Saudi J Kidney Dis Transplant 2006;17(4):511-515

Saudi Journal of Kidney Diseases and Transplantation

Original Article

Retrospective Analysis of Factors Affecting the Progression of Chronic Renal Failure in Adult Polycystic Kidney Disease

Ebadur Rahman Ahmed*, Muhammed A. Tashkandi*, Sahpar Nahrir**, Abdurrahim Maulana***

*Alnoor hospital, **Hera General Hospital, ***King Abdulaziz hospital, Mekka, Saudi Arabia

ABSTRACT. Autosomal dominant polycystic kidney disease (ADPKD) is the commonest congenital cystic renal disease. Factors such as hypertension, urinary tract infection, hematuria, and proteinuria may affect the progression to chronic renal failure in ADPKD patients. Therapeutic interventions, such as the use of angiotensin converting enzyme inhibitors (ACEI) or diet modification, may impact the natural progression of the disease. We aim in this study to review a registry of ADPKD patients in order to compare the slow and fast progressors and identify possible predictors of progression and interventions that slow the progression of this disease. Sheffield Kidney Institute (SKI), one of the largest kidney institutes in Northern Europe, has registered a large number of ADPKD patients since 1981. SKI's computer network contains a wide range of information on these patients. We selected 94 adult polycystic patients from the SKI for retrospective analysis of factors affecting progression to chronic renal failure. Patients who doubled their s. creatinine in ≤ 36 months were considered fast progressors (FP), while those who doubled their s. creatinine in > 36 months were regarded as slow progressors (SP). There were 70 patients in the FP group and 24 patients in the SP group. A third group of 137 patients consisted of non-progressors (NP) who had stable s. creatinine levels during the same period. We found that the incidence of hypertension, UTI, macroscopic and microscopic hematuria, and overt proteinuria in the FP group was higher than in the SP and NP groups. Modification of some factors, such as hypertension and UTI, may decrease the rate of the deterioration of renal function.

Key Words: Adult, Polycystic, Kidney, Disease, Hypertension, Hematuria, Proteinuria, Urinary, Infection.

Reprint request and correspondence to:

Dr. Ebadur Rahman
Department of Nephrology
Alnoor Hospital, Mekka
Kingdom of Saudi Arabia
E-mail: ebadurmr@hotmail.com

Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is the commonest congenital cystic renal disease. However, its pathogenesis and progression to chronic renal failure are not

clearly understood. Factors such as hypertension, urinary tract infection, hematuria, and proteinuria may affect the progression to chronic renal failure in ADPKD patients. [1-9]

Therapeutic interventions, such as the use of angiotensin converting enzyme inhibitors (ACEI) or diet modification, may impact the natural course of progression of the disease. [10-14]

We aim in this study to review a registry of ADPKD patients in order to compare the slow and fast progressors and identify possible predictors of progression and interventions to slow down the progression of this disease.

Materials and Methods

Sheffield Kidney Institute (SKI), one of the largest kidney institutes in Northern Europe, has registered a large number of ADPKD patients since 1981. SKI is a computer network that contains a wide range of information on these patients. 94 adult polycystic patients were selected from the SKI for retrospective analysis of factors affecting progression to chronic renal failure. Patients who doubled their s. creatinine in < 36 months were considered fast progressors (FP), while those who doubled the s. creatinine in over 36 months were regarded as slow progressors (SP). A third group consisted of non progressors (NP) whose renal function remained stable during the study period. There were 70 patients in the FP group, 24 patients in the SP group, and 137 patients in NP group.

The effects of gender, documented active and recurrent urinary tract infection (UTI), gross and microscopic hematuria, >300mg/24hrs or 2+ proteinuria, hypertension (defined as systolic values of ≥160 mmHg and a diastolic values ≥ 90mmHg during the time of progression prior to any replacement therapy), and use of angiotensin converting enzyme inhibitors on progression in the study groups were analyzed.

The mean systolic and mean diastolic pressures were calculated for each patient from at least three readings before therapeutic intervention. The duration of hypertension prior to any replacement therapy was also calculated. In order to evaluate the severity of the hypertension, the number of drugs used to control hypertension was also compared among the study groups.

Statistical Analysis

We compared the groups by using non-parametric tests. The significance of the differences of the continuous variables (i.e. blood pressure) between the study groups was tested by the Wilcoxon Ranksum test. The significance of discontinuous variables (UTI, hematuria, and drugs) among the study groups were estimated by the Chi-squared test. The P value was set as significant if $P < 0.05$.

Results

Table 1 shows the characteristics and risk factors of progression in the different study groups. There was no significant difference in the gender composition among the study groups. A total of 29 patients in the progressors group had UTIs, mostly in the FP group; 11 patients had recurrent UTIs. The prevalence of UTI in the NP group was 18 patients (13.1%). There was a significant statistical difference in the prevalence of UTI between the FP and NP groups (p value <0.01). The prevalence of proteinuria was 5.7% and 4.1% in the fast and slow progressors, respectively. In the NP group, the incidence of proteinuria was 2.9%. None of these patients had proteinuria of more than 1 g/24h. Because of this very small number, statistical tests were not performed. The prevalence of microscopic hematuria was 25.7%, 29%, and 8.7% in the FP, SP, and NP groups, respectively. On

Table 1. The characteristics and risk factors of progression in the different study groups.

	FP (N=70)	SP(N=24)	NP (N=137)	P value
Males	38 (54 %)	16 (66%)	56 (40%)	
Female/male	1.2/1	2/1	0.7/1	NS
Single UTI	15 (21.4%)	3 (12.5%)	13(9.45%)	0.01*
Recurrent UTI	10 (14.3%)	1 (4%)	6 (4.4%)	0.01*
Proteinuria <1g/24-h	1 (1.4%)	4 (16%)	4 (2.9%)	
Proteinuria >1g/ 24-h	4 (5.7%)	1(4.1%)	0(0%)	
Macroscopic hematuria	18 (25%)	7(29%)	12(8.7%)	0.05**
Microscopic hematuria	5(7.1%)	1(4.1%)	2(1.5%)	0.01***
Mean systolic blood pressure	142.5	140	NA	NS
Mean diastolic blood pressure	89	87.7	NA	NS
Median of mean arterial pressure	105	105.5	NA	NS
Duration of hypertension (years)	10	8	NA	NS
No drug	9 (12.9%)	4 (16.6%)	75 (54.7%)	0.01***
Single drug	21 (30%)	4 (16.6%)	23 (16.7%)	0.01***
Two drugs	15 (21.4%)	8 (33.3%)	15 (10.9%)	0.01***
Three or more drugs	25 (35.7%)	8 (33.3%)	10 (7.3%)	0.01***
ACE-inhibitors	21 (30%)	9 (37.5%)	14 (10.2%)	NS

Fast progressor (FP), slow progressor (SP), non-progressors (NP). NA: not available.
* Between FP and SP. ** Between FP and NP. *** Between NP and both FP and SP.

the other hand, the incidence of macroscopic hematuria in the FP group was 7.1%. This was higher than in the SP and NP groups, where the prevalence of macroscopic hematuria was 4.1% and 1.5%, respectively. However, a statistically significant difference was found between the FP and NP groups ($p<0.05$). The prevalence of microscopic hematuria was not significantly different between the FP and SP groups but was significant between both of these and the NP group ($p <0.01$). The prevalence of recurrent hematuria was higher in the FP group than in the other groups. In the FP and SP groups, 81 out of 94 (86%) patients were hypertensive. the prevalence of hypertension was significantly lower in the NP group, since only 55 out of 137 (40%) patients were hypertensive, ($p <0.001$). The mean arterial pressure, mean systolic pressure, and mean diastolic pressure in the FP group were found to be slightly higher than in the SP group, but this was statistically not significant. Furthermore, the difference in duration of hypertension between the FP and SP groups was not significant. The prevalence of drug resistant hypertension (requiring 3 or more antihyper-tensives for satisfactory control of BP) was found to be slightly higher in FP group than in the SP and the NP groups. However, there was no statistically significant difference in the use of multiple antihypertensives or ACEIs between the FP and SP groups. Because of lack of data, the blood pressure values of non progressors could not be obtained.

Discussion

With the limitations inherent in retrospective analysis, the factors affecting the progression of chronic kidney disease (CKD) in ADPKD were analyzed. We found that the prevalence of UTI, macroscopic and microscopic hematuria, and overt proteinuria in the FP group was higher than in the SP and NP groups. This suggests an association between these factors and the progression of CKD in ADPKD patients.

An association with the fast progression of CKD in ADPKD patients who had macrohematuria, especially before the age of 30 years, has been shown by other studies. [15] The same result was obtained for overt proteinuria. [16]

The prevalence of hypertension was significantly higher in the FP and SP groups than in the NP group. This implies that hypertension may be an important factor for the progression of CKD in ADPKD patients. Other investigators also observed the deleterious effect of hypertension on the progression of CKD when they compared hypertensives with and without any interventions. [17-22]

The utilization of ACEIs was not significantly different between the FP and SP groups. This is largely due to a small number of patients in our study. The observations described in the MDRD study suggested a low benefit of the ACEIs in the prevention of progression of CKD in ADPKD patients. [14]

We found no gender effect on the progression of CKD in ADPKD patients after the GFR falls below 25 ml/min/1.73m^2. The MDRD study reported the same conclusion on the gender effect on CKD progression. [5]

We conclude that the progression of CKD in ADPKD patients can be affected by several factors, such as hypertension, proteinuria, hematuria, and UTI. These factors may result in the rapid deterioration of renal function and progression towards end–stage renal failure. Modification of some factors, such hypertension and UTI, may decrease the rate of the deterioration of renal function.

References

1. Churchill DN, Bear JC, Morgan J, Payne RH, Mc Manamon PJ, Gault MH. Prognosis of adult onset polycystic kidney disease re-evaluated. Kidney Int 1984;26:190-3.
2. Gabow PA. Autosomal dominant polycystic kidney disease- more than a renal disease. Am J Kidney Dis 1990;16: 403-13.
3. Gabow PA, Johnson AM, Kaehny WD, et al. Factors affecting the progression of renal disease in autosomal-dominant polycystic kidney disease. Kidney Int 1992;41:1311-19.
4. Gabow PA, Chapman AB, Johnson AM, et al. Renal structure and hypertension in autosomal dominant polycystic kidney disease. Kidney Int 1990;38:117-80.
5. Gretz N, Zeier M, Geberth S, Strauch M, Ritz E. Is gender a determinant for evolution of renal failure? A study in autosmal dominant polycystic kidney disease. American Journal of Kidney Dis 1989;14:178-83.
6. Higashihara E, Aso Y, Shimazaki J, Ito H, Koiso K, Sakai O. Clinical aspects of polycystic kidney disease. J Urol 1992;147:329-32.
7. Franz KA, Reubi FC. Rate of functional deterioration in polycystic kidney disease. Kidney Int 1983;23:526-9.
8. Paarfrey PS, Bear JC, Morgan J, et al. The diagnosis and prognosis of autosomal dominant polycystic kidney disease. N Engl J Med 1990;323:1085-90.
9. Torra R, Badenas C, Darnell A, et al. Linkage, clinical features and prognosis of autosomal dominant polycystic kidney disease types 1 and 2. J Am Soc Nephrol 1996;7:2142-51.
10. Simon HB, Thompson GJ. Congenital renal polycystic disease, a clinical and therapeutic study of three hundred sixty-six caases. J Am Med Assoc 1955;159:657-62.
11. Campanacci L, Fabris B, Fischetti F, Bardelli M, Vran F, Carretta R. ACE inhibition in renal disease: risks and benefits. Clin Exp Hypertens 1993;15:173-86.
12. Maschio G, Alberti D, Janin G, et al. Effect of the angiotensin-converting-enzyme inhibitor benazepril on the progression of chronic renal insufficiency. N Engl J Med 1996;334:939-44.
13. Kanno Y, Suzuki H, Okada H, Takenaka T, Saruta T. Calcium channel blockers versus ACE inhibitors as antihypertensives in polycystic kidney disease. QJM 1996;89: 65-70.

14. Klahr S, Levey AS, Beck GJ, et al. The effects of dietary protein restriction and blood-pressure control on the progression of chronic renal disease. N Eng J Med 1994;330:877-84.
15. Klahr S, Breyer JA, Beck GJ, et al. Dietary protein restriction, blood pressure control, and the progression of polycystic kidney disease. J Am Soc Nephrol 1995;5:2037-47.
16. Gabow PA, Duley I, Johnson AM. Clinical profiles of gross hematuria in autosomal dominant polycystic kidney disease. Am J Kidney Dis 1992;20:140-3.
17. Chapman AB, Johnson AM, Gabow PA, Schrier RW. Overt proteinuria and microalbuminuria in autosomal dominant polycystic kidney disease. J Am Soc Nephrol 1994;5(6):1349-54.
18. Alvestrand A, Gutierrez A, Bucht H, Bergstrom J. Reduction of blood pressure retards the progression of chronic renal failure in man. Nephrol Dial Transplant 1988;3:624-31.
19. Bell PE, Hossack KF, Gabow PA, Durr JA, Johnson AM, Schrier RW. Hypertension in autosomal dominant polycystic kidney disease. Kidney Int 1988;34:683-90.
20. Gabow PA, Chapman AB, Johnson Am, et al. Renal structure and hypertension in autosomal dominant polycysti kidney disease. Kidney Int 1990;38:1177-80.
21. Gonzalo A, Gallego A, Rivera M, Orte L, Ortuno J. Shape of the relationship between hypertension and the rate of progression of renal failure in autosomal dominant polycystic kidney disease. Nephron 1992;62: 52-7.
22. Hansson L, Karlander LE, Lundgren W, Peterson LE. Hypertension in polycystic kidney disease. Scand J Urol Nephrol 1974;8:203-5.
23. Valvo E, Gammaro L, tessitore N, et al. Hypertension of polycystic kidney disease: mechanisms and hemodynamic alterations. Am J Nephrol 1985;5:176-81.