Validation of Continuous Glucose Monitoring in Children and Adolescents With Cystic Fibrosis

A prospective cohort study

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OBJECTIVE — To validate continuous glucose monitoring (CGM) in children and adolescents with cystic fibrosis.

RESEARCH DESIGN AND METHODS — Paired oral glucose tolerance tests (OGTTs) and CGM monitoring was undertaken in 102 children and adolescents with cystic fibrosis (age 9.5–19.0 years) at baseline (CGM1) and after 12 months (CGM2). CGM validity was assessed by reliability, reproducibility, and repeatability.

RESULTS — CGM was reliable with a Bland-Altman agreement between CGM and OGTT of 0.81 mmol/l (95% CI for bias ± 2.90 mmol/l) and good correlation between the two (r = 0.74–0.9; P < 0.01). CGM was reproducible with no significant differences in the coefficient of variation of the CGM assessment between visits and repeatable with a mean difference between CGM1 and CGM2 of 0.09 mmol/l (95% CI for difference ± 0.46 mmol/l) and a discriminant ratio of 13.0 and 15.1, respectively.

CONCLUSIONS — In this cohort of children and adolescents with cystic fibrosis, CGM performed on two occasions over a 12-month period was reliable, reproducible, and repeatable.

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Statistical analysis

All data were extracted from the Medtronic Mini Med Solutions CGM sensor, MMT-730 version 3.0c (3.0.128). Mean and SD of the interstitial glucose concentrations for all CGM recordings were derived. Analysis was performed in SPSS version 15.

Validity of CGM in children and adolescents with CF was assessed by determination of reliability, reproducibility, and repeatability. Reliability was assessed by...
Bland-Altman analysis of agreement (9,10) along with Pearson’s correlation coefficient. Reproducibility tested the null hypothesis that the mean difference between the coefficients of variation (CVs) of observations was zero using a paired Student’s t test. Reproducibility was derived from Bland-Altman analysis and calculation of a discriminant ratio (DR) (11). Data are expressed as mean values with 95% CIs where appropriate. Significance was set at the 5% level.

RESULTS — A total of 104 out of 160 children and adolescents with CF (aged 9.5–19.0 years) were studied. A total of 102 valid CGM results were obtained at CGM1 and 92 at CGM2. The average number of valid CGM sensor readings used was 710 (range 499–1,410).

Mean interstitial glucose for all children and adolescents with CF was $6.7 \pm 2.3$ mmol/l (means ± SD) on CGM1 and $7.0 \pm 2.6$ mmol/l CGM2. Mean interstitial glucose for NGT, IGT, and CF-related diabetes is shown in Table 1. All values were significantly higher than in normal healthy nondiabetic subjects (mean $5.1 \pm 0.7$ mmol/l, $P < 0.0001$).

Table 1—Validity of CGM at visit 1 (CGM1) and visit 2 (CGM2) in 102 children and adolescents with cystic fibrosis ($n = 102$)

|                  | NGT* | IGT* | CFRD* | Control subjects |
|------------------|------|------|-------|------------------|
|                  | CGM1 | CGM2 | CGM1  | CGM2             |
| Interstitial glucose (mmol/l)† | 6.25 ± 1.84 | 6.35 ± 1.85 | 6.97 ± 2.65 | 6.56 ± 2.60 |
| CV (%)†          | 23.2 | 25.5 | 25.0  | 28.5             |
| DR               | 10.1 | 9.1  | 10.3  | 7.6              |
| Interstitial glucose (mmol/l)‡ | 6.25 ± 1.84 | 6.35 ± 1.85 | 6.97 ± 2.65 | 6.56 ± 2.60 |
| CV (%)‡          | 23.2 | 25.5 | 25.0  | 28.5             |
| DR               | 10.1 | 9.1  | 10.3  | 7.6              |

Data are mean ± SD, percent, and DR. Validity is based on reliability, reproducibility, and repeatability measures. *The baseline glucose tolerance category is based on standard oral glucose tolerance testing 2-h glucose concentrations: NGT <7.8, IGT 7.8–11, and CFRD >11.1 (8). Normal healthy control subject data shown to be significantly different from all children and adolescents with CF; $t P < 0.001$.

Repeatability. The mean difference between CGM1 and CGM2 interstitial glucose concentrations was $0.09 \pm 2.38$ mmol/l with 95% CI for the difference of $\pm 0.46$ mmol/l. The DRs (the variability of an individual to the variability of the group) for CGM1 and CGM2 were 13.0 and 15.1, respectively. Subgroup DRs are shown in Table 1 and indicate that CGM has the ability to identify subjects with high variability, such as CF-related diabetics, within this cohort of children and adolescents with CF.

CONCLUSIONS — This study demonstrates that CGM is a valid method for assessing glycemia in children and adolescents with CF, extending similar observations in adults with CF (7). The validation of CGM in children and adolescents with CF is essential before other prospective research can be undertaken with CGM in children and adolescents with cystic fibrosis and is warranted because of the higher glucose concentrations observed in these patients compared with the general population.

As expected, there was a linear correlation between five-point OGTT plasma blood glucose and the corresponding CGM glucose readings ($r = 0.74–0.91$). Rather than use correlation or Clarke error grid analysis, which both describe association, we used Bland-Altman analysis of agreement (9,10). The mean difference between the two methods was $0.81 \pm 2.90$ mmol/l with a 95% CI $\pm 2.90$ mmol/l, which is a reasonably acceptable bias for clinical practice.

CGM was reproducible in children with CF with varying degrees of glucose intolerance, since there were no significant differences in the CVs of the CGM assessment between visits, irrespective of diagnosis.

Finally, we have demonstrated that CGM was repeatable as the mean difference between CGM1, and CGM2 was 0.09 mmol/l Further, all DRs were $>1$, indicating that CGM has the ability to discriminate between different subjects and allow comparison between subjects.

In conclusion, CGM is a valid measure of glycemia in children and adolescents with CF. These observations suggest that CGM is not influenced by the CF chloride channel defect and has become a useful tool for the assessment of glycemia in children and adolescents with CF.

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