# Clinical Experience With the Addition of Pramlintide in Patients With Insulin-Requiring Type 2 Diabetes

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Pramlintide, a synthetic amylin analog, was approved for type 2 diabetes as an adjunct treatment in patients who have failed to achieve desired glycemic control, despite optimal insulin therapy, with or without concomitant administration of oral antidiabetes agents (1). In clinical trials, pramlintide added to insulin treatment in patients with type 2 diabetes was shown to reduce postprandial glucose levels, improve glycemic control, and promote weight loss (2–8). We reviewed the medical records of our patients with type 2 diabetes who were on pramlintide in addition to insulin treatment to assess the efficacy of mealtime pramlintide on glycemic control and cardiometabolic risk factors in a single endocrine clinical practice setting.

## RESEARCH DESIGN AND METHODS

We retrospectively studied laboratory and medical parameters of 92 insulin-treated adult patients with type 2 diabetes (54 female, 38 male, aged 24–80 years) recorded at baseline, 12 ± 4 weeks, and 24 ± 4 weeks after initiating pramlintide therapy. Medical and laboratory information were pulled from the main database of the Metabolic Center of Louisiana through a query that extracted information on all patients with type 2 diabetes treated with insulin who were unable to achieve glycemic control and who had completed at least 24 weeks of pramlintide treatment from June 2005 to November 2006. Patients with type 1 diabetes, patients with type 2 diabetes not on insulin, and patients with normal blood glucose were excluded. The primary efficacy end point was the change in A1C from baseline to 24 weeks. Secondary efficacy end points included the changes in lipids, abdominal girth, BMI, and total body weight over time (from baseline to 24 weeks). We also evaluated information about changes in dose(s) of other antidiabetes medications and lipid-lowering agents. The first 100 patients meeting inclusion/exclusion criteria with a complete set of pre-, intermediate, and posttreatment primary and secondary end point variables were used to avoid selection bias; 8 of these patients were subsequently excluded from the data analyses because some of their laboratory tests were performed at a different site and could not be compared. The Western Institutional Review Board approved the retrospective study protocol and waived consent.

### Statistical analysis

The data were analyzed using a SS × Trials design (repeated measures at baseline, 12 weeks, and 24 weeks of treatment). Multinomial logistic regression analyses were performed to correct for confounding variables. Significance was accepted at $P < 0.05$ (two-tailed test).

## RESULTS

The study population of 54 women and 38 men encompassed a wide range of ages (24–80 years), body weights, and entry A1C values. The majority of patients were overweight or obese. Glycemic control, anthropometric parameters, and serum lipid levels at baseline and at 24 weeks after start of pramlintide therapy are shown in Table 1. Mean A1C fell significantly ($P = 0.0125$) from baseline to end point after adjunctive pramlintide treatment (from 8.3 to 7.86% at 24 weeks). The decrease in A1C with pramlintide at 24 weeks was accompanied by a significant reduction ($P = 0.029$) in average body weight (104.4 to 103.2 kg). A reduction in A1C with pramlintide treatment occurred despite the reduction of premeal insulin and minimal adjustments in basal insulin doses and oral hypoglycemic agents.

The majority of patients exhibited a progressive decrease ($P = 0.019$) in BMI; however, mean abdominal girth did not significantly change from baseline (111.8 cm) to the posttreatment 24-week visit (111.5 cm; $P > 0.05$). Lipid profiles showed improvement over the treatment period; however, only the reduction of mean LDL cholesterol levels was statistically significant ($P = 0.029$) (Table 1). Improvements in lipid profiles with adjunct pramlintide were not attributable to changes in lipid-lowering agents. Neither sex ($P = 0.3$) nor age ($P = 0.5$) were significant independent predictors of A1C or BMI when interactions between parameters were considered over patient visits.

## CONCLUSIONS

While several clinical trials in patients with type 2 diabetes have consistently shown that the addition of pramlintide to preexisting insulin regimens led to a further improvement in glycemic control (2–5), this retrospective analysis provides further insight into the potential clinical benefits of adjunctive therapy with pramlintide in this patient population. Pramlintide improved glycemic control in our patients regardless of age, sex, body weight, diabetes duration, and preexisting antihyperglycemic therapy. In our predominantly obese patient population, we observed reduc-

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A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

**Table 1—*Summary of body composition, A1C, and lipid levels before and after treatment with pramlintide >24 weeks***

| Parameter | Baseline | Pramlintide (>24 weeks) | *P* |
|---|---|---|---|
| A1C (%) | 8.32 ± 0.17 | 7.86 ± 0.16 | 0.0125 |
| Body weight (kg) | 104.4 ± 2.1 | 103.2 ± 2.07 | 0.029 |
| BMI (kg/m$^2$) | 35.2 ± 0.6 | 34.7 ± 0.6 | 0.019 |
| Abdominal girth (cm) | 111.76 ± 1.5 | 111.5 ± 1.4 | 0.5 |
| Cholesterol (mmol/l) | 4.65 ± 0.13 | 4.46 ± 0.12 | 0.06 |
| Triglyceride (mmol/l) | 1.78 ± 0.11 | 1.72 ± 0.13 | 0.61 |
| HDL cholesterol (mmol/l) | 1.29 ± 0.05 | 1.25 ± 0.05 | 0.15 |
| LDL cholesterol (mmol/l) | 2.57 ± 0.1 | 2.38 ± 0.09 | 0.029 |

Data are means ± SE.

tions in A1C with pramlintide therapy that were generally associated with a mean weight loss. It is also worth mentioning that the observed weight reduction with pramlintide therapy occurred in patients who had been on established insulin therapy and who had not been required to change their diet and exercise regimen. This weight loss may be attributed not only to pramlintide but also to decreased insulin doses; treatment with insulin and oral antihyperglycemic agents, with the exception of metformin (9,10), is frequently accompanied by weight gain. A notable finding in our study is the fact that abdominal girth did not consistently decrease despite weight loss and lower BMI.

When interpreting the magnitude of A1C reductions with pramlintide treatment, it is important to recognize that pramlintide was added as an adjunct to the preexisting diabetes regimen. It can be concluded that the pramlintide in conjunction with insulin therapy is efficacious in improving glycemic control and reducing body weight in patients with type 2 diabetes. While we acknowledge some limitations of our study design, pramlintide as an adjunctive therapy to insulin and other antidiabetes medications appears to be a potential treatment option for overweight insulin-requiring patients with type 2 diabetes. Future prospective randomized studies designed to further explore the clinical significance of our findings are needed.

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