

Evaluation of Type 2 diabetes mellitus with insulin thereby

Done by
Mustafa Raheem

Supervisor
Prof. Mahmood shaker



كلية الطب
جامعة النهرين

تأسست عام ١٩٨٧

CONTENTS

Abstract	Page 1
Aim of study	Page 2
Introduction	Page 3
Persons and methods	Page 4
Results	Page 5
Discussion	Page 6
Conclusion	Page 7
References	Page 8

Abstract

In type 2 diabetes mellitus, oral hypoglycemic agents and analogues of glucagon-like peptide-1 provide adequate glycemic control early in the disease. Insulin therapy becomes necessary for those with advanced disease. Further, some experts recommend electively starting insulin therapy in early diabetes. This review addresses practical approaches to insulin therapy, particularly when it is indicated and which regimen to use.

Guidelines from professional societies differ on these points (1, 2) as do individual clinicians. Moreover, antidiabetic treatment is an evolving topic. Many new drugs—oral agents as well as injectable analogues of glucagon-like peptide-1 (GLP1) and insulin formulations—have become available in the last 15 years.

Aim of study :

Many patients with type 2 diabetes eventually need insulin, as their ability to produce their own insulin from pancreatic beta cells declines progressively (3). The questions remain as to when insulin therapy should be started, and which regimen is the most appropriate

Introduction :

A number of landmark randomized clinical trials established that insulin therapy reduces microvascular complications (4, 5). In addition, recent follow-up data from the U.K. Prospective Diabetes Study (UKPDS) suggest that early insulin treatment also lowers macrovascular risk in type 2 diabetes (6). Whereas there is consensus on the need for insulin, controversy exists on how to initiate and intensify insulin therapy. The options for the practical implementation of insulin therapy are many. In this presentation, we will give an overview of the evidence on the various insulin regimens commonly used to treat type 2 diabetes.

Secondary analyses of the aforementioned landmark trials endeavored to establish a glycemic threshold value below which no complications would occur. The UKPDS found no evidence for such a threshold for A1C, but instead showed that better glycemic control was associated with reduced risks of complications over the whole glycemic range (“the lower the better”) (7). For the management of type 2 diabetes, this resulted in the recommendation to “maintain glycemic levels as close to the nondiabetic range as possible” (8). However, in contrast to the UKPDS, the Kumamoto study observed a threshold, with no exacerbation of microvascular complications in patients with type 2 diabetes whose A1C was <6.5%, suggesting no additional benefit in lowering A1C below this level. Moreover, the intensive glycemia treatment arm of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, targeting A1C <6.0%, was discontinued because of higher mortality in this group compared with the standard therapy group targeting A1C from 7.0 to 7.9% (8). Therefore, the American Diabetes Association (ADA) recommendation of an A1C target <7.0% seems the most balanced compromise at present (9).

Another important conclusion of the UKPDS was that the risk reductions in long-term complications were related to the levels of glycemic control achieved, rather than to a specific glucose-lowering agent. This has left health care providers and patients with the difficult task of choosing from the wide variety of glucose-lowering interventions currently available.

When considering the effectiveness, tolerability, and cost of the various diabetes treatments, insulin is not only the most potent, but also the most cost-effective intervention (10). Although insulin has no upper dose limit and numerous trials established that glycemic goals could be attained by using adequate insulin doses in clinical practice, many patients have elevated A1C levels and experience years of uncontrolled hyperglycemia (10). Moreover, the Steno-2 Study demonstrated that only a minority of patients reached the intensive A1C target of <6.5%, compared with a far greater percentage of patients who reached the respective intensive treatment goals for blood pressure and serum lipid levels (11). Apparently, the initiation and intensification of insulin therapy is not as straightforward and simple as we had hoped. In accordance with the ADA and the European Association for the Study of Diabetes (EASD) , we advocate an algorithmic approach for the start and adjustment of insulin treatment, with modifications for individual patients as needed. This review contains an overview of the currently available insulin preparations and an outline of the merits and disadvantages of the various regimens commonly used for the initiation and intensification of insulin therapy in patients with type 2 diabetes. Our aim is to assist clinicians in designing individualized management plans for insulin therapy in type 2 diabetic patients.

When glycemic control worsens or is not adequate despite the use of oral hypoglycemic agents, often the next step is to add basal insulin therapy, ie, once-daily doses of a long-acting insulin.

the rationale for combining insulin with oral therapy is minimization of the adverse effects of insulin treatment, i.e., hypoglycemia and weight gain (44). Combination of insulin with metformin is indeed associated with better glycemic control, fewer hypoglycemic events, and less weight gain than treatment with insulin alone (45)

The only consistent advantage of such combined therapy is reduced insulin dose requirements, which may result in less daily injections, easier dose titration, and improved compliance (46).

So NPH, detemir, or glargine?

Most often, glargine or detemir (Levemir) insulin is used. Detemir can also be given twice daily if needed. If cost is a concern, neutral protamine Hagedorn (NPH, Humulin N, Novolin N) insulin once daily at bedtime or twice daily is a reasonable alternative.

Rapid-acting insulin analogues (lispro, aspart, and glulisine) control postprandial glucose levels better than regular insulin and cause less hypoglycemia. Their pharmacokinetics enable them to be taken within a few minutes of the start of a meal, or even after the meal if the patient forgets to take an injection before the meal.

For example, in one study,³⁶ taking aspart immediately before the meal provided better glycemic control than taking regular insulin 30 minutes before meals. In a basal-bolus regimen, the use of aspart along with detemir resulted in glycemic control similar to that provided by twice-daily NPH and regular insulin, with less hypoglycemia.³⁷

Acknowledgments

Persons and methods:

Study is done on 25 person with type 2 diabetes mellitus on insulin therapy

The questionnaire ask them about: age, HBA1c, diagnosis, complication, type of insulin and regimes

Results

Table 1: Age of Patients with type 2 diabetes mellitus.

		Frequency	Percent
Valid	From 45 to 55 years	3	12.0
	From 55 to 65 years	8	32.0
	Above 65 years	14	56.0
	Total	25	100.0

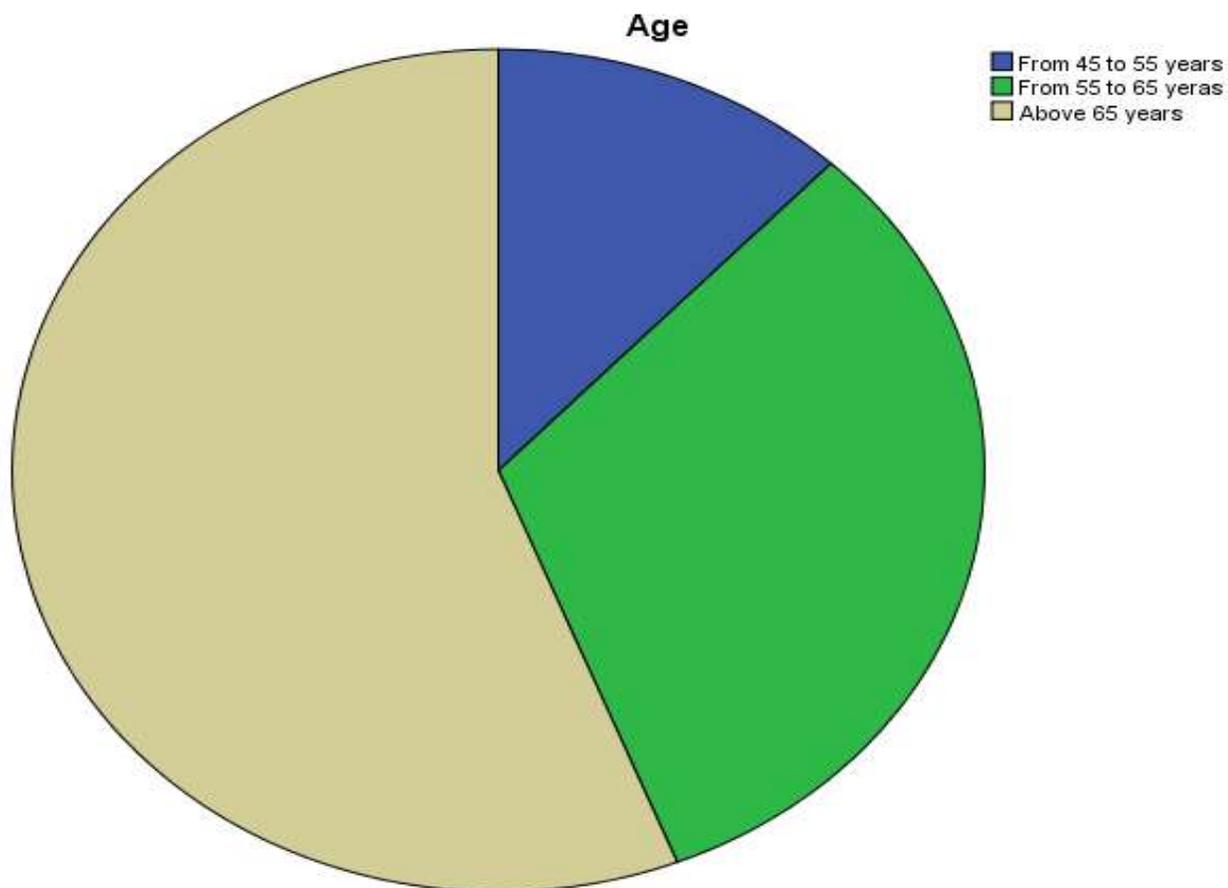


Table 2: the time of diagnosis of type 2 DM.

Time Of Diagnosis	Frequency	Percent
Since 1 To 5 years	3	12.0
Since 5 To 10 years	14	56.0
since more than 10 years	8	32.0
Total	25	100.0

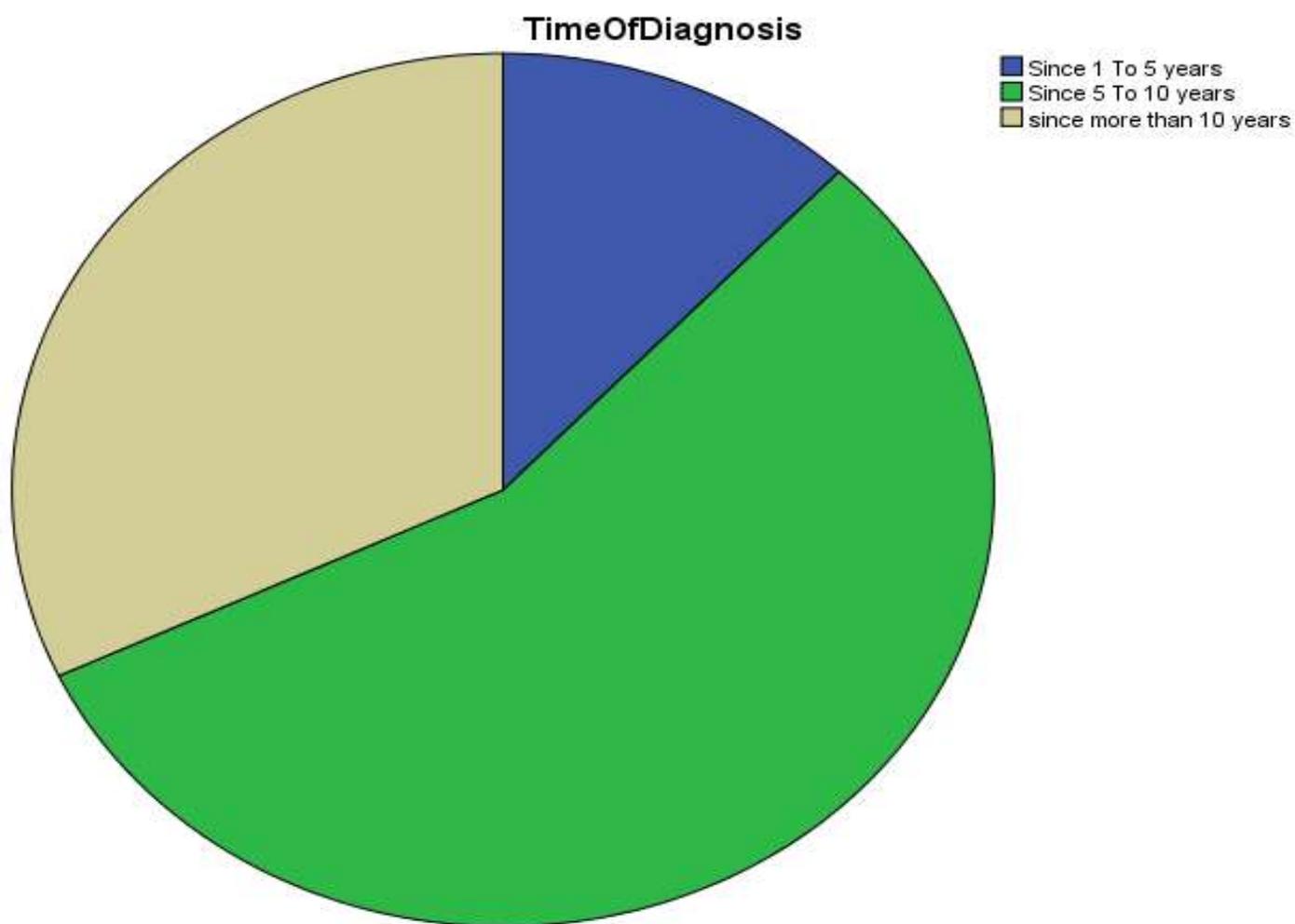


Table 3: the values of HbA1c of DM2 patients.

HbA1c	Frequency	Percent
From 6.5 to 8.5	2	8.0
From 8.5 to 10.5	7	28.0
Above 10.5	16	64.0
Total	25	100.0

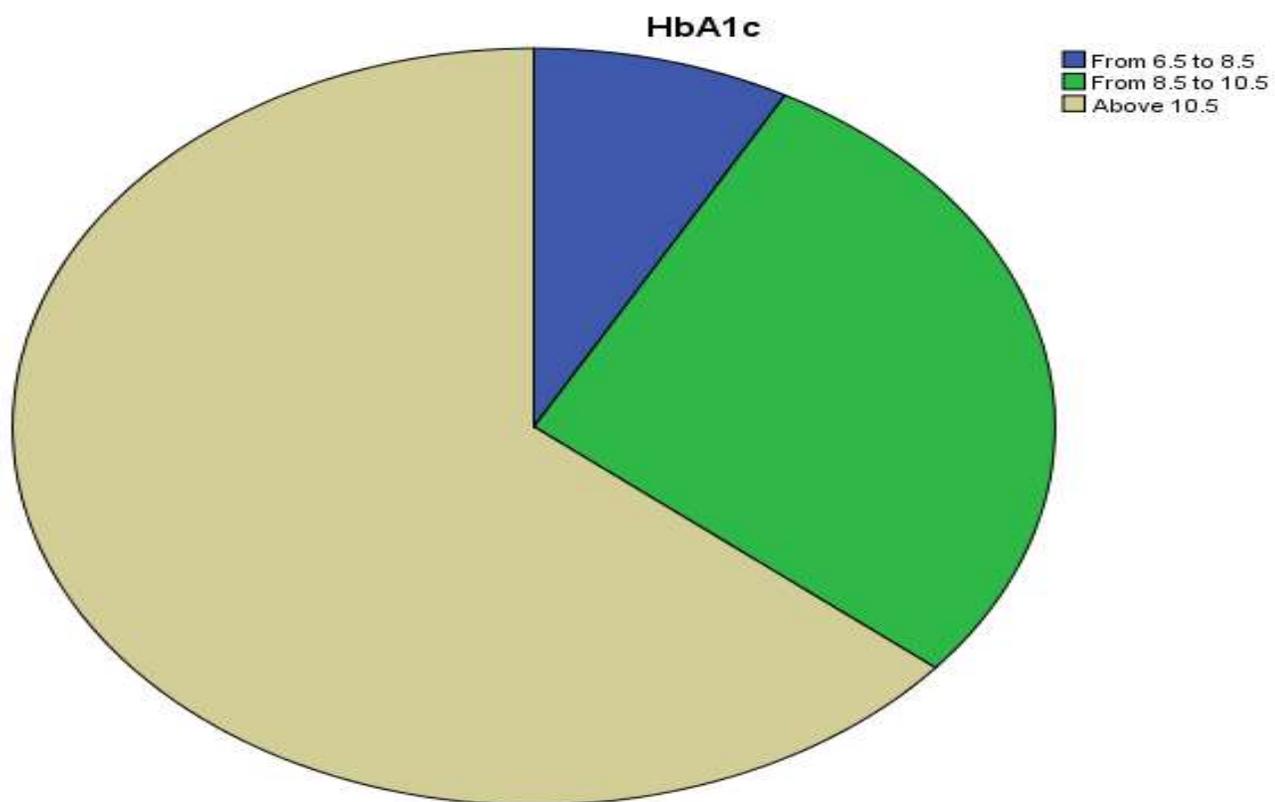


Table 4: the use of medications and insulin therapy by DM2 patients

	Used	Not Used
Oral Anti-diabetics	25(100%)	0(0.0%)
Insulin	25(100%)	0(0.0%)

Table 5: the complications of type 2 DM

Complication	Frequency	Percent
major complications	2	8.0
minor complications	9	36.0
both complications	14	56.0
Total	25	100.0

Table 6: the correlations between the Hba1c and age, insulin therapy and complications.

		HbA1c			P-value
		From 6.5 to 8.5	From 8.5 to 10.5	Above 10.5	
Age	From 45 to 55 years	1	1	1	0.38
	From 55 to 65 years	0	3	5	
	Above 65 years	1	3	10	
Time Of Diagnosis	Since 1 To 5 years	1	1	1	0.08
	Since 5 To 10 years	0	6	8	
	since more than 10 years	1	0	7	
Insulin	On Insulin	2	7	16	0.98
	Not on Insulin	0	0	0	
complications	major complications	0	0	2	0.11
	minor complications	2	4	3	
	both complications	0	3	11	

Discussion

According to age of diagnosis in table (1) the results tell that people above 65 years more liable to use insulin in comparison with others this agree with other studies

According to HBA1c in table (3) most patients have results > 10.5 despite using insulin and oral antidiabetic drugs the cause related

Conclusion :

Because most type 2 diabetic patients have residual endogenous insulin secretion, the rationale for imitating the physiological insulin secretion pattern is less convincing than in type 1 diabetes.

Glycemic treatment should be stepwise with swift introduction of successive interventions after treatment failure (i.e., A1C $\geq 7.0\%$). Insulin should be initiated when A1C is $\geq 7.0\%$ after 2–3 months of dual oral therapy. The preferred regimen for insulin initiation in type 2 diabetes is once-daily basal insulin. In addition to timely initiation, rapid titration of the dose is indispensable for successful insulin therapy.

Typically patients are on about 20–30 units of insulin in combination with oral agents when fasting or pre-prandial blood glucose levels are at target. Despite this, the HbA1c may remain elevated. In this situation, moving to a twice daily dose of insulin could be considered and specific attention paid to controlling post-prandial rises. For some, the addition of a short-acting insulin analogue before the larger meal, the so-called ‘basal plus’ regimen

Many studies have evaluated how to use insulin effectively for the treatment of type 2 diabetes. Two- and four-dose regimens of NPH improved glycemic control but caused basal hyperinsulinemia.³⁶ The addition of 70/30 insulin (a premixed formulation with 30% fast-acting insulin and 70% intermediate-acting insulin) before supper to glimepiride (Amaryl) restored glycemic control more quickly than did 70/30 insulin alone, without producing severe hypoglycemia.²⁵ The addition of NPH to glipizide (Glucotrol) was superior to high- and low-dose NPH alone in

restoring glycemic control.**37** Combination therapy with an intermediate-acting insulin at bedtime plus metformin was superior to bedtime insulin plus glyburide and metformin, bedtime insulin plus glyburide, and insulin twice daily and produced no weight gain.**18** The addition of evening NPH to existing oral agents was similar in efficacy to morning NPH plus an existing antidiabetic agent, a two-injection regimen of 70/30 insulin, multiple injections, and oral hypoglycemic agents alone; however, this regimen did not induce as much weight gain and hyperinsulinemia.**38**

References

1. UK Prospective Diabetes Study 16. Overview of 6 years' therapy of type II diabetes: a progressive disease. UK Prospective Diabetes Study Group. *Diabetes* 1995; 44:1249–1258.
2. Nathan DM, Buse JB, Davidson MB, et al; American Diabetes Association. 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.
3. Rodbard HW, Jellinger PS, Davidson JA, et al. Statement by an American Association of Clinical Endocrinologists/American College of Endocrinology consensus panel on type 2 diabetes mellitus: an algorithm for glycemic control. *Endocr Pract* 2009; 15:540–558
4. 1. U.K. Prospective Diabetes Study (UKPDS) Group Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). *Lancet* 1998; 352: 837– 853
[PubMed] [Google Scholar]
5. 2. Ohkubo Y, Kishikawa H, Araki E, Miyata T, Isami S, Motoyoshi S, Kojima Y, Furuyoshi N, Shichiri M: Intensive insulin therapy prevents the progression of diabetic microvascular complications in Japanese patients with non-insulin-dependent diabetes mellitus: a randomized prospective 6-year study. *Diabetes Res Clin Pract* 1995; 28: 103– 117 [PubMed] [Google Scholar]

6. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HA: 10-year follow-up of intensive glucose control in type 2 diabetes. *N Engl J Med* 2008; 359: 1577– 1589 [[PubMed](#)] [[Google Scholar](#)]
7. 4. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, Hadden D, Turner RC, Holman RR: Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000; 321: 405– 412 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
8. 5. Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, Zinman B: 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 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
9. 6. Action to Control Cardiovascular Risk in Diabetes Study Group Effects of intensive glucose lowering in type 2 diabetes. *N Engl J Med* 2008; 358: 2545– 2559 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
10. 7. American Diabetes Association Standards of medical care in diabetes: 2009. *Diabetes Care* 2009; 32: S13– S61 [[PMC free article](#)] [[PubMed](#)] [[Google Scholar](#)]
11. Nathan DM: Initial management of glycemia in type 2 diabetes mellitus. *N Engl J Med* 2002; 347: 1342– 1349 [[PubMed](#)] [[Google Scholar](#)]
12. Brown JB, Nichols GA, Perry A: The burden of treatment failure in type 2 diabetes. *Diabetes Care* 2004;27: 1535– 1540 [[PubMed](#)] [[Google Scholar](#)]
13. 10. Gaede P, Vedel P, Larsen N, Jensen GVH, Parving HH, Pedersen O: Multifactorial intervention and cardiovascular disease in

patients with type 2 diabetes. N Engl J Med 2003; 348: 383– 393
[\[PubMed\]](#) [\[Google Scholar\]](#)

Questionnaire :

Age :

Diagnosis :

HbA1c :

Medication :

Insulin :

Complication :