclusion, 41 percent of patients treated with Humalog Mix75/25 achieved an A1C level of 7 percent or lower. The ADA recommends a target A1C of less than 7.0 percent. Twenty-two percent of patients on Lantus achieved an a1C level of 7 percent or lower at the end of the study.
- Humalog Mix 75/25 was associated with a smaller rise in glucose levels after participants ate breakfast and dinner meals.
 - The average rise in post-breakfast glucose levels for Humalog Mix75/25 was 18 mg/dL compared to 47 mg/dL for Lantus.

- o The average rise in post-dinner glucose level was 14 mg/dL for Humalog Mix75/25 and 40 mg/dL for Lantus.
- After 16 weeks of treatment, patients taking Lantus had lower rates of hypoglycemia compared to those treated with Humalog Mix75/25. On average, patients treated with Lantus had .39 episodes per month compared to .68 episodes per month for those on Humalog Mix75/25. No instances of severe hypoglycemia were reported in either study arm.
 - o Among participants, the rate of hypoglycemia during sleep was similar after 16 weeks of treatment with each insulin (.14 episodes per patient per month with Humalog Mix 75/25 vs.. .24 episodes per patient per month with Lantus).

Study two consisted of 97 patients from Europe whose blood sugar was not under control despite treatment with insulin therapy one or twice a day, or insulin combination with oral medications. All patients were treated with bedtime NPH plus metformin for a six-week lead-in period, so that apples could be compared to apples, so to speak. As in study one, participants received 32 weeks of treatment, - 16 weeks each with Humalog Mix75/25 and Lantus Both insulins were given with metformin

Results of study showed that:

- The A1C at endpoint was the primary objective of this study. The average A1C at endpoint for Humalog Mix75/25 was 7.5 percent and for Lantus 8.1 percent.
- On average, patients treated with Humalog Mix75/25 showed a greater reduction in A1C levels compared to those same patients treated with Lantus (1 percent vs.. 0.42 percent respectively).
- At the study's conclusion, 30 percent of patients on Humalog Mix75/25 achieved a target A1C level of seven percent or lower, compared to 12 percent on Lantus.
- On average, the increase in glucose levels after all three main meals (breakfast, lunch and dinner) were 27 mg/dL lower among patients treated with Humalog Mix75/25 compared to Lantus. As expected, fasting blood glucose levels were lower in the Lantus group (the average was 127 mg/dL for Lantus and 140 mg/dL for Humalog Mix75/25).
- Overall hypoglycemia rates were not significantly different between either treatment arm and no instances of severe hypoglycemia were reported in either group.
 - o However, on average, patients treated with Humalog Mix75/25 had fewer episodes of hypoglycemia during sleep than those patients with Lantus (.14 episodes per patients per month compared to .34 episodes per patients per month.)

"These data are further evidence of the benefit of using a pre-mixed insulin at mealtimes compared with once daily insulin," said John Holcombe, M.D., a diabetes medical advisor at Lilly. "Moreover, the results of this study support the growing body of evidence that suggests controlling blood sugar levels at mealtimes is important in achieving overall improved glycemic control in patients with type 2 diabetes."

About Humalog Mix75/25

Humalog Mix75/25 is for use in patients with diabetes to control high blood sugar. Humalog Mix75/25 starts lowering blood glucose more quickly than regular human insulin, allowing for convenient dosing immediately before a meal (within 15 minutes). By combining the benefits of the rapid-acting Humalog with an intermediate-acting insulin, Humalog Mix75/25 provides blood glucose control throughout the day - at mealtime, between meals, and at nighttime. It is available by prescription only. Humalog Mix75/25 is not indicated for use with metformin.

Important Safety Information

Potential side effects associated with the use of all insulins include low blood sugar, weight gain, low blood potassium, changes in fat tissue at the side of injection, and allergic reactions, both general and local. Humalog Mix75/25 should not be mixed with another insulin. Starting or changing insulin therapy should be done cautiously and only under medical supervision.

For full prescribing information on Humalog Mix75/25 go to www.Humalog.com. or call 1-800-LILLYRX. For full prescribing information on Lantus, go to www.Lantus.com.

About Eli Lilly and Company

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Humalog® Mix75/25™ (75% insulin lispro protamine suspension, 25% insulin lispro injection [rDNA origin], Lilly)
Lantus® (insulin glargine [rDNA origin] injection), Aventis Pharmaceuticals)



Humalog Mix75/25 Pen