adjusted dosing using insulin detemir and a simplified algorithm (Group 1) was non-inferior to physician-directed standard-of-care dosing (Group 2). Detemir was started in either group once daily at bedtime as an add-on therapy to any other glucose-lowering regimens, or as a replacement of previous basal insulin in patients with type 2 diabetes. The primary outcome measure was HbA1c reduction from baseline.

Randomization was done at the site level. Patients from sites assigned to Group 1 adjusted their detemir dose every 3 days based on mean fasting blood glucose (FBG) values using the following simplified algorithm: mean FBG <4.4 mmol/L, reduce dose by 3U; FBG between 4.4 and 6.1 mmol/L, no change; FBG >6.1 mmol/L, increase by 3U. Detemir dose for Group 2 patients was adjusted by physicians according to the standard of care.

Mean baseline HbA1c was 8.5%. At 26 weeks, mean HbA1c was 7.9% for patients in Group 1 and 8.0% in patients in Group 2 group ($p=0.01$ between groups; $p<0.0001$ vs baseline for both groups). FBG, which was 9.7 mmol/L (178 mg/dL) at baseline, dropped to 7.8 mmol/L (143 mg/dL) in patients in Group 1 and to 8.4 mmol/L (154 mg/dL) in Group 2 patients ($p<0.0001$ between groups; $p<0.0001$ versus baseline for both groups). As expected, the reductions in HbA1c observed in the insulin-naïve subjects in Group 1 and Group 2 were substantially greater, with no significant differences between groups (-1.1% vs -1.0%, respectively; $p=0.09$ between groups; $p<0.0001$ vs baseline for both groups)

At 26 weeks most patients (88%) remained on once-daily insulin detemir (91% in Group 1, 85% in Group 2). The mean daily insulin detemir dose at 26 weeks was 0.7 and 0.5 U/kg, in Groups 1 and 2, respectively. Among insulin-naïve patients, rates of once-daily insulin detemir dosing were higher (95% in Group 1, 92% in Group 2).

At study end, the overall rates of daytime and major hypoglycemia (event/patient/year) were significantly reduced in both groups versus baseline ($p<0.05$). Daytime, nocturnal and overall hypoglycemia were significantly lower Group 2 versus Group 1 ($p<0.0001$). Weight remained constant in Group 1 but dropped from 98.2 kg to 97.9 kg in Group 2.

In summary, Prof. Meneghini said that basal insulin titration was successfully carried out in primary care practices. “Compared with standard-of-care, the 303 Algorithm resulted in better or equal improvement in glycemia with slightly greater incidence of non-major hypoglycemia, and no significant weight gain.”

MITRE: No Benefit for Continuous Glucose Monitoring Devices

The MITRE (Minimally Invasive Technology Role and Evaluation) Study, a randomized controlled trial of continuous glucose monitoring device use, showed them to be of no greater benefit than standard care. Stanton Newman, PhD, University College, London, UK, reported that all groups, including controls, had a sustained reduction of HbA1c.

Prof. Newman said that prior to MITRE, clinical trial evidence regarding the use of continuous glucose monitoring devices was limited by small sample size, the inclusion primarily of type 1 diabetes patients, and the increased attention given to those receiving the continuous glucose monitoring device. The objective of MITRE was to compare the benefits of using the GlucoWatch® G2™ Biographer (Animas) and the Continuous Glucose Monitoring System (CGMS®, MiniMed) on HbA1c versus attention control and standard treatment in a randomized controlled trial. Percentage change in HbA1c from baseline to 6, 12, and 18 months was the primary endpoint.

Patients were randomly assigned to one of MITRE’s four study arms (~100 patients each). The groups differed as follows:

- Standard Control (baseline visit only asked to test capillary blood glucose at normal frequency with Lifescan Onetouch Ultra Meter®), continued with standard care.
- Attention Control (feedback based on self-monitoring of blood glucose)
- GlucoWatch (used at times of patient choice; recommended minimum of 4x/month and maximum of 4x/week)
- CGMS (fitted at 3, 6, and 12 weeks and worn for 72 hours each time)

The participants in the two treatment groups and the attention placebo group attended three research visits. The attention control group was included to control for the impact of increased levels of contact with health care professionals in the two device groups. Planned visits were conducted with nurses trained specifically on use of the MITRE devices, interpretation of blood glucose results and delivery of appropriate feedback to patients.

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Prof. Hanas concluded, "I think the best we can do for our young children is to give them as good a start as possible through helping them achieve a low HbA1c."

Psychological Aspects in Children and Adolescents with Diabetes

There have been great advances in diabetes care over the years, with better drugs, better glucose testing and sophisticated drug delivery devices—all resulting in reduced late complications. "But while modern treatment may be better, it is still a heavy burden," stated Johnny Ludvigsson, MD, Linköping University, Sweden. He began by cautioning his audience that he is a pediatrician, not a psychologist, and his presentation would be personal and *not* balanced or scientific.

Because treatment according to the best and latest evidence is actually more complicated with more injections, more reliance on blood glucose determinations, more knowledge about diet and more skill in adjusting insulin doses—compliance is crucial and *motivation* remains the key to maintaining optimal treatment. "In spite of all our efforts, teams, and modern devices, many children and teenagers hate their diabetes." Many patients have a decreased quality of life, and depression and low self-esteem are more common among those with diabetes. Furthermore, anorexia, bulimia, and suicide are all overrepresented in diabetic populations. Also, even with active insulin treatment and carbohydrate counting, the most delicious foods need to avoided.

Once diabetes has been diagnosed, the tone of life changes and is characterized by "musts," "shoulds," "have tos," prescriptions, reminders, rules, and principles. On top of that are requirements, threats, and demands. For teenagers whose natural impulse is to test and push against boundaries, their lives are dragged in the opposite direction by "don'ts" and by strict time requirements regarding injections and meals and medical visits. "No wonder some patients give up!" Prof. Ludvigsson commented.

What can pediatricians do? "Our attitude/policy and care at diagnosis is crucial," he said. Most important is the caregiver's ability to listen and empathize, and to affirm the range of the newly diagnosed patient's feelings and questions. Information must be given honestly, but with optimism. The messages that life will not be "normal" and that rules have to be followed have to be conveyed, but so does the message that life can be "long, exciting, and happy." It is important to be aware, as well, that communication goes beyond words to body language and tone of voice.

The time period around diagnosis, the pediatrician needs to remember, is a psychological crisis for both patient and family. Efforts to include the family and other key people in the education process are important. Furthermore, the attitude that needs to be developed is that learning occurs through the problems that arise. Therefore, questions are to be expected, and the pediatrician can be expected to make sure that understanding and solutions are available.

When HbA1c is high, the underlying causes can be many, including wrong advice, inadequate science, and the patient's own fluctuating hormones or behaviors. For solutions to be found, an atmosphere of mutual confidence based more on encouragement than criticism is crucial. "We can like the patient, but dislike the disease/metabolic control—and convey the message: You are good, but your HbA1c is too high. Diabetes is our common enemy!" Out of a foundation of collaboration, short-term goals and realistic agreements can be established. In view of the complexities of modern regimens, Prof. Ludvigsson concluded, "The fundamentals of treatment of diabetes in children and adolescents—insulin, love, and care—are more relevant than ever before."

MITRE Study Results continued from page 12

The study population included individuals ≥18 years of age with insulin-requiring diabetes (≥2 injections/day), diabetes duration >6 months, and two consecutive HbA1c measurements ≥7.5%.

Mean age was ~52 years (55% men) with 57% having type 1 diabetes. Mean HbA1c, which was 9.1% at baseline, declined in all groups, although the effect waned over time. At 18 months, the reduction was 1% for the GlucoWatch group and between 4% and 5% for the other groups, with no significant differences at any time point. In the GlucoWatch group 15% of patients achieved a reduction of 12.5% from baseline HbA1c versus 29% in the CGMS group. None of the differences was significant at any time point.

Monitor use declined over time, with 20% continuing to use the GlucoWatch and 67% continuing to use CGMS. Hypoglycemic events were similar between groups. CGMS-derived information tended to alter clinical feedback more than that from GlucoWatch.

Prof. Newman concluded, "There was no group effect on HbA1c of minimally invasive monitors relative to attention control or standard control." He commented also that with all groups showing a sustained HbA1c reduction, trial participation may have led to improved metabolic control, obscuring any effects of devices.