นิพนธ์ต้นฉบับ • Original Article

การควบคุมเบาหวาน การตรวจพบโปรตีนในปัสสาวะและเบาหวานเข้าจอประสาทตา ในคลินิกเบาหวานโรงพยาบาลเพชรบูรณ์

วิกรม สุธีเวสารัช
กลุ่มงานอายุรกรรม โรงพยาบาลเพชรบูรณ์

Diabetic Control, Proteinuria and Diabetic Retinopathy in Diabetes Clinic at Petchabun Hospital

Wikrom Sutheewesaraj
Department of Medicine, Petchabun Hospital

หลักการและเหตุผล: การศึกษานี้นำข้อมูลจากผลการตรวจและการสืบค้นต่างๆที่รวบรวมจากการตรวจตามปกติในคลินิกเบาหวาน ช่วงเวลาหนึ่งปี ระหว่างวันที่ 1 ก.ค. 2546 - 30 มิ.ย.2547 มาวิเคราะห์เพื่อตอบคำถามว่าภาพรวมของการควบคุมเบาหวานได้ถึงเกณฑ์มาตรฐานมากน้อยเพียงไร

วัตถุประสงค์:

1. เพื่อประเมินการควบคุมเบาหวาน ซึ่งครอบคลุมถึง ระดับน้ำตาลในเลือด ความดันเลือด และระดับไขมันในเลือด ในผู้ป่วยเบาหวาน
2. หาความชุกของการตรวจพบโปรตีนในปัสสาวะ และเบาหวานเข้าจอประสาทตา

รูปแบบ: การศึกษาแบบตัดขวาง เชิงพรรณนา

สถานที่ทำการศึกษา: คลินิกเบาหวาน โรงพยาบาลเพชรบูรณ์

การวัดผล: ดัชนีมวลร่างกาย ระดับน้ำตาลกลูโคสในเลือดขณะอดอาหาร ฮีโมโกลบินเอวันซี ความดันเลือด ระดับไขมันในเลือด โปรตีนในปัสสาวะ ซีรัมครีอาตินีน ผลตรวจจอตา

ผลการศึกษา: จำนวนผู้ป่วยเบาหวานทั้งหมด 1,960 คน ผู้ป่วยที่แพทย์วินิจฉัยว่าความดันเลือดสูงร่วมด้วยหรือความดันเลือดมากกว่าหรือเท่ากับ 130/80 ม.ม.ปรอท มีร้อยละ 62.1 ผู้ป่วยที่แพทย์วินิจฉัยว่าระดับไขมันผิดปกติในเลือดร่วมด้วยหรือได้รับยาลดระดับไขมันในเลือดมีร้อยละ 36.3 ดัชนีมวลกายมากกว่าหรือเท่ากับ 25 กก./ตรม. มีร้อยละ 55.4 ผู้ป่วยที่ควบคุมระดับน้ำตาลกลูโคสในเลือดขณะอดอาหารมากกว่าหรือเท่ากับ 130 มก./ดล. มีร้อยละ 61.6 ความดันเลือดมากกว่าหรือเท่ากับ 130/80 ม.ม.ปรอท มีร้อยละ 48.3 และระดับไขมันแอลดีแอลโคเลสเตอรอลมากกว่าหรือเท่ากับ 100 มก./ดล. มีร้อยละ 36.3 ความชุกของการตรวจพบโปรตีนในปัสสาวะ และเบาหวานเข้าจอประสาทตา เท่ากับ ร้อยละ 12.3 และ 13.9

Background: During a one-year period between July 1, 2003 and June 30, 2004 routine diabetic control parameters were collected into the database for every patient's visit to the diabetes clinic. Investigations were done to each patient in a casual manner and the available data were analyzed. The result should give an insight toward care improvement for the clinic.

Objectives:

1. Evaluate the control of diabetes mellitus including blood glucose, hypertension and dyslipidemia in the diabetes clinic at Petchabun hospital
2. Determine the prevalence of overt proteinuria and diabetic retinopathy in the clinic

Design: cross-sectional, descriptive study

Setting: diabetes clinic, Petchabun Hospital, Petchabun Province

Measures: body mass index, fasting blood glucose, hemoglobin A1C, blood pressure, lipid profiles, proteinuria, serum creatinine, fundoscopic examination

Results: Total number of diabetic patients was 1,960. Associated hypertension and dyslipidemia were 62.1% and 36.3%, respectively. Prevalence of body mass index of ≥ 25 kg/sqm was 55.4%. Patients with average fasting blood glucose ≥ 130 mg/dl were 61.6%. Patients with average blood pressure ≥ 130/80 mmHg were 48.3%. Patients with average low-density lipoprotein cholesterol of ≥ 100 mg/dl were 36.3%. Prevalence of overt proteinuria and diabetic retinopathy were 12.3% and 13.9%.

สรุป: ควรให้ความสำคัญในการปรับปรุงการควบคุมทั้งระดับน้ำตาล ความดันเลือด และระดับไขมันในเลือด ในคลินิกเบาหวานให้ได้มาตรฐานมากยิ่งขึ้น

Conclusion: There is room for improvement in diabetic control at the diabetes clinic.

Key words: diabetes mellitus, diabetic complications, microvascular complications, Petchabun

ศรีนครินทร์เวชสาร 2547; 19(4), 226-232 • Srinagarind Med J 2004; 19(4), 226-232

Introduction

Management of diabetes comprises not only glucose control but also control of hypertension and dyslipidemia in order to minimize their common long-term complications, i.e., atherosclerosis and its consequences. Poorly controlled diabetic patients suffer from macrovascular as well as microvascular complications including retinopathy, nephropathy and neuropathy [1-3]. While the ultimate goal is to decrease morbidity and mortality, doctor's intermediate concern's whether diabetic control's within the target range.

The aim of the study was to evaluate the control of diabetes mellitus (DM) which include controlling blood glucose, blood pressure and dyslipidemia, and to determine the prevalence of retinopathy and overt proteinuria in diabetes clinic at Petchabun Hospital. The author hoped that the knowledge would give an insight toward care improvement for the clinic.

Materials and methods

A cross-sectional study was carried out in all patients attending the diabetes clinic during one year period from July 1, 2003 to June 30, 2004. All types of DM except gestational type were included. Routine diabetic control parameters were collected and inputted into the clinic database for every patient's visit during the period. The parameters were body weight (BW), fasting blood glucose (FBG) by portable capillary whole blood glucose meter, blood pressure (BP) by standard manual application of mercury sphygmomanometer, hemoglobin A_1C (Hb A_1C), urinalysis (U/A) where proteinuria was measured by reagent strip with discrete result ranging from negative, trace, 1+, 2+, 3+, 4+, serum creatinine (Cr), serum total cholesterol (TC), serum triglyceride (TG), serum high-density lipoprotein cholesterol(HDL-C), serum low-density lipoprotein cholesterol (LDL-C) and fundoscopic exam by ophthalmologist.

FBG, BW and BP were recorded in every visit, while Hb A1C, U/A, Cr, TC, TG, HDL-C, LDL-C were collected only after doctor's order but every result was recorded. In addition to direct measurement, LDL-C was also derived from calculation by Friedewald's formula [4]: LDL-C = TC-(HDL-C+TG/5) whenever TG<400 mg/dL and three samples collected on the same day. Each patient may have no, one or more records of Hb A_1C, U/A, Cr, TC, TG, HDL-C, LDL-C. Fundoscopic examination was recorded by only one of the four doctors taking part in the clinic thus each patient may have no, one or more records during the one year period and only a fraction of the fundoscopic examinations was recorded.

Fundoscopic examinations done before the study period were also included as possible but only to identify patient with retinopathy. These values were excluded in the statistic calculation elsewhere.

Body mass index (BMI) was calculated from each patient's latest BW and height and rounded to integer. BMI $\geq$ 25 kg/sqm identified patients with obesity.

One or more of these means identified patients with HT

1. Doctor's diagnosis
2. Three consecutive systolic BP reach 130 mmHg and/or three consecutive diastolic BP reach 80 mmHg

One or more of these means identified patients with dyslipidemia

1. Doctor's diagnosis
2. Prescribed medication against dyslipidemia

Patients with overt proteinuria were identified by latest two U/A revealed "grade 1+ or more" proteinuria or latest one U/A revealed "grade 2+" proteinuria. All U/A with sediments, i.e., red cell $\geq$ 3-5/HPF and/or white cell $\geq$5-10/HPF, were excluded.

Patients with diabetic retinopathy (DR) were identified by ophthalmologist's diagnosis of either non-proliferative DR (NPDR) or proliferative DR (PDR).

Prescription data were derived from prescription database of the hospital.

Statistical analyses were carried out using simple descriptive analysis such as frequency, percentage, means, standard deviation and range. Selection biases of investigation or examination were shown using Z-test or Chi-square test.

Results

As shown in Table 1, total number of DM patients was 1,960. Male to female ratio was 1: 2.27.The patients' age ranged from 23-104 years with mean 58.8 years. The majority of patients (93.7%) were between 40-79 years old.

According to the study criteria, HT and dyslipidemia were found in 62.1% and 36.3%, respectively.

All patients had at least one FBG, BP record in the database. The average FBG was 145.6 mg/dL. The average BP was 126.6/77.4 mmHg.

Mean, S.D. and range of other parameters were based on only available data. There were differences between the tested or examined group and not-tested or not-examined group as shown in table 2. Patients with diagnosis of associated HT or dyslipidemia were likely to be tested or examined. Younger age was also a significant factor of doctor's order to many tests while older age promoted more creatinine test.

Eighty five percent of patients had both body weight and height record sufficient to calculate BMI. BMI ranged from 14-76 kg/sqm with mean 25.59 kg/sqm. The prevalence of obesity was 55.6%.

Only 27.2% were sent for Hb A1C test. The average Hb A1C was 6.67% with range of 3.2-12.1%. Among these patients, the average FBG was 143.4 mg/dL (range 74-328 mg/dL), which was not significantly different from that of the not-tested group with average FBG = 146.4 mg/dL ($p = 0.11$). However, the tested group was younger with mean age 57.7 vs. 59.3 years ($p = 0.004$) and had a slightly more male to female ratio ($p = 0.042$).

Records of LDL-C were derived from 2 ways, direct measurement and calculation. Patients had one or more record. Among these patients, the (53.4%) average LDL-C was 114.4 mg/dL.

The mean serum creatinine of 59.0% of patients was 1.34 mg/dL. Older patients were more likely to be tested as noted above.

According to the latest practice recommendation from American Diabetes Association[12], target range of blood pressure is < 130/80 mmHg, target range of prepandrial plasma glucose is 90-130 mg/dL and target range of

Table 1 Characteristics of diabetic patients

	Total patients	Number	Per cent	
Sex (male : female)	1,960	600 : 1,360	30.6 : 69.4	
HT	1,960	1,218	62.1	
Dyslipidemia	1,960	711	36.3	
Obesity	1,666(85.0%)	927	55.6	
	Total patients	**Mean ***	**S.D. ***	**Range ***
Age (years)	1,960	58.8	11.3	23-104
BMI (kg/sqm)	1,666(85.0%)	25.59	4.70	14-76
Average systolic BP (mmHg)	1,960	126.6	7.66	90-178
Average diastolic BP (mmHg)	1,960	77.4	4.37	60-96
Average FBG (mg/dL)	1,960	145.6	42.3	64-541
Average Hb A1C (%)	534(27.2%)	6.67	1.60	3.20-12.10
Average TC (mg/dL)	735(37.5%)	197.5	46.6	53-612
Average TG (mg/dL)	883(45.1%)	187.1	126.0	29-1320
Average HDL-C (mg/dL)	801(40.9%)	48.3	10.6	23-113
Average LDL-C (mg/dL)	1,046(53.4%)	114.4	32.4	16-249
Average serum creatinine (mg/dL)	1,157(59.0%)	1.34	0.86	0.1-10.4

* mean, S.D. and range of available data

Table 2 Significant difference between tested and not-tested group *

Test or examination	Odds ratio between tested and not-tested			Mean value of tested group / Mean value of not-tested group			
	Diagnosis of HT	Diagnosis of Dyslipidemia	Male sex	Age	Average FBG	Average SBP	Average DBP
BMI	1.660			58.6/60.2		127.2/128.6	
Hb A_1C	1.324		1.247	57.7/59.3			
LDL-C	2.166	14.786				127.8/126.8	77.8/77.3
TC		5.251					
TG	1.603	6.572		58.2/59.4			
HDL-C	1.891	5.881		58.2/59.3			
Cr	1.392	1.790		59.7/57.7		128.1/126.4	77.8/77.2
Urine protein	3.371	2.135		58.0/59.3			
Fundoscopy	4.523	2.300					

* show only data with statistically significant difference by Z-test (odds ratio) or Chi-square test(mean)

LDL-C is <100 mg/dL. Table 3 shows numbers of patients whose diabetic control was outside target range.

1. 61.6% of patients in the clinic had average FBG ≥130 mg/dL.
2. Among 1,218 patients with associated HT, 60.3% had average BP ≥130/80 mmHg.
3. As high as 43.3% of total 1,960 patients were never tested for any serum lipid in the one-year period.
4. Among 711 patients with associated dyslipidemia, 68.8% had average LDL-C ≥100 mg/dL.

642 patients had one or more record of U/A without sedimentation. Among these patients, 5.1% had proteinuria 1+ or more in the latest 2 consecutive U/A during this period. More than 7.2% had proteinuria 2+ or more in the latest U/A, this made the overall prevalence of overt proteinuria under the study criteria 12.3%. Another 11.1% had one record of 1+ proteinuria in the latest U/A and had to be tested more to rule out non-persistent proteinuria. There was no record of proteinuria within the same day with record of systolic BP ≥180 mmHg or diastolic BP ≥110 mmHg.

Only 302 patients (15.4%) were both sent for fundoscopy and recorded into the database. The prevalence of DR was 13.9% (NPDR:PDR = 20:1).

Discussions

This study included all types of DM except gestational type because gestational DM presents in short term and has different target range of control from other types. There was no discrimination between type 1 and 2 in the database. No data of duration of diabetes, foot evaluation, complications such as neuropahty or macrovascular complications were taken into analysis.

Per cent of patients whose diabetic control parameter was outside target range was used to assess diabetic care in this study. Although the target cannot be applied appropriately to all patients, e.g., optimum diabetic control may be unnecessary in short life expectancy, etc, data has shown that better glycemic, blood pressure or lipid control were needed in a large portion of the patients. Annual screening of Hb A1C, lipid profile, kidney function and U/A were also inadequate.

The prevalence of HT in this study (62.1%) was higher than many other studies in the past 5-9 owing to diagnostic criteria following the latest practice recommendation. Three consecutive high systolic BP's or diastolic BP's triggered automatic diagnosis of each patient by computer program. With this method of diagnosis, doctors sometimes did not realize that their patients have associated HT. It may be the reason why as high as 60.3% of patients with associated HT had average BP higher than target range. Unlike dyslipidemia, patients who took antihypertensives were not included as associated HT because many antihypertensives are prescribed for other indications. For example, ACEI or ARB may be prescribed for proteinuria, ACEI, ARB or beta-blockers for ischemic heart disease or congestive heart failure, propranolol for history of variceal bleeding, etc. So the prevalence might even be an underestimate.

Only 56.7% of patients were sent to any lipid test at

Table 3 Patients whose diabetic control was outside target range

Glycemic control	**Total**		**Number**		**%**
Average FBG ≥130 mg/dL	1,960		1,207		61.6
Average Hb A1C ≥ 7%	534		224		41.9
Blood pressure control	**Number**		**Average BP ≥130/80 mmHg**		**%**
Total	1,960		947		48.3
Diagnosis of HT	1,218		734		60.3
No diagnosis of HT	742		213		28.7
Lipid control	**Number**	**Never sent for any lipid test**	**%**	**Average LDL-C ≥ 100 mg/dL**	**%**
Total	1,960	849	43.3	712	36.3
Diagnosis of dyslipidemia	711	49	6.8	489	68.8
No diagnosis of dyslipidemia	1249	800	64.1	223	17.9

Table 4 Overt proteinuria and retinopathy

Characteristics		**Number**	**Per cent**
Proteinuria status			
No overt proteinuria		563	87.7
	negative or trace	492	76.6
	1+ only once	71	11.1
Overt proteinuria		79	12.3
	≥1+ at least twice	33	5.1
	≥2+ at least once	46	7.2
		(n=642)	100
Fundoscopy			
No DR		260	86.1
DR		42	13.9
	NPDR	40	13.2
	PDR	2	0.7
		(n=302)	100

least once in the year, which was inadequate. The primary target of lipid-lowering therapy is LDL-C. In diabetic patients, goal is below 100 mg/dL. Thus only 31.2% with diagnosis of associated dyslipidemia achieved the goal. However, success or failure cannot be measured by this fraction only. At any level of LDL-C, for a given mg/dL change in the LDL-C level, the change in relative risk of coronary heart disease is the same as at any other LDL-C level. Moreover, when baseline LDL-C was very high, it would be difficult to decrease to 100 mg/dL because even with high dose statins or lipid-lowering drug combinations, LDL-C reductions > 50% often cannot be achieved[13].

Proteinuria instead of albuminuria was used to assume diabetic nephropahty (DN) at the clinic. False negative could be from insensitivity of the dipstick method where grade 1+ and 2+ imply proteinuria about 300 and 1,000 mg/day respectively in an average person with daily urine output 1,000 ml. False positive could be from non-glomerular proteinuria or other causes of glomerular proteinuria. The criteria excluded only-once 1+ proteinuria

Table 5 Prevalence of DN and DR among various studies (%)

	Number	DN	DR
Siriraj[7]	781	8.6	21.4
Chula[8]	469	17.1	3.2
Rajavithi[9]	1,171	11.2	23.8
Srinagarind[6]	207	12.5	25.1
Lerdsin[5]	420	16.7	28.8
Banphaeo[10]	158	8.2	30.4
Chonburi[11]	206	31.0	35.4
Petchabun (number)		12.3 (642)	13.9 (302)

to rule out non-persistent proteinuria which could be from causes such as exercise within 24 hours, infection, fever, congestive heart failure, marked hyperglycemia, marked hypertension, pyuria and hematuria[14].

Comparison of DN among various studies was difficult because of differences in method and definition. Some studies used grade 2+ [5,6,10] while other used grade 1+ [11] as cut-off point. This study mixed and complicated the criteria. Comparison of DN as well as DR was displayed on Table 10. Prevalence of DR in this study appeared lower than most other studies. Further pre-designed study is needed to confirm this information.

Conclusion

In diabetes clinic at Petchabun Hospital, better control of fasting blood glucose, blood pressure and LDL-cholesterol were needed in 61.6, 48.3 and 36.3%, respectively. Prevalence of overt proteinuria and DR were 12.3% and 13.9%. There is room for improvement in diabetic control at the clinic.

Acknowledgement

The author would like to thank the following persons for their support: Mrs. Ammala Pangkaew; Mrs. Piyathida Ruangjan; Mrs. Saithong Han-In; Mr. Pramote Sanguanvong; Mr.Sakchai Satthanont; Mrs. Mayuree Jantho; Dr. Bongkoj Jiramethathorn; Dr. Pisit Wathanawithookoon, Dr. Kobchai Jiracharnchai, Dr. Nantakorn Bunpan, Dr. Apichai Seehawong; Dr. Chaicharn Suebsurikul

References

1. Thai Multicenter / Research Group on Diabetes Mellitus. Vascular complications in NIDDM in Thailand. Diabetes Res Clin Pract 1994; 25: 61-9.
2. UK Prospective Diabetes Study 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: 837-53.
3. UK Prospective Diabetes Study Group: Effect of intensive blood glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998; 352: 854-65.
4. Friedewald WT, Levy RS, Fredrickson DS. Estimation of the concentrations of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. Clin Chem 1972; 18: 499-502.
5. Tanamai J. Diabetic Control and Complications in Diabetic Clinic, Lerdsin Hospital. Bull Dept Med Serv 1995; 20: 147-154.
6. Bhuripanyo P, Graisopa S, Suwanwatana C, Prasertkaew S, Kiatsayompoo S, Bhuripanyo K, et al. Vascular complications in NIDDM in Srinagarind Hospital, Khon Kaen. J Med Assoc Thai 1992; 10: 570-7.
7. Tandhanand S, Nitiyanant W, Makarasara C, Vannasaeng S, Vichayanrat A. Chapter 6. Epidmiology of diabetes mellitus in Southeast Asia. In : Bajaj JS. ed. Diabetes mellitus in developing countries. New Delhi : Interprint 1984 p.51-4.
8. Bunnag SC, Chandraprasert S, Svetarundra B, et al. Prevalence of vascular complications in diabetes at Chulalongkorn University Hospital. J Asean Fed Endocr Soc 1982 ; 2 :13-8.

9. Serirat S, Kachaceewa U, Sunthornthepvarakul T, Watanachote S, Kalayanarooj S, Makarasara C, et al. Chronic complications in Thai patients with NIDDM. Intern Med 1990; 6: 124-7.
10. Siriwechadaruks P. Chronic complications in NIDDM at Banphaeo Hospital. Bull Dept Med Serv 1996; 21: 377-85.
11. Kwanjaipanich R, Tengtrirat C, Nanna K, Laiwatanapaisal S. Vascular complications in type 2 diabetes mellitus at Chonburi Hospital, Thailand. Intern Med J Thai 2002:18:122-30.
12. American Diabetes Association. Standards of medical care for patients with DM. Diabetes Care 2004; 27 (Suppl 1): S15-35.
13. National Cholesterol Education Program. Implications of Recent Clinical Trials for the National Cholesterol Education Program Adult Treatment Panel III Guidelines. Circulation. 2004; 110: 227-239.
14. American Diabetes Association. Nephropathy in Diabetes. Diabetes Care 2004; 27 (Suppl 1): S79-83.