Original article

Inadequate glycaemic control and antidiabetic therapy among inpatients with type 2 diabetes in Guangdong Province of China

BI Yan, YAN Jin-hua, LIAO Zhi-hong, LI Yan-bing, ZENG Long-yi, TANG Kuan-xiao, XUE Yao-ming, YANG Hua-zhang, LI Lu, CAI De-hong, WU Ge, ZHANG Fan, LIN Shao-da, XIAO Zheng-hua, ZHU Da-long and WENG Jian-ping

Keywords: type 2 diabetes; inpatient; glycaemic control; antidiabetic therapy

Background Diabetes mellitus has become epidemic in recent years in China. We investigated the prevalence of hyperglycaemia and inadequate glycaemic control among type 2 diabetic inpatients from ten university teaching hospitals in Guangdong Province, China.

Methods Inadequate glycaemic control in diabetic patients was defined as HbA1c ≥ 6.5%. Therapeutic regimens included no-intervention, lifestyle only, oral antilglycemic agents (OA), insulin plus OA (insulin+OA), or insulin only. Antidiabetic management included monotherapy, double therapy, triple or quadruple therapy.

Results Among 493 diabetic inpatients with known history, 75% had HbA1c ≥ 6.5%. Inadequate glucose control rates were more frequently seen in patients on insulin+OA regimen (97%) than on OA regimen (71%) (P <0.001), and more frequent in patients on combination therapy (81%–86%) than monotherapy (75%) (P <0.05). Patients on insulin differed significantly from patients on OA by mean HbA1c, glycemic control rate, diabetes duration, microvascular complications, and BMI (P <0.01).

Conclusions This study showed that glycemic control of type 2 diabetic patients deteriorated for patients who received insulin and initiation time of insulin was usually delayed. It is up to clinicians to move from the traditional stepwise therapy to a more active and early combination antidiabetic therapy to provide better glucose control.

Chin Med J 2008;121(8):677-681

The prevalence of diabetes mellitus has dramatically increased in recent years in China, an estimated 40 million nationwide have diabetes. A similar, disproportionate number of hospitalized patients have diabetes. In the USA, the prevalence of diabetes in hospitalized adults is conservatively estimated at 12.4%–25.0% and for every two patients diagnosed with diabetes in the hospital, there may be at least one other patient in the hospital with unrecognized diabetes, who is at risk for poor outcomes and safety issues, as well as higher health care costs. However, the prevalence and an accurate estimate of the number of patients admitted to hospitals with diabetes in China have never been reported because type 2 diabetes is underdiagnosed in hospital settings.

The prevalence of diabetes is increasing in China, but glycaemic control appears to be deteriorating. Glycaemic control remains the major therapeutic objective for diabetics. United Kingdom Prospective Diabetes Study reported that a lower HbA1c level decreased the risk of complications. For this reason, the International Diabetes Federation in 2005 advised people with diabetes to maintain an HbA1c level lower than 6.5% to minimize the development of complications.7 Recently, new recommendations from the American Diabetes Association for the management of type 2 diabetes suggest that HbA1c level should be maintained less than 7%, call for more rapid initiation of oral medications and...
insulin therapy and recommend early use of insulin for patients with A1c >9%. However, despite the introduction of new antidiabetic agents and treatment guidelines, many studies have shown that the prevalence of inadequate control remains high. According to the United Kingdom General Practice Database from 1998 to 2002, the proportion of patients with type 2 diabetes and HbA1c over 6.5% was 88%. In 2003, a survey of control of glucose for type 2 diabetic patients in China showed the prevalence of patients with HbA1c ≥ 6.5% was 88.5%. These results indicate that optimal glycaemic control is not achieved in many, perhaps the majority, of patients with diabetes.

Recently, a survey of diabetes mellitus was taken among inpatients in Guangdong Province of China. To gain a broader understanding of the current quality of inpatient diabetic management, we analyzed: (1) the general antidiabetic therapy and glycaemic control among patients with type 2 diabetes; and (2) the relationship between glycaemic control rate and antidiabetic managements.

METHODS

Clinical case selection
Data were derived from the survey of diabetes among inpatients in Guangdong Province. The survey was conducted among adult inpatients registered in the departments of medicine, surgery, gynaecology, traditional Chinese medicine, dermatology, ophthalmology, ENT, stomatology, rehabilitation, and neurology in ten university teaching hospitals of Guangdong, China during the week before Diabetes Day, 14th November, 2004. Department of paediatrics, organ replacement surgery, obstetrics, infection, and radiotherapy were excluded.

The program has been described in detail before. The fasting plasma glucose (FPG) levels were screened when the 8753 patients investigated were hospitalized. The determination of diabetic status in epidemiological studies is based on the measurement of the fasting plasma glucose level (FPG ≥ 7.0 mmol/L). Those with the FPG levels within 5.6 – 6.9 mmol/L with no medical history of diabetes underwent a 75 g oral glucose tolerance test (OGTT). Complications associated with diabetes, including microvascular complications (neuropathy, nephropathy and retinopathy) and macrovascular complications (stroke and myocardial infarction) were diagnosed by a specialist after the diagnosis of diabetes.

For the purpose of analysis for glycaemic control and antiglycaemic therapy in type 2 diabetic inpatients, we defined the study sample as subjects with a medical history of type 2 diabetes diagnosed by an endocrinologist. Patients were excluded for the following reasons: type 1 diabetes (n=13), gestational diabetes mellitus (n=13), other types and uncertain types of diabetes (n=78), refusing the blood test for HbA1c and incomplete medical records (n=132). There remained 493 inpatients enrolled for analysis of inadequate glucose control.

The study design and protocol conformed to the Guidelines of the Declaration of Helsinki (1975 and 1983), were approved by the Medical Research and Ethics Committee of Sun Yat-sen University and by the equivalent Committee at each centre. All patients gave informed, witnessed consent.

Study methods
Inadequate glucose control rates were calculated by the proportion of type 2 diabetic inpatients with HbA1c ≥ 6.5% according to International Diabetes Federation 2005. Five therapeutic regimens were defined for this study: no intervention; lifestyle only; diet and exercise only; oral antiglycaemic agents (OA) only; insulin plus OA (insulin+OA); and insulin only. Additionally, three antidiabetic managements were defined as: monotherapy, only one antidiabetic agent was used; double therapy, two kinds of antidiabetic agents were used; triple or quadruple therapy, three or four kinds of agents were used.

Analytical methods
Fasting blood samples were collected and HbA1c measured uniformly at the First Affiliated Hospital, Sun Yat-sen University. The HbA1c level was measured by high performance liquid chromatogram assay and the upper limit of normal was 6.2%. Blood glucose and serum lipids were measured by using standard methodology at laboratories of individual centres. Because the blood glucose and serum lipids measurements were standardized to the same reference method, there were no differences in normal range or upper limit.

Statistical analyses
All measurements were expressed as mean ± standard deviation (SD). Statistical analyses were conducted using SPSS10.0. Statistical differences between groups were determined using two tailed, unpaired Student’s t and χ² tests. A P value less than 0.05 was considered statistically significant.

RESULTS
There were 493 patients who met the inclusion criteria for this analysis. The enrolled patients (245 men and 248 women) were aged (63.6 ± 12.3) years, with diabetes for (6.5±6.4) years. The mean HbA1c was (8.0±2.3)%. Seventy-five percent of type 2 diabetic inpatients had an HbA1c level equal to or greater than 6.5%.

Characteristic differences between therapeutic regimens
Among the therapeutic regimens in our study, 45.2% inpatients received insulin only, 12% received insulin+OA, 28.4% received OA only, 5.5% experienced lifestyle intervention only and the other 8.9% had no intervention (Table 1). The proportion of insulin use (insulin only and insulin+OA) increased in patients with a longer duration of diabetes,
The rates of inadequate glucose control in type 2 diabetic patients with combination therapy were higher compared with patients in OA and lifestyle only groups. Patients with inadequate glycaemic control differed significantly from patients who were in good glycaemic control group by diabetes duration and type of diabetic therapy. There was no difference in sex or complications between inadequate glycaemic control and good glycaemic control. In addition, more patients in the inadequate glycaemic control group were prescribed OA plus insulin than in the good control group (Table 3).

**DISCUSSION**

Until recently, diabetic status in hospitalized patients was not a major therapeutic focus for clinicians, especially if patients were 77% of the insulin only treated group, 97% of the insulin+OA group, 71% of the OA only group, 52% of the lifestyle only regimen group and 59% of the non-intervention group (Table 1). Mean HbA1c levels in insulin and insulin+OA groups were significantly higher compared with patients in OA and lifestyle only groups. Patients with inadequate glycaemic control differed significantly from patients who were in good glycaemic control group by diabetes duration and type of diabetic therapy. There was no difference in sex or complications between inadequate glycaemic control and good glycaemic control. In addition, more patients in the inadequate glycaemic control group were prescribed OA plus insulin than in the good control group (Table 3).
the patient had no history of diabetes. This is partly because of a lack of epidemiological data of hyperglycaemia in hospitalized patients in China and partly because of a lack of caution regarding adverse outcomes from asymptomatic hyperglycaemia. In fact, many studies have shown a higher mortality and morbidity among inpatients of undiagnosed diabetes in cardiac surgery, myocardial infarction, and critical illness.13-16

We report the prevalence of hyperglycaemia in hospitalized patients for the first time.11 Of the 8753 inpatients investigated, 15.1% had diabetes and 4.9% IGR. Of those inpatients with diabetes, 8.3% (n=729) had a known history of diabetes, 6.8% were diagnosed as newly diabetics with no medical history of diabetes before admission, showing that 45% of the inpatient diabetics were unrecognized. Of the new onset diabetics, 4% (n=353) had FPG ≥7.0 mmol/L on admission and 2.8% were diagnosed diabetic according to OGTT, which indicate that OGTT can detect further unrecognized diabetes in hospital setting. The results indicate that hospitalized diabetics in China is underdiagnosed and an urgent need for clinicians to take a high priority to screen and manage hyperglycaemia.

However, whether hospitalized hyperglycaemia is an acute response or a reflection of underlying diabetes has been controversial. A prospective study on impaired glucose metabolism with myocardial infarction and no previous diagnosis of diabetes mellitus showed that impaired glucose tolerance at discharge and after 3 months were 66% and 65%.17 Another study on stroke in nondiabetics showed similar results,18 indicating that elevated glucose levels in hospital are not only related to stress induced by acute event.

The present study analysed the tiered approach to type 2 diabetes management to control glucose, which often leads to delay in both achievement and maintenance of glucose control.19,20 The average duration of diabetes in the insulin only and insulin plus OA groups was 6.9 years and 10.8 years, while the disease duration in the OA only group was 5.3 years. This indicates that use of insulin is usually the last choice for the stepwise approach to type 2 diabetes management. The proportions of microvascular complications in the insulin treated groups were higher than those in the OA treated group, which might be one reason for the choice of insulin therapy. One study showed that there were some barriers to starting insulin when treatment goals are not achieved.19 By the time patients with type 2 diabetes are treated with insulin, they usually have had diabetes for over 10 years and have established complications.20

In the present study, patients with inadequate glycaemic control were likely to be prescribed insulin plus OA and the inadequate glycaemic control rate and mean HbA1c level in the insulin plus OA and insulin only groups were higher than in the group treated with only OA. This indicates that clinicians tried to switch to insulin therapy usually when glucose control was difficult to maintain by oral antidiabetic agents. For stepwise approach, the first step is lifestyle modification, followed by treatment with a single oral antidiabetic agent gradually increased to maximal recommended dose before combination therapy is introduced.12 In a prospective well controlled study, Brown et al21 found that the average patient accumulated nearly 10 years of excess glycaemia burden of HbA1c >7.0% from diagnosis until the initiation of insulin therapy. In our study, patients who were treated with only OA were heavier than those on an insulin only regimen, thus indicating that metabolic control of patients on insulin use might have deteriorated before they had to turn to insulin therapy.

The highest inadequate glucose control rate was in combination therapy (81% to 96%) compared with monotherapy (75%). The average duration of diabetes in the monotherapy group was 6 years while in the combination groups were 7.7 to 10.5 years. This suggests that a delay often occurs between monotherapy and combination therapy. A study showed that the mean number of months that elapsed until a new or additional treatment was started ranged from 26.5 months (metformin monotherapy) to 35.1 months (sulfonylurea monotherapy).19 The consensus statement from the American Diabetes Association in 2006 states that the goal of diabetes management is to achieve and maintain glycaemic levels as close to the nondiabetic range as possible, to change interventions at as rapid a pace as blood levels allows and more rapid initiation of both oral medications and insulin therapy.2

The present study has two limitations. First, the study provided a simplistic view of a complex disease process in which patients’ HbA1c rose and fell over time. A longitudinal study is required to examine the relationship between treatment and the disease. Second, the study population were inpatients with type 2 diabetes, whose management approach could not be exactly examined as a whole and the expectation is that a larger group of outpatients should have been studied. Nonetheless, the

### Table 3. Characteristics of inpatients with type 2 diabetes mellitus according to HbA1c values

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Good control HbA1c&lt;6.5%</th>
<th>Inadequate control HbA1c≥6.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (%)</td>
<td>123 (25)</td>
<td>370 (75)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n (%))</td>
<td>63 (51)</td>
<td>182 (49)</td>
</tr>
<tr>
<td>Female (n (%))</td>
<td>60 (49)</td>
<td>188 (51)</td>
</tr>
<tr>
<td>Age (year)</td>
<td>64.4±13.2</td>
<td>62.8±12.7</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.9±4.2</td>
<td>22.8±5.1</td>
</tr>
<tr>
<td>Mean diabetes duration (year)</td>
<td>5.06±6.34</td>
<td>6.75±6.42*</td>
</tr>
<tr>
<td>Diabetes therapy number (n (%))</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>28 (23)</td>
<td>40 (11)</td>
</tr>
<tr>
<td>OA only</td>
<td>41 (33)</td>
<td>99 (27)</td>
</tr>
<tr>
<td>Insulin+OA</td>
<td>2 (2)</td>
<td>57 (15)</td>
</tr>
<tr>
<td>Insulin only</td>
<td>52 (42)</td>
<td>174 (47)</td>
</tr>
<tr>
<td>Patient number of microvascular complications (n (%))</td>
<td>51 (41)</td>
<td>202 (55)</td>
</tr>
</tbody>
</table>

*P<0.05 vs monotherapy group. BMI: body mass index; OA: oral antidiabetic agents.

The present study assessed the tiered approach to type 2 diabetes to control glucose, which often leads to delay in both achievement and maintenance of glucose control.19,20 The average duration of diabetes in the insulin only and insulin plus OA groups was 6.9 years and 10.8 years, while the disease duration in the OA only
Inadequate glucose control rate (75%) in this study was lower than the results from diabetes control in China in 2003 (88.5%). Differences between the enrolled subjects as well as regional differences could explain the responsible factors. Although our study had some limitations, it still provides a basis for future nationwide research to improve the strategies to treat type 2 diabetes.

In summary, the present study showed the following: (1) the prevalence of diabetes in hospitalized adult patients is a common finding and nearly half were undiagnosed diabetes, which should generate an urgent need for clinicians to make screening for diabetes in hospitalized patients a priority in China. (2) Glycaemic control of type 2 diabetic patients deteriorated while patients received insulin, suggesting that initiation time of insulin is usually delayed and microvascular complications often occur during the change from monotherapy to combination therapy, which calls for a need for intensified efforts to treat type 2 diabetic patients to recommended levels.

Competing interests: None declared.

Acknowledgements: The author would like to thank all the participated patients, centres and coordinators for this study.

REFERENCES


(Received December 12, 2007)
Edited by LIU Dong-yun