

Underutilization of insulin and better metabolic control. A NOVA clinic experience

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SUMMARY

OBJECTIVE: To present the results of metabolic control in patients with type 2 Diabetes Mellitus from a private clinic in Northern Mexico,

METHODS: This cross-sectional study used retrospective data obtained from electronic records from a private outpatient clinic at the end of 2018. Inclusion criteria were a diagnosis of T2DM and age ≥ 18 years. Baseline characteristics (age, gender, drug use) were reported. The achievement of glycated hemoglobin goals was established as $<7\%$.

RESULTS: A total of 3820 patients were evaluated. Their mean age was 59.86 years (± 15.01). Of the population, 46.72% were men, and 53.28% were women. Glycated hemoglobin goals were adequate in 1872 (54%) patients. There were 3247 patients (85%) treated with oral medications, of which 1948 (60%) reported glycated hemoglobin less than 7%. Insulin use was reported in 573 (15%) patients, with 115 (20%) reporting glycated hemoglobin less than 7%. The most frequently used basal insulin was glargine in 401 (70%) patients.

CONCLUSIONS: Our findings are clearly higher than the control rate reported by our national health surveys of 25% with glycated hemoglobin $< 7\%$, but similar to that reported in other countries. The most commonly used therapeutic scheme was the combination of oral hypoglycemic agents. The percentage of cases that include insulin in their treatment was lower. Clinical inertia to insulin initiation and intensification has been defined as an important cause of this problem.

KEYWORDS: Diabetes mellitus. Insulin. Hypoglycemic agents.

INTRODUCTION

As the prevalence of type 2 diabetes (T2DM) globally increases, the need for improved disease prevention and management strategies becomes urgent. The International Diabetes Federation estimates that 415 million (1 in 11 persons) individuals have DM, and this will increase to 642 million or almost 10% of the general population by 2040¹. There are great individual, societal, and economic costs associated with DM, which can

be heightened by microvascular complications, such as retinopathy and neuropathy, conditions that have been attenuated by better glycemic control. Macrovascular complications are relatively better abated by lipid and blood pressure control². However, for individuals with DM, cardiovascular disease (CVD) remains the most prevalent cause of morbidity and mortality in both men and women³. Studies show that insulin initiation

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is often delayed until after multiple oral antidiabetic drug failures and deterioration of glycemic control well beyond recommended guidelines^{4,5}. Clinical inertia to insulin initiation and intensification has been defined as an important cause of this problem in Mexico^{6,7}.

The objective of this report is to present the results of the metabolic control of patients with T2DM from a private clinic in Northern Mexico, emphasizing the proportion of patients that achieve target goals.

METHODS

This cross-sectional study used patient data obtained during 2018 from electronic records from the private outpatient clinic of the Hospital Clinica Nova in San Nicolas de los Garza, Mexico, where all diagnostic procedures and treatments were free of charge to patients, given by general internists. Inclusion criteria were a diagnosis of T2DM and age ≥ 18 years. We excluded pregnant patients, patients with type 1 DM, and patients with acute metabolic complications, such as diabetic ketoacidosis and hyperglycemic hyperosmolar state. Baseline characteristics, including age, gender, and drug use, were reported. Hemoglobin A1c (A1c) goal was established as $< 7\%$ following ADA 2018 recommendations⁸. The study was approved by the local research ethics committee. Statistics were reported as frequencies, percentages, and central tendency. When comparing different treatments to the therapeutic goal, $p < 0.05$ was considered significant.

RESULTS

A total of 3820 patients were evaluated. The mean age was 59.86 years (15.01); 46.72% were men, and 53.28% were women. A1c goals were adequate in 2063 (54%) of patients.

Of the 3247 patients (85%) treated with oral medications, 1948 (60%) had an A1c less than 7%. In most cases, treatment was combined using 2 to 4 drugs, including metformin (66.34%). Insulin use was reported in 573 (15%) patients, either with insulin alone or insulin combined with oral agents. The most frequently used

insulin was glargine, reported in 401 (70%) patients; pre-mixed insulin in 115 (20%); and other types of insulin (NPH, detemir, degludec) in 57 (10%). In patients with insulin treatment, the A1c target was met in 115 (20%). There is a significant difference in glycemic control in favor of oral medication compared to insulin ($\chi^2=31.68$, $p<0.00001$). Other measures to treat cardiovascular risk factors, such as statins and acetylsalicylic acid, were used by a small percentage of patients ($< 20\%$).

DISCUSSION

The control of T2DM in our clinic was 54%. Our findings are clearly higher than the control rate reported in the national health survey in Mexico of 25% with A1c $< 7\%$ ^{6,7}, although similar to results reported by primary care doctors of the Spanish healthcare system⁹. Other recent publications from the United States reported that overall glycemic control has not improved and remains poor among nearly a quarter of younger patients¹⁰.

The most frequent therapeutic scheme was the combination of oral hypoglycemic agents with metformin in a large proportion with good glycemic control. This is similar to previous studies, in which up to 80% of patients with DM were taking oral treatment, along with a tendency to reduce the use of sulfonylureas^{11,12}. New treatment schemes that include glycosuric or GLP agonist drugs have yet to represent a significant proportion in our studies, due to them being just recently added to our therapeutic tools¹³. It is very important to establish appropriate guidelines for the selection of OHAs. We use metformin as monotherapy and combination therapy, and its association with other drugs will depend on the patient's clinical characteristics and the efficacy, side effects, mechanism of action, risk of hypoglycemia, the effect on body weight, patient preference, and combined comorbidity. Interestingly, newer antihyperglycemic medications such as the GLP-1 RAs and SGLT-2 inhibitors showed significant promise in recent clinical trials in terms of providing CV benefit via their favorable effect on traditional CV-risk factors. GLP-1 agonists provided more benefits in terms of improving vascular risk factors and atherosclerosis, whereas SGLT-2 inhibitors improved HF outcomes and CV mortality^{14,15}. Real-world data evaluating SGLT-2 inhibitors use in T2DM patients confirmed the findings of EMPA-REG OUTCOME study and also showed that SGLT-2 inhibition could have CV benefit in patients with low CV risk¹⁴.

TABLE 1.

	A1c $< 7\%$ (n,%)	A1c $> 7\%$ (n,%)
N= 3820	2063(54)	1757(46)
Oral Treatment (n=3247)*	1948(60)	1299(40)
Insulin (n=573)	115(20)	458(80)

*Differences between oral and insulin metabolic control: $P < 0.00001$

We have recently published our findings in relation to one of these classes of medications¹³. More detailed studies, perhaps using patient and physician questionnaires, should attempt to establish the reasons for a delay in intensification, particularly among older people with DM and those with comorbidities.

The percentage of cases that included insulin in their treatment was lower than that reported in other countries where it is greater than 30 %¹⁶; however, it is similar to the 13% in the national survey⁶, despite the low rate of insulin use, the control measured by A1c is similar to that of developed countries¹⁰, perhaps due to the option of combining two or more non-insulin drugs, or the significant delay in the initiation of insulin treatment after glycemic failure with oral antidiabetic drugs^{11,12}. Initiation of insulin treatment with basal analogs insulin is often a preferred option for primary care physicians for its relatively low risk of hypoglycemia or in patients with a history of hypoglycemia with human insulins^{11,12,17}; however, there is no fixed standard for intensification of insulin treatment in patients who continue to have poor glycemic control after insulin initiation. However, the use of other schemes is infrequent¹⁸. Moreover, it is important that studies on clinical inertia be carried out regularly to keep up with the changes in patient demographics, therapy options, and clinical guidelines¹⁹. We speculate that these patients may have been on very low doses of insulin and have low adherence to medical treatment. This hypothesis could be the basis for further research.

In our country, age, a high body mass index, stress in a private setting, and longer duration of DM and insulin use have been found as the main cause of chronic poor control. Fasting blood glucose is the method frequently used to assess glycemic control and A1c, considered the gold standard, is used in less than 10% of cases^{6,7}.

The strengths of the present analysis include cohort size, which corresponds to a private clinic where the first level of care are internists, with institutional coverage of all antidiabetic drugs approved in our country and a multidisciplinary team for the care of patients with DM.

We are also developing a multidisciplinary coaching strategy in outpatient “problem” patients under both oral and insulin medications, using all clinical evaluation and biomarkers as determinations of peptide C in the decision making, personalizing of diabetes care ranking the following aspects: Pathophysiology (insulin resistance or insulin deficiency), Potency (effectiveness),

Precaution (security), Perks (non-glycemic effects), Practicalities (consistency with the treatment), and Price (our clinic provides coverage), all this in addition to personalized goals according to age and comorbidities. The main limitation of our cross-sectional study is its design: an electronic database with unidentified data variables such as body mass index, insulin dose, time of evolution of chronic poor control, dose intensification or titrations, treatment adherence, among others, selection bias because the population is from a secondary-care hospital clinic. No subanalysis of results that could modify these data was performed; for example, for geriatric patients whose therapeutic goals are more flexible. Also, no pharmacodynamic study was performed. Our goals are to continue increased medical education including structured programs in DM both for patients and physicians and to try to create preventive, predictive, personalized and precise care, along with informing about and prescribing medication for cardiovascular risk factors, such as the use of statins and aspirin, which is low in our clinic. We will also continue promoting independent medical education for the attending physician as a strategy for improving clinical inertia and providing personalized care.

CONCLUSION

Our patients’ glycemic control is similar to that reported around the world, but higher than that reported in our country. The use of oral hypoglycemics in combination is the most frequently used therapeutic strategy. Insulin treatment represents only a small percentage with insufficient control. The prescription of drugs for cardiovascular risk factors, like statin and aspirin, is an area of opportunity due to its infrequent indication. The management of T2DM calls for employing a holistic risk factor control approach with conventional T2DM medications and adequate control of additional cardiovascular risk factors.

Conflict of interest

None

Sources of funding

None

Author contributions

All authors contributed to the study design, data analysis, data interpretation, and writing of the manuscript

RESUMO

OBJETIVO: Apresentar os resultados do controle metabólico de pacientes com Diabetes Mellitus tipo 2 em uma clínica privada no norte do México,

MÉTODOS: Este estudo transversal utilizou dados retrospectivos obtidos em prontuários eletrônicos de um ambulatório privado no final de 2018. Os critérios de inclusão foram o diagnóstico de DM2 e idade ≥ 18 anos. Características basais (idade, sexo, uso de drogas) foram relatadas. A realização de metas de hemoglobina glicada foi estabelecida como $<7\%$.

RESULTADOS: Um total de 3820 pacientes foram avaliados. A média de idade foi de 59,86 anos (+/- 15,01). Da população, 46,72% eram homens e 53,28% eram mulheres. Objetivos de hemoglobina glicada foram adequados em 1872 (54%) pacientes. Havia 3247 pacientes (85%) tratados com medicamentos orais relatando em 1948 (60%) menos de 7%. O uso de insulina foi relatado em 573 (15%) pacientes, com 115 (20%) relatando menos de 7%. A insulina basal mais utilizada foi a glargina, em 401 (70%) pacientes.

CONCLUSÕES: Nossos resultados são claramente mais altos do que a taxa de controle relatada por nossos levantamentos nacionais de saúde de 25% com hemoglobina glicada $<7\%$, mas semelhante à relatada em outros países. O esquema terapêutico mais utilizado foi a combinação de hipoglicemiantes orais. A porcentagem de casos que incluem insulina no tratamento foi menor. A inércia clínica à iniciação e intensificação da insulina tem sido definida como uma importante causa desse problema.

PALAVRAS-CHAVES: Diabetes mellitus. Insulina. Hipoglicemiantes

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