Abstract

- A recent study conducted in Brazil including *over 6,000* patients showed that only 10.4% of type 1 and 26.8% of type 2 diabetics presented adequate glycemic control with A1C <7%(1).
- Current approaches to promote glycemic control are mostly based in A1C levels, requiring lengthy implementation and contributing to clinical inertia.
- This proof-of-concept, randomized and controlled clinical trial was developed to find an effective, safe, reliable, low cost and easily implementable method for achieving glycemic control with intensive diagnostic, educational and pharmacological interventions.
- The use of combined 5MBG-derived concepts such as weekly mean glycemia (WMG), glycemic variability (SD) and glycemic profile can substantially improve the evaluation of glycemic control, allowing weekly corrections of therapeutic strategy and a faster migration to normal glycemic levels.
- This intensive intervention strategy promoted rapid improvement in glycemic control, variability, and A1C within 6 weeks using 7 point glycemic profiles 3 days per week and weekly clinic visits in up to 82% of the patients in the intensive group. Prevalence of hypoglycemia (< 60 mg/dL) was low and similar in both groups.

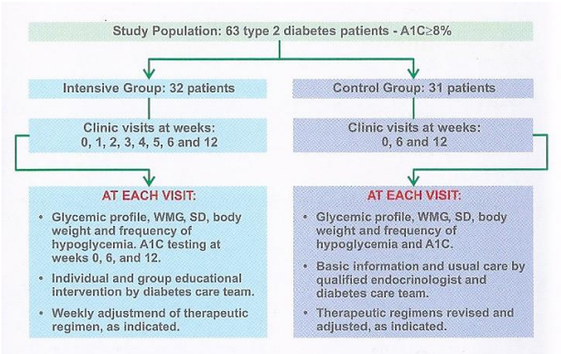
Objectives

- Primary objective of this clinical trial was to evaluate the efficacy and safety of an "Intensive Monitoring, Education, and Therapy (IMET)" Program (intensive group) *vs.* standard "real life" care (control group).

  Primary outcomes were WMG, SD, A1C and prevalence of hypoglycemia at weeks 0, 6 and 12.

Patients and Methods

- Patients were randomly allocated to one of the following study arms: Intensive and Control *(cf.* Figure).



- Study population: 63 type 2 adult patients of both sexes up to 75 years of age with poor glycemic control (A1C ≥ 8%) and poor response to therapy before entering the study.
- All patients received glucose meters and test strips (Accu-Chek Perfoma - Roche Diagnostics) to practice SMBG (6 to 7 tests/day for 3 days in a week). During weekly visits data from the meters were downloaded for computerized analysis by special software (Accu-Chek 360^0 - Roche Diagnostics).
- Patients in both the Intensive and Control groups were treated with diet and mono, dual, or triple therapy regimens with metformin, sulfonylureas, nateglinide, rosiglitazone, and/or insulin, at their physician's discretion.

STATISTICAL ANALYSIS

- Analysis within individuals: "each patient as their own control".
- *t* tests of differences between Week 0 and Week 6 or Week 12 one-sided for WMG, SD, A1C; two-sided for Weight.
- Unpaired *t* tests of Intensive vs Control groups using differences between Baselines and Weeks 6 or 12.
- z-test of frequency of hypoglycemia for Intensive vs Control groups for Weeks 0 - 6 and Weeks 0 - 12.
- After correction for baseline WMG or baseline A1C one obtains *even* more impressive levels of statistical significance.

Results

• Summary of study results:

PARAMETER	INTENSIVE GROUP (Mean ± sem)			CONTROL GROUP (Mean ± sem)			INTENSIVE GROUP *vs* CONTROL GROUP	
	Week 0	*Change* Week 0 to Week 6	*Change* Week 0 to Week 12	Week 0	*Change* Week 0 to Week 6	*Change* Week 0 to Week 12	P 6 weeks	P 12 weeks
WMG (mg/dL)	216.45 ± 5.57	-76.65 ± 8.92 ****	-60.96 ± 10.55 ****	210.20 ± 9.27	-20.46 ± 8.08 **	-34.11 ± 10.25 **	0.00001 ***	0.038 *
SD (mg/dL)	69.37 ± 4.12	-16.30 ± 3.12 ****	-15.75 ± 3.00 ****	65.95 ± 4.04	-5.04 ± 3.12 NS	-7.20 ± 3.52 *	0.010 *	0.036 *
A1C (%)	10.29 ± 0.25	-1.82 ± 0.16 ****	-2.26 ± 0.23 ****	10.01 ± 0.25	-0.66 ± 0.22 **	-1.29 ± 0.24 ***	0.00001 ***	0.003 **
WEIGHT (kg)	86.42 ± 3.41	-0.10 ± 0.40 NS	0.12 ± 0.60 NS	76.65 ± 2.76	0.05 ± 0.28 NS	0.73 ± 0.35 *	0.76 NS	0.39 NS

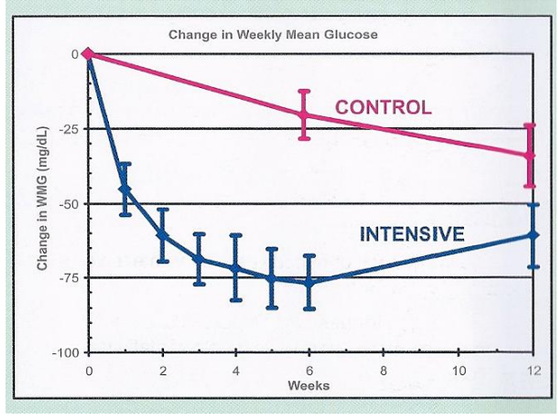
**** P < 0.000001 *** P < 0.001 ** P < 0.01 * P < 0.05 NS P > 0.05

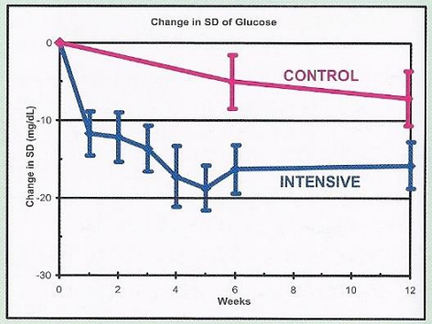
% of Glucose Values < 60 mg/dL	INTENSIVE GROUP § (Mean ± sem)	CONTROL GROUP § (Mean ± sem)	P 12 weeks
	4.11 ± 0.96 %	2.24 ± 0.64 %	> 0.05 NS

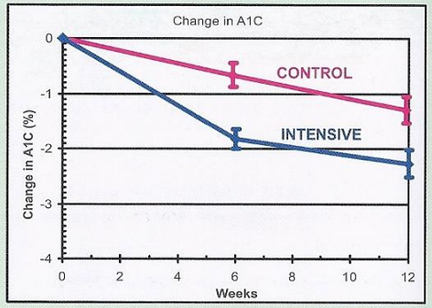
§ No reports of severe hypoglycemia in either group.

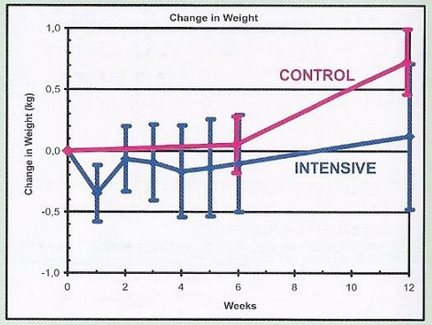
- Evolution of WMG, A1C, SD and Body Weight - Intensive vs. Control Groups

Change in WMG, SO, A1C and Weight,
Week 0 to Week 12, Control vs. Intensive Groups









CORRESPONDING AUTHOR:

Augusto Pimazoni-Netto, MD

Diabetes Education and
Control Group Kidney and Hypertension Hospital
Federal University of Sao Paulo, Brazil

E-mail: pimazoni@uol.com.br

Conclusions

- The Intensive Program resulted in a very prompt clinically significant reduction in WMG, A1C, SD, with no change in weight. Smaller but significant favorable changes in WMG, A1C and SD were seen for the control group.
- The differences between Intensive Group and Control Group were statistically significant for WMG, SD, and A1C at both Week 6 and Week 12.
- No significant changes in weight were seen in any group.
- The risk of hypoglycemia was not statistically significantly increased in the subjects receiving Intensive therapy.
- Changes in WMG are highly correlated with Baseline WMG. Similary, changes in A1C and SD are highly correlated with Baseline A1C: Greater improvement is seen in sugjects with higher baselines.
- The Intensive Therapy protocol (IMET) with Monitoring, Education and Frequent adjustment of Therapy can result in dramatic improvement of glycemia (WMG < 150 mg/dL; SD < 50 mg/dL) within a matter of a few weeks in nearly all subjects. We estimate that the long-term benefits of this rapid improvement should considerably outweight the costs.
- Seven-point glucose profiles, performed 3 days each week for 6 weeks and then at 6 weeks intervals, provides the information needed for rapid adjustment of therapy.
- The "IMET" Protocol deserves further evaluation in multiple clinics and patient populations to evaluate its generalizability and long-term sustainability. We plan to conduct such studies.

Reference

1. Mendes AB, Fittipaldi JAS, Neves RCS et al. Prevalence and correlates of inadequate glycaemic control: results from a nationwide survey in 6,671 adults with diabetes in Brazil. Acta Diabetol. 2010 Jun;47(2):137-45. Epub 2009 Aug 5.

MEMBERS OF THE DIABETES EDUCATION AND CONTROL GROUP
KIDNEY AND HYPERTENSION HOSPITAL
FEDERAL UNIVERSITY OF SAO PAULO, BRAZIL

Amanda Pires - Anita Sachs - Aparecida Fátima Bueno - Bianca Pires - Camila Costa - Clarissa Uezima - Ednir Apostólico - Eráclíton de Souza - Fátima Regina da Silva - Fernanda Carvalho - Graça Camara - Irma Cianfrone - Kátia Martins - Kátia Niglio - Maria da Gloria Carvalho - Maria Gabriela Cavicchioli - Mário da Silva Júnior - Marta Darhouni - Milena Alves - Mônica Gamba - Patrícia Fan - Patrícia Monteagudo - Patrícia Zach - Priscila Broinizi - Regina Niglio - Rene Araújo - Ricardo Santos - Sheilla Silveira - Sonia Ramos - Tarcila Campos - Viviane Nascimento.

Diabetes Education and Control Group
UNIFESP

KIDNEY AND HYPERTENSION HOSPITAL
Federal University of Sao Paulo - Brazil

UNIFESP
UNIVERSIDADE FEDERAL DE SÃO PAULO
1933

Rapid Improvement in Glycemic Control, Variability, and A 1 C within 6 Weeks using 7 Point Glycemic Profiles 3 Days Per Week and Weekly Clinic Visits: A Randomized Controlled Trial In Type 2 Diabetes

Pimazoni-Netto, A.[1], Rodbard, D.[2], Pires, A.L.[3], and Zanella, M.T.[4]

On behalf of *Diabetes Education and Control Group*
Kidney and Hypertension Hospital,
Federal University of *Sao Paulo, Brazil .*

[1] Coordinator, Diabetes Education and Control Group;
[2] Biomedical Informatics Consultants, Potomac, MD, USA;
[3] Nutritionist and Study Monitor;
[4] Full Professor of Endocrinology