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An algorithm for the treatment of type 2 diabetes in Latin America

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Summary: Diabetes is a principal and growing health concern in Latin America, accounting for significant mortality and morbidities. Large, randomized, prospective trials of various interventional therapies in patients with both type 1 and type 2 diabetes have demonstrated that reductions in hyperglycaemia and management of diabetes-related risk factors can significantly reduce the micro- and macrovascular complications of diabetes. Therefore, patients with type 2 diabetes will benefit from more aggressive treatment regimens to help decrease the occurrence and rate of progression of diabetic complications. Given the many complexities of diabetes management, it is often difficult for general practice physicians to stay abreast of emerging treatment strategies and therapies. Owing to the high prevalence of type 2 diabetes in Latin America, the majority of patients with diabetes are treated by generalists rather than specialists. This article was intended to assist physicians and other healthcare professionals in developing and using effective treatment strategies to stem the growing epidemic of diabetes and its complications in Latin America.

Keywords: diabetes treatment, AIC, glycaemic control, self-monitoring of blood glucose

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Introduction

A group of physicians met on 18 January 2003 in San Jose, Costa Rica, to develop an algorithm for treating patients with type 2 diabetes mellitus. Attendees included physicians representing a cross-sectional view of type 2 diabetes in various Latin American regions. The purpose of this al gorithm was to provide a stepwise approach to the treatment of type 2 diabetes, including detection/diagnosis and initiation of education, nutrition therapy, exercise therapy, pharmacologic therapy and monitoring. This article presents a perspective on the increasing need for treatment guidelines in Latin America and discusses the epidemiology of type 2 diabetes in Latin America as it relates to the challenges faced by the physicians trying to control this disease and its complications.

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Overview

Diabetes is a principal health concern in Latin America. It is estimated that over 19 million Latin Americans have diabetes, affecting 10–15% of the adult population [1–3]. Undiagnosed diabetes further compounds the problem. It is estimated that over 30% (up to 90% in some rural areas) of people with type 2 diabetes are undiagnosed [4]. Furthermore, Latinos in the US report greater functional impairment with the disease, and their diabetes mortality rates are higher than those of European Americans [5]; the annual number of deaths in 2000 caused by diabetes mellitus was estimated at 339 035 in Latin America and the Caribbean [6]. Unless effective preventive measures are established, the number of people with diabetes in Latin America will increase to approximately 40 million by 2025 [1,2].

Owing to the high prevalence of type 2 diabetes in Latin America, the majority of patients with diabetes are treated by generalists rather than specialists, as in most parts of the world. The inherent complexity of diabetes treatment, combined with continuous introduction of new therapies and treatment strategies, is often overwhelming for general practitioners who must remain current in a variety of disease states and treatment modalities. Therefore, it is valuable to develop a clear and concise treatment algorithm to assist clinicians in the detection and treatment of type 2 diabetes.

Epidemiology of Type 2 Diabetes in Latin America

Cultural and Ethnic Diversity

Latin America comprises more than two dozen countries, covering an area twice the size of Europe. Despite its size, Latin America has just over half of the population of Europe (about 450 million in 1995) [1].

The population of Latin America is very diverse. Over 60% of Latin Americans can be classified as mestizos (a mixture of white and Native Americans), though the distribution of this population varies widely, from less than 20% in Argentina and Uruguay to more than 80% in Paraguay, Ecuador and Honduras [7]. In some countries, such as Bolivia, Peru and Guatemala, more than one-third of the population is Native American. In addition, a large proportion of black descendants are found in Brazil, Colombia, Panama and the Caribbean Islands. This diversity, however, is only one of many factors associated with the increase in diabetes in Latin America.

Geographical Diversity and Effects of Urbanization

In addition to a population that represents an assortment of ethnic and cultural backgrounds, the natural environment of Latin America is also very diverse. It is logical, then, that the observed prevalence of a disease, such as type 2 diabetes, which is affected by both cultural and environmental influence, also varies widely in Latin America. Studies have shown the occurrence of diabetes to range from less than 1% in some Native American communities and rural populations [8] to more than 10% in some urban populations (reports from Mexico) [4].

Two-thirds of Latin Americans are now urbanized (ranging from 40 to 90% in different countries), but migration to urban areas is rapidly increasing these figures [4]. Some studies have shown that 30–40% of the people with type 2 diabetes living in Latin American cities are undiagnosed; in some rural areas, undiagnosed type 2 diabetes can be as high as 90% [4].

Effects of Age

The age pyramid is also changing. In most Latin American countries, approximately one-third of the population is at or over 30 years of age. Ten years ago, the proportion was less than one-fourth [4]. In all Latin American countries, the prevalence of type 2 diabetes increased with age [4]. This is particularly important, as the age distribution in Latin America has changed. For example, in Colombia, between 1985 and 1993, the total population has increased by 29%; however, the major changes occurred in the age groups over 30 years, which showed a 46% increase [4]. Overall, the population over 60 years is increasing at an annual rate of about 3%, whereas the US rate is less than 0.5% [7].

Complications

The few studies that have looked at complications in newly diagnosed patients (Argentina and Colombia) show that prevalence is high; the prevalence of retinopathy ranges between 16 and 21%, nephropathy between 12 and 23% and neuropathy between 25 and 40% [7]. Patients also experience other confounding risk factors, such as dyslipidaemia, hypertension, coronary heart disease, peripheral vascular disease and cardiovascular disease; in general, the prevalence of dyslipidaemia ranges from 35% in San Jose, Costa Rica to 53% in Bogotá, Colombia, while the frequency of hypertension ranges from 28% in La Plata, Argentina to 40% in San Jose, Costa Rica [4]. It is important to note that studies of African Caribbean and Latino patients have shown no difference in complications when glycaemia is controlled [9,10].

In summary, although the epidemiological data presented here are not the result of standardized studies throughout Latin America, they do fulfil a need where little or no information is available. The isolated efforts of epidemiologists have brought attention to the diversity of diabetes epidemiology in Latin America, showing that much of the population of Latin America is at high risk for diabetes and that the prevalence of diabetic complications varies throughout Latin America. Moreover, prevalence of diabetes is increasing at a rapid pace. It is apparent that patients with type 2 diabetes require more aggressive treatment regimens to help decrease the occurrence and rate of progression of diabetic complications. The purpose of this article was to assist physicians and other healthcare professionals in developing and utilizing effective treatment strategies to stem the growing epidemic of diabetes and its complications in Latin America.

Pathophysiology of Type 2 Diabetes

Progression of Insulin Resistance and β-cell Deterioration

Type 2 diabetes is a progressive disease characterized, initially, by persistent insulin resistance and compensatory hyperinsulinaemia [11]. As shown in figure 1, pancreatic β-cells gradually lose their ability to respond with appropriate insulin secretion to a glucose challenge. Eventual loss of first-phase insulin response and reduced suppression of hepatic glucose output after meals lead to impaired glucose tolerance (IGT), indicated by postprandial hyperglycaemia [12]. Progressive decrease of insulin secretion and insulin sensitivity lead to an absolute increase in hepatic glucose output. When hepatic glucose output exceeds glucose utilization, fasting hyperglycaemia results [12].

It is important to observe that the majority of individuals who are insulin resistant do not go on developing type 2 diabetes [13]. Therefore, it has been suggested that although insulin resistance and impaired insulin secretion are both important in the pathogenesis of type 2 diabetes, insulin resistance appears to be primarily acquired (through obesity and sedentary lifestyle), while impaired insulin secretion is the primary genetic defect [14].

Impact of Glycaemic Control

Large, randomized, prospective trials have shown that reductions in hyperglycaemia, in conjunction with management of diabetes-related risk factors, significantly reduce the micro- and macrovascular complications in patients with type 1 and type 2 diabetes [15–17]. These trials demonstrated a 30–35% reduction in microvascular complications per 1% absolute reduction of glycated haemoglobin. Epidemiological data from the UKPDS also showed a 14–16% decrease in macrovascular complications for every 1% absolute reduction in glycated haemoglobin with no glycaemic threshold for a substantive change in the risk for any of the clinical outcomes studied [18]. Risk reduction extended into the normal range for glycated haemoglobin.

To achieve maximum benefit from treatment, many researchers and clinicians now believe that glycated haemoglobin values must be kept close to <6.5%, which is slightly above normal range in non-diabetic

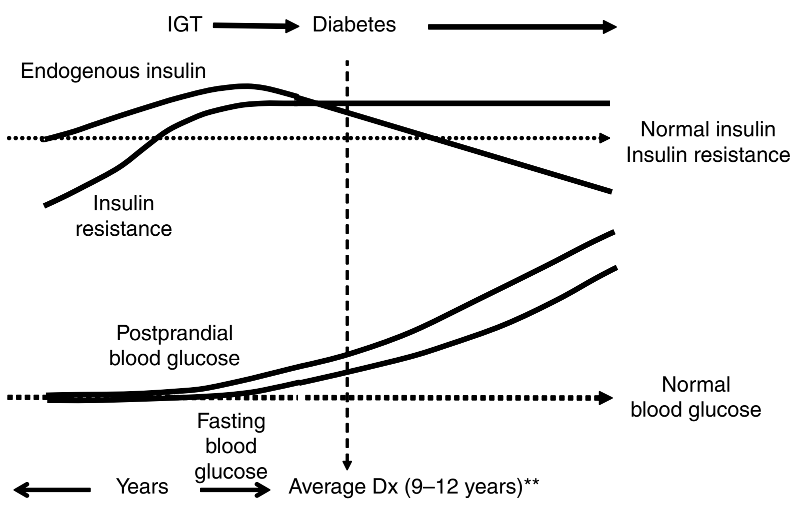

Fig. 1 Conceptual rendering of type 2 diabetes progression [31,67]. Dx, diagnosis.

patients (<6%) [19,20]. A key factor in achieving optimal A1C levels is achieving and maintaining near-normal postprandial glucose, as well as fasting and preprandial glucose control.

Management of Risk Factors

Microvascular Disease

Maintaining good glycaemic control is an effective strategy for reducing the development and progression of microvascular complications, such as retinopathy, nephropathy and neuropathy. The UKPDS showed a direct benefit of treating hypertension in both micro- and macrovascular disease [21]. However, in addition to achieving glycaemic control, it is important to perform periodic assessments of the patient to detect the presence/severity of these complications. Tables 1 and 5 provide treatment targets and suggested frequency for assessing these micro- and macrovascular complications in diabetic patients.

Macrovascular Disease

Although the link between glycaemic control and macrovascular complications stems from epidemiological studies, clinical trial data demonstrate that obesity, hypertension, dyslipidaemia and procoagulant state have a direct impact on macrovascular disease [22,23]. While obesity has always been a key risk factor for the development of type 2 diabetes, it can also make diabetes management more complicated, often worsening metabolic abnormalities, such as insulin resistance, hyperglycaemia, hyperinsulinaemia and dyslipidaemia.

Table 1 Goals of treatment

Measurement	Target values
A1C (%)	≤6.5* [19,20]
Fasting/preprandial (mg/dl)	<110† [19,20]
2-h postprandial (mg/dl)	<140 [20]
Blood pressure (mmHg)	<130/80 [42]
Fasting lipids (mg/dl)	
LDL cholesterol	<100 [42]
HDL cholesterol	>40 (men) [42]
	>50 (women)‡ [42]
Triglycerides	<150 [42]
Microalbuminuria	<30 μ/mg creatinine (spot) [42]
	<30 mg/24 h [42]

*Standardized to DCCT methodology (upper limit: 6.1%).
†Plasma equivalent.
‡Suggested.
HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Conversely, findings from the Diabetes Prevention Programme (DPP) and other studies clearly show that modest weight loss (5–10% of body weight) and regular physical activity can prevent or delay the progression from IGT to type 2 diabetes [24–26].

Treatment of dyslipidaemia is also an important component in the prevention and treatment of macrovascular disease. A study by Pyorala *et al.* [27] revealed that treatment of dyslipidaemia resulted in a 28% reduction in cardiovascular events in patients with type 2 diabetes. Rubins *et al.* [28] showed a significant 41% reduction in cardiovascular death in diabetic men treated with a fibrate.

Although atherosclerosis and vascular thrombosis are considered major contributors to mortality, it is generally accepted that platelets are also contributory [29]. There is substantial evidence that supports low-dose aspirin therapy as a primary prevention strategy in men and women with diabetes who are at high risk for cardiovascular events [30].

Treatment Algorithm

The overall goals of diabetes management are to achieve good metabolic control and to prevent the micro- and macrovascular complications of diabetes. Figure 2 presents a treatment algorithm that clinicians may find helpful in developing treatment regimens for patients. It is important to observe that treatment plans should be individualized to each patient (figure 2).

Although there are no data available specific to Latin America, Harris *et al.* [31] showed that patients may have diabetes 9–12 years prior to diagnosis. As a result, patients are often not identified until they present with one or more diabetic complications. Therefore, the first step in treatment is to assess each patient in terms of glycaemic control and presence/degree of complications.

Step 1. Risk Assessment

The following are the key measurements used to assess glycaemic control and risk for diabetic complications.

A1C – Haemoglobin A1C

A1C testing is considered the gold standard in monitoring glycaemic control. A1C is used to assess glycaemic levels over a 2- to 3-month period (see table 1 for A1C target).

Microalbuminuria

Microalbuminuria testing is used to detect the development or progression of diabetic nephropathy;

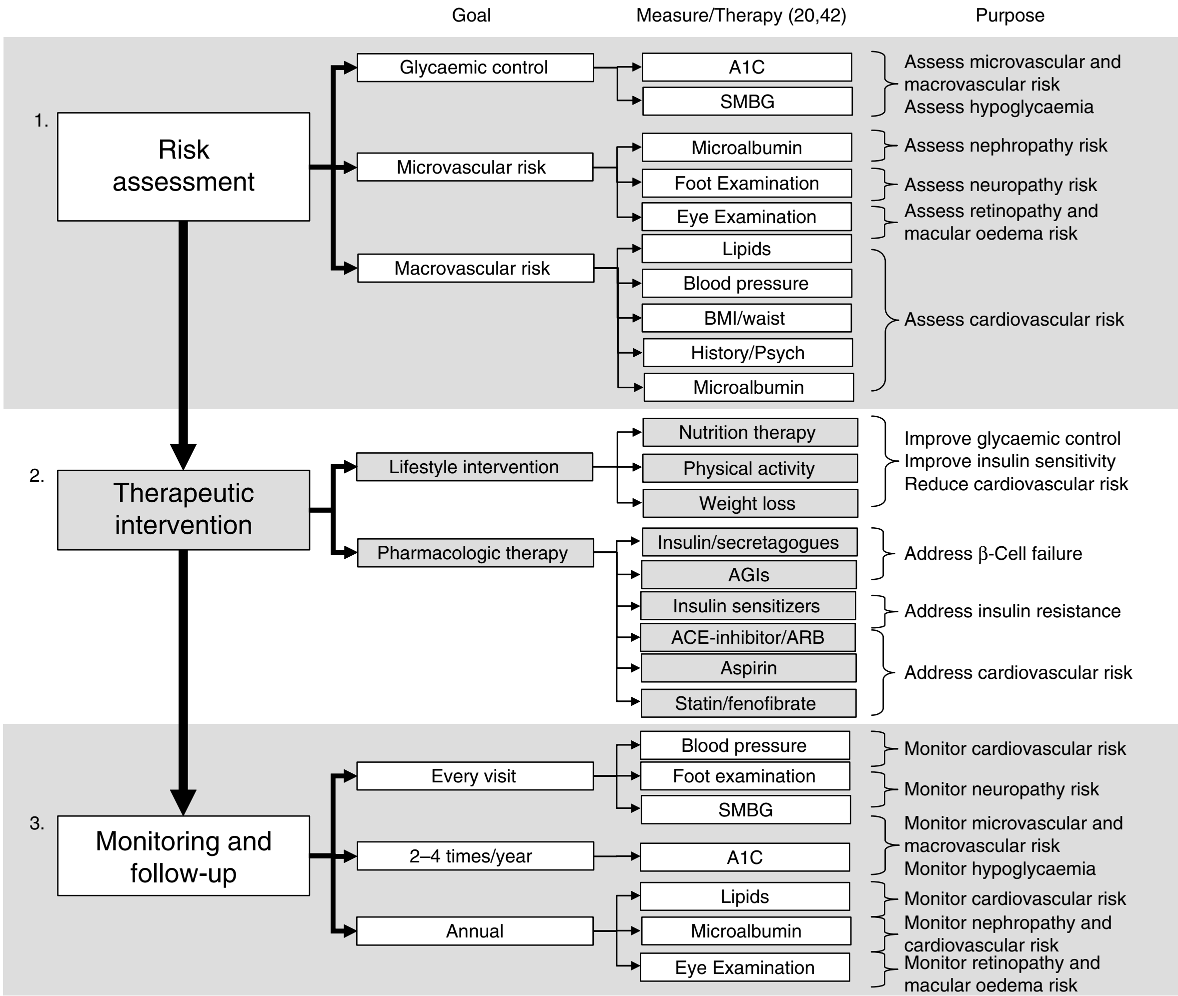

Fig. 2 Treatment algorithm. AGI, α-glucosidase inhibitors; SMBG, self-monitoring of blood glucose.

microalbuminuria is also a risk factor for cardiovascular disease in type 2 diabetes (see table 1 for laboratory values).

Foot Examination

Regular foot examinations are critical in identifying and assessing peripheral vascular disease and diabetic neuropathy. Clinicians should perform a foot examination at every patient visit. It is also valuable to teach patients to perform self-examinations. This will help identify abnormalities earlier and reinforce the importance of good glycaemic control.

Eye Examination

Diabetes is the leading cause of blindness in adults. Patients with diabetes should have a thorough eye examination (through dilated pupils) at the time of diagnosis and then annually to detect presence/progression of retinopathy and/or macular oedema.

Lipids

Recommended goals for lipid levels are presented in table 1. Levels should be checked annually for patients with normal or controlled lipids. Levels should be checked more frequently in patients with dyslipidaemia or in those who are changing/adjusting medication.

Blood Pressure

Blood pressure should be checked at every patient visit. Table 1 presents recommended targets for patients with diabetes.

BMI/Waist Circumference

Body mass index (BMI) [weight (kg) divided by height squared (m^2), kg/m^2] is the clinical standard for measuring obesity. However, a strong correlation has been found between BMI and a simple measurement of the waistline across the navel. Despres *et al.* showed that a 100-cm (40-inch) waistline measurement can be used as a cut point for central obesity in men [32]; a circumference of 35 inches can be used to determine obesity in women [33]. Waist measurement can be performed quickly in the office and can be easily explained to the patient.

History

Personal interviews are needed to identify other risk factors such as smoking or excessive use of alcohol. It is also important to screen for depression; up to 30% of patients with diabetes suffer from depression and anxiety [34,35]. Another common disorder in men is erectile dysfunction; up to 75% of diabetic men will experience consistent or recurrent inability to achieve and maintain an erection adequate for sexual performance in their lifetime [36]. It is estimated that more than 50% of men with diabetes will develop erectile dysfunction within 10 years of disease onset [37]. These conditions have been proven to have a significant impact not only on general health but also on the patient's adherence to self-care plans and clinical outcomes. Identification of symptoms and signs associated with hyperglycaemia (i.e. urinary tract infections, blurred vision, skin infections and vaginitis) can be accomplished through a careful history.

Because diabetes is a self-managed disorder, patients must possess the knowledge and skills to effectively manage their disease. Therefore, it is important to assess patient's self-management skills and then to provide appropriate education to address knowledge/skill deficits.

Step 2. Therapeutic Intervention

Lifestyle Intervention

Not all patients are diagnosed at the same stage during the disease progression. If a patient with type 2 diabetes is diagnosed relatively early in the process, the first step is usually lifestyle intervention. Numerous studies have shown that regular exercise, a low-fat/high-fibre diet and moderate weight loss (5–10% of body weight) improve insulin sensitivity and reduce cardiovascular risk [38,39]. Lifestyle intervention (diet and moderate weight loss) has been shown to lower A1C levels up to 1–2% [40].

Exercise

Regular physical activity provides significant cardiovascular benefits to patients, including improved circulation, respiratory system, blood pressure and insulin sensitivity [41]. A regimen of brisk walking is an easy exercise programme to initiate because it requires no special equipment and can be performed indoors and outdoors. When discussing exercise with patients, clinicians should encourage them to select an activity that is enjoyable; otherwise, they will not follow the regimen. It is also important to make the patient start slowly (10 min/day) and gradually work up to 30–45 min of brisk walking, 4–5 days per week. Patients should be evaluated for any health issues (cardiovascular risk and peripheral neuropathy) that would contraindicate a specific exercise.

Nutrition

Modification of dietary habits can positively affect both glycaemic control and cardiovascular risk [42]. Reducing total daily caloric intake and a more even distribution of calories consumed during the day can significantly improve postprandial glucose levels and overall glycaemic control. Limiting fat intake and increasing dietary fibre have been shown to improve cardiovascular risk factors as well. Current recommendations for meal composition include:

- Carbohydrate (preferably complex) and monounsaturated fat together should provide 60–70% of energy intake; however, the metabolic profile and need for weight loss should be considered when determining the monounsaturated fat content of the diet [43]. Less than 10% of energy intake should be derived from saturated fats [43].
- Protein should make up 15–20% of caloric intake [43].
- Consume 20–30 g fibre for each 2000 total calories consumed daily [43].

Whenever possible, patients should be encouraged to meet with a qualified dietician for instruction in nutrition and meal planning.

Weight Loss

Combining regular exercise with low-fat/high-fibre meals and reduced caloric intake leads to gradual weight loss in most patients. Furthermore, even modest weight loss can significantly improve insulin sensitivity and overall glucose control and reduce cardiovascular risk [24]. Key concepts to communicate with patients include:

- Modest weight loss (5–10% of body weight) significantly improves health.
- Weight loss occurs when patients expend more calories than they consume.
- Loss of 0.45 kg of body fat requires a reduction/expenditure of 3500 calories.
- Record progress (weight, waist measurement, adherence to exercise and daily food diary).

Table 2 presents a method for calculating required daily caloric intake based on patient's activity levels.

Table 2 Calculation for estimated daily caloric intake requirement based on activity level

Activity factor	Females	Males
Sedentary (no activity)	27	29
Light activity	31	33
Active	35	38
Very active	40	44

Daily calories = target weight (kg) × activity factor.

Self-Monitoring of Blood Glucose

Self-monitoring of blood glucose (SMBG) data generated by the patient provide important information regarding glucose levels throughout the day. This allows clinicians and patients to make informed decisions when adjusting meal plans and medication regimens. The frequency of SMBG has been closely linked with improved outcomes as measured by A1C levels [44]. A recent study by Schwedes showed that post-meal monitoring improved glycaemic control in patients with type 2 diabetes who were not treated with insulin [45]. Figure 3 presents a staggered testing regimen that provides key information about preprandial and postprandial glucose control without requiring excessive testing. Patients should follow this regimen when they change/adjust therapy. This is also a useful testing regimen to follow 2 weeks prior to their next office visit.

	Breakfast		Lunch		Supper		Bedtime
	Pre	Post	Pre	Post	Pre	Post	
Monday	X	X					
Tuesday			X	X			
Wednesday	X				X	X	
Thursday	X	X					
Friday			X	X			
Saturday	X				X	X	
Sunday	X	X					

Fig. 3 Staggered regimen for self-monitoring of blood glucose (SMBG).

Education

Diabetes is a lifelong, self-managed disease that requires patients to master a variety of cognitive and physical skills. Patients should be exposed to an education programme to receive instructions regarding the necessary management skills. Basic diabetes education should include:

- Information about diabetes risks and complications.
- Training in identifying and treating acute complications (hyperglycaemia and hypoglycaemia).
- Training in SMBG, including testing procedure, meter/sensor care and maintenance, documentation and utilization of test results
- Instruction in medications, including dosages, insulin administration (if needed), storage, drug interactions and avoidance/treatment of hypoglycaemia
- Instruction in meal planning, including food selection, portion control and calorie reduction strategies
- Instruction/guidance in exercise, including methods for avoiding/treating hypoglycaemia

Pharmacologic Intervention

Nutrition and physical activity remain the cornerstones of effective diabetes treatment. As the β-cell function deteriorates, more intensive therapies are required, either to produce more insulin or to enable the body to utilize insulin more efficiently. In most cases, type 2 diabetes patients will eventually require insulin in their regimens.

If diet and exercise fail to achieve the glycaemic target of ≤6.5% A1C, pharmacologic therapy will be required (table 1). It is important to point out that UKPDS data show that there is a clear benefit in lowering A1C levels into the normal range, <6.1% [17,18].

Although severe hypoglycaemia is rare in patients with type 2 diabetes, the fear of hypoglycaemia may be an obstacle to achieving tight glycaemic control; this fear is not justified. The VA Cooperative Study [46] showed severe hypoglycaemic reactions to be extremely rare among intensively treated patients and not significantly different from those among conventionally treated patients. The Kumamoto study [16] showed no severe hypoglycaemia over 8 years in either treatment group. Although the UKPDS did show severe hypoglycaemia in intensively treated patients (0.1–2.3% per year), depending on the therapy, severe hypoglycaemia (0.03% per year) was also reported by patients treated with diet therapy alone, which calls into question the actual incidence of true severe hypoglycaemia [17,47]. Furthermore, new oral medications and insulin analogues allow for much tighter glycaemic control without increasing severe hypoglycaemia [48–57]. Therefore, it is possible to intervene with drugs that improve glycaemia, without increasing the risk of hypoglycaemia. However, A1C levels above 6.5% should be treated to achieve and maintain target A1C levels. Figure 4 presents recommendations for pharmacologic therapy based on A1C levels.

Because type 2 diabetes is a progressive disease, pharmacologic therapy must be continually monitored and adjusted to address persistent insulin resistance and β-cell deterioration. A1C levels should be measured every 3 months in patients who are not controlled or undergoing a change in therapy. Therapy modifications should then be made based on the 3-month A1C value and SMBG data. Patients who are well controlled should have A1C levels measured at least every 6 months (preferably four times per year).

Secretagogues

Secretagogues stimulate insulin production. There are two types of secretagogues: (i) sulfonylureas and (ii) glinides. A key consideration when using a sulfonylurea is the potential for hypoglycaemia; therefore, therapy should be initiated using the lowest dosage. New rapid-acting glinide formulations (repaglinide and nateglinide), which are taken at meal time, were developed to address postprandial glucose [58,59]. These postprandial medications can be beneficial in the early stages of diabetes and are beneficial when used in elderly patients or in those who are at increased risk for hypoglycaemia.

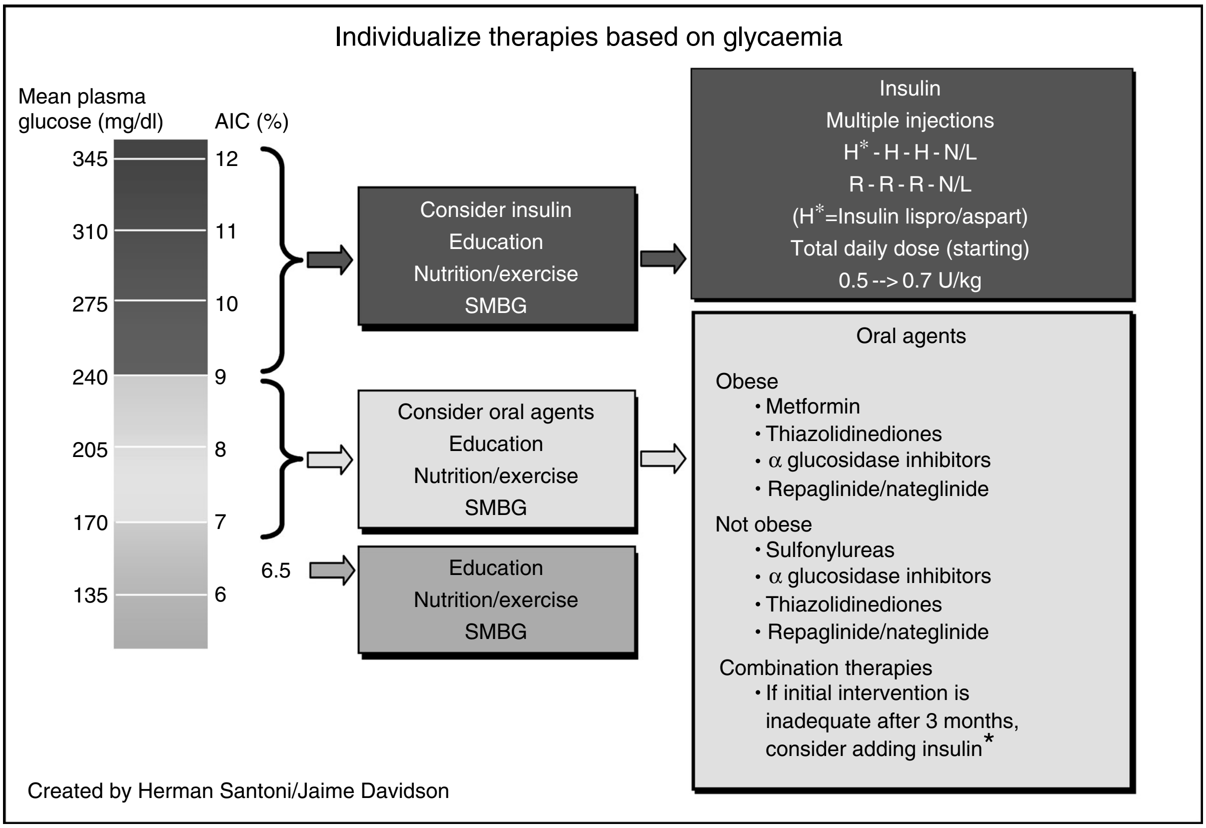

Fig. 4 Pharmacologic therapy. *NPH at bedtime or premixed rapid/long-acting at meals (0.1–0.5 U/kg/day starting dose) eliminate or reduce sulfonylurea to half of maximum dose.

Sensitizers (Metformin and Thiazolidinediones)

Metformin helps reduce hepatic glucose output and facilitates some additional insulin sensitivity in peripheral tissues. Metformin is a popular option, especially in patients who are obese and insulin resistant. It has an added benefit of weight reduction in many patients. Side effects of metformin therapy can include gastrointestinal (GI) disturbances. Metformin is contraindicated in patients with congestive heart failure, liver disease or impaired renal function (creatinine 1.4 mg/dl, women; 1.5 mg/dl, men) [60].

Thiazolidinediones (TZDs), such as pioglitazone and rosiglitazone, are effective in increasing insulin sensitivity in muscle and fat tissue. They improve glycaemic control and also provide a significant benefit by improving lipid profiles. Liver function tests must be performed every 2 months during the first year of treatment and periodically thereafter to detect abnormalities, which have been linked to troglitazone, an earlier compound [61,62]. TZDs are contraindicated in patients with liver function test (LFT) $>3\times$ normal and New York Heart Association class III and IV cardiac functional status [61,62]. It is important to refer to the full prescribing information for each agent.

α-Glucosidase Inhibitors

α-Glucosidase inhibitors (AGIs) (acarbose and miglitol) provide postprandial glucose control by slowing the absorption of carbohydrates from the intestines. Side effects may include flatulence, abdominal pain and diarrhoea. It has been shown that slow titration usually resolves gastrointestinal side effects over time [63,64].

Fixed Combination Oral Agents

New oral medications that combine metformin with glibenclamide [53] or glyburide [54] provide an additional option for controlling glycaemia. Although these combinations provide added convenience to the patient, titration can be more difficult because of the fixed dosage. It is important to observe that these combinations have the same contraindications as their component compounds.

Insulin

Because insulin immediately reduces glucose levels, it may be advisable to automatically prescribe insulin when A1C levels are ≥9% (mean plasma glucose ≥240 mg/dl) or if the patient is very symptomatic, even though oral therapies have not been utilized yet [42]. Initial insulin therapy reverses glucose toxicity, permitting the subsequent use of oral agents. Insulin therapy can be a single bedtime injection of intermediate- or long-acting insulin [neutral protamine nagedorn (NPH), glargine, lente and ultralente] or a combination of insulin and oral agents or an intensive insulin regimen, using intermediate- or long-acting insulin for basal coverage and rapid-acting insulin analogues (lispro and aspart) at meals. Premixed insulin preparations (rapid + intermediate acting) are also available. Figure 5 presents examples of common insulin regimens. Patients should be considered for insulin treatment when any of the following occurs:

- Unintended weight loss
- Diabetic ketoacidosis
- Acute metabolic stress (i.e. infection, myocardial infarction and surgery)
- Failure to reach goals on oral agents
- Recurrence of acute complications
- Pregnancy

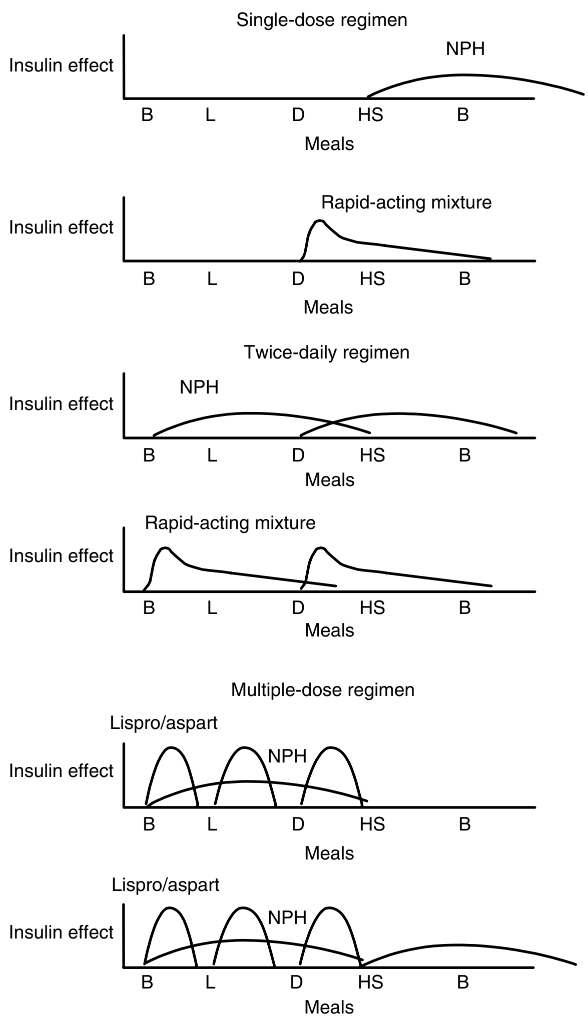

Fig. 5 Common insulin regimens.

The total initial daily insulin dose should be based on ideal body weight and is determined by the following calculation: 0.5–0.7 U/kg [16,17,56]. Although this calculation serves as a starting point for therapy, patients often show a varied response to insulin treatment that will necessitate individualization of the regimen. It is important to observe that higher insulin dosages may be required because most type 2 diabetes patients are insulin resistant; dosages of 1.0–1.5 U/kg are not uncommon and should be used as needed [56]. Table 3 provides guidelines for adjusting NPH insulin dosages. Often insulin is used in combination with oral agents to enhance glucose control.

Combination Therapy

The following combination therapies are approved; the first two are the most commonly used. It is important to check package inserts to ensure the safety of all combined medications: (i) sulfonylurea + metformin; (ii) sulfonylurea + TZD; (iii) sulfonylurea + AGI; (iv) metformin + TZD; (v) metformin + AGI; (vi) metformin + sulfonylureas + TZD; (vi) metformin + glinides; (vii) insulin + sulfonylureas; (viii) insulin + metformin; (ix) insulin + TZD.

Table 4 presents the average effect of these medications (monotherapy and combination therapy) on glycaemic levels. The data presented in table 4 show that combination oral therapy can lower A1C by 1.5–2.0%. Therefore, even when combined with effective lifestyle intervention, which can reduce A1C levels by 1.0–1.5%, patients with ≥9% A1C values would benefit by adding insulin to their therapy, especially those who are symptomatic.

Table 3 Recommendations for adjusting insulin dosages [56]

NPH algorithm
Adjust evening NPH according to average fasting glucose last 3–7 days
BG<80 mg/dl − 2U
>80–100 mg/dl no adjustment
>100–120 mg/dl + 2U
>120–140 mg/dl + 4U
>140–180 mg/dl + 6U
>180 mg/dl + 8U
Lispro or regular, AC meals
According to meal, same adjustment per meal
At breakfast based on prelunch readings
At lunch based on presupper readings
At supper based on hs readings

AC, before; BG, blood glucose; hs, bedtime.

Table 4 Impact of oral therapies on A1C levels [58–64,66]

	Fasting plasma glucose reduction (mg/dl)	% A1C reduction
Sulfonylureas (second generation)	50–60	1.0–2.0
Acarbose	15–30	0.5–1.0
Metformin	50–78	1.0–2.0
Thiazolidinedione	14–48	0.8–1.0
Nateglinide	–	0.5–1.0
Repaglinide	50.0	1.5–2.0
Metformin + sulfonylurea	63.5	1.7
Metformin + thiazolidinedione†	48.0	0.8
Thiazolidinedione + glyburide	31–56	0.7–1.8
Thiazolidinedione + insulin	34.9–48.8	0.84–1.41
Insulin	150*	>5.0*

*Depending on the number of units.
†Data from the study of patients inadequately controlled on 2.5 g/day of metformin [62].
Improvement in glycaemic control can vary, depending on the agents used.

Step 3. Monitoring Therapy and Risk

Type 2 diabetes is a progressive disease that must be monitored regularly. Although diet and exercise remain the cornerstones of therapy, it is imperative to be aggressive in achieving and maintaining the glycaemic targets – A1C, fasting glucose and postprandial glucose. This requires regular follow-up every 3 months to assess glycaemic control and to escalate therapy by increasing the dose and/or adding an additional agent. Patients should be brought into acceptable glycaemic control as early as possible to prevent/minimize the development of complications [65]. Therefore, therapy adjustment should be timely and aggressive. Because type 2 diabetes involves progressive β-cell failure, insulin therapy should be initiated when needed and without hesitation. It is also important to closely monitor risk factors for cardiovascular disease and other diabetic complications. Table 5 provides guidelines for frequency of laboratory testing and physical assessment.

Conclusion

Diabetes is a devastating disease with significant costs, both financial and human. As diabetes prevalence accelerates over the next decade in Latin America, healthcare providers and public health organizations will be challenged to find effective ways to control diabetes and reduce its complications. Studies have clearly shown that achieving and maintaining near-normal glycaemia and managing risk factors can prevent or significantly reduce the development/severity of diabetic complications.

Table 5 Frequency of laboratory testing/physical assessment [20,42]

Each patient visit	
	Blood pressure
	Self-monitoring of blood glucose data
	Foot exam
3–6 months	
	A1C
	3 months for uncontrolled diabetes or regimen change
	6 months (minimum) for controlled diabetes, preferably every 3 months
Annual	
	Lipids*
	Microalbumin*
	Eye exam*

*Should be performed more frequently if complications are present or therapy is changed.

However, implementing effective treatment strategies is a challenge to patients and healthcare providers, especially general practitioners who must manage a variety of illnesses and disorders in their patient populations.

The Latin American treatment algorithm is a living and evolving document. As new treatment options are developed, this algorithm will require modification. However, the basic concepts on which it is formed will not change. Education, nutrition, exercise and SMBG will remain the cornerstones of therapy for patients with type 2 diabetes. Pharmacologic therapy must be utilized and intensified in patients as their diabetes progresses.

The stepwise approach to modifying therapy must be shortened and intensified to more quickly achieve and maintain target glycaemic levels. This will require a new paradigm in how physicians approach type 2 diabetes management. The intention of this algorithm is to help physicians improve the long-term care of their patients with type 2 diabetes by standardizing treatment. The goal was to reduce the development of the complications associated with the disease. Owing to its utility and simplicity, this algorithm has been submitted to the Latin American Diabetes Association for use by clinicians in Latin America. Utilization of this treatment algorithm, in addition to individualized treatment plans, should enhance clinicians' abilities to provide optimal care for their patients.

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