The Rate of Checking Urine Microalbumin and Aspirin Primary Prevention in Type 2 DM

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Background: *The American Diabetic Association recommends type 2 Diabetes Mellitus (DM) to take aspirin therapy as a primary preventive way. It should be implemented in cases that are aged over 40 with at least one additional risk such as hypertension, obesity, dyslipidemia. Urine microalbumin now also ranks as a major risk factor for atherosclerosis.*
Objectives: *The authors aimed to evaluate the rate of urine microalbumin determination and the use of such preventative aspirin therapy at Srinagarind Hospital.*
Material and Method: *The authors randomly selected the charts of type 2 diabetics treated for at least one year at the hospital's outpatient department by a block of four techniques. The inclusion criteria were aged more than 40 years old and never had any atherosclerotic events. Cases were excluded if they had a history of aspirin allergy or active upper gastrointestinal bleeding. By the end of July, 2004, 109 patients were enrolled (44 males).*
Results: *The mean age and duration of diagnosed diabetes mellitus was 60.8 and 7.4 years, respectively. Forty-four cases (40.4%) were checked for urine microalbumin. Eight cases had microalbuminuria and four cases had macroalbuminuria. Every case was treated with aspirin because they had at least one additional atherosclerotic risk factor, mostly more than two. But aspirin therapy was used in only 35 cases (32.1%) with the appropriate dose in only six cases (17.1%).*
Conclusion: *Physicians should consider more about checking urine microalbumin and aspirin as primary prevention in type 2 DM.*

Keywords: *Microalbuminuria, Aspirin, Primary prevention, Atherosclerosis, DM type 2*

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Type 2 Diabetes Mellitus (Type 2 DM) is a major risk factor for atherosclerosis[1,2] and usually has a greater burden than other atherosclerotic risk factors in non-diabetics. Cardiovascular events are the most important cause of death among diabetics[3]. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) cited urine microalbumin as a major risk factor for atherosclerosis[4]. In addition, the American Diabetes Association (ADA) recommends aspirin as a treatment for primary prevention among high-risk diabetic patients[5].

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As follow-on, the authors investigated the rate of checking of urine microalbumin and practice of aspirin therapy as a primary prevention in type 2 DM at Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, Thailand. Furthermore, the full profile of diabetics was studied. The authors' aim was to encourage physicians to routinely test urine for microalbumin and prescribe aspirin therapy when appropriate.

Material and Method

The authors reviewed the charts of type 2 DM who were more than 40 years of age, had been treated for at least one year, and never experienced any atherosclerotic events (*i.e.* ischemic heart disease, stroke or peripheral artery disease). The patients were excluded if they had a history of aspirin allergy or

active upper gastrointestinal bleeding. Cases were randomly selected by the block of four techniques from the patients' list. The patient profile (including age, sex, duration of diabetes, body weight, height, lipid profile, HbA1C level, urinalysis, urine microalbumin level and aspirin treatment) was reviewed. The atherosclerotic risk factors were counted in each case. Each one of these factors were defined as one atherosclerotic risk factor; hypertension, smokers, obesity (body mass index, BMI > 25 kg/m^2), dyslipidemia, physical inactivity,a family history of sudden death in males under 55 or females under 65, and urine microalbuminuria. The following criteria for dyslipidemia were checked. The acceptable level of fasting Triglyceride (Tg) was less than150 mg/dL, High Density Lipoprotein cholesterol (HDL-c) was more than 40 mg/dL, and Low Density Lipoprotein cholesterol (LDL-c) was less than 100 mg/dL. Aspirin therapy as primary prevention should be implemented in cases of type 2 DM who are older than 40 years with at least one atherosclerotic risk factor. The appropriate use of aspirin was between 75 and 162 mg/day. The data were analyzed by SPSS version 11. A p-value of < 0.05 was considered significant.

Results

There were 109 diabetic patients included in the present study; 44 (40.4%) were males. The mean age was 60.8 $\pm$ 11.1 years of age (range, 40-91). The mean duration before diagnosis was 7.4 $\pm$ 6.0 years. Seventy-eight cases (71.6%) had no recorded height or BMI; 16 cases (14.7%) had never been checked for A1C; and 13 cases (11.9%) did not know their lipid levels.

BMI averaged 26.2 kg/m^2 ranging from 20.9-38.2. Of the 31 cases with known BMI, 18 cases (58.1%) had BMI > 25 kg/m^2, eight cases (25.8%) were between 23.0 and 24.9 kg/m^2, and five cases (16.1%) were < 23 kg/m^2.

The mean A1C value and standard deviation for the 93 cases (85.3%) was 7.1 $\pm$ 3.3% (range, 4.1-14.5%). Intensive diabetic control (A1C < 7%) was practiced in 21 cases (22.6%); with a 95% confidence interval of 14.8, 32.7 (Table 1).

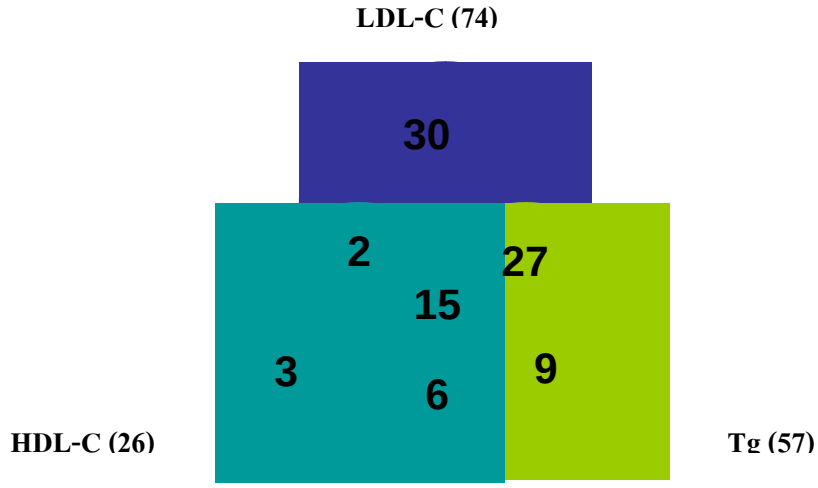
The lipid profiles were checked in 96 cases (88.1%). According to the criteria for dyslipidemia mentioned above, 88 (91.7%) patients had a lipid abnormality in at least one of three values. There were only eight cases that had all acceptable lipid values. High LDL-c was the most common abnormality (either alone or in combination with other lipid values) as shown in Table 1. The number of case that had high LDL-c, high Tg, low HDL-c, high LDL-c with high Tg, high LDL-c with low HDL-c, high Tg with low HDL-c, high LDL-c with high Tg and low HDL-c was 30, 9, 3, 27, 2, 6, 15, respectively (Fig. 1). The mean (SD) of serum cholesterol was 195.7 (89.3), Tg was 204.5 (197.0), HDL-c was 42.0 (20.5), and LDL-c was 111.6 (60.6). Although the mean of all lipid values was nearly normal, there were more than ninety percent of lipid abnormalities demonstrated in individuals. No correlation was found between A1C and age, sex, duration of diabetes, BMI, or any of the lipid profiles.

A large number (49 cases or 45.0%) of cases had never been checked for either urine microalbumin or urinalysis. Urine microalbumin was done in forty-four cases (40.4%). Both routine urinalysis and urine

Table 1. Demonstrates the number, percentage, and 95% confident interval of obesity, well controlled DM, and lipid abnormalities

Variables	N (%)	95%CI
BMI $\geq$ 25 kg/m^2 (of 31 cases)	18 (58.1)	39.3, 75.0
A1C < 7% (of 93 cases)	21 (22.6)	14.8, 32.7
Lipid profile (of 96 cases)		
High LDL-c (total cases)	74 (77.1)	67.2, 84.8
High Tg (total cases)	57 (59.4)	48.9, 69.1
Low HDL-c (total cases)	26 (27.1)	18.8, 37.3
High Tg and low HDL-c	6 (6.3)	2.6, 13.7
High Tg and high LDL-c	27 (28.1)	19.6, 38.4
Low HDL-c and high LDL-c	2 (2.1)	0.4, 8.1
High Tg, high LDL-c and low HDL-c	15 (15.6)	9.3, 24.8

Note: BMI; body mass index, A1C; hemoglobin A1C, LDL-c; low density lipoprotein cholesterol, HDL; low density lipoprotein cholesterol, N; number of cases, CI; confident interval



Note: LDL-c; low density lipoprotein cholesterol, HDL-c; high density lipoprotein cholesterol, Tg; fasting triglyceride

Fig. 1 Shows the number of cases that had lipid abnormalities in each type (alone and combination)

microalbuminuria were done in only ten cases. The correlations of urine strip and urine microalbumin were studied in 44 cases (Table 2). Both tests were not consistent with each other. For example, four cases had trace proteinuria by urine strip but urine microalbumin level was less than 30 mg per day. Microalbuminuria and macroalbuminuria were found in 8 and 4 cases, respectively (Table 2). The nine patients with gouty arthritis had their serum checked for the level of uric acid.

Regarding atherosclerotic risk factor count, every case had at least one risk factor with the maximum at six. Most of the patients had two to four major risk factors for atherosclerosis (Table 3). There were 69 cases (63.3%) that had more than three major risk factors. According to ADA guideline, all of the enrolled cases should be treated with aspirin. Only 35 cases (32.1%) were treated with aspirin. The appropriate dose was prescribed in six of 35 cases (17.1%) as shown in Table 3.

Discussion

Type 2 Diabetes Mellitus (type 2 DM) is a major risk factor for atherosclerosis; so much so that it is defined as equivalent to coronary heart disease[6]. Furthermore, coronary heart disease is a major cause of morbidity and mortality among diabetics[7]. No difference was found in macrovascular disease in the intensive and conventional group in a prospective study of diabetics in the UK[8]. However, a subgroup analysis suggested that reducing the A1C by 1% was associated with 15% reduction of stroke and 18% reduction in myocardial infarction. In addition, aspirin

Table 2. Shows the result of urine microalbumin in 44 cases correlated with result of routine urinalysis. Result of urinalysis was revealed by urine protein representing negative, trace, or 1+ by urine strip. Correlation is shown by row (n = 44)

Urinalysis (urine protein)	Urine microalbumin			Total, N
	< 30 mg/day, N	30-300 mg/day, N	> 300 mg/day, N	
Not done	26	5	3	34
Negative	2	2	1	5
Trace	4	0	0	4
1+	0	1	0	1
Total	32	8	4	44

Note: mg; milligram, N; number of cases

Table 3. Reveals the number of cases that had one to six atherosclerotic risk factors correlated with number of case receiving aspirin therapy and appropriate dose of aspirin. Correlation is shown by row

No. of risk factor	N	Aspirin therapy, N	Appropriated dose, N
1	12	2	1
2	28	5	0
3	34	10	1
4	28	13	2
5	6	4	2
6	1	1	0
Total	109	35 (32.1%)	6 (17.1%)

Note: No.; number, N; number of cases

as a primary prevention and treatment of other atherosclerotic risk factors (*i.e.* obesity, dyslipidemia, smoking cessation, and hypertension) is also an important strategy[5].

The baseline characteristics of type 2 DM in our out-patient department, who were free from atherosclerotic events, showed obesity in 58.1%, successful intensive therapy in 22.6% and dyslipidemia in 91.7%. Hypertriglyceridemia with low HDL is the most common pattern of dyslipidemia in type 2 DM[5] and was found in only 6.3%. In this study, 77% of cases had a high value of LDL-c (alone or in combination with high Tg or low HDL-c). It may imply that statin therapy should be considered in most diabetic patients. There was no correlation between A1C and age, sex, BMI, duration of diabetes or any particular lipid profiles. The small number of subjects in the present study may limit the reliability of this analysis. The main problem in the present study was incomplete data on the out-patient card. Missing data included height (71.6%), urine microalbumin (59.6%) and smoking habit - all of which are significant risk factors in themselves.

Microalbuminuria is the earliest marker of diabetic nephropathy and is associated with an increased risk of cardiovascular disease in both diabetics and nondiabetics[9]. The rate of checking urine microalbumin in our setting was 40.4%. Microalbuminuria was detected in eight of 44 cases (18.2%). According to Table 2, the urine microalbumin test is a more accurate indicator than the urine strip because of higher sensitivity. However, routine urinalysis is also important. One should rule out any other causes of proteinuria by urine strip. In summary, yearly urinalysis and/or urine microalbumin should be used to detect early diabetic nephropathy in type 2 DM. Routine urinalysis should be done first. If there is no detection of protein or abnormal cellular abnormality, urine microalbumin should be further done by using 24 hours urine examination or spot urine for protein-creatinine index. Serum uric acid is now also becoming a cardiovascular risk factor[10]. It may be routinely checked in the near future for evaluating atherosclerotic risk. In the authors' review, only nine cases were checked for the level of uric acid because all of them had gouty arthritis. It was just a routine evaluation.

According to the ADA guideline, the atherosclerotic risk count should be considered in all Type 2 DM cases for considering aspirin as primary prevention. It is appropriate to prescribe aspirin in those older than 40 years old and having at least one additional risk factor such as a family history of CVD, hypertension, smoking, dyslipidemia, or albuminuria. Every case in the present study had at least one atherosclerotic risk factor, with a maximum range of six. The median number was 3. Combining with Type 2 DM, most cases were identified as the high risk group for atherosclerotic events. Aspirin should have been used in all cases but there were only 35 of 109 cases (32.1%) taking aspirin. The suggestive dose is 75-162 mg/day for both primary and secondary prevention[5]. The appropriate dose was prescribed in only 17.1% (6 of 35). The rate and dose of aspirin therapy were still at a lower rate (32.1%) and a lower dose (82.9%) than the ADA recommendation. However, the side effects of aspirin are important and patients must be made aware of them before starting treatment.

The A1C level, the lipid profiles, urine microalbumin, BUN, and creatinine should be checked annually in diabetics. A1C must be checked more frequently (3-4 times a year) in cases of poor control. In addition, aspirin therapy and other strategies (*i.e.* lipid therapy, weight control, smoking cessation, and

physical activities) should be implemented as appropriate.

Conclusion

Physicians should think about checking urine microalbumin, doing an atherosclerotic risk count, and using an aspirin therapy as they are all important as diabetic control in type 2 DM.

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อัตราการตรวจแอลบูมินในปัสสาวะและการให้ยาแอสไพรินเพื่อป้องกันโรคหลอดเลือดและหัวใจในผู้ป่วยเบาหวานชนิดที่ 2

กิตติศักดิ์ สวรรยาวิสุทธิ์, ปณิตา ลิมปะวัฒนะ, อรรจนี มหรรฆานุเคราะห์, ไชยสิทธิ์ วงศ์วิภาพร

American Diabetic Association ได้แนะนำให้มีการให้ยาแอสไพรินแก่ผู้ป่วยเบาหวานชนิดที่ 2 ที่ยังไม่เกิดโรคหลอดเลือดและหัวใจที่มีอายุมากกว่า 40 ปีและมีปัจจัยเสี่ยงอาทิ ความดันโลหิตสูง อ้วนหรือไขมันผิดปกติ การตรวจพบแอลบูมินในปัสสาวะก็จัดเป็นอีกปัจจัยเสี่ยงหนึ่งที่สำคัญในการเกิดโรคหลอดเลือดและหัวใจ การศึกษานี้ต้องการศึกษาว่ามีอัตราการตรวจแอลบูมินในปัสสาวะและการให้ยาแอสไพรินในผู้ป่วยเบาหวานที่รับการรักษาที่โรงพยาบาลศรีนครินทร์มากน้อยเพียงใด เกณฑ์ที่คัดเลือกผู้ป่วยเข้ารับการศึกษาคือ ผู้ป่วยเบาหวานชนิดที่ 2 ที่ได้รับการรักษาอย่างต่อเนื่องเป็นเวลาอย่างน้อย 1 ปีและยังไม่เคยเกิดโรคหลอดเลือดและหัวใจ หากผู้ป่วยมีประวัติแพ้ยาแอสไพรินหรือมีประวัติการเกิดเลือดออกในทางเดินอาหารจะถูกตัดออกจากการศึกษา ผู้ป่วยที่เข้าเกณฑ์จะถูกสุ่มศึกษาโดยวิธี block of four มีผู้ป่วยที่เข้าร่วมการศึกษา 109 ราย เป็นชาย 44 ราย อายุเฉลี่ย 60.8 ปี เป็นเบาหวานมาแล้วเฉลี่ย 7.4 ปี มีผู้ป่วยจำนวน 44 รายที่ได้รับการตรวจหาแอลบูมินในปัสสาวะ โดย 8 รายเข้าได้กับภาวะ microalbuminuria และ 4 รายเข้าได้ กับภาวะ macroalbuminuria ผู้ป่วยทุกรายควรได้รับการรักษาด้วยยาแอสไพรินเนื่องจากมีปัจจัยเสี่ยงต่อการเกิดโรคหลอดเลือดและหัวใจอย่างน้อย 1 ข้อ (ส่วนมากมีปัจจัยเสี่ยงมากกว่าหรือเท่ากับ 2 ข้อ) แต่มีการใช้ยาเพียงร้อยละ 32.1 และด้วยขนาดยาที่เหมาะสมเพียงร้อยละ 17.1 โดยสรุป แพทย์ควรตระหนักถึงการส่งตรวจหาแอลบูมินในปัสสาวะ และพิจารณาการรักษาด้วยยาแอสไพรินในผู้ป่วยเบาหวาน ชนิดที่ 2 ให้มากขึ้นและถูกต้องมากขึ้น