INSULIN REQUIREMENT REDUCTION IN INSULIN TREATED TYPE 2 DIABETES PATIENTS DURING HOSPITALIZATION

DANA CIOBANU[1], SIMONA CLUS[1], ROXANA MOSCU[1], IOAN A.VEREŞIU [1,2], GABRIELA ROMAN[1,2]

[1]Emergency County Hospital Cluj, Clinical Center of Diabetes, Nutrition, Metabolic Diseases, Cluj-Napoca, Romania
[2]Iuliu Haţieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania

Abstract

Introduction. *Key elements for glycaemic control in diabetes mellitus are treatment adherence and lifestyle optimization.*

Aim. *Our objective was to evaluate modifications in insulin requirements and glycaemic values comparing first and last hospitalization days.*

Patients and methods. *We performed a retrospective observational study of 211 patients admitted in Clinical Center of Diabetes Cluj. Inclusion criteria were type 2 diabetes mellitus insulin treated; exclusion criteria were newly diagnosed diabetes, sever metabolic imbalance.*

Results. *The sample study consisted of 56.4% women, aged 61.6±9.8 years, diabetes duration 13.3±8.1 years, hospitalized 2-14 days, blood glucose monitored 2-8 times/day. In the analyzed patients: HbA1c 9.1±1.6%, BMI 32.5±6.3 kg/m^2, GRF 75.3±23.4 ml/min. Diabetes microvascular complications were neuropathy 77.7%, retinopathy 60.2% and nephropathy 40.2%. Drugs added when discharged: Metfomin 61.6%, DiPeptidilPeptidase IV inhibitor 2.75%, GLP-1 analog 1.9%, PPAR-γ agonist 2.8%, Glinides 1% of the patients. Sulfonylurea was stopped in 9 patients out of 14. Insulin regimen when admitted compared when discharged were modified: basal 21.3% to 25.1%, intensive 41.2% to 51.7%, mixed 37.4% la 22.4%, in 2 patients insulin was interrupted. Last day insulin requirement (0.77±0.41 UI/kg) compared with first day (0.87±0.5 UI/kg) were statistically significant reduced (p<0.001, N=209). Last day (153.3±33.3 mg/dl) medium glycaemic levels compared with first day (199±53.9 mg/dl) were statistically significant reduced (p<0.001, N=211). Insulin requirements were reduced in 14.2% patients exclusively by diet modifications (changing home diet with hospital diet, no physical activity). Dietary intake was reduced by 500 kcal and was observed insulin requirement reduction by 0.08 U/kg, median glycaemia reduction by 62 mg/dl at median BMI 29.7 kg/m^2.*

Conclusions. *The analysis demonstrates glycaemic control improvement although decreased insulin requirements due to dietary intake control. Insulin regimens were modified for increasing flexibility. Metfomin was added according with current recommendations.*

Keywords: insulin requirement, reduction, type 2 diabetes, hospitalization.

Introduction

Type 2 diabetes mellitus is a chronic progressive metabolic disease leading to multiple microvascular and macrovascular complications. The control of the disease and the prevention of complications are necessary to be done early and multidirectional in order to reduce the risk of long-term complications and increase the quality of life [1]. Screening programs for early detection of the complications are useful in diagnosing and stopping the progressions of diabetes and also the associated pathology: obesity, hypertension, dyslipidemia. Key elements for glycaemic control in diabetes mellitus are treatment adherence and lifestyle optimization. This requires continuing medical care and ongoing patient self-management education and support. A large body of evidence exists that supports a range of interventions to improve diabetes outcomes as in

Adress for correspondence: danam_b@yahoo.com

UKPDS and ACCORD studies [2,3]. The idea of the study began from the authors' clinical observation: improved glycaemic control despite overall reduced total insulin dose during hospitalization.

The objective of this study was to evaluate modifications in insulin requirements and glycaemic levels comparing first and last hospitalization days in patients with insulin treated type 2 diabetes.

Patients and methods

We performed a retrospective observational study of 211 consecutive patients selected out of 623 patients admitted in Clinical Center of Diabetes Cluj from June 2011 to February 2012. The inclusion criteria were adults with insulin treated type 2 diabetes mellitus. There were excluded patients with newly diagnosed diabetes, on oral medication only, having sever metabolic imbalance, end stage renal disease or acute infectious disease. Anthropometric data were collected: age, gender, height, weight. We calculated body mass index according to the formula: weight/height² (kg/m^2) and we used World Health Organization criteria for defining: normal weight, overweight and obesity. Glycated hemoglobin (HbA1c), serum creatinine, albuminuria were determined. Total hospitalization days, numbers of blood glucose monitoring, hypoglycemic events and insulin requirements for the first and last days of admission were registered. Renal disease was diagnosed according to the following criteria: estimated glomerular filtration rate (GFR) by MDRD calculator [4] <60 ml/min or GRF >60 ml/min and albuminuria >30 mg/g [5]. The foot exam using Toronto score [6] and ophthalmoscopy were performed for screening diabetes chronic complications. All subject previously signed written consent.

Statistical analysis was performed using the SPSS v.13.0 package. Arithmetic mean and standard deviations were calculated to describe quantitative variables, frequencies and percentages were used for qualitative variables. Student t-test was used to compare two variables with normal distribution and ANOVA was used for more samples. A p-value≤0.05 was considered statistically significant.

Results

The main clinical characteristics of patients included in the study are shown in Table I.

Table I. Patients characteristics. (Means±standard deviation for continuous variables and number or percent for categorical variables).

Parameter	Patients (N=211)
Women (%)	56.4
Age (years)	61.6±9.8
Body Mass Index (kg/m^2)	32.5±6.3
HbA1c (%)	9.1±1.6
Diabetes duration (days)	13.3±8.1
Hospitalization period (days)	2-14
Blood glucose monitoring (times/day)	2-8

Overweight and obese patients represented 91.5% of studied population.

Diabetes microvascular complications are represented in figure 1.

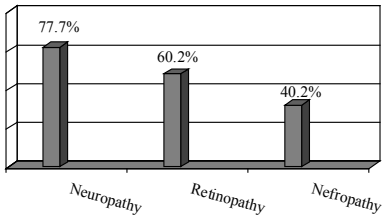

Figure 1. Diabetes chronic complications.

Insulin regimens were modified when admitted compared with when discharged: basal 21.3% to 25.1%, basal-bolus 41.2% to 51.7%, premixed 37.4% la 22.4%. Insulin was stopped in 2 patients. Insulin regimens are represented in figure 2.

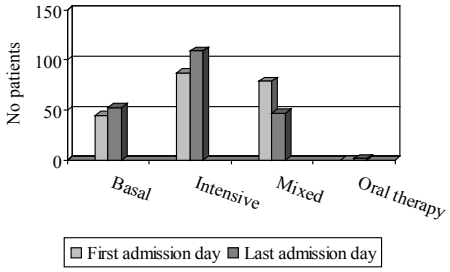

Figure 2. Insulin regimens.

Last day (0.77±0.41 U/kg) insulin requirement compared with first day (0.87±0.5 U/kg) were statistically significant reduced (p<0.001, N=209).

Last day medium glycaemic values (153.3±33.3 mg/dl) compared with first day (199±53.9 mg/dl) were statistically significant reduced (p<0.001, N=211). There were no statistical differences in BMI, hypoglycemic event and number of blood glucose testing. Analyzing data in stratifying intervals of HbA1c we found statistically significant reduced levels of glycaemia for all intervals. Insulin dose reduction was statistically significant reduced only for HbA1c<10%. Results are presented in Table II.

Table II. HbA1c intervals, first and last days values compare (t-Student).

HbA1c(%)	No. patients	p value	
		Glycaemic values	Insulin dose
<7	13	0.014	0.03
7-8	43	<0.001	0.007
8-10	96	<0.001	0.003
>10	57	<0.001	0.27

Insulin requirements were reduced in 14.2% patients exclusively by diet modifications (changing home diet

with hospital diet, no physical activity). Dietary intake was reduced by 500 kcal and was observed insulin requirement reduction by 0.08 U/kg, median glycaemic reduction by 62 mg/dl at median BMI 29.7 kg/m^2. Results are presented in figure 3.

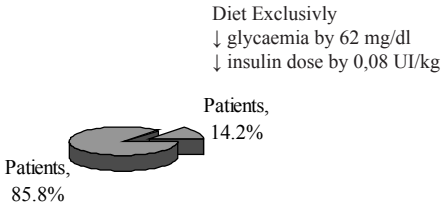

Figure 3. Insulin dose reduction.

Treatment with Metformin was newly introduced in 14% of the patients and supplemented in 61.6% of the patients (figure 4).

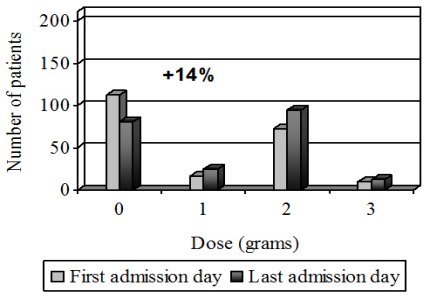

Figure 4. Metfomin therapy.

Drugs added when discharged were DiPeptidilPeptidase IV inhibitor 2.75%, GLP-1 analog 1.9%, PPAR-γ agonist 2.8%, Glinides 1% of the patients. Sulfonylurea was stopped in 9 patients out of 14. Results are presented in figure 5.

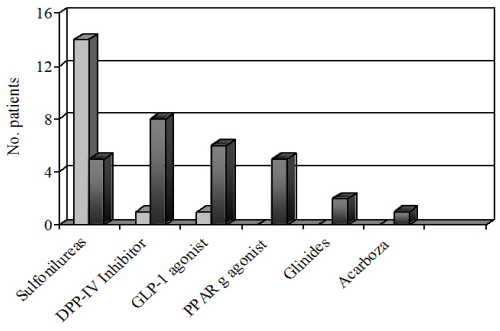

Figure 5. Oral drug therapy.

Discussions

Glycaemic control can be assessed by determining HbA1c every 2-3 months. Higher values than 7% in HbA1c makes lifestyle optimizations -diet and physical exercise- and treatment intensifications necessary [7]. Reduced calories intake combined with adding new-drug therapy in some cases and intensified blood glucose monitoring determines reduction in insulin dose together with improved blood glucose. This hypothesis was the tested in our study. In LOOK-AHEAD study is a large clinical trial designed to determine whether weight loss will improve glycemia in patients with type 2 diabetes. One-year results of the intensive lifestyle intervention in this trial show an average 8.6% weight loss and significant reduction of A1C [8].

Meta-analyses suggest that overall each new class of noninsulin agents added to initial therapy lowers A1C around 0.9-1.1%. Metfomin is the first drug indicated in the treatment of type 2 diabetes and must be maintain unless contraindications appear [9]. In our study group Metfomin was introduced according to international recommendations during hospitalization. Insulin treatment is needed in type 2 diabetes when all combined oral agents fail to maintain glycamia within targets. Adding insulin leads to increased risk for weight gain [10] and hypoglycemia [11]. Daily blood glucose monitoring is mandatory for adjusting insulin dose. Large number of insulin treated type 2 patients perform one or two test a day; in our study median testing in first and last admissions day was 2 to 8 times/day. This intensified glycaemic control helped us better adjust insulin dosage.

In the study group patients associated microvascular complication related to diabetes and obesity. In other large studies peripheral polyneuropathy had an incidence of 20% [12], retinopathy 50% [13] and nephropathy 25% [14]. This shows a higher prevalence of the analyzed populations analyzed in our study than in general population with type 2 diabetes. Explanation may relay in the diabetes' duration and prolonged impaired glycaemic control.

Conclusions

The analysis demonstrates glycaemic control improvement although insulin requirements were decreased due to dietary intake control and mare intensive blood glucose monitoring. Insulin regimens were modified for increasing treatment flexibility. Metfomin was added according with current recommendations.

References

1. American Diabetes Association. Standard of Medical Care-2012. Diabetes Care, 2012; 35(1):11-63.

2 Stratton IM, Adler AI, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ, 2000; 321:405-412.

3. Ismail-Beigi F, Craven T, Banerji MA, et al; ACCORD trial group. Effect of intensive treatment of hyperglycemia on microvascular outcomes in type 2 diabetes: an analysis of the ACCORD randomized trial. Lancet, 2010; 376:419-430.

4. National Kidney Foundation. KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease. Am J Kidney Dis, 2007; 49(2):S1-

S180.
5. Giles P, Rylance P, Crothers D. New results from the Modification of Diet in Renal Disease study: the importance of clinical outcomes in test strategies for early chronic kidney disease. QJM, 2007; 101(2):155-158.
6. Bril V, Perkins BA. Validation of the Toronto Clinical Scoring System for Diabetic Polyneuropathy. Diabetes Care, 2002; 25(11):2048-2052.
7. Nathan DM, Buse JB, Davidson MB, et al.; American Diabetes Association; European Association for Study of Diabetes. Medical management of hyperglycemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care, 2009; 32:193-203.
8. Wing RR. Look AHEAD Research Group. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. Arch Intern Med, 2010; 170:1566-1575.
9. Bennett WL, Maruthur NM, Singh S, et al. Comparative effectiveness and safety of medications for type 2 diabetes: an update including new drugs and 2-drug combinations. Ann Intern Med, 2011; 154:602-613.
10. Buysschaert M, Paris I, Selvais P, Oriot P, Preumont V. Glycaemic control and weight changes in patients with type 2 diabetes intensified to three insulin regimens after therapeutic failure to exenatide. Acta Clin Belg, 2012; 67(4):250-254.
11. Brod M, Rana A, Barnett AH. Impact of self-treated hypoglycemia in type 2 diabetes: a multinational survey in patients and physicians. Curr Med Res Opin, 2012; 28(12):1947-1958.
12. Boulton A, Vinik A, Arezzo J, et al. Diabetic neuropaties. A Statement of the American Diabetes Association. Diabetes Care, 2005; 28:956-962.
13. Kempen J, O'Colmain Bm et al. For the Eye Disease Prevalence Research group. The prevalence of diabetic retinopathy among adults in the United States. Arh Ophtalmol, 2004; 122:552-563.
14. Rossing P. Prediction, progression and prevention of diabetic nephropathy. The Minkowski Lecture 2005. Diabetologia, 2006; 49:11-19.