Risk factors for progression of chronic kidney disease in diabetic patients

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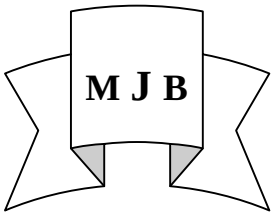

Abstract

Background

The incidence and progression of renal injury vary substantially among individuals who are at-risk for **kidney disease**.Prediction of increased risk of occurrence or progression of CKD enables clinicians to identify individuals who may benefit from closer supervision of care or more intensive disease modifying interventions.

Method

Between march 2005 and July 2007, 151 patients (69 male, 82 female,) with stage 4 chronic renal failure(CRF) defined by a creatinine clearance (Ccr) of 16–30 ml/min(15)from A-forat Al-awsat , and Alsader teaching hospital, all of them had a regular follow-up from baseline Ccr until the the end of the follow-up period, or the GFR become <15 ml/min,(stage 5 CKD).

Results:

Serum calcium and hemoglobin were significantly lower in patients whose GFR progressed to stage 5 CKD (group (A)), than in patients did not enter stage 5 CKD(group(B)) , baseline urine protein and erythrocyte sedimentation rate were significantly higher in group (A) than in group (B) .The differences between other parameters between patients of the 2 groups were not significant .

Conclusion:

In conclusion our study suggest that baseline hypocalcaemia , anemia , high ESR , and proteinuria are independent predictors for progression of CKD.

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عوامل خطر تدهور اعتلال الكلى السكري

الخلاصة

ان تدهور امراض الكلية المزمنة مختلف بين الاشخاص المصابين بها ،معرفة عوامل الخطر و علامات التدهور يساعد المعالج السريري على تعيين المصابين الذين يستفادون من العناية الطبية المشددة، او التدخلات العلاجية المركزة ز

الطريقة:

تضم الدراسة ١٥١ مريضا (٦٩ رجلا و ٨٢ امرأة) يعانون من إمراض الكلى المزمن الدرجة الرابعة(نسبة تصفية الكرياتنين اكثر من ١٥ مل/الدقيقة) بسبب اعتلال الكلى السكري ، تابعنا حلتهم المرضية لمدة سنة ،لنرى مدى نسبة التدهور عند كل مريض بحيث يدخل الدرجة الخامسة (نسبة تصفية الكريانين اقل من ١٥ مل/الدقيقة).

النتائج:

ان نسبة الكلسيوم و الهيموغلوبين في الدم في مرضى المجموعة الأولى (المرضى الذين و صلوا الى الدرجة الخامسة من الاعتلال الكلوي المزمن) هي اقل مما في مرضى المجموعة الثانية (المرضى الذين لم يصلوا الى تلك الدرجة) ، كما ان نسبة الزلال في الإدرار و نسبة ترسب الكريات الحمراء(ESR) اكبر عند مرضى المجموعة الأولى مما لدى مرضى المجموعة الثانية.

الاستنتاجات:

ان هذه الدراسة تشير إلى ان فقر الدم و قلة الكالسيوم في الدم و الزلال في الادرار و ارتفاع نسبة ترسب كريات الدم الحمراء هي عوامل و علامات خطر لتدهور مرض الكلية المزمن في مرضى الاعتلال السكري ،مما يدعو الى عناية طبية مشددة، و تدخلات علاجية مركز.

Introduction

End srage renal disease(ESRD) is a major health problem , resulting in considerable increasae in morbidity and mortality , decrease in quality of life and a substantial cost from renal replacement therapies (1 , 2).Slowing the progression of renal failure thus appears to be a major therapeutic challenge for the coming years (3) .

For example, 8% of new patients with type 2 diabetes mellitus already have proteinuria at diagnosis (4). Among patients with type 2 diabetes mellitus who are initially free of proteinuria, the 20-yr risk of diabetic nephropathy is 41% (4). After proteinuria occurs, the subsequent 10-yr risk of progressive chronic kidney disease is 11% (5). Thus, about half of those with type 2 diabetes will develop nephropathy and 10% of these individuals will experience progressive loss of renal function. Variable risk of impaired renal function has also been reported among hypertensive subjects. At study entry, 5.9% of the Hypertension Detection and Follow-up Program trial participants had a serum creatinine of 1.5 mg/dl or greater and 2.3% of the 8683 participants with serial serum creatinine measurements over 5 year experienced clinically significant loss of renal function (6).

Similarly, the rate of loss of renal function among individuals with chronic kidney disease(CKD) also displays considerable person-to-person variability. For example, the Modification of Diet in Renal Disease (MDRD) study reported that the mean (SD) rate of decline in GFR during follow-up was 3.8 (± 4.2) ml/min per yr for patients with moderate and 4.0 (± 3.1) ml/min per yr for those with severe renal insufficiency at baseline (7). Substantial proportions of each group, 19% and 11%, respectively, showed no progression during follow-up, further indicating variability in progression.

Prediction of increased risk of occurrence or progression of CKD enables clinicians to identify individuals who may benefit from closer supervision of care or more intensive disease modifying interventions(8).For chronic kidney disease, interest has focused on risk factors for its occurrence and rate of progression. Information about these risk factors can be used in risk prediction (9,10).

Information about the rate of change in renal function over time can serve as a measure of disease progression .Progression of CKD can be measured using serum creatinine (11), reciprocal of the serum creatinine (12), Cockcroft-Gault estimated glomerluar filtration rate(GFR), (or similar estimating equation) (13,14).

We therefore aimed to evaluate the factors which associated with decline in GFR in diabetic patients with CKD.

Patients and methods

Between march 2005 and July 2007, 151 patients (69 male, 82 female,) with stage 4 chronic renal failure(CRF) defined by a creatinine clearance (Ccr) of 16–30 ml/min(15) , from A-forat Al-awsat , and Alsader teaching hospital, all of them had a regular follow-up from baseline Ccr until the the end of the follow-up period, or the GFR become <15 ml/min,(stage 5 CKD)(15), and gave their informed consent to participate in a study of risk factors of progression of renal disease .

All were ambulatory and managed as outpatients. Among them, 32 patients reached the end poiont (i.e: GFR <15)(group(A)) . The remaining 119 CKD patients had not yet reached the end point and served as controls [group (B)]. Primary renal disease was diabetic nephropathy in all ptients.

Each patient had at least 4 visits per year, or at more frequent intervals according to the degree of CRF, with assessment of blood pressure, antihypertensive medication [i., beta-blockers, calcium-channel blockers and angiotensin-converting enzyme (ACE) inhibitors], and serum creatinine at each visit. The majority of patients treated with ACE inhibitors had this treatment at the start

of follow-up (>85%). Creatinine clearance (Ccr) was estimated for each subject from serum creatinine concentration using the Gault and Cockroft formula, which takes into account age, body weight and gender. Clinical and laboratory parameters taken into account for correlation analysis were the baseline values at the start of the follow up.

Statistics

At screening ,normally distributed variables are expressed as mean (SD),otherwise as median (range). Differences between groups were tested using Student's *t*_test, P_value <0.05 was considered significant (two_tailed).

Result

The total numbers of patients are 151 with stage 4 CKD(baseline GFR between 15 and 30 mil/min)(15) .

We divided the patients into 2 groups , group (A) involved 119 patients whose GFR did not progress to the end point (i.e: their GFR were >15 mil/min) after one year , and group (2) involved 32 patients with GFR of <15 mil//min after one year .Baseline characters of patients are shown in table (I).

Serum calcium and hemoglobin were significantly lower in group(A) than in the group(B), baseline urine protein and erythrocyte sedimentation rate were significantly higher in group (A) than in group (B) ,as shown in table(II).The differences between other parameters between patients of the 2 groups were not significant ,see table(II).

We observed that the progression of chronic kidney disease proportionated with the numbers of abnormalities in these four parameters (serum calcium , hemoglobin , erythrocyte sedimentation rate ESR , and urine protein). Where only 26% of patients with no one of these abnormalities in baseline measure progress to GFR <15 mil/min within one year , while 62-66 % of patients with one abnormality(either anemia , hypocalcaemia , proteinuria or high ESR) , and 85% of patients with all these 4 abnormalities progress to GFR < 15% mil/min within one year .

Discussion

The major finding of this study is that the decline in GFR of diabetic patients with chronic kidney disease patients is more in those with baseline anemia , hypocalcaemia , high ESR , and proteinuria .these finding are with agreement with other studies (16-20). The differences between arterial blood pressure and baseline total serum cholesterol and baseline serum creatinine of the 2 groups were not significant. This is in agree with previous studies (21,22)

Variability of risk for the occurrence and progression of CKD suggests that biologically relevant characteristics exist that influence the occurrence or course of the renal disease (12). The variable progression of CKD among individuals with autosomal dominant polycystic kidney disease (ADPKD) illustrates this concept. The mutation of the polycystin gene that occurs within family members is a necessary risk factor for ADPKD. However, family members who inherit the same mutation demonstrate highly variable rates of progression to ESRD (12). The within-family heterogeneity of time of onset of ESRD indicates that the rate of progression of CKD among individuals with the same ADPKD gene is associated with one or more independent exposures other than the mutation itself. Combinations of causal factors that result in rapid progression to ESRD define sufficient causes for early loss of renal function among ADPKD patients (23)..

Even though a risk factor need not be causal, the concept has considerable utility in developing disease prevention and control strategies. Risk factors can be used to identify individuals at high risk for the occurrence and progression of CKD(8) .

Prediction of increased risk of occurrence or progression of CKD enables clinicians to identify individuals who may benefit from closer supervision of care or more intensive disease modifying interventions(8). For

chronic kidney disease, interest has focused on risk factors for its occurrence and rate of progression. Information about these risk factors can be used in risk prediction (9,10).

Conclusion

In conclusion our study suggest that baseline hypocalcaemia , anemia , high ESR , and proteinuria are independent predictors for progression of CKD , and the progression correlates with number of these abnormalities .So closer supervision of care or more intensive disease modifying interventions for patients with these abnormalities .

The predictability of these factors for occurrence and progression of CKD in patients with non- diabetic nephropathy need to be evaluated .

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Table (1) baseline characters of patients.

Parameters	Values
Age(year)	47 ± 16
Sex:M/F ratio	1:1.19 (69/82)
s.cr(mg/dl)	3.4 ± 1.7
GFR(mil/min)	21.8 ± 7.7
MAPB(mmHg)	86 ± 13
FBS(mmol/l)	6.1 ± 0.9
S.ca (mg/d)	8.2 ± 1.7
Urine protein(gm/24hour)	0.63 ± 0.39
Hb (gm/dl)	9.7 ± 2.1
ESR	44 ± 16

Table(2) baseline characters of each group.

Parameters	Group(A)	Group(B)	p-value*
Age(year)	46 ± 15	49 ± 16	NS
Sex:M/F ratio	1:1.18(56/66)	1:12 (13/16)	NS
S.cr (mg/dl)**	3.2 ± 1.2	3.5 ± 0.9	NS
GFR (ml/min	22.5 ± 5.2	21.1 ± 4.4	NS
MAPB***(mmgH)	85 ± 11	87 ± 12	NS
24 urine protein(mg/dl)	0.7 ± 0.43	1.3 ± 0.55	<0.05
S.calcium(mg/dl)	9.2 ± 0.75	7.8 ± 1.3	<0.05
S.phosphorus (mg/dl)	2.6 ± 0.6	2.8 ± 0.5	NS
Hb(mg/dl)	10.5 ± 1.5	7.5 ± 1.3	<0.05
ESR(	25 ± 15	53 ± 19	<0.05
T.S.cholesterol(mmol/l)	6.1±1.2	6.2±1.3	NS

- * p-value<0.05 is significant
- ** s.cr= serum creatinine
- ***MABP=mean arterial blood pressure