Contents available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

International Diabetes Federation

Time to and factors associated with insulin initiation in patients with type 2 diabetes mellitus

Jorge Enrique Machado-Alba [a,*], *Manuel Enrique Machado-Duque* [b], *Paula Andrea Moreno-Gutierrez* [c]

[a] *Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira, Audifarma S.A, Paraje la Julita, AA: 97, 660003 Pereira, Risaralda, Colombia*

[b] *Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia, Universidad Tecnológica de Pereira, Pereira, Colombia*

[c] *Grupo de Investigación en Farmacoepidemiología y Farmacovigilancia. Universidad Tecnológica de Pereira, Audifarma S.A., Pereira, Colombia*

ARTICLE INFO

Article history:
Received 12 August 2014
Received in revised form
3 December 2014
Accepted 14 January 2015
Available online 21 January 2015

Keywords:
Type 2 diabetes mellitus
Hyperglycemia
Hypoglycemic agents
Insulin
Pharmacoepidemiology
Colombia. (MeSH)

ABSTRACT

Aims: Determine the time between the start of oral antidiabetic therapy (OAD) and the initiation of insulin therapy and to establish factors associated with insulin prescription among patients with type 2 diabetes mellitus (T2DM) in Colombia.

Methods: Cohort, retrospective, population-based study. We identify patients with T2DM who started OAD therapy between 1 January 2007 and 31 December 2008, and a 5-year follow-up was performed. Kaplan–Meier survival analysis for time to start insulin therapy was generated and factors associated with insulin initiation were determined using logistic regression.

Results: A total of 1042 patients (52.4% women), mean age 63.4 years at the start of pharmacological treatment. After 5 years, 272 patients (26.1%) initiated insulin therapy. Using combination therapy of metformin and glibenclamide was associated with greater risk of insulin initiation (OR: 1.64, 95%CI: 1.12–2.40, $p = 0.010$), while being a male over 45 years of age (OR: 0.59, 95%CI: 0.37–0.96, $p = 0.034$) and initiating OAD therapy with metformin (OR: 0.30, 95%CI: 0.20–0.46, $p < 0.001$) reduced the risk of insulin use.

Conclusions: After 5 years of OAD treatment, 26.1% of people with T2DM started insulin therapy. Age, sex and type of initial OAD affected the probability of switching to insulin in these patients in Colombia.

1. Introduction

Latin America is experiencing a remarkable epidemiological transformation. Type 2 diabetes mellitus (T2DM) and other chronic non-communicable diseases are now the major health problems [1,2]. Tissue insulin resistance, followed by progressive decline in β-cell function that promotes disease worsening are the primary cause of this complex metabolic and endocrine disease [3].

Multiple pharmacologic therapies have been developed for diabetes, always with adjuvant lifestyle changes [4,5]. Therapy

* Corresponding author. Tel.: +57 3108326970; fax: +57 63137822.
E-mail addresses: machado@utp.edu.co, jormach66@hotmail.com (J.E. Machado-Alba).
http://dx.doi.org/10.1016/j.diabres.2015.01.018
0168-8227/

usually starts with oral hypoglycemic, such as metformin, sulfonylurea or incretins, which are very effective in achieving glycemic control [1,6]. Adequate treatment also reduces micro and macrovascular complications and reduce mortality [7,8]. When oral therapy is insufficient to reach the goals of clinical practice guidelines, the addition of other drugs is recommended including starting insulin therapy [5,9,10]. The United Kingdom Prospective Diabetes Study (UKPDS) reported that about half of patients required insulin therapy six years after therapy onset and that this could be explained by progressive β-cell impairment [11].

A number of patients are hesitant to begin insulin therapy because of factors such injection site pain, risk of adverse reactions, weight gain and the complexity of the therapy [9,12,13]. Therefore, after education about the disease, types of insulin, dose and dosage forms, therapeutic goals and glucose monitoring, the treating physician and the patient must make the treatment decision [14–17].

Diabetes management is a topic of concern for Latin American health care systems due to its high economic and social burden [18,19]. The objective of this study was to assess how much time elapses between the onset of oral therapy for diabetes and the addition of insulin therapy, and related factors in patients with Colombia.

2. Materials and methods

A retrospective cohort study was conducted with patients with T2DM from a population database from one health-care service provider. Survival analysis was used to assess the time elapsed between hypoglycemic medication onset and the addition of any type of insulin therapy on persons affiliated with the Colombian health system (SGSSS).

2.1. Subjects

Patients included were ≥18 years old, from both genders, lived in Pereira, Colombia, had a diagnosis of T2DM and started oral hypoglycemic medication between 1 January 2007 and 31 December 2008. Monthly follow-up was performed for a period of 5 years or until the patient began taking insulin.

Information was obtained from dispensing records from a private company (Audifarma S.A.), and a database was constructed using Microsoft Excel 2010 and checked by a pharmacoepidemiologist physician.

2.2. Variables included

(1) Socio-demographic: age, sex (additional subgroups created for analysis: men ≥45 years and women ≥55 years) [20].
(2) Pharmacologic: oral hypoglycemic; biguanides (metformin), sulfonylureas (glibenclamide, gliclazide, etc.), insulin (isophane insulin (NPH), zinc crystalline insulin, glargine insulin, glulisine detemir, aspartat, lispro) according to the Anatomical Therapeutic Chemical classification system (ATC).
(3) Comedication: (a) antihypertensive (Agents acting on the renin-angiotensin system, β-blocking agents, thiazides, Calcium channel blockers); (b) Hypolipidemic (statins, fibrates, bile acid sequestrant resins, ezetimibe), (c) antiplatelet agents (salicylic acid, clopidogrel).

2.3. Statistical methods

Data analysis was conducted using IBM SPSS Statistics version 22.0 for Windows (IBM, Chicago, USA). The start of follow-up was considered as the moment when a patient began hypoglycemic therapy (time $0 - t_o$), monthly time scales were used and insulin therapy initiation was defined as the survival analysis event (time $k - t_k$). The database included variables for date of initiation of hypoglycemic drug and insulin therapy, time elapsed (months) for initiation and onset of therapy any time during the 60 months of follow-up for each person. Subjects that initiated therapy during the first year of pharmacological management were categorized as *early insulin therapy*. Patients that never started insulin therapy were categorized as *censured* and those who left the health-care services company during the observation period were categorized as *lost in follow up*. Patients that continued hypoglycemic oral medication despite insulin therapy initiation were also included.

Survival analysis was performed to assess the time elapsed from time zero t_o (oral hypoglycemic therapy initiation) to time t_k (initiation of insulin therapy), where survival was the difference between $t_k - t_o$. The outcome variable was the onset of insulin therapy on T2DM treatment. Hazard ratio or $h(t)$, is the instantaneous risk of outcome occurrence at a certain time and was assessed for patients that started treatment using glibenclamide or metformin. Differences among groups were estimated through a Log Rank test (Mantel–Cox). Risk of initiation at any time of insulin therapy and risk for early insulin therapy were estimated using logistic regression analysis; a p value of <0.05 was considered significant.

The protocol was reviewed by the Bioethics Committee of the Universidad Tecnológica of Pereira (Pereira, Colombia); it was approved as ''research without risk'' and guaranteed the anonymity of the patients, following the principles of the Declaration of Helsinki.

3. Results

There were 1042 patients with T2DM that started oral hypoglycemic therapy between January 1st of 2007 and December 31th of 2008 in Pereira, Colombia. Among the patient population, 546 (52.4%) were women, mean age at the beginning of the observation period was 63.4 years (range: 21 to 98 years). During the 5 years of follow-up, 272 patients (26.1%) started insulin therapy, of which more than half (55.0%) were women. Socio-demographic characteristics and statistical differences among treatment groups are show in Table 1.

The oral agents started by patients is shown in Table 1. As for first insulin regimen, the most frequent was NPH ($n = 160$, 58.8%), then NPH + zinc crystalline insulin ($n = 43$, 15.8%), glargine insulin ($n = 34$, 12.5%), glargine + glulisine ($n = 20$, 7.3%) and other schemes ($n = 15$, 5.6%).