

***Glycemic Control in Adult Type 1 Diabetes Patients from a Brazilian Country City: Comparison Between a Multidisciplinary and a Routine Endocrinological Approach***

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**ABSTRACT**

**Objective:** To evaluate the metabolic control of a cohort of adult type 1 diabetes mellitus (T1DM) patients assisted in a public Diabetes Center (DC) that follows the rules of a national diabetes society. **Methods:** We compared for one year the metabolic control and the characteristics of 175 T1DM patients attended by a multidisciplinary team in a DC (test group) with 30 patients assisted only by endocrinologists at a public endocrinology outpatient center (control group). **Results:** The test group presented a larger proportion of well-controlled patients ( $p= 0.002$ ). The proportions (test x control group) were as follows: 51.4% x 16.7% in the subgroup with A1C < 7%; 21.7% x 36.7% in the subgroup with A1C between 7.1% and 8.0%; and 26.9% x 46.7% in the subgroup with A1C > 8%. Patients assisted in the DC presented a likelihood 4.38 times higher of reaching levels of A1C up to 7%. **Conclusions:** This study shows the effectiveness of a DC and emphasizes the importance of education, adherence and multidisciplinary as cornerstones for the treatment, showing that in developing countries it is possible to treat T1DM with satisfactory results. (**Arq Bras Endocrinol Metab 2006;50/5:944-950**)

**Keywords:** Diabetes mellitus, type 1; Insulin; Health services; Patient education; Brazil.

**RESUMO**

**Controle Glicêmico em Pacientes Adultos com Diabetes do Tipo 1 em Uma Cidade Brasileira: Comparação entre Abordagem Multidisciplinar e Endocrinológica de Rotina.**

**Objetivo:** Avaliar o controle metabólico de uma coorte de pacientes adultos com diabetes do tipo 1 (DM1) atendidos em um Centro de Diabetes (CD) que segue as normas da Sociedade Brasileira de Diabetes. **Métodos:** Foram comparados o controle glicêmico e as características de 175 pacientes com DM1 atendidos por uma equipe multidisciplinar em um CD (grupo teste) com 30 pacientes assistidos em um ambulatório de endocrinologia geral (grupo controle) durante um ano. **Resultados:** O grupo teste apresentou uma maior proporção de pacientes bem controlados ( $p= 0,002$ ). As proporções (grupo teste x grupo controle) foram: 51,4% x 16,7% no subgrupo com A1C < 7%; 21,7% x 36,7% no subgrupo com A1C entre 7,1% e 8,0%; e 26,9% x 46,7% no subgrupo com A1C > 8%. Os pacientes atendidos no CD apresentaram probabilidade 4,38 vezes maior de atingir níveis de A1C até 7%. **Conclusão:** O estudo mostra a efetividade do CD e enfatiza a importância da educação, aderência e da multidisciplinaridade como pedras angulares do tratamento, mostrando ser possível tratar o DM1 nos países em desenvolvimento com resultados satisfatórios. (**Arq Bras Endocrinol Metab 2006;50/5:944-950**)

**Descritores:** Diabetes mellitus tipo 1; Insulina; Serviços de saúde; Educação do paciente; Brasil

**T**YPE 1 DIABETES MELLITUS (T1DM) corresponds to approximately 10% of all the cases of diabetes and affects between 10 and 20 million individuals worldwide (1). In about 40% of the cases, T1DM appears during the adult age, which begins, in general, less dramatically and eventually can be confused with type 2 diabetes in lean patients (2).

The prevalence of T1DM varies among the studied areas (3) and according to the International Diabetes Federation (IDF) data, this disease is present in approximately 0.11% of the general population of South American countries (4).

Nowadays, it is well established that a great percentage of primary and secondary prevention of chronic diabetes complications can be achieved with a good glycemic control — levels of glycosylated hemoglobin (A1C) up to 7% — as much in T1DM (5) as in type 2 diabetes mellitus (T2DM) (6), resulting in a reduction of its morbi-mortality and costs (7-9). There are studies showing that in T1DM a significant increase of the prevalence of microangiopathic complications occur when A1C levels are higher than 8%, suggesting such level to be the maximum accepted limit (10-12).

In developing countries, although DM represents a serious public health concern, strict glycemic control is difficult to achieve, owing to financial constraints, cultural obstacles, and lack of adequate infrastructure underlying public services. However, it is known that even in developed countries (13) the goal of reaching an ideal glycemic control is still a great challenge.

In Brazil, the Ministry of Health has been implementing programs to reduce DM impact on the population's health and the national budget. One of the strategies adopted was to stimulate and to implement the creation of Diabetes Centers (DC), where patients are accepted to be cared for by a multidisciplinary team and receive enough insulin vials until the next consultation. Conversely, the continuous supply of insulin is still a critical point in many developing countries (14).

Such Brazilian Diabetes Society guidelines began to be implemented more than a decade ago, but so far, its impact on the glycemic control of DM patients has not been evaluated.

Considering that the adult's T1DM, in spite of being characterized for an insulinopenic state (as in T1DM in the youth), has a more stable behavior (2), and taking into account the complexity of the T2DM treatment (the approach to insulin secretion alteration, insulin resistance, arterial hypertension and dyslipidemia that frequently occur in those patients), we supposed that T1DM in the adult would be a good model

for an initial evaluation of the impact of a DC on the patients' glycemic control.

So, the objective of this study was to evaluate the glycemic control of a cohort of adult T1DM patients, treated in a DC of a medium-sized city (Juiz de Fora, Brazil), which follows the recommendations of the Brazilian Diabetes Society, during a one-year period (2003).

## **MATERIAL AND METHODS**

### **Type 1 Diabetes Mellitus population studied**

According to the Brazilian Diabetes Society calculation method, it is estimated that there are about 7,632 diagnosed diabetics in Juiz de Fora (approximately 763 Type 1 and 6,869 Type 2) out of a population of 439,716 inhabitants (15).

### **Description of the outpatient centers**

The DC of the Public Health Office of Juiz de Fora has a waiting room, five medical offices, a meeting room with audiovisual system, an insulin storage room, and offices for a social assistant, a nutritionist and a head nurse/diabetes educator. In addition, there is a pre-appointment room where the nurse checks patient's body weight, height, blood pressure, abdominal circumference and capillary blood glucose. After the doctor's appointment, the patient receives the insulin vials with a kit for application and the next consultation is scheduled.

The DC patients benefit from the services of a multidisciplinary team comprised of five endocrinologists, a nutritionist, a social assistant, three nurses, two administrative auxiliaries, and a head nurse certified by the Ministry of Health in diabetes education. When the patient is admitted to DC or whenever a doctor detects some situation that jeopardizes the treatment compliance, the head nurse supplies information to the patient about insulin use, diet, hypoglycemia, foot care and lifestyle. The patients attend bimonthly meetings with all the DC board, in groups of up to 10 patients, where the education strategies are focused using audiovisual methods and discussion groups about nutrition, exercise regimens and foot care, among other topics. The consultations with each member of the DC board last about 60 minutes.

The DC distributes about 4,000 NPH insulin vials a month. At the DC, a great emphasis is placed upon education and the necessity of bimonthly appointment, which is a condition for the patient to still receive continuous free insulin.

Juiz de Fora City has also a public general endocrinology center (EC), where, unlike the DC, any kind of endocrinopathy is treated. At the EC only endocrinologists attend the patients without a multidisciplinary approach.

Due to the fact that at both the DC and the EC only NPH insulin is available, all patients are treated with 1 or 2 daily applications of this kind of insulin (fasting and bedtime). The DC and the EC do not offer dipsticks for self-management (capillary glycemia or glycosuria) and the patients' metabolic control is assessed according to A1C and fasting blood glucose (FBG) levels.

### **Patients**

One hundred and seventy five patient records of adult T1DM patients who have received the whole multidisciplinary support available in the DC were analyzed (test group). The records of 30 adult T1DM patients in attendance at the EC were taken as a control group. T1DM was classified as the patients for whom the use of insulin was necessary since the onset of the symptoms in order to normalize the glycemic levels, in agreement with the World Health Organization criteria (16).

Patients with T1DM were eligible for inclusion if they were aged equal or above 20 years old at diagnosis and had at least six consultations at the DC in 2003. The patients from the EC have attended up to three consultations during the same period. None of the studied patients had clinical signs of chronic complications. The local ethics committee approved the study.

### **Methods**

The annual (2003) average of the A1C (high performance liquid chromatography, normal value up to 6%) and fasting plasma glucose — FPG — (enzymatic colorimetric method, normal value: 70 to 100 mg/dl= 3.9 to 5.6 mmol/l) were calculated for each patient.

Aiming to assess glycemic control, all patients in our study were divided into three subgroups according to the A1C value: subgroup A (A1C up to 7%), subgroup B (A1C between 7.1 and 8%) and subgroup C (A1C higher than 8%).

Age and gender were analyzed along with DM duration in years, age at the diabetes onset, mean body mass index (BMI) in kg/m<sup>2</sup>, daily mean NPH insulin dose in U/kg/day, number of daily insulin applications, patient compliance and acute complications from the database.

In the present study, it was considered as a dietary indiscretion the reported consumption of food with sucrose at least three times a week (17), without includ-

ing the use of sweets consumed during hypoglycemic episodes. It was considered as a drug misuse any omission in the insulin use reported by the patient (18).

To evaluate the occurrence of acute complications, only hypoglycemic episodes in which the patient reported the classic symptoms followed by an improvement after the ingestion of sweets were computed, having been considered as serious the hypoglycemia that needed the help of others, or with loss of consciousness (19). Ketoacidosis episodes were computed after being confirmed by the hospital discharge summary.

In order to compare the glycemic control between the test (DC) and control (EC) groups, the patients' proportions were considered, in both groups, according to the three subgroups of A1C.

### **Statistical analysis**

Continuous variables are expressed as mean  $\pm$  SD. The categorical variables are expressed as proportions. The comparison of means among the three subgroups was analyzed through the one-way ANOVA, the differences between two means through the Student's t-test (double tail) and the differences among proportions through the chi-square or Fisher's exact test. A logistic binary regression was performed in the whole sample (205 patients) in order to quantify the association between the treatment center (DC or EC) and the glycemic control (outcome), considering other variables that could affect the A1C levels. A p value less than 5% was considered statistically significant. The statistical package Minitab version 14.0 was used to analyze the data.

## **RESULTS**

### **Description of the test (DC) and control (EC) groups**

The test and the control groups were similar to each other in relation to age, gender, time of DM diagnosis, age at clinical picture onset, BMI, number of daily applications of insulin, mean daily dose of insulin, proportion of reports of insulin misuse, and hypoglycemia and ketoacidosis episodes. In the control group, there were more reports of dietary indiscretions and the daily amount of NPH insulin used was greater. The means of the A1C and FPG were lower in the test group, without any overlap between the 99% confidence intervals. These results are summarized in table 1. The patients' proportion with A1C > 7% that took two applications was greater than those who took just

**Table 1.** Characteristics of patients in the test and control groups after one year.

	Test Group (n= 175)	Control Group (n= 30)	p value
Age (years)	42.4 ± 14.2	42.6 ± 13.2	0.949
Gender (M/F)	83/92	13/17	0.698
Disease duration (years)	12.9 ± 9.2	12.5 ± 8.5	0.812
Age at DM onset (years)	29.4 ± 8.4	30.0 ± 12.0	0.721
FPG (mmol/l)*	9.6 ± 2.5 (9.1 to 10.1)	11.0 ± 1.6 (10.2 to 11.8)	0.003
A1C (%)*	7.28 ± 1.70 (6.94 to 7.61)	8.36 ± 1.07 (7.82 to 8.99)	0.001
NPH mean dose (U/kg/day)*	0.98 ± 0.47	1.23 ± 0.94	0.025
BMI (kg/m <sup>2</sup> )	27.3 ± 17.1	28.6 ± 4.4	0.679
Number of doses(1 dose/2 doses)	50/125	6/24	0.383
Dietary indiscretions*	42	13	0.043
Drug misuse	24	5	0.776
Hypoglycemic episodes	40	3	0.149
Ketoacidotic episodes	3	1	0.472
Number of consultations	6	up to 3	—

Data are n or mean ± SD. Values between brackets represent the 99% confidence interval.  
\*p< 5%. The factor used to convert mg/dl to mmol/l was 0.05551.

one application in both the test group (p= 0.039) and the control group (p= 0.041), as verified by the Fisher's exact test.

#### Analysis of the test group (DC) according to A1C values

The three subgroups (A, B and C) of the test group were similar to each other regarding age, gender, time of DM diagnosis, age of DM onset, mean daily dose of NPH insulin, BMI, number of reports of dietary indiscretions and drug misuse, and number of hypoglycemia reports. In the subgroups with A1C > 7% (B and C) the patients' proportion that took 2 daily applications of NPH insulin was greater. The only three ketoacidosis reports in the test group occurred in the subgroup B. The mean values of A1C were the following: 6.0 ± 0.67% in the subgroup A, 7.51 ± 0.3% in the subgroup B and 9.6 ± 1.15% in the subgroup C. The results are shown in table 2.

#### Comparison of glycemic control (DC x EC)

Comparing the test group with the control group, the former presented a higher proportion of well-controlled patients ( $\chi^2= 12.45$ , df= 2, p= 0.002). The proportions (test group x control group) were the following: 51.4% x 16.7% in subgroup A (A1C < 7%), 21.7% x 36.7% in subgroup B (A1C between 7.1% and 8.0%) and 26.9% x 46.7% in subgroup C (A1C > 8%), as illustrated in figure 1.

#### Impact of the DC approach

The logistic regression analysis performed had as a dependent binary variable the groups with A1C up to 7% and A1C > 7%. The numeric independent variables were the patients' age, time of DM diagnosis,

mean insulin daily dose, and number of daily insulin applications. The independent binary variable was the treatment center (DC x EC). The results showed that age (p= 0.307), time from DM diagnosis (p= 0.801), daily insulin dose (p= 0.284) and number of applications (p= 0.082) did not present significant influence on the tested outcome (A1C up to 7% x A1C > 7%). However, the center where the patient was assisted was the factor of decisive influence (p= 0.006, positive coefficient of 1.48), showing that patients assisted at the DC presented a likelihood 4.38 times higher of presenting levels of A1C up to 7% (OR= 4.38, 95% CI= 1.53 to 12.57, p= 0.006). All the assumptions of the logistic regression analysis were verified (Log-Likelihood test: p< 0.001) and the model's goodness-of-fit was confirmed by the tests of Pearson (p= 0.415) and Hosmer-Lemeshow (p= 0.108). The association measures were solid (Goodman-Kruskal Gamma coefficient= 0.34) (20).

#### DISCUSSION

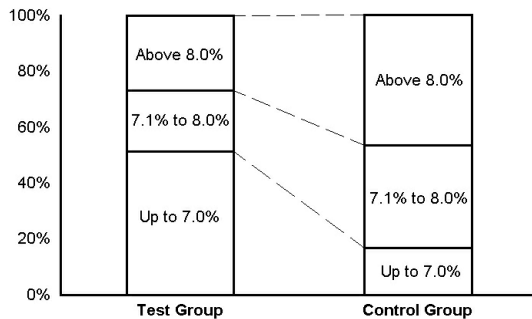
According to the estimated T1DM prevalence and the population of the city studied, our work included about 23% of them. There are patients that do not adapt to the DC regimen, such as consultation periodicity and participation in the weekly groups of DM education.

In the period of the study (1 year), there were a significant proportion of patients with desirable metabolic control in the test group, despite the fact that all patients (due to a limitation of basic resources, like fast-acting insulin and dipsticks for self-management supply) were treated with conventional insulin therapy

**Table 2.** Characteristics of patients in the test group, according to the A1C interval after one year.

	Subgroup A (n= 90) A1C < 7.0%	Subgroup B (n= 38) A1C: 7.1% to 8.0%	Subgroup C (n= 47) A1C > 8.0%	p value
Age (years)	41.7 ± 13.7	41.2 ± 14.6	44.6 ± 14.8	0.459
Gender (M/F)	45/45	19/19	19/28	0.532
Disease duration (years)	12.5 ± 8.9	12.6 ± 9.7	14.2 ± 9.4	0.595
Age at DM onset (years)	29.2 ± 8.3	28.6 ± 8.2	30.4 ± 8.9	0.596
NPH mean dose (U/kg/day)	0.95 ± 0.46	1.10 ± 0.42	1.04 ± 0.5	0.211
BMI (kg/m <sup>2</sup> )	27.8 ± 23.1	26.0 ± 5.9	27.2 ± 6.4	0.855
Number of doses (1 dose/2 doses)*	32/58	4/34	14/33	0.016
Dietary indiscretions	22	7	13	0.606
Drug misuse	13	8	3	0.142
FPG (mmol/l)*	7.7 ± 1.0	10.0 ± 0.4	13.1 ± 1.7	0.001
Hypoglycemic episodes	23	7	10	0.650
Ketoacidotic episodes*	0	3	0	0.006

Data are n or mean ± SD. \*p < 5%.



**Figure 1.** Patients' proportions according to the A1C level subgroups in the test group (n= 175) and in the control group (n= 30).

(one or two daily applications of NPH). However, similar reports exist both in national and international literature (21,22). As our sample was composed by adult T1DM patients, perhaps with a larger endogenous insulin reserve (23), glycemic control may have been facilitated. Data from a Belgian study of children and adolescents using up to two daily insulin doses, showed that 62% of the studied group reached a good metabolic control (22), as well as demonstrated by another Brazilian study (21).

The frequency of DC consultations (which was bimonthly in our study), specialists care and a structured DM education service might have collaborated in obtaining results with the use of conventional insulin therapy (22,24).

This approach with one or two daily insulin applications, for several reasons, is still frequently used in several countries in the treatment of T1DM. A multicentric study (13) involving 18 countries showed that 60% of the T1DM patients were in the regimen of two daily insulin doses and 34% of them presented good glycemic control — an inferior percentage in

comparison to our group and in the studies previously mentioned (21,22), perhaps because the analyzed patients had not been assisted in structured DCs.

Anyway, regardless of the therapeutic modality utilized, the percentage of patients that do not reach the ideal metabolic control worldwide is still high even with intensive insulin therapy, including developed countries (10,24,25).

It is known that T1DM is a disease that requires great commitment by patients to reach the desired goals. The patients' compliance is difficult to achieve, perhaps providing an explanation for the difficulty in getting the desired metabolic control, as mentioned above.

It is plausible to presume that the multidisciplinary team's effort for improving the patients' adherence explain the relatively high amount of patients with better metabolic control at the DC (26).

In regards to the ideal metabolic control (A1C up to 7%), 51.4% of the patients assisted at the DC reached such goal, versus only 16.7% in the control group. In addition, it was statistically confirmed that the patients assisted at the DC presented a likelihood 4.38 times higher of reaching levels of A1C up to 7%.

The characteristics of the patients studied, such as gender, duration of the disease, age at the onset of the disease, mean dose of insulin used and BMI do not differ from other national (27-29) and international (5) studies. Given a more advanced age of our patients, it is possible that some of them presented LADA, although patients with LADA sometimes do not require insulin at diagnosis (30).

The T1DM diagnosis could not be confirmed with laboratorial methods, since autoantibody measurement was not available where the study was carried out; furthermore nowadays the precise diagnosis of T1DM is far from straightforward (2,31-34).

In the test group, the patients with worse metabolic control used two insulin applications more frequently than the group with better control. It is probable that the option of changing from one to two applications had been based on this criterion. Although a study accomplished in Belgium demonstrated no difference in the metabolic control of patients using insulin two or four times a day (22).

The number of reports of dietary indiscretions and drug misuse was equivalent in the three studied subgroups of the test group. In the control group, there were more dietary indiscretions, showing fewer adherences of these patients.

There were 43 hypoglycemia reports in our sample without the need of help from others for the patients' recovery. In fact, the studies show that the frequency of serious hypoglycemia is directly related to intensive glycemic control (5,35).

The four episodes of reported ketoacidosis occurred in patients due to omission of insulin use.

Anyway, 26.9% of the patients of the test group maintained levels of A1C above 8%. Besides the possibilities discussed above, it is probable that the simultaneous use of fast-acting insulin and self-management could improve this situation. Accordingly to Almeida et al. (29), in Latin America only Brazil, Cuba and Costa Rica distribute insulin gratuitously, and only Costa Rica, among 12 studied countries, supplies necessary material for the patients' self-management.

Several limitations of our study must be considered concerning the generalization of our results. We studied adult T1DM with a probably better insulin reserve, our patients were very adherent to the proceedings of the DC and we carried out a historical cohort analysis (in the future prospective clinical trials may assess our results).

Besides, in our study it is possible that mild hypoglycemia episodes may have occurred and this fact could be related to the found A1C levels, although in the control group the mean dose of NPH insulin was larger. We could not evaluate this fact due to the lack of self-management of the capillary glycemia.

Probably the chief fact that could explain our relatively good results concerning the glycemic control is that all the patients were completely adherent to the DC rules, furthermore other studies showed that when the therapeutic strategies are very complex, they can impair the patients' adherence (36,37).

To sum up, this study demonstrated that patients attended by a structured multidisciplinary team, with emphasis on the patient's education with good adherence, continuous supply of insulin, were

capable of reaching satisfactory results even without resources for self-management of the glycemia and using only NPH insulin, evidencing that in developing countries it is possible to improve the patients' glycemic control even when intensive insulin therapy is not available.

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