

Program Helps Teens Lose Weight, Cut Lipids

BY KERRI WACHTER

BALTIMORE — An intensive multidisciplinary weight-loss program can help obese adolescents lose weight and reduce lipid levels, a small study has shown.

By combining clinical care, nutrition, behavioral counseling, and exercise guidance, 28 teens in the program significantly reduced their body mass index by an average of 3 kg/m², Dr. Susan J. Wool-

ford reported in a poster session at the annual meeting of the Pediatric Academic Societies. The teens had significant reductions in fasting total cholesterol, LDL, and triglycerides, said Dr. Woolford of the division of general pediatrics at the University of Michigan, Ann Arbor.

The Michigan Pediatric Outpatient Weight Evaluation and Reduction (MPOWER) program helps obese adolescents aged 12-17 years identify causes

of their weight gain as a strategy for reducing their weight. During the first visit, patients receive a complete medical evaluation including lab tests aimed at identifying possible causes for, and complications from, their weight gain. Patients with complications from their obesity may be referred to other University of Michigan subspecialty clinics.

A registered dietitian provides personalized dietary assessments and nutrition

education. The program's family-focused treatment of obesity includes dietitian home visits to assess barriers to weight loss and help families improve the likelihood of success.

The program includes regular visits with pediatric therapists who specialize in weight loss. They work with families to help motivate behavioral changes and build confidence in new lifestyle habits. Each patient receives fitness evaluations and regular physical activity instruction from a physiologist. Exercise classes are tailored to adolescents, and a well-equipped exercise facility is accessible. Patients are taught new kinetic skills to help them become more active in their home environment.

The retrospective study included obese adolescents enrolled in the MPOWER program between April 2007 and July 2008 with a BMI greater than or equal to the 95th percentile for age and sex. Patients were excluded if they were taking cholesterol-lowering medications or obeso-genic medications (such as steroids), or had a moderately severe mental illness.

They were weighed weekly, and their height was measured at weeks 1, 12, and 23. Lipids were measured at weeks 1 and 23. The researchers calculated mean changes in weight and BMI using measurements taken at weeks 1 and 23. Differences in fasting lipid levels at weeks 1 and 23 were calculated.

Twenty-eight patients completed 6 months in the program and their initial and final laboratory levels were available. Mean age was 15 years; 69% were female. Almost half (44%) received Medicaid. Most patients were white (64%) and 28% were black.

Final mean fasting levels of total cholesterol, LDL, and triglycerides were significantly lower than were the initial mean levels. The mean reduction in fasting total cholesterol was 7 mg/dL, with a final average level of 156.6 mg/dL. Fourteen patients had borderline or elevated initial total cholesterol levels (greater than 170 mg/dL). Eleven of these patients reduced their total cholesterol over 6 months. Eight had final levels in the normal range.

Mean reduction in fasting LDL was 2.7 mg/dL, with a final average level of 98 mg/dL. Eleven patients had borderline or elevated initial LDL (greater than 110 mg/dL). Nine of them reduced their LDL. Six had final levels in the normal range.

The mean reduction in fasting triglycerides was 24.2 mg/dL, with a final mean level of 97.6 mg/dL. Eight patients had elevated initial triglyceride levels (greater than 150 mg/dL). Seven of these patients reduced their triglycerides levels to the normal range. Two teens with strong family histories of dyslipidemia had lipid levels that did not decrease with weight loss. Three teens who initially had normal lipid levels had elevated final levels, but all three lost weight during the program.

The study was funded by the University of Michigan Pediatric Comprehensive Weight Management Center. ■

Reference: 1. Bode BW, Strange P. Efficacy, safety, and pump compatibility of insulin aspart used in continuous subcutaneous insulin infusion therapy in patients with type 1 diabetes. *Diabetes Care*. 2001;24(1):69-72.

NovoLog® (insulin aspart [rDNA origin] injection)

Rx only

BRIEF SUMMARY. Please consult package insert for full prescribing information.

INDICATIONS AND USAGE: NovoLog® is an insulin analog indicated to improve glycemic control in adults and children with diabetes mellitus.

CONTRAINDICATIONS: NovoLog® is contraindicated during episodes of hypoglycemia and in patients hypersensitive to NovoLog® or one of its excipients.

WARNINGS AND PRECAUTIONS: Administration: NovoLog® has a more rapid onset of action and a shorter duration of activity than regular human insulin. An injection of NovoLog® should immediately be followed by a meal within 5-10 minutes. Because of NovoLog®'s short duration of action, a longer acting insulin should also be used in patients with type 1 diabetes and may also be needed in patients with type 2 diabetes. Glucose monitoring is recommended for all patients with diabetes and is particularly important for patients using external pump infusion therapy. Any change of insulin dose should be made cautiously and only under medical supervision. Changing from one insulin product to another or changing the insulin strength may result in the need for a change in dosage. As with all insulin preparations, the time course of NovoLog® action may vary in different individuals or at different times in the same individual and is dependent on many conditions, including the site of injection, local blood supply, temperature, and physical activity. Patients who change their level of physical activity or meal plan may require adjustment of insulin dosages. Insulin requirements may be altered during illness, emotional disturbances, or other stresses. Patients using continuous subcutaneous insulin infusion pump therapy must be trained to administer insulin by injection and have alternate insulin therapy available in case of pump failure.

Hypoglycemia: Hypoglycemia is the most common adverse effect of all insulin therapies, including NovoLog®. Severe hypoglycemia may lead to unconsciousness and/or convulsions and may result in temporary or permanent impairment of brain function or death. Severe hypoglycemia requiring the assistance of another person and/or parenteral glucose infusion or glucagon administration has been observed in clinical trials with insulin, including trials with NovoLog®. The timing of hypoglycemia usually reflects the time-action profile of the administered insulin formulations [see *Clinical Pharmacology*]. Other factors such as changes in food intake (e.g., amount of food or timing of meals), injection site, exercise, and concomitant medications may also alter the risk of hypoglycemia [see *Drug Interactions*]. As with all insulins, use caution in patients with hypoglycemia unawareness and in patients who may be predisposed to hypoglycemia (e.g., patients who are fasting or have erratic food intake). The patient's ability to concentrate and react may be impaired as a result of hypoglycemia. This may present a risk in situations where these abilities are especially important, such as driving or operating other machinery. Rapid changes in serum glucose levels may induce symptoms of hypoglycemia in persons with diabetes, regardless of the glucose value. Early warning symptoms of hypoglycemia may be different or less pronounced under certain conditions, such as longstanding diabetes, diabetic nerve disease, use of medications such as beta-blockers, or intensified diabetes control [see *Drug Interactions*]. These situations may result in severe hypoglycemia (and, possibly, loss of consciousness) prior to the patient's awareness of hypoglycemia. Intravenously administered insulin has a more rapid onset of action than subcutaneously administered insulin, requiring more close monitoring for hypoglycemia. **Hypokalemia:** All insulin products, including NovoLog®, cause a shift in potassium from the extracellular to intracellular space, possibly leading to hypokalemia that, if left untreated, may cause respiratory paralysis, ventricular arrhythmia, and death. Use caution in patients who may be at risk for hypokalemia (e.g., patients using potassium-lowering medications, patients taking medications sensitive to serum potassium concentrations, and patients receiving intravenously administered insulin). **Renal Impairment:** As with other insulins, the dose requirements for NovoLog® may be reduced in patients with renal impairment [see *Clinical Pharmacology*]. **Hepatic Impairment:** As with other insulins, the dose requirements for NovoLog® may be reduced in patients with hepatic impairment [see *Clinical Pharmacology*]. **Hypersensitivity and Allergic Reactions: Local Reactions -** As with other insulin therapy, patients may experience redness, swelling, or itching at the site of NovoLog® injection. These reactions usually resolve in a few days to a few weeks, but in some occasions, may require discontinuation of NovoLog®. In some instances, these reactions may be related to factors other than insulin, such as irritants in a skin cleansing agent or poor injection technique. Localized reactions and generalized myalgias have been reported with injected metacresol, which is an excipient in NovoLog®. **Systemic Reactions -** Severe, life-threatening, generalized allergy, including anaphylaxis, may occur with any insulin product, including NovoLog®. Anaphylactic reactions with NovoLog® have been reported post-approval. Generalized allergy to insulin may also cause whole body rash (including pruritus), dyspnea, wheezing, hypotension, tachycardia, or diaphoresis. In controlled clinical trials, allergic reactions were reported in 3 of 735 patients (0.4%) treated with regular human insulin and 10 of 1394 patients (0.7%) treated with NovoLog®. In controlled and uncontrolled clinical trials, 3 of 2341 (0.1%) NovoLog®-treated patients discontinued due to allergic reactions. **Antibody Production:** Increases in anti-insulin antibody titers that react with both human insulin and insulin aspart have been observed in patients treated with NovoLog®. Increases in anti-insulin antibodies are observed more frequently with NovoLog® than with regular human insulin. Data from a 12-month controlled trial in patients with type 1 diabetes suggest that the increase in these antibodies is transient, and the differences in antibody levels between the regular human insulin and insulin aspart treatment groups observed at 3 and 6 months were no longer evident at 12 months. The clinical significance of these antibodies is not known. These antibodies do not appear to cause deterioration in glycemic control or necessitate increases in insulin dose. **Mixing of Insulins:** Mixing NovoLog® with NPH human insulin immediately before injection attenuates the peak concentration of NovoLog®, without significantly affecting the time to peak concentration or total bioavailability of NovoLog®. If NovoLog® is mixed with NPH human insulin, NovoLog® should be drawn into the syringe first, and the mixture should be injected immediately after mixing. The efficacy and safety of mixing NovoLog® with insulin preparations produced by other manufacturers have not been studied. Insulin mixtures should not be administered intravenously. **Subcutaneous continuous insulin infusion by external pump: When used in an external subcutaneous insulin infusion pump, NovoLog® should not be mixed with any other insulin or diluent.** When using NovoLog® in an external insulin pump, the NovoLog®-specific information should be followed (e.g., in-use time, frequency of changing infusion sets) because NovoLog®-specific information may differ from general pump manual instructions. Pump or infusion set malfunctions or insulin degradation can lead to a rapid onset of hyperglycemia and ketosis because of the small subcutaneous depot of insulin. This is especially pertinent for rapid-acting insulin analogs that are more rapidly absorbed through skin and have a shorter duration of action. Prompt identification and correction of the cause of hyperglycemia or ketosis is necessary. Interim therapy with subcutaneous injection may be required [see *Dosage and Administration, Warnings and Precautions, How Supplied/Storage and Handling, and Patient Counseling Information*]. NovoLog® is recommended for use in pump systems suitable for insulin infusion as listed below. **Pumps:** MiniMed 500 series and other equivalent pumps. **Reservoirs and infusion sets:** NovoLog® is recommended for use in reservoir and infusion sets that are compatible with insulin and the specific pump. In-vitro studies

have shown that pump malfunction, loss of metacresol, and insulin degradation, may occur when NovoLog® is maintained in a pump system for longer than 48 hours. Reservoirs and infusion sets should be changed at least every 48 hours. NovoLog® should not be exposed to temperatures greater than 37°C (98.6°F). **NovoLog® that will be used in a pump should not be mixed with other insulin or with a diluent** [see *Dosage and Administration, Warnings and Precautions and How Supplied/Storage and Handling, Patient Counseling Information*].

ADVERSE REACTIONS: Clinical Trial Experience: Because clinical trials are conducted under widely varying designs, the adverse reaction rates reported in one clinical trial may not be easily compared to those rates reported in another clinical trial, and may not reflect the rates actually observed in clinical practice. **Hypoglycemia:** Hypoglycemia is the most commonly observed adverse reaction in patients using insulin, including NovoLog® [see *Warnings and Precautions*]. **Insulin initiation and glucose control intensification:** Intensification or rapid improvement in glucose control has been associated with a transitory, reversible ophthalmologic refraction disorder, worsening of diabetic retinopathy, and acute painful peripheral neuropathy. However, long-term glycemic control decreases the risk of diabetic retinopathy and neuropathy. **Lipodystrophy:** Long-term use of insulin, including NovoLog®, can cause lipodystrophy at the site of repeated insulin injections or infusion. Lipodystrophy includes lipohypertrophy (thickening of adipose tissue) and lipatrophy (thinning of adipose tissue), and may affect insulin absorption. Rotate insulin injection or infusion sites within the same region to reduce the risk of lipodystrophy. **Weight gain:** Weight gain can occur with some insulin therapies, including NovoLog®, and has been attributed to the anabolic effects of insulin and the decrease in glucosuria. **Peripheral Edema:** Insulin may cause sodium retention and edema, particularly if previously poor metabolic control is improved by intensified insulin therapy. **Frequencies of adverse drug reactions:** The frequencies of adverse drug reactions during NovoLog® clinical trials in patients with type 1 diabetes mellitus and type 2 diabetes mellitus are listed in the tables below.

Table 1: Treatment-Emergent Adverse Events in Patients with Type 1 Diabetes Mellitus (Adverse events with frequency ≥ 5% and occurring more frequently with NovoLog® compared to human regular insulin are listed)

Preferred Term	NovoLog® + NPH N=596		Human Regular Insulin + NPH N=286	
	N	(%)	N	(%)
Hypoglycemia*	448	75%	205	72%
Headache	70	12%	28	10%
Injury accidental	65	11%	29	10%
Nausea	43	7%	13	5%
Diarrhea	28	5%	9	3%

*Hypoglycemia is defined as an episode of blood glucose concentration <45 mg/dL with or without symptoms. See *Clinical Studies* for the incidence of serious hypoglycemia in the individual clinical trials.

Table 2: Treatment-Emergent Adverse Events in Patients with Type 2 Diabetes Mellitus (except for hypoglycemia, adverse events with frequency ≥ 5% and occurring more frequently with NovoLog® compared to human regular insulin are listed)

	NovoLog® + NPH N=91		Human Regular Insulin + NPH N=91	
	N	(%)	N	(%)
Hypoglycemia*	25	27%	33	36%
Hyporeflexia	10	11%	6	7%
Onychomycosis	9	10%	5	5%
Sensory disturbance	8	9%	6	7%
Urinary tract infection	7	8%	6	7%
Chest pain	5	5%	3	3%
Headache	5	5%	3	3%
Skin disorder	5	5%	2	2%
Abdominal pain	5	5%	1	1%
Sinusitis	5	5%	1	1%

*Hypoglycemia is defined as an episode of blood glucose concentration <45 mg/dL, with or without symptoms. See *Clinical Studies* for the incidence of serious hypoglycemia in the individual clinical trials.

Postmarketing Data: The following additional adverse reactions have been identified during postapproval use of NovoLog®. Because these adverse reactions are reported voluntarily from a population of uncertain size, it is generally not possible to reliably estimate their frequency. Medication errors in which other insulins have been accidentally substituted for NovoLog® have been identified during postapproval use [see *Patient Counseling Information*].

OVERDOSAGE: Excess insulin administration may cause hypoglycemia and, particularly when given intravenously, hypokalemia. Mild episodes of hypoglycemia usually can be treated with oral glucose. Adjustments in drug dosage, meal patterns, or exercise, may be needed. More severe episodes with coma, seizure, or neurologic impairment may be treated with intramuscular/subcutaneous glucagon or concentrated intravenous glucose. Sustained carbohydrate intake and observation may be necessary because hypoglycemia may recur after apparent clinical recovery. Hypokalemia must be corrected appropriately.

More detailed information is available on request.

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NovoLog® is covered by US Patent Nos 5,618,913; 5,866,538; and other patents pending.

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NovoLog®
insulin aspart (rDNA origin) injection