

NUEVAS INSULINAS, SENSORES DE GLUCOSA Y SISTEMAS DE LIBERACIÓN EN NIÑOS CON DIABETES TIPO 1

Denis Daneman MB BCh FRCPC

Professor of Pediatrics. University of Toronto. Chief - Division of Endocrinology. The Hospital for Sick Children. Toronto, Canada.

Although advanced complications are rare in youth, the demonstration of metabolic memory in follow-up studies of the DCCT cohort, demands implementation of tight glycemic control in all individuals with T1D as early as possible after diagnosis. This is particularly difficult in the pediatric population owing to the increased risk for hazardous hypoglycemia, fluctuating insulin requirements due to exercise, illness, variable carbohydrate intake, as well as psychosocial and physiological issues related to age, puberty and weight gain. Furthermore, adolescents with T1D have higher average HbA1c levels compared to those in the adult population. For the moment better outcomes for children and teens with T1D depend in large part on the ability to more appropriately tailor the insulin regimen for each individual. The presentation will review: use of insulin analogs, newer monitoring systems and delivery devices.

A. INSULINS

Different centers use different approaches to insulin therapy, with increasingly more using basal-bolus approaches with either multiple daily insulin injections (MDI) or CSII. MDI has traditionally comprised NPH or Ultralente given once or twice daily as the basal insulin with regular human insulin boluses before meals. With the availability of both fast- and very long-acting insulin analogues, MDI now mainly uses insulin glargine (Lantus) or detemir (Levemir) as the basal insulin and insulin lispro (Humalog) or aspart (Novorapid/Novolog) as the premeal boluses. CSII employs fast-acting insulin analogues in a continuous basal rate with premeal boluses. When basal-bolus routines are meticulously used together with the other aspects of management, at least a proportion of individuals with T1D are able to maintain near normal glycemic control.

Both a meta-analysis and Cochrane Review compared intensive therapy regimens with fast-acting insulin analogues to regular insulin. A small (-0.1 to -0.15%), but significant decrease in HbA1c was seen with the analogues, with comparable results between the analogues and regular insulin in terms of overall hypoglycemia. Quality of life was significantly better with analogue use, due

largely to the shorter interval between injection and food intake.

A number of RCTs as well as observational studies have evaluated insulin glargine or detemir in adults and children with T1D. All subjects in these trials used basal-bolus insulin regimens. Most found no differences in HbA1c levels between groups receiving insulin glargine or detemir and those receiving NPH. A few reported significant HbA1c decreases of 0.1-0.5% when insulin glargine was compared to NPH or Ultralente. Some studies reported less night- or day-time hypoglycemia or less severe hypoglycemic events in those receiving insulin glargine.

Studies in children and adolescents with T1D using insulin analogues show similar findings to those in adults.

B. MONITORING GLYCEMIC CONTROL

Self-monitoring of blood glucose (SMBG) is fundamental to good diabetes care. More frequent monitoring is generally associated with lower HbA1c levels, avoidance of hypoglycemia and lifestyle flexibility when the results are used to assist the individual in their dietary choices, physical activity and insulin doses.

Available glucose monitors are now much smaller, require very small amounts of blood (2-10 mL), are faster at providing a result (5-15 sec), and can be used at sites other than fingertips. Verification of accuracy of SMBG is required by comparing results obtained on the patient's meter with a simultaneous specimen sent to the laboratory.

Most meters incorporate data management systems; however, maintaining a blood glucose logbook is necessary to detect patterns of glucose control and make appropriate dose adjustments. Recently, continuous glucose monitoring technologies with subcutaneous sensors, have become increasingly used in clinical care as a means of accessing more complete glycemic data than is available with traditional SMBG.

While SMBG reflects day-to-day variations in blood glucose levels, long-term control is best measured by HbA1c levels, reflecting average glycemia over the previous 90-120 days. Each laboratory needs to standardize its HbA1c as-

say against either the DCCT or another internationally recognized reference laboratory since there are no universal standards against which individual assays can be calibrated.

Insulin and monitoring are two of the many aspects of the comprehensive management of T1D in childhood, others being attention to meal planning, psychosocial issues, physical activity and other nonbasal conditions.

REFERENCES

1. Bui H, Perlman K, Daneman D. Glucose monitoring: future directions. *Pediatric Diabetes* 6:50-62, 2005.
9. National Institute for clinical Excellence (December 2002): Guidance on the use of long acting insulin analogues for the treatment of diabetes-insulin glargine. Technology appraisal guidelines No.53.
10. Rami B, Schober E. Postprandial glycaemia after regular and lispro insulin in children and adolescents with diabetes. *Eur J Pediatr* 2000;156:838-40.
11. Ford-Adams ME, Murphy NP, Moore EJ, Edge A, Ong KL, mWatts AP, et al. Insulin lispro, a potential role in preventing nocturnal hypoglycemia in young children with diabetes mellitus. *Diabet Med* 2003;20:656-60.
12. Deeb LC, Holcombe JH, Brunelle R, Zalani S, Brink S, Jenner M, et al. Insulin lispro lowers postprandial glucose in prepubertal children with diabetes. *Pediatrics* 2001;108(5):1175
13. Rutledge KS, Chase HP, Klingensmith GL, Walrvens PA, Slover RH, Garg SK. Effectiveness of postprandial humalog in toddlers with diabetes. *Pediatrics* 1997;100:968-72.
14. Chase HP, Dixon B, Pearson J, Fiallo-Scharer R, Walravens P, Klingensmith G, Rewers Marian, Garg SK. Reduced hypoglycemic episodes and improved glycemic control in children with type 1 diabetes using insulin glargine and neutral protamine hagedorn insulin. *J Pediatr* 2003;143:737-40.
15. Chapman TM and Perry CM. Insulin detemir: a review of its use in the management of type 1 and 2 diabetes mellitus. *Drugs* 2004;64(22):2577-95.
16. Mohn A, Strang S, Wernicke-panten K, Lang AM, Edge JA, Dunger DB. Nocturnal glucose control and free insulin levels in children with type 1 diabetes by use of the long acting insulin HOE 901 as part of a three injection regimen. *Diabetes Care* 2000;23(4):557-9.
17. Danne T, Lupke K, Walte K, Schuetz W, Galil M. Insulin detemir is characterized by a consistent pharmacokinetic profile across age-groups in children, adolescents, and adults with type 1 diabetes. *Diabetes Care* 2003;26:3087-92.
18. Schober E, Schoenle E, Van Dyk J, Wenicke-Panten K. The pediatric study group of insulin glargine. Comparative trial between insulin glargine and NPH insulin in children and adolescents with type 1 diabetes mellitus. *J Pediatric Endocrinol Metabol* 2002;15:369-76.
19. Garg SK, Carmain JA, Braddy KC, Anderson JH, Vignati L, Jennings MK, Chase HP. Pre-meal insulin analogue insulin Lispro vs Humulin R Insulin treatment in youth subjects with type 1 diabetes. *Diab Med* 1996;13(1):47-52.
20. Holcombe JH, Zalani S, Arora VK, Mast CJ, for the Lispro in adolescents study group. comparison of insulin lispro with regular human insulin for the treatment of type 1 diabetes in adolescents. *Clin Ther* 2002;24:629-38.
21. Home P, Bartley P, Russel Jones D, Hanaire-Broutin H, Heeg J, Abrams P, et al. (Study to Evaluate the Administration of Detemir Insulin Efficacy, Safety and Suitability (STEADINESS) Study Group). Insulin Detemir Offers Improved Glycemic Control Compared With NPH Insulin in People With Type 1 Diabetes. *Diabetes care* 2004;27:1081-7.
22. Fritsche A, Haring H. At last, a weight neutral insulin? *Int J Obes Relat Metab Disord* 2004;28(s2):S41-6.
23. Tamborlane WV, Bonfig W, Boland E. Recent advances in treatment of youth with type 1 diabetes: better care through technology. *Diabet Med* 2001;18:864-70.