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Type 2 diabetes: Prescription patterns and treatment outcomes of IDMPS survey in Argentina

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ABSTRACT

Aim: To assess prescription patterns for treatment of type 2 diabetes (T2D) and their outcomes in the IDMPS survey in Argentina.
Methods: Data from 2551 people with T2D recruited from 210 physicians participating in IDMPS surveys in Argentina (2006 to 2012 waves) were recorded, including medical history, medications, glycemic control, blood pressure, and lipid status.
Results: Most people were treated with oral glucose-lowering drugs (OGLDs) (65%), followed by combinations of these drugs plus insulin (22%) and only insulin (13%). These percentages varied according to T2D duration, the frequency of OGLDs decreasing while contrastingly and only insulin increasing (under 5 years versus over 10 years of disease duration, respectively). Average systolic blood pressure (SBP), HbA1c and LDL-c were significantly higher in patients treated with insulin either alone or associated with OGLDs. The percentage of people at target values for these parameters was also lower in these two groups. The percentage of people that reached simultaneous goal treatment values for BP, HbA1c and LDL-c levels was markedly low.
Conclusion: Prescription patterns for treatment of T2D follows a chronological trend and the percentage of people at goal values (HbA1c, BP and LDL-c values) was significantly lower in people receiving insulin. These data must be carefully considered by health and academic authorities in order to implement effective strategies to modify this situation.

1. Introduction

Type 2 diabetes (T2D) is the most common clinical form of diabetes worldwide, its chronic complications increasing cost of care and impacting negatively on quality of life of people with this disease [1–4]. T2D is frequently associated with other cardiovascular risk factors (CVRF) which potentiate development and progression of chronic complications [5].

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Attainment of treatment goals for hyperglycemia and associated CVRF, particularly when reached simultaneously, can effectively prevent chronic complications [6].

Elsewhere, different scientific organizations have developed and published guidelines with standardized algorithms to attain appropriate treatment goals, thereby facilitating management of people with diabetes and associated CVRF [5,7,8]. These algorithms establish sequential, progressive steps ranging from adoption of healthy life styles and different oral glucose lowering drugs (OGLDs) to insulin injections. However, chronic complications still represent a heavy burden on patients and health care organizations in many countries worldwide [1].

The dissociation between successful prevention of chronic complications obtained in randomized control studies and failure to reproduce these results in real world management might result from inappropriate treatment by the management group. This assumption, however, must be proved in order to identify potential effective strategies to modify inadequate behavior of physicians and health care teams in patient management.

We have attempted to obtain an objective answer to this problem by analyzing data recorded in the International Diabetes Management Practices Study (IDMPS) survey implemented in the 2006–2012 period in Argentina. This analysis focused mainly on the characterization and comparison of people with T2D as well as the degree of clinical, metabolic, and therapeutic control obtained in their management.

2. Methods

2.1. Study design

IDMPS is an international, multicenter, prospective, observational study of patients with diabetes. Its survey design followed STROBE guidelines as described elsewhere [9,10].

Briefly, IDMPS is composed of 5 cross-sectional registries (called "waves") in a 5-year period to assess changing practices in management of people with diabetes. Each wave consists of two phases: a 2-week cross-sectional registry and a 9-month longitudinal survey. A 3-month interval separates the end of the longitudinal survey and the start of the next wave. Our current report analyzed only cross-sectional registry data for people with T2D (according to ADA criteria [5]) in Argentina.

2.2. Data collection and outcome measures

Although the IDMPS survey included a wide range of data, this report considers only medical history, medications, glycemic control, blood pressure, and lipid status. Outcome measures analyzed included attainment of treatment goals defined as HbA1c $\leq$ 7%, blood pressure $\leq$ 130/80 mmHg, and LDL cholesterol $\leq$ 100 mg/dl [5].

2.3. Sample size estimation and selection of physicians

The number of subjects to be recruited in each participating country was determined on the assumption that insulin is the least prescribed therapy, and the sample was determined in order to establish the frequency of insulin-treated patients [9,10]. Therefore, 210 Argentinian physicians with experience in initiation and titration of insulin therapy (95% either endocrinologists or diabetologists) were invited and accepted to participate. Physicians with these characteristics participated in the 5 waves implemented in Argentina –most of them working in different ones-, collecting data from 2719 patients with T2D. Patients included in one wave cannot be included in another, thus there is not patients overlapping among waves. Of these, 168 patients were treated only with diet and physical activity, and were not included in the study; therefore, we analyzed 2551 patients treated with different drugs.

2.4. Study implementation

A steering committee advised the project team on study design and registry structure, monitored study progress, reviewed and validated all study-related documents, and proposed and approved decisions on protocol amendments, analyses, and publications. The study was coordinated by Sanofi-Aventis Intercontinental; in each country the study was advocated by a leading diabetologist who compiled and endorsed the list of investigators being assisted by local Sanofi-Aventis staff to accomplish this task. Ethics approval was obtained from institutional boards of each country and all participants provided written informed consent to participate.

2.5. Data analysis

Statistical analyses utilized the Statistical Package for Social Sciences version 15 (SPSS Inc., Chicago, IL, US). Descriptive statistics are presented as percentages and mean ± standard deviation (SD). Comparisons for continuous variables were analyzed by ANOVA, student *t*-test, Mann-Whitney *U* test and Kruskall-Wallis test according to the data distribution profile. Chi-square test was used for proportions. Significance was established at $p \leq 0.05$.

3. Results

As shown in Fig. 1, most people with T2D were treated with OGLDs (65%), followed by a combination of these drugs plus insulin (22%) and only insulin (13%).

These percentages varied according to T2D duration: frequency of OGLD usage went down whereas only insulin went up comparing people ill for under 5 years versus more than 10 years of disease duration (from 86 to 46% and from 4 to 21%, respectively) (Fig. 2).

Most of the OGLDs were represented by metformin (84%), sulphonylureas (49%), thiazolidinediones (19%) and DPP4i (10%) with non-significant differences among waves.

Patients treated only with insulin followed two different regimes: most applied basal insulin whereas a smaller percentage used a basal-bolus regime and a minor percentage premixed insulin. For the basal regime, most patients received human insulin (73%) whereas for the prandial corrections they mostly took analogs (68%).

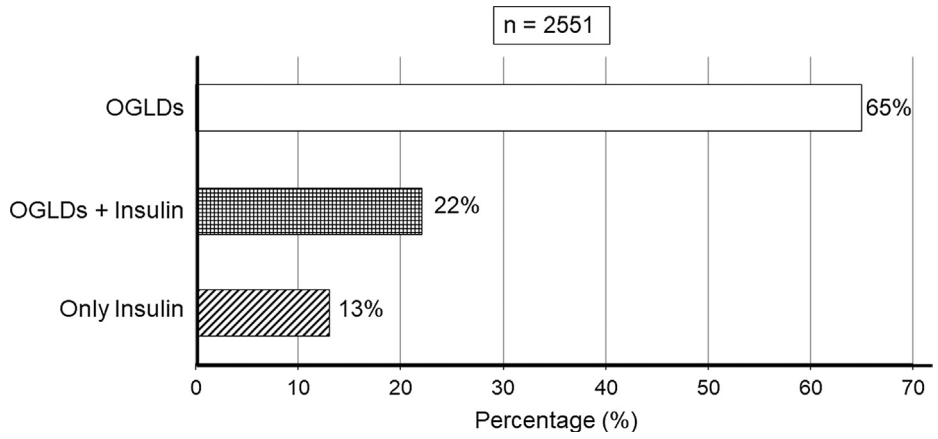

Fig. 1 – Type of treatment. **The figure shows the frequency use (percentage) of different drugs prescribed for the control of hyperglycemia in our population of people with T2D.**

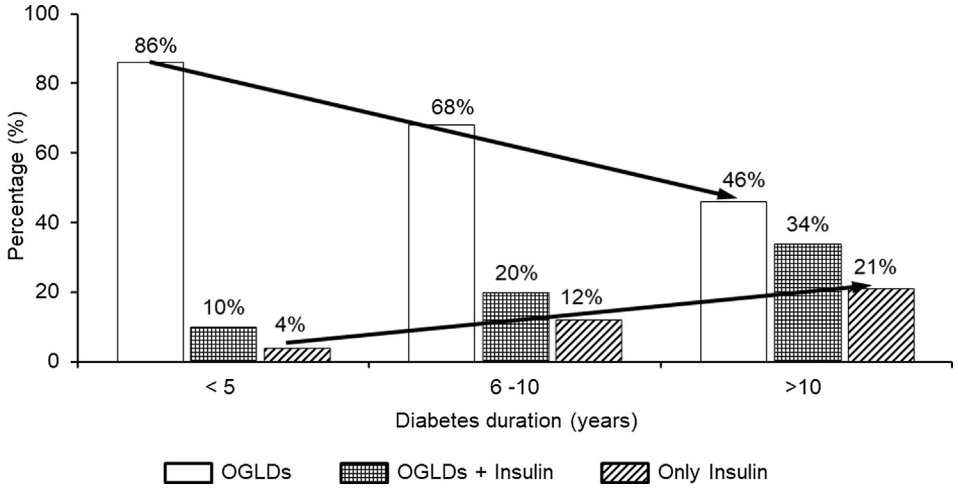

Fig. 2 – Treatment type and disease duration. **The figure shows the opposite trend of OGLD and insulin prescription in people with T2D according to disease duration. The former trend follows a comparable reported pattern of chronological decrease of β-cell mass and function.**

Table 1 – Clinical and metabolic characteristics according to treatment.

Parameter	Only OGLDs (n = 1662)		OGLDs + Insulin (n = 555)		Insulin alone (n = 334)		p-value
Female (%)	47.5%	(773)	50.4%	(272)	48.8%	(159)	0.514
Age (years)	63.0 ± 11.3	(1661)	63.6 ± 10.3	(555)	66.4 ± 10.6	(333)	0.000
Diabetes duration (years)	8.2 ± 7.4	(1604)	14.2 ± 8.8	(539)	15.4 ± 9.6	(318)	0.000
Waist circumference (cm)	103.0 ± 13.7	(1649)	105.5 ± 14.8	(551)	100.1 ± 14.4	(325)	0.000
BMI (kg/m^2)	30.7 ± 5.4	(1659)	31.7 ± 5.9	(553)	29.2 ± 5.3	(332)	0.000
Complications (%)	34.1%	(5 6 7)	59.8%	(332)	68.6%	(229)	0.000
SBP (mmHg)	129.5 ± 14.8	(1651)	131.4 ± 14.5	(552)	130.9 ± 15.5	(331)	0.022
DBP (mmHg)	78.5 ± 9.5	(1652)	78.8 ± 9.4	(552)	78.1 ± 9.7	(331)	0.633
Fasting blood glucose (mg/dL)	132.9 ± 42.2	(1599)	147.0 ± 57.8	(539)	145.8 ± 62.7	(322)	0.000
HbA1c (%)	6.9 ± 1.4	(1551)	8.1 ± 1.7	(538)	8.0 ± 1.8	(319)	0.000
Total Cholesterol (mg/dL)	189.5 ± 38.0	(1547)	188.1 ± 38.9	(515)	190.1 ± 40.5	(308)	0.721
HDL-c (mg/dL)	49.5 ± 15.7	(1482)	49.5 ± 20.6	(494)	50.0 ± 14.6	(281)	0.924
LDL-c (mg/dL)	110.5 ± 33.2	(1425)	110.6 ± 33.9	(482)	114.8 ± 34.1	(274)	0.137
Triglyceride (mg/dL)	152.4 ± 78.9	(1536)	154.8 ± 92.4	(506)	142.1 ± 93.5	(301)	0.093

OGLD: Oral glucose lowering drug; BMI: Body Mass Index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

People treated only with insulin had significantly lower BMI and waist circumference than the other two treatment groups (Table 1). Percentage of people with BMI >30 and 35 Kg/m^2 was lower in the group treated only with insulin.

Chronic complications (micro and macroangiopatic expressed both together) showed significantly lower percentage in the group of people treated only with OGLDs than in the other ones (Table 1).

Systolic blood pressure was significantly higher in patients treated with insulin, either alone or associated with OGLDs. The percentage of people at target values of both systolic and diastolic blood pressure (130/80 mmHg) was lower in the group treated with OGLDs plus insulin (Table 2).

Significantly higher average HbA1c levels were recorded in people treated with insulin, either alone or associated with OGLDs. The percentage of people treated with OGLDs with HbA1c levels ≤ 7.0% decreased according to diabetes duration while that percentage was significantly lower in the group treated with insulin, either alone or combined with OGLDs. However, these two last percentages were independent of disease duration (Fig. 3).

Dyslipidemia was present in around 70% of the overall population and they received statins in 80% of all the cases (data not shown). Average values of LDL-c were significantly higher in the group treated only with insulin, and the percentage of people at goal values for this parameter (<100 mg/dL) was lower. Opposite results were recorded in triglyceride levels: they were significantly lower in people treated with insulin alone and the percentage of people at goal values (<150 mg/dL) was higher.

Finally, when we focused on people that simultaneously attained goal treatment values for BP, HbA1c and LDL-c levels, we found a very low percentage in all groups, but even lower in those treated with insulin alone or combined with OLGDs (Table 2).

4. Discussion

Our study provides objective information on treatment patterns prescribed by physicians familiarized with insulin prescription to people with T2D and on their clinical and metabolic outcomes throughout Argentina.

Table 2 – Percentage of people at goal values on different parameters.

Parameter	Only OGLDs		OGLDs + Insulin		Insulin alone		p-value
	%	n	%	n	%	n	
Normal weight	12.2	1658	9.4	553	20.8	332	
Overweight	38.5	1658	34.5	553	39.8	332	
Obesity	49.3	1658	56.1	553	39.5	332	
HbA1c < 7%	61.6	1551	29.0	538	31.3	319	0.000
SBP/DBP < 130/80 mmHg	25.4	1652	18.3	552	25.1	331	0.003
Total Chol. < 200 mg/dL	63.0	1547	63.7	515	61.4	308	0.796
LDL-c < 100 mg/dL	40.4	1431	38.2	487	34.5	278	0.165
Triglycerides < 150 mg/dL	59.8	1536	60.7	506	68.8	301	0.014
Multi targets (HbA1c < 7%, SBP/DBP < 130/80 mmHg and LDL-c < 100 mg/dL)	5.5		1.5		2.7		0.002

N changes in each parameter because it depends on the number of cases with pertinent data in the individual records.
OGLD: Oral glucose lowering drug; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

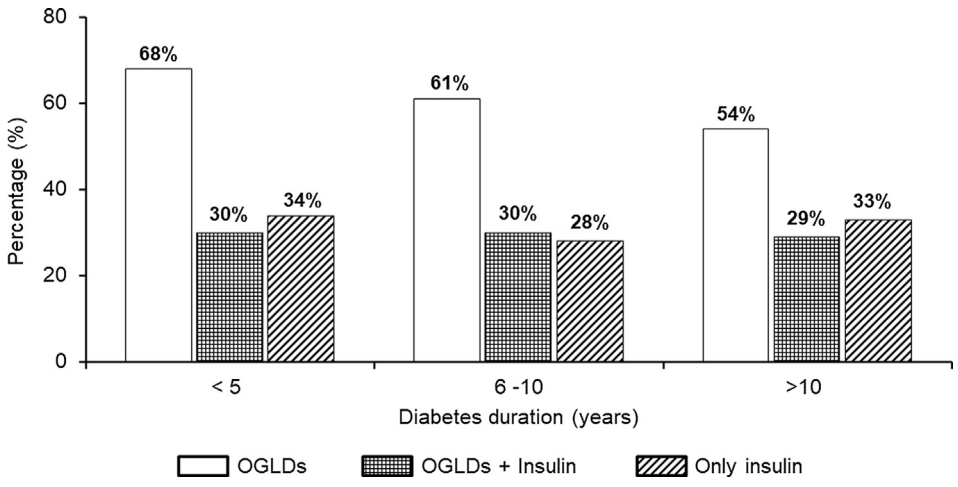

Fig. 3 – HbA1c on target (≤7.0%). The figure represents the percentage of HbA1c values at goal recorded in our population of people with T2D according to the type of treatment employed to control hypeglycemia.

Evidence recorded showed that over half of T2D patients are treated with OGLDs, whereas insulin is chronologically and progressively added until it becomes the only medication effective to treat these patients. Concomitantly, within the group treated with OGLDs the percentage of people with HbA1c ≤ 7.0% decreases according to T2D duration; this phenomenon has also been reported by other authors [11]. Thus, the trend of treatment prescription and the percentage of people at goal values apparently follow the natural time-course of the life of β-cell mass/function. Indeed, these cells are widely accepted to show a progressive decrease starting at the early stage of impaired fasting glucose [12–14]. Also, this trend follows the chronological progressive algorithm proposed by most treatment guidelines in order to attain HbA1c levels able to prevent development and progression of chronic complications [5,7,8]. However, data from our study population show that the use of insulin to control hyperglycemia is far from attain this aim: the percentage of people with HbA1c < 7.0% markedly decreased instead of improving when insulin was added to T2D treatment, independent of disease duration. This poor metabolic control associated with insulin treatment is clinically reflected in the significantly larger percentage of complications recorded in both groups of patients receiving insulin (Table 1).

Other authors have reported similar difficulties to attain target HbA1c values: in their randomized A1chieve study, Home et al mentioned that despite the large reduction of HbA1c values recorded, the percentage people achieving a target value of <7.0% was disappointing, reflecting -among other difficulties- the limited titration of insulin doses over their study period [15]. In a short review on insulin therapy in people with T2D other authors leaded again by Home mentioned that in randomized clinical trials glycemic control to Hba1c levels of 7.0% is not easily achieved and maintain [16].

Further, comparable lower target Hba1c levels in patients with T2D treated with insulin were reported in Lebanon [17], and also in Latin America [18,19].

In our case the failure to attain target HbA1c values with insulin treatment could be ascribed to an inappropriate insulin regime and dosage prescription, assumption supported by the low BMI and waist circumference found for this group of patients (Table 1). It may also suggest that our physician-patient couple is not as efficient as endogenous β cells to control glucose homeostasis.

We might also consider that while most of our patients received human NPH insulin for the basal regime, the opposite situation occurs with rapid acting insulin; in the latter case most patients are treated with analogs. Thus, these data show the selective prescription pattern of our physicians that settle another issue to consider. In fact, despite several randomized clinical trials have been proved the effectiveness of analogs use to treat people with type 2 diabetes with inadequate glycaemic control we need to accept that frequently real world conditions are from those of such trials. Thus, It is necessary to adopt an individualized approach for insulin prescription regime considering the benefits and risks of each treatment approach and the attitude and preferences of each patient to attain successful metabolic control [20].

Altogether these data might draw the attention of health care authorities to the need to implement strategies that (a) effectively prolong the function of endogenous β cells protecting them against glucolipotoxicity [21] and (b) to improve the current inappropriate management of insulin therapy. The first condition requires early diagnosis of T2D –starting at the stage of prediabetes- when the patient still has enough β-cell mass/function, a condition not properly met in our country [22,23]. Also, β-cell protection requires attainment of target HbA1c values -to avoid glucotoxicity- plus effective control of serum lipid profile levels to prevent the deleterious effect of high levels of triglyceride and LDL-c [24–27]. Education of physicians, health care team members, and people with T2D is a cost-effective tool to implement these recommendations [28,29].

Our data also present some further warnings: despite reported evidence that multifactorial control of risk factors lowers the risk of death from cardiovascular causes in a cost-effective manner [5,30], our population of people with T2D treated only with insulin attained low percentages of blood pressure and serum lipids at goal values; the situation was worse when composite therapeutic goals are considered. Comparable low rates of composite parameters at goal values: HbA1c, blood pressure, and LDL-c were also reported in different European countries, across Europe, and in the US, with values around 5% as in our case [11,31–36].

Although statistically significant, our current evidence should be interpreted with caution because: (a) it was obtained from an observational rather than a prospective controlled study and (b) it has a selection bias because physician recruitment criteria were based on physicians' experience with insulin treatments (see material and methods). However, the latter condition might also indicate that the magnitude of poor metabolic outcomes recorded in our group of people treated with insulin may be larger in the primary care physician population.

Briefly, our data shows that, at least in our population and during the time-period considered, people with T2D are: (a) mainly treated with OGLDs in a disease duration-dependent manner, with progressive increase of patients treated with insulin alone or combined with oral drugs; (b) patients treated with insulin attained a low percentage of HbA1c values <7.0%; and (c) this percentage was even lower when considering combined cardiovascular risk factors at goal. This situation must be carefully considered by health and academic authorities in order to implement effective strategies – such as implementation of diabetes education at every level - to effectively modify this situation. We postulate that the implementation of improved strategies would decrease the heavy socioeconomic burden derived from poorly controlled people with T2D.

5. Conclusions

In our country treatment of hyperglycemia in people with T2D mainly depends on disease duration with a progressive increase of insulin prescription. A low percentage of those treated with insulin attain treatment target values (HbA1c < 7.0%) thus facilitating the development and progression of chronic complications. The situation is even worse when considering combined cardiovascular risk factors at

goal (1.5–2.7%). This situation could be effectively overcome by implementation of diabetes education at every care level.

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Conflict of interest

The authors Juan.J.Gagliardino and Jorge Elgart do not present a conflict of interest. Ivanna Querzoli, Lujan Forti and Jean Marc Chantelot are employees of Sanofi.

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