# THE EFFECTS OF SUBCUTANEOUS INSULIN INFUSION VERSUS MULTIPLE INSULIN INJECTIONS ON GLUCOSE VARIABILITY IN YOUNG ADULTS WITH TYPE 1 DIABETES: THE METRO STUDY

*M.I. Maiorino*[1], M. Petrizzo[2], G. Bellastella[1], M. Gicchino[2], O. Casciano[1], P. Cirillo[1], M. Caputo[1], A. Sarnataro[2], F. Castaldo[1], O. Romano[1], D. Giugliano[1], K. Esposito[1].

*[1]University of Campania "Luigi Vanvitelli", Department of Medical, Surgical, Neurological, Metabolic Sciences and Aging, Naples, Italy. [2]University of Campania "Luigi Vanvitelli", Diabetes Unit, Naples, Italy.*

## Introduction

The aim of the present study was to evaluate the long-term effects of continuous subcutaneuous insulin infusion (CSII), as compared with multiple daily injections of insulin (MDI), on glucose variability, assessed with continuous glucose monitoring (CGM), in a population of young adults with type 1 diabetes with sub-optimal glycemic control. To this purpose, we used data of the Management and technology for Transition (METRO) study, a longitudinal observational study of type 1 diabetic patients in transition from the pediatric clinic to the adult diabetes care center (1,2).

## Methods

Patients aged 18-30 years and considered eligible for insulin pump therapy were included in the study. Ninety-eight patients who started CSII therapy and 125 who remained in MDI completed a 2-year follow-up. Glucose variability was assessed with continuous glucose monitoring using blood glucose standard deviation (BGSD), mean amplitude of glycemic excursions (MAGE), continuous overlapping net glycemic action (CONGA-2h), low blood glucose index (LBGI), high blood glucose index (HBGI), daily risk range (ADRR). Secondary end-points were HbA1c, fasting glucose, frequency of hypoglycemia, insulin dose, lipids profile, blood pressure, and treatment satisfaction (DTSQ).

***Figure 1*** *- HbA1c Levels, MAGE, fasting glucose, and insulin dose at 6, 12, and 24 months in all the study patients according to insulin regimen. Values are means ± SE. Asterisks denote significant differences for all comparisons between pump therapy and injection therapy at each time point. * P<0.05; **P<0.01; ***P<0.001.*

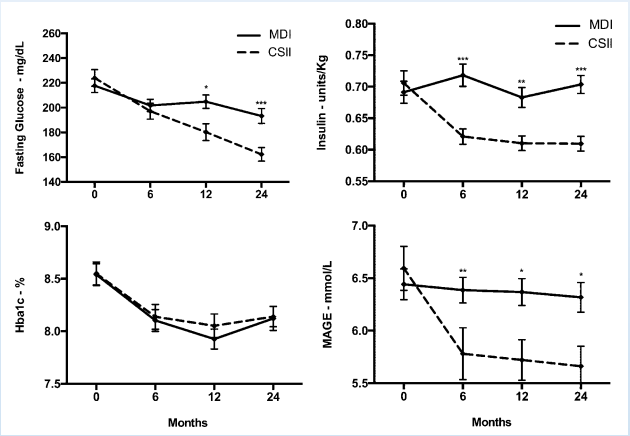


***Table 2*** *- Frequency of hypoglycemic events according to the treatment regimen*

| | Baseline | | | 2 years | | |
|---|---|---|---|---|---|---|
| Events, n | CSII (n = 98) | MDI (n = 125) | P | CSII (n = 98) | MDI (n = 125) | P |
| **Daily hypoglycemia, n (%)** | | | | | | |
| 0 | 0 (0.00) | 1 (0.80) | | 10 (10.20) | 1 (0.80) | |
| ≥ 1 | 98 (100.0) | 124 (99.20) | 0.37 | 88 (89.80) | 124 (99.20) | <0.01 |
| **Nocturnal hypoglycemia, n (%)** | | | | | | |
| 0 | 53 (54.08) | 69 (55.20) | | 71 (72.45) | 64 (51.20) | |
| ≥ 1 | 45 (45.92) | 56 (44.80) | 0.87 | 27 (27.55) | 61 (48.80) | <0.01 |
| **Severe hypoglycemia, n (%)** | | | | | | |
| 0 | 69 (70.41) | 84 (67.20) | | 88 (89.80) | 99 (79.20) | |
| ≥ 1 | 29 (29.59) | 41 (32.80) | 0.61 | 10 (10.20) | 26 (20.80) | <0.05 |

***Table 1*** *– Main outcomes at 2 years. [a] Adjusted with the propensity score*

| | CSII (n = 98) | | | MDI (n = 125) | | | | |
|---|---|---|---|---|---|---|---|---|
| **Parameter** | **Baseline** | **Endpoint** | **Difference** | **Baseline** | **Endpoint** | **Difference** | **Adjusted Difference[a] (95% CI)** | **P value** |
| Weight, Kg | 70.7 ± 10.7 | 71.6 ± 10.7 | 0.85 ± 3.73 | 69.9 ± 9.5 | 70.3 ± 10.0 | 0.45 ± 4.48 | 0.63 (-2.11, 3.42) | 0.65 |
| BMI, kg/m$^2$ | 24.8 ± 3.3 | 25.1 ± 3.2 | 0.32 ± 1.49 | 24.2 ± 2.9 | 24.4 ± 2.7 | 0.23 ± 1.75 | 0.12 (-0.65, 0.93) | 0.75 |
| FG, mg/dL | 224.1 ± 67.1 | 162.3 ± 54.5 | -61.73 ± 72.4 | 217.8 ± 61.7 | 193.3 ± 67.5 | -24.5 ± 74.6 | -31.2 (-47.91, -14.42) | <0.001 |
| HbA1c, % | 8.6 ± 1.1 | 8.1 ± 1.0 | -0.41 ± 1.07 | 8.5 ± 1.2 | 8.1 ± 1.3 | -0.42 ± 1.0 | 0.05 (-0.26, 0.35) | 0.77 |
| Insulin dose, UI/kg | 0.73 ± 0.2 | 0.63 ± 0.1 | -0.10 ± 0.14 | 0.72 ± 0.2 | 0.73 ± 0.2 | 0.01 ± 0.14 | -0.1 (-0.15, -0.06) | <0.001 |
| MAGE, mmol/L | 6.6 ± 2.1 | 5.7 ± 1.9 | -0.93 ± 2.55 | 6.4 ± 1.6 | 6.3 ± 1.6 | -0.12 ± 1.03 | -0.74 (-1.22, -0.26) | <0.01 |
| CONGA-2h, mmol/L | 6.6 ± 1.6 | 6.3 ± 1.7 | -0.31 ± 1.47 | 6.6 ± 1.8 | 6.4 ± 1.8 | -0.19 ± 0.92 | -0.01 (-0.48, 0.46) | 0.97 |
| SD, mmol/L | 3.3 ± 0.8 | 3.2 ± 0.8 | -0.17 ± 0.79 | 3.6 ± 0.8 | 3.5 ± 0.8 | -0.06 ± 0.54 | -0.3 (-0.52, -0.10) | <0.01 |
| HBGI | 8.5 ± 3.4 | 7.6 ± 3.0 | -0.87 ± 3.28 | 8.9 ± 3.9 | 8.4 ± 3.3 | -0.53 ± 2.16 | -0.9 (-1.8, 0.05) | 0.06 |
| LBGI | 5.5 ± 1.7 | 5.0 ± 1.9 | -0.56 ± 1.3 | 5.5 ± 1.2 | 5.2 ± 1.4 | -0.29 ± 1.06 | -0.15 (-0.56, 0.26) | 0.47 |
| ADRR | 31.9 ± 8.6 | 30.3 ± 8.0 | -1.61 ± 5.22 | 32.1 ± 7.5 | 30.5 ± 6.8 | -1.56 ± 2.61 | -0.05 (-2.10, 2.05) | 0.97 |
| DTSQ total score | 27.5 ± 3.5 | 29.1 ± 3.7 | 1 (0, 3) | 27.4 ± 3.7 | 28.2 ± 3.4 | 1 (-1, 2) | 0.5 (-0.42, 1.52) | 0.27 |
| perceived hypoglycemia | 3 (2, 4) | 2 (1, 3) | -1 (-2,0) | 3 (2, 4) | 3 (2, 3) | -1 (-1, 0) | -0.5 (-0.83, -0.21) | <0.01 |
| perceived hyperglycemia | 2 (2, 3) | 2 (1, 3) | 0 (-1, 1) | 2 (2, 3) | 2 (1, 3) | -0.5 (-1, 0) | -0.02 (-0.35, 0.30) | 0.93 |

*For legends refer to Introduction and Methods*

## Results

MAGE and BGSD decreased in both groups, with an adjusted differences of -0.74 mmol/L (95% confidence interval [CI] -1.22 to -0.26, P=0.003) and -0.3 (CI -0.52 to -0.1, P = 0.005) favoring the pump-therapy group (Tab.1, Fig.1). No significant differences between groups in the other variability indexes were observed (Tab.1). HbA1c decreased in both groups without significant difference (0.05, -0.26, 0.35, P = 0.77); fasting glucose, insulin dose and overall hypoglycemia (daily, nocturnal, and severe) decreased more in patients with CSII, as compared with those with MDI (Fig.1, Tab.2).

## Conclusion

Among young adult with type 1 diabetes transitioning from the pediatric care, the use of CSII is associated with lower glucose variability, fasting glycemia and overall hypoglycemic events than MDI during a 2-year period of follow-up.

## References

1. Maiorino MI, et al. Reducing glucose variability with continuous subcutaneous insulin infusion increases endothelial progenitor cells in type 1 diabetes: an observational study. *Endocrine*. 2016;52:244-52.

2. Maiorino MI, et al. Treatment satisfaction and glycemic control in young Type 1 diabetic patients in transition from pediatric health care: CSII versus MDI. *Endocrine*. 2014;46:256-62.