A1c below 7% is not enough.

Additional information from Continuous Glucose Monitoring is relevant in DM1 patients.

Gomez-Peralta, F; Santos-Mazo, E; Abreu-Padín, C; Pujante-Alarcón, P.

Diabetes Unit. Endocrinology and Nutrition Department. Clínica Universitaria de Navarra. Pamplona, Spain.

Glycated hemoglobin A1c (A1c) is the main method to assess the glycemic control in diabetes mellitus type 1 (DM1). It reflects the glycemic exposure during the past three months. Nevertheless, A1c doesn't provide information about glycemic variability. Frequency and intensity of glycemic excursions is extremely important for the quality of life of the people with DM1, as the time spent in hypoglycemia. Continuous glucose monitoring systems (CGMS) can describe and quantify these glycemic excursions.

Aims:

1.- Define the glycemic profile in DM1 patients with different glycemic control.

2.- Look for correlation of time spent in hyper-, hypoglycemia and glycemic variability with A1c.

Subjects and methods

One hundred and four patients with DM1 (56 women, age: 37.5 + 16.4 years) were studied using the continuous subcutaneous glucose monitoring system *CGMS™ (Minimed Medtronic ™, Ca, USA)*. Simultaneously we measure A1c value. All the patients wore the sensor during more than 72 hours. 12 patients were using insulin subcutaneous continuous infusor (ISCI) and the rest multiple doses of insulin (MDI). We analyzed the entire group and separately subjects with A1c < 7% and those with A1c > 9%.

Results

Mean ± standard deviation of A1c was 8.3 ± 1.1 (%). It's statistically correlated with the following data of continuous glucose monitoring (CGM): mean glucose (176 mg/dl, r =0.64, *p<0.001*), minimum glucose (51.18 mg/dl, r =0.28, *p= 0.04*), maximum glucose (342 mg/dl, r =0.47, *p <0.001*), number of glucose excursions (14, r = -0.23, *p = 0.019*), time spent over 180 mg/dl (45% , r= 0.62, *p <0.001*), time spent into the range 80-180 mg/dl (44%, r= -0.54, *p < 0.001*), time spent under 80 mg/dl (11%, r = -0.47, *p <0.001*), glucose area over 180 mg/dl (32, r = 0.62, *p<0.001*) and glucose area under 80 mg/dl (32, r = -0.36, *p<0.001*). These results confirm that CGM is representative of the global glycemic control of DM1 patients (Table 1).

When we divide the entire group according to the level of A1c correlations are maintained in the bad control subgroup (A1c >9%) for the CGM parameters reflecting hyperglycemia, but the correlation is absent for all the CGM parameters in the group of patients with A1c bellow 7% (Table 2).

Correlation with A1c	A1c <7%	A1c >9%	TOTAL
n	20	26	104
Hb A1c (%) mean	6.5	10.3	8.3
Glycaemia mean (mg/dl)	-0.02	0.58**	0.64**
% time >180 (mg/dl)	-0.05	0.53**	0.62**
% time 80-180 (mg/dl)	0.11	-0.54**	-0.54**
% time <80 (mg/dl)	-0.05	-0.27	-0.47**
glucose area >180 (mg/dl)	-0.04	0.59**	0.62**
glucose area <80 (mg/dl)	0.02	-0.12	-0.36**

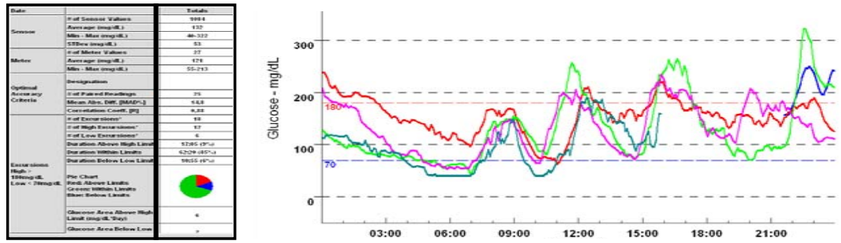
Table 1: Correlation (r Pearson, ** p <0.01) A1c – CGMS data of the total group and the groups with A1c < 7% and A1c > 9%

A 1c <7% (n=20)	Mean + SD
A1c (%)	6.5 + 0.4
Glycaemia mean (mg/dl)	141.3 + 30
Standard deviation	60 + 15
time > 180 mg/dl (%)	25 + 17
time 80-180 mg/dl (%)	55 + 14
time < 80 mg/dl (%)	19 + 11
Glucose Area > 180 mg/dl	14.4 + 12
Glucose Area < 80 mg/dl	4.1 + 3

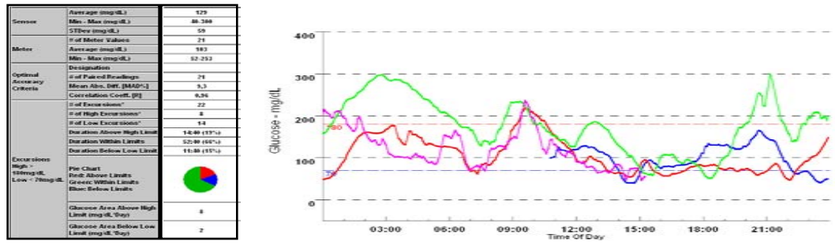
Table 2: CGMS data of the group with A1c < 7%

Some practical examples

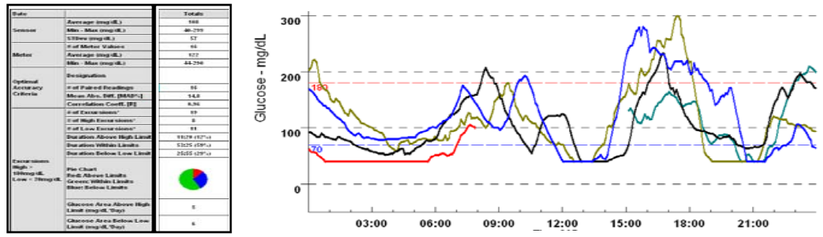
Case 1.- A1c **7.2 %** (1 glargine bedtime + lyspro preprandial)



Case 2.- A1c = **6.9%**, 32 y old woman with ISCI



Case 3.- A1c = **7%**, 29 y old man, previously satisfied with his treatment: 2 NPH/day + lyspro preprandial



Conclusions

1) In DM1 patients, A1c is better correlated with CGMS data reflecting hyperglycemia, indicating that A1c is a good marker of "glycemic load" but it doesn't inform about time and intensity of hypoglycemia.

2) In the group of patients with an "optimal glucose control" in terms of A1c (<7%), correlation of CGMS data with A1c disappears and 45% of the time is spent "out of range (80-180).". Nearly 20% of the time (4.8 hours per day) the glucose level remains under 80 mg/dl.

3) Additional information about the "real" glycemic profile obtained from CGMS is clinically relevant for patients with DM1, particularly in those with A1c in the objective range.