An evaluation of insulin therapy initiation among patients with type 2 diabetes attending a public health facility in South Africa

Mayet L, MBChB, MMed(Sc), Principal Medical Officer
Diabetes Unit, Addington Hospital, KwaZulu-Natal
Naidoo SS, MBChB, FCFP, MMed, Head of Department
Department of Family Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal
Corresponding author: Leila Mayet, e-mail: selim@mweb.co.za
Keywords: type 2 diabetes mellitus, insulin requirements, prescription

Abstract

Background: Clinically effective interventions that could reduce diabetic patients' risk of long-term complications are needed to contain the rising cost of diabetes care associated with the increasing prevalence of this condition. Good glycaemic control needs to be rapidly attained and maintained by the appropriate initiation and adjustment of glucose-lowering therapy. In patients with insulin-requiring type 2 diabetes who are not at goal glycaemia, this translates to the initiation and intensification of insulin therapy. The aim of this study was to evaluate the appropriateness of the initiation of insulin therapy in patients with poorly controlled insulin-requiring type 2 diabetes.

Method: This descriptive retrospective study evaluated treatment regimens, dose adjustments and glycated haemoglobin A_{1c} (HbA_{1c}) measurements extracted from records of patients with type 2 diabetes suitable for inclusion. The observation period spanned the 24 months retrospective to study start. Data collected were transcribed into a spreadsheet suitable for statistical analysis.

Results: Of the overall cohort of patients with insulin-requiring type 2 diabetes (n = 131), only 45.8% (n = 60) were commenced on insulin during the observation period, of whom 51.7% had subsequent adjustment of insulin dosage. Mean HbA_{1c} at insulin initiation was 10.29% (± 2.42), and 10.63% (± 1.93) after adjustment of insulin dose (p-value > 0.05). Of those who remained on oral glucose-lowering therapy (n = 71), 57.7% had no change in medication dosage throughout the study period. Overall, 81.35% remained ≥ 1% above goal HbA_{1c} by the end of the study period.

Conclusion: This study found a discrepancy in the appropriate use and adjustment of insulin therapy according to metabolic status.

Ⓟ Peer reviewed. (Submitted: 2012-01-05. Accepted: 2012-03-07.) © SAAFP
S Afr Fam Pract 2012;54(6):525-530

Introduction

Diabetes care is expensive. The greater proportion of overall expenditure relates to the costs of managing the morbidity associated with the long-term, end-organ complications of diabetes.[1] In the face of the predicted rise in the prevalence of type 2 diabetes,[2] effective interventions to restore and maintain target glycaemia make good clinical and economic sense.

Several landmark clinical trials have demonstrated that the normalisation of glucose levels is critical for protecting patients with type 2 diabetes from long-term complications.[3-6]

Most patients will require progressively intensified glucose-lowering medication to reach and maintain target glycaemia, as type 2 diabetes mellitus is a progressive condition in which glycaemia deteriorates over time.[7-9]

The Society for Endocrinology, Metabolism and Diabetes of South Africa (SEMDSA) and the American Diabetes Association (ADA) recommend that the goal of glucose-lowering therapy is a haemoglobin A_{1c} (HbA_{1c}) level of < 7%, and the re-evaluation of therapeutic regimens if HbA_{1c} measures are consistently ≥ 7%.[7-9]

In patients with type 2 diabetes on a treatment regimen of maximum oral hypoglycaemic agents (OHAs), an HbA_{1c} measure of ≥ 7% should act as a trigger for the timely initiation of insulin therapy to effect good glycaemic control.[7-9]

A slow transition from maximum OHA treatment to insulin therapy, to achieve target glycaemia, may result in expensive-to-manage, long-term complications of type 2 diabetes mellitus, which translates to an increase in the burden of the disease.[10,11]

Timely initiation of insulin therapy is defined as the commencement of insulin in patients with type 2 diabetes who are not at recommended target glycaemia, despite taking maximum doses of OHAs.[8,10,12] Such patients are deemed "insulin-requiring".

A maximum dose of OHAs is defined as metformin 2 550 mg daily, or the maximum tolerated dose, together with either glibenclemide 15 mg daily, or gliclazide 320 mg daily.[9,13]

The aim of this study was to analyse prescribing practices for the management of patients with type 2 diabetes in terms of metabolic parameters and treatment regimens, as observed from patient records. The purpose was to assess and evaluate the appropriateness of the initiation of insulin therapy in patients with poorly controlled insulin-requiring type 2 diabetes.

Method

This descriptive retrospective study analysed data extracted from files of patients with insulin-requiring type 2 diabetes attending the medical outpatients' department of a large regional public sector hospital in KwaZulu-Natal. Approximately 1 500 patients with chronic medical conditions are seen in a month at this medical outpatients' department, of whom approximately 30% have diabetes. Attending medical officers review these patients every six months, and prescribe ongoing treatment.

Records of patients with type 2 diabetes mellitus were eligible for inclusion if patients made at least four visits to the study clinic during the observation period, if the most recent visit occurred within six months prior to start of the study, if patients had HbA_{1c} measures of ≥ 7% on two or more occasions, and ≥ 3 months apart during the same period.

The period of observation was the 24 months retrospective to the start of the study.

The maximum number of files meeting the inclusion criteria (n = 247) was sampled over a one-month period from the registry of records of all diabetic patients who attended the study site over the same period (n = 463).

Of these, files of all patients commenced on an insulin regimen during the observation period, and files of all patients on maximum OHA therapy over the same period, were identified. Following consultation with a biostatistician, it was decided to sample 50% of the files that met the inclusion criteria. Patient files ending in an even number were selected, and made up the final study sample (n = 131).

Treatment regimen information and dose adjustments were collected and recorded, together with HbA_{1c} measurements which were obtained from the designated hospital laboratory database.

The hospital laboratory method of HbA_{1c} measurement is by ion-exchange, high-performance liquid chromatography, with a co-efficient variation of 1.15% in line with the Diabetes Control and Complications Trial standardisation of HbA_{1c} assays that have an acceptable co-efficient variation of < 4%.[14]

Patient data were recorded at five time points:

- Time 1: Most recent clinic visit within the six months retrospective to study start
- Time 2: Time 1 minus six months
- Time 3: Time 1 minus 12 months
- Time 4: Time 1 minus 18 months
- Time 5: Time 1 minus 24 months.

Age, sex, race, and concomitant conditions were recorded, but were only used for the demographics and description of the study cohort.

Data collected were entered into an Excel® spreadsheet, and then transcribed into a spreadsheet package suitable for statistical analysis.

In this study, descriptive analysis was performed in order to report and summarise the findings. Frequency counts, percentages and 95% confidence intervals were reported for categorical variables. Summary statistics such as mean, standard deviation and range were reported for quantitative variables. A paired t-test was performed to compare the mean HbA_{1c} level at initiation of the insulin therapy, with the HbA_{1c} level at the most recent clinic visit. A p-value value of < 0.05 was considered to be statistically significant.

Approval to conduct this study was granted by the University of KwaZulu-Natal, and by the hospital management.

Results

Two hundred and forty-seven patient records were suitable for extraction of data, and 131 made up the final study sample. Of these, 54.2% (n = 71) were of patients on maximum OHAs, and 45.8% (n = 60) of patients commenced on insulin within the 24-month observation period (Table I).

In total, 338 HbA_{1c} levels were measured over the observation period; a mean of 2.58 (± 0.67) and 2.53 (± 0.65) for the OHA and insulin subsets, respectively. Patients had several measurements of HbA_{1c} ≥ 7% before having insulin initiated [1.6 (± 0.80)] (Table II).

Table I: Cohort characteristics

Characteristic	Cohort	
	Frequency	Percentage (%)
Overall cohort	131	100
Maximum OHAs	71	54.2
Insulin	60	45.8
Age (years)*	59 (±10)	
Female	92	70.0
Race		
Black	36	27.3
Caucasian	14	10.7
Indian	74	56.4
Mixed	7	5.7
Concomitant conditions		
Hypertension	107	81.0
Dyslipidaemia	63	47.6
Ischaemic heart disease	36	27.6

* Age given as mean ± standard deviation

Table II: Metabolic characteristics of cohort

Parameter	OHA		Insulin		Cohort	
	Mean	SD	Mean	SD	Mean	SD
Number HbA_{1c} per point	2.58	0.67	2.53	0.65	2.56	0.66
Number HbA_{1c} before change to insulin			1.60	0.80		
HbA_{1c} Vo*	8.56	1.63	10.02	3.18	9.28	2.4
HbA_{1c} Vi**	8.39	1.93***	10.29	2.42****	9.22	2.22
HbA_{1c} Vr*****	9.58	1.71	10.63	1.93****	9.75	1.87

* Beginning of observation period, ** Change of medication viz. initiate insulin or change in oral hypoglycaemic dose, *** Oral hypoglycaemic doses adjusted to maximum tolerable dose for metformin and not actual intensification of oral therapy, **** p-value difference of glycaemic control between Vi and Vr = 0.312, ***** Most recent visit ("final" visit)

Of the overall cohort, the only change in oral therapy was an adjustment to maximum tolerable doses for metformin (22.9%), and not intensification of oral therapy (Table III). Of the OHA subset, 57.7% did not have any adjustment of medication dosage throughout the observation period.

By the most recent visit, the majority of the overall cohort remained at suboptimal glycaemic control (Table IV).

Discussion

Adequate metabolic control is key to reduced risk of diabetes complications.[3-6] Both SEMDSA and the ADA recommend the goal of glucose-lowering therapy to be an HbA_{1c} level of < 7%, and the re-evaluation of therapeutic regimens if HbA_{1c} measures remain consistently ≥ 7%.[7-9] Thus, the appropriate use and adjustment of glucose-lowering medication according to metabolic parameters, HbA_{1c}, is critical for good glycaemic control.

Table III: Medical regimen adjustment characteristics

Parameter (24-month observation period)	Percentage of overall cohort
No change in therapy at all	31.3
Change to tolerable OHA dose	22.9
Change in insulin dose after initiation	51.7
No change in insulin dose after initiation	48.3

Table IV: Glycaemic status of cohort at the end of study

HbA_{1c}	Total cohort	OHA arm	Insulin arm
< 7%*	17.7%	10.3%	23.1%
≥ 7%**	83.3%	89.7%	76.9%
≥ 8%	81.3%***	76.1%***	86.7%[e]

* Optimal or goal glycaemia, ** Suboptimal glycaemia, *** Percentage of suboptimal group with HbA_{1c} ≥ 1% above goal

Initiation of insulin

Several studies and standard treatment policies recommend the initiation of insulin in patients with type 2 diabetes on maximum dual oral therapy when the HbA_{1c} level remains consistently ≥ 7%.[5,7-9]

While insulin is recommended in patients not achieving glycaemic control on maximum OHAs, this study demonstrated that only a small proportion of patients had actually been commenced on insulin therapy. Of the overall cohort, 45.8% were commenced on an insulin regimen during the 24-month observation period, while 54.2% remained on maximum OHAs, despite having a mean HbA_{1c} above 7% (9.58 ±1.71%) by the end of the study observation period.

These proportions are comparable to those shown by Kirkman et al[15] where, of 275 insulin-requiring diabetic patients, only 40% were taking insulin. Similarly, upon analysis of pharmacy data from a United Kingdom database, Fox et al[16] showed that, at an HbA_{1c} cut-off of > 7.5%, 41% and 52% of patients with insulin-requiring type 2 diabetes were still on ≥ 2 OHAs by 1998 and 2002, respectively.

In a similar study, also by analysis of data from a UK database, Rubino et al[17] estimated that if followed up for five years, only 25% of patients with insulin-requiring type 2 diabetes will have insulin initiated within 1.8 years, and 50% within 4.9 years. By comparison, in the 2005 Canadian Evaluation study,[18] only 12% of insulin-requiring type 2 diabetic patients had insulin introduced for better glycaemic control.

Two South African studies reported that most patients with diabetes were found to be insulin requiring, yet remained at poor glycaemia because of frequent rare modification

of glucose-lowering medications and insulin not being prescribed.[19,20]

Early addition of insulin is recommended as an efficient way of achieving target glycaemia, and could lead to a substantial decrease in patients' long-term risk of developing complications.[3,21,22]

In this study, the mean level of HbA_{1c} at which insulin was initiated was 10.29% (± 2.42).

Late introduction of insulin therapy has been demonstrated by several international studies,[10,12,23] where glucose-lowering action was triggered by an HbA_{1c} level of ≥ 9%, while Dailey[25] demonstrated that the trigger for intensifying treatment was an HbA_{1c} ≥ 10%.

Harris et al[10] further demonstrated that at the time of initiation of insulin, 74% of his study cohort already had one diabetes-related complication, suggesting a prolonged period of above-target HbA_{1c} levels.

According to Hirsch et al and Spellman,[24-26] an HbA_{1c} level of ≥ 1% above goal is a clear indication for the introduction of insulin in patients with type 2 diabetes who fail to respond to maximum OHA therapy.

Of those patients who remained on OHAs throughout this study, the mean HbA_{1c} measured at the end of the observation period (9.58 ± 1.71%) was ≥ 1% above goal, and is suggestive of a delay in the initiation of insulin according to metabolic parameters.

The mean level of HbA_{1c} at which insulin was commenced (10.29 ± 2.42%), together with the number of HbA_{1c} levels ≥ 7% (1.60 ± 0.80) that were considered before insulin was initiated, is also suggestive of a delay in making the necessary transition from OHA therapy to insulin therapy using HbA_{1c} levels as a guide.

Rapid attainment of good glycaemic control is critical in improving outcomes in patients with diabetes. It is recommended that, in patients with insulin-requiring type 2 diabetes, insulin should be started within three to six months, if combination oral therapy cannot achieve HbA_{1c} goals.[27]

In this study, the slow transition from OHA therapy to insulin was evidenced by the 57.7% of patients on maximum OHA therapy who did not have any alteration to their therapy over the total 24-month period of observation.

Such findings are not peculiar to this study. Harris et al[10] showed that healthcare professionals waited an average of 9.2 years before initiating insulin in patients with type 2 diabetes mellitus, at which point HbA_{1c} levels were well above target, and resultant diabetes complications had begun to develop.

Delayed introduction of insulin has also been reported by Nathan,[11] who found that patients had diabetes for 10-15 years before being treated with insulin.

Intensification of therapy

Appropriate medication change, adjustment and titration represent the major strategies for lowering glucose levels, and are necessary for effective and successful diabetes care.[28]

Of the subset of patients commenced on insulin, 51.7% had an adjustment of insulin dose, including the addition of a second insulin type, while 48.3% did not have any change in dose after insulin was commenced. More than half (57.7%) of the OHA subset did not have any change in therapy for the duration of observation, despite having a mean HbA_{1c} above 7% (9.58 ± 1.71%) by the most recent visit.

Several international studies have shown that the frequency of dose adjustment of medication was less than expected for patients with inadequate glycaemic control. Reports of the proportion of patients with above-goal HbA_{1c} levels, who did not have intensification of anti-diabetic therapy, varied from 23-54%.[23,29,30]

While proportions are not reported, an audit of primary care services in Cape Town revealed that fewer than half of the clinic visits resulted in any change of diabetes management.[31]

Patients attending this study clinic have their HbA_{1c} levels measured a month prior to their visit to the doctor. This, together with the fact that these HbA_{1c} results are easily retrievable from the laboratory database, presents an opportunity to assess and optimise diabetes treatment at every doctor's visit.

In this study, there was no statistically significant change in mean HbA_{1c} level at the time of initiation of insulin (10.29 ± 2.42%) and the mean HbA_{1c} level at the end of the observation period (10.63 ± 1.93%) (p-value = 0.312), suggesting that although there was some intensification of hypoglycaemic treatment, it was not adequate to achieve target glycaemic control.

While the practice of the study clinic is to refer patients initiated on insulin to their local primary health clinic for up-titration of doses on a weekly basis, the persistently above-normal HbA_{1c} levels at follow-up clinic visits suggest a deviation from this prescribing practice.

In this study, the frequency of intensification of therapy was less than expected, as evidenced by the low proportion of medication adjustment in patients not meeting recommended therapeutic goals.

Diabetes care measures

The HbA_{1c} assay has become the gold standard measurement of chronic glycaemia, and is used as an index of mean plasma glucose levels.[14] It is recommended that the HbA_{1c} is measured every six months to guide clinicians' treatment decisions.[7-9,14]

In total, 338 HbA_{1c} levels were measured over the 24-month observation period, giving a mean number of HbA_{1c} measurements for the OHA and the insulin subsets as 2.58 (± 0.67) and 2.53 (± 0.65), respectively.

This frequency of HbA_{1c} measurement suggests a favourable level of quality measure in terms of HbA_{1c} testing. However, this does not necessarily translate into adequate metabolic control, as evidenced by the above-goal mean HbA_{1c} (9.75 ± 1.87%), and the high proportion of patients with suboptimal control (83.3%) at the final visit of the observation period.

In South Africa, Van Zyl and Rheeder[1] showed that annual HbA_{1c} measurements rose from 70% of patients tested, to 94% tested after the implementation of a physician diabetes education programme, and reported that such findings were similar to the proportion of diabetes care measures carried out by American clinics.

In a study conducted by Grant[12] to assess the quality of care provided at clinics in America, overall levels of quality measure of HbA_{1c} were good, yet quality of care was deemed low in terms of proportions of patients not meeting goal glycaemia. Such findings were confirmed in Canada by Harris and Worrall,[32] and in the UK by Fox et al.[16]

End-study glycaemia

Both SEMDSA and the ADA recommend the goal of therapy to be an HbA_{1c} level of < 7%.[7-9]

In this study cohort, the proportion of patients meeting goal glycaemia was disappointingly low. Despite the introduction of insulin, 76.9% of this subset remained at suboptimal glycaemic control by the end of the observation period, with 86.7% of these having "final" HbA_{1c} measures ≥ 1% above goal HbA_{1c} of < 7%.

Of the patients remaining on maximum OHA therapy, only 10.3% achieved target glycaemic control, with 76.1% having "final" HbA_{1c} measures ≥ 1% above goal HbA_{1c} of < 7%.

These results are comparable with those demonstrated by Steyn et al[33] in the Western Cape, where 76% of patients with type 2 diabetes mellitus had HbA_{1c} levels ≥ 1% above the upper limit of normal.

Similar suboptimal control has been reported by Erasmus et al[34] in a study conducted in South Africa, in which only 20.1% of patients achieved HbA_{1c} levels of < 7%, irrespective of sex, duration of diabetes, body mass index, educational status, dietary advice, or type of treatment.

Failure to achieve targets, even once insulin was commenced, was shown by Gough et al[35] in the UK, and Hayward and Manning[36] in America. After a mean of two years of insulin therapy, Gough et al[35] reported that 81% of subjects had HbA_{1c} values of > 7%, while Hayward and Manning[36] reported 60% of subjects had HbA_{1c} levels of ≥ 8%.

Limitations

Some limitations have been identified in interpreting the findings from this study. A single site was studied, the study sample was small, and the results described are those of a very specific study cohort, and thus may be subject to selection bias.

Conclusion

In this study cohort, a discrepancy in the appropriate use and adjustment of insulin therapy according to metabolic status was evident, based on analysis of metabolic and treatment regimen data extracted from patient files.

The results of this study demonstrated a slow transition from OHA therapy to insulin therapy in poorly controlled insulin-requiring type 2 diabetes. Intensification of therapy was not adequate, resulting in HbA_{1c} levels remaining well above recommended targets, and the majority of patients remaining poorly controlled by the end of the observation period. Such prolonged exposure to hyperglycaemia may increase the risk of developing unwanted, expensive-to-treat, long-term complications associated with type 2 diabetes mellitus.

While barriers to insulin initiation need to be identified and addressed, appropriate medication adjustment and intensification is critical for good glycaemic control and improved patient outcomes, thereby reducing the burden of disease.

The awareness for the timely transition from oral glucose-lowering therapy to insulin therapy needs to be built into the clinical practice of healthcare professionals who manage and treat patients with type 2 diabetes mellitus.

The simple, well-documented practice of using an HbA_{1c} level of ≥ 7% as an alert to trigger appropriate adjustment of glucose-lowering therapy is recommended. Once this awareness to alter therapy has been created, barriers to insulin initiation need to be addressed and taken into consideration when implementing insulin therapy in patients with insulin-requiring type 2 diabetes.

Acknowledgements

Acknowledgement is given to Stephan van der Linde, Biostatistics Department, UKZN, and Dr John Gill, Medical Outpatient Department, Addington Hospital.

References

1. Van Zyl DG, Rheeder P. Physician education programme improves quality of diabetes care. S Af J Med. 2004;94(6):455-459.
2. Mbanya JN, Motala AA, Sogngwi E, et al. Diabetes in Sub-Saharan Africa. Lancet. 2010;375(9733):2254-2266.
3. Intensive blood glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study group. Lancet. 1998;352(9131):837-853.
4. The effects of intensive treatment on the development and progression of long term complications in IDDM. Diabetes Control and Complications Trial and Research Group. N Engl J Med. 1993;329(14):977-986.
5. Stratton IM, Adler AE, Neil HA, et al. Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. BMJ. 2000;321(7258):405-412.
6. Ohkubo Y, Kishikawa H, Araki E. 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(2):103-117.
7. American Diabetes Association. Standards of medical care in diabetes - 2009. Diabetes Care. 2009;3(Suppl 1):S13-S61.
8. Nathan DM, Buse JB, Davidson MB, et al. Management of hyperglycaemia in type 2 diabetes: a consensus algorithm for the initiation and adjustment of therapy. Diabetes Care. 2006;29(8):1963-1972. (Erratum, Diabetes Care. 2006;29(8):2816-2818).
9. The Society for Endocrinology, Metabolism and Diabetes of South Africa [homepage on the Internet]. c2011. Available from: www.semdsa.org.za/files/Diabetes%20Guidelines
10. Harris SB, Kapor J, Lank C, et al. Clinical inertia in patients with T2DM requiring insulin in family practice. Can Fam Physican. 2010;56(12):e418-e424.
11. Nathan D. Initial glycaemia in type 2 diabetes mellitus. N Engl J Med. 2002;347(17):1342-1349.
12. Grant RW, Buse JB, Meigs JB. Quality of diabetes care in US academic medical centres. Diabetes Care. 2005;28(2):337-342.
13. National programme for control and management of Diabetes Type 2 at primary level. Western Cape Government [homepage on the Internet]. c2011. Available from: www.westerncape.gov.za/Text/2003/diabetes.pdf
14. Goldstein DE, Little RR, Lorenz RA, et al. Tests of glycaemia in diabetes. Diabetes Care. 2004;27(7):1761-1773.
15. Kirkman MS, Williams SR, Caffrey HH, Marrero DG. Impact of a programme to improve adherence to diabetes guidelines by primary care physicians. Diabetes Care. 2002;25(11):1946-1951.
16. Fox KM, Gerber RA, Bolinder B, et al. Prevalence of inadequate glycaemic control among patients with type 2 diabetes in the United Kingdom general practice research database: a series of retrospective analyses of data from 1998 through 2002. Clin Ther. 2006;28(3):388-395.
17. Rubino A, McQuay LJ, Gough SC, et al. Delayed initiation of subcutaneous insulin therapy after failure of oral glucose-lowering agents in patients with type 2 diabetes: a population-based analysis in the UK. Diabet Med. 2007;24(12):1412-1418.
18. Harris SB, Ekoé JM, Zdanowicz Y, Webster-Bogaert S. Glycaemic control and morbidity in the Canadian primary care setting (results of the Diabetes in Canada Study). Diabetes Res Clin Pract. 2005;70(1):90-97.
19. Rotchford AP, Rotchford KM. Diabetes in rural South Africa: an assessment of care and complications. S Afr Med J. 2002;92(7):536-541.
20. Levitt NS, Bradshaw D, Zwarenstein MF, et al. Audit of public sector primary diabetes care in Cape Town, South Africa: high prevalence of complications, uncontrolled hyperglycaemia and hypertension. Diabet Med. 1997;14(12):1073-1077.
21. Riddle MC. The under use of insulin therapy in North America. Diabetes Metab Res. 2002;18(Suppl 3):S42-S49.
22. Riddle MC. Timely addition of insulin to oral therapy for type 2 diabetes. Diabetes Care. 2002;25(2):395-396.
23. Brown JP, Nichols GA. Slow response to loss of glycaemic control in type 2 diabetes mellitus. Am J Manag Care. 2003;9(3):213-217.
24. Hirsch IB, Bergenstal RM, Parkin CG, et al. A real-world approach to insulin therapy in primary care practice. Clin Diabetes. 2005;23:78-86.
25. Spellman CW. Insulin therapy for maximal glycaemic control in type 2 diabetes mellitus. J Am Osteopath Assoc. 2007;107(7):260-269.
26. Spellman CW. Achieving glycaemic control: cornerstone in the treatment of patients with multiple metabolic risk factors. J Am Osteopath Assoc. 2009;109(5 Suppl):8-13.
27. Dailey GE. Early insulin: an important therapeutic strategy. Diabetes Care. 2005;28(1):220-221.
28. Swinnen SG, Hoekstra JB, De Vries JH. Insulin therapy for type 2 diabetes. Diabetes Care. 2009;32 (Suppl 2):S253-S259.
29. El-Kebbi IM, Ziemer DC, Gallina DL, et al. Phillips diabetes in urban African-Americans. XV. Identification of barriers to provider adherence to management protocols. Diabetes Care. 1999;22(10):1617-1620.
30. Wetzler HP, Snyder JW. Linking pharmacy and laboratory data to assess the appropriateness of care in patients with diabetes. Diabetes Care. 2000;23(11):1637-1641.
31. Levitt NS, Zwarenstein MF, Doepfmer S, et al. Public sector primary care of diabetics: a record review of quality of care in Cape Town. S Afr Med J. 1996;86(Suppl):1013-1017.
32. Harris SB, Worrall G, Macaulay A, et al. Diabetes management in Canada: baseline results of the Group Practice Diabetes Management study. Can J Diabetes. 2006;30(2):131-137.
33. Steyn K, Levitt NS, Patel M, et al. Hypertension and diabetes: poor care for patients at community health centres. JEMDSA. 2008;13(2):64-70.
34. Erasmus RT, Blanco Blanco E, Okesina AB, et al. Assessment of glycaemic control in stable type 2 black South African diabetics attending a peri-urban clinic. Postgrad Med J. 1999;75(888):603-606.
35. Gough S, Frandsen KB, Toft AD. Glycaemic control and cardiovascular risk in isulin-treated patients with type 2 diabetes in Germany and the UK (abstract). Rome, Italy: European Association for the Study of Diabetes; 2008.
36. Hayward RA, Manning WG, Kaplan SH, et al. Starting insulin therapy in patients with type 2 diabetes: effectiveness, complications and resource utilization. JAMA. 1997;278(20):1663-1669.