SHORT COMMUNICATION

A COMPARATIVE STUDY OF CREATININE CLEARANCE RATE IN TYPE I (IDDM) AND II (NIDDM) DIABETIC PATIENTS*

C. ADITHAN, G. SRIRAM, R. P. SWAMINATHAN[1], C. H. SHASHINDRAN, M. KRISHNAN[2], J. S. BAPNA AND S. CHANDRASEKAR[1].

Departments of Pharmacology, Medicine[1] and Ophthalmology[2]
Jawaharlal Institute of Postgraduate Medical Education and Research,
Pondicherry - 605 006

(Received on August 18, 1988)

Summary : The endogenous creatinine clearance test was done in 14 Type I and 15 Type II poorly controlled diabetic patients and compared with respective age matched healthy volunteers. Type I diabetics had significantly lower creatinine clearance rate, body mass index and serum albumin levels when compared to their control group. In Type II diabetics these values remained unaltered. Both Type I and Type II diabetics had significantly higher blood sugar and glycosylated haemoglobin levels. The creatinine clearance rate had significant positive correlation with patients' body mass index and serum albumin levels. This suggests that the undernutrition of Type I diabetics may be responsible for the decreased creatinine clearance.

Key words : Diabetes mellitus undernutrition creatinine clearance

INTRODUCTION

The creatinine clearance rate (CCR) is commonly used for estimation of glomerular function of kidney. It has been reported in Western population that CCR is significantly increased in Type I (1, 2) and unchanged in Type II diabetes mellitus (3) of short duration. Many studies were conducted about the renal function of Indian diabetics with clinical manifestations of nephropathy (4, 5, 6). However, there is paucity of data on this topic among diabetic patients without nephropathy. An earlier study reported that 28% of Indian diabetics had sub-normal CCR (7). But in this study the patient details such as type of diabetes and nutritional status were not given. The data obtained from Western population cannot be extrapolated to Indian subjects due to difference in nutritional status (8) Under-nutrition (9) and low dietary protein intake (10) were shown to reduce CCR. In view of the above, the present study was carried out to estimate the CCR in Indian diabetic patients without having any clinical evidence of nephropathy and short duration of illness.

MATERIALS AND METHODS

The study was conducted in 54 subjects of whom 14 were Type I (IDDM) and 15 were Type II (NIDDM) poorly controlled diabetic patients. The age matched controls for Type I and Type II diabetics were 12 and 13 respectively. The diabetic patients had no clinical signs of diabetic microangiopathy or disease affecting kidney functions. Their serum creatinine and urinary sediments (protein) were normal. Their blood pressure was within normal limits. The duration of diabetes varied from three months to five years. The diabetics were

*Supported by grant No. 6/8/84-STP-II from Department of Science and Technology, New Delhi.

receiving irregular treatment of insulin and glybenclamide. They were not receiving any other drugs. All the subjects were admitted in the hospital ward. They were placed on a diet free from meat, tea and coffee, one day prior to the study. The biochemical parameters determined in all patients prior to creatinine clearance test are given in the Table

The creatinine clearance test was done as described earlier (9). After emptying the bladder, urine was collected for six hours. Blood was collected for serum creatinine estimation after 3 h of starting the urine collection. The creatinine concentration in urine and serum were estimated by spectrophotometric methods (11). Serum albumin, blood sugar, urea and glycosylated haemoglobin (HbA_1) levels were determined using reagent kits (Stangen Immuno diagnostics, Hyderabad). The creatinine clearance was calculated using the formula :

$$CCR = \frac{UV}{P} \times \frac{1.73}{A}$$

where 'U' is the urine creatinine in mg per ml, 'V' is the urine output in ml per minute, 'P' is the serum creatinine concentration in mg per ml and 'A' is the body surface area in square meters. Statistical analysis was done using student 't' test.

RESULTS AND DISCUSSION

The results of the study are given in the Table. The diabetics had significantly higher HbA_1 and fasting blood sugar values indicating poor control of the disease Type I diabetic patients were found to be undernourished as evidenced by their significantly lower body weight and serum albumin values (Table). The CCR was significantly reduced in them and not in Type II diabetics when compared to their respective eontrols. None of the diabetics had high creatinine clearance values suggestive of glomerular hyperfiltration which was reported in Western diabetic population (1, 2).

Since the diabetic status of both types of diabetic patients are comparable it is possible that the reduced creatinine clearance seen in Type I diabetics could be due to undernutrition. This is supported by the presence of significant correlation between

TABLE I : The biological and biochemical data of diabetic patients and healthy volunteers.

Subjects	*Age (yrs)*	*Weight (kg)*	*Body mass index (Weight/height²)*	*Albumin (gm%)*	*Fasting blood sugar (mmol/l)*	*HbA_1 (%)*	*Blood Urea (mg%)*	*Serum creatinine (mg%)*	*Creatinine clearance rate (ml/mt)*
Group I									
Control	24 8	55.6	19.55	3.81	3.09	7.2	21.1	1.12	104.0
(n=12)	±1.8	±1.6	±0.65	±0.04	±0.12	±0.4	±0.6	±0.05	±5.8
Type I	25.6	40.6*	15.40*	3.16*	12.67*	14.2*	21.6	1.14	63.7*
diabetics	±1.7	±1.5	±0.60	±1.10	±1.47	±0.8	±1.6	±0.12	±5.5
(n=14)									
Group II									
Control	55.4	49.8	18.73	3.71	3.55	8.5	23.3	0.97	78.8
(n=13)	±2.2	±2.2	±0.61	±0.08	±0.05	±0.4	±1.2	±0.06	±4.3
Type II	52.5	54.5	20.35	3.51	11.34*	12.5*	21.2	1.10	75.3
diabetics	±1.6	±2.4	±0.97	±0.09	±1.11	±0.8	±1.2	±0.11	±4.7
(n=15)									

Values are mean±SEM

*P<0.001 when compared to respective controls.

CCR and body mass index ($r=0.605$, $d.f.=24$, $p<0.001$) and serum albumin levels ($r=0.570$, $d.f.=24$, $p<0.01$). Further, low protein dietary intake was shown to reduce CCR in healthy volunteers (12, 13) and in Type I diabetics (10). This effect occurred independently of changes in plasma glucose concentration (10, 14). It has been reported earlier that CCR is reduced in undernourished non-diabetic subjects (9). Our study supports the earlier observation that protein or aminoacid metabolism may be important for the expression of the renal haemodynamic disturbances of early diabetes (15, 16).

The CCR was unchanged in type II diabetics which is similar to data obtained in Western subjects (3). This may be explained on the basis that these patients were not undernourished and their body weight and serum albumin levels were comparable with that of controls (Table). However, Type II diabetics and their age matched controls had lower creatinine clearance values than the younger age matched control subjects of Type I diabetics which could be due to age related decline in glomerular function (17).

Our study thus shows that creatinine clearance rate is decreased in Type I diabetes of short duration which is contrary to Western reports. This may be related to poor nutritional status of Indian diabetics.

ACKNOWLEDGEMENTS

The financial assistance received through grant No. 6/8/84-STP II from Department of Science and Technology, New Delhi and Mr. S. Manoharan's secretarial assistance are gratefully acknowledged.

REFERENCES

1. Ditzel J and Junker K. Abnormal glomerular filtration rate, renal plasma flow and renal protein excretion in recent and short term diabetics. *Br Med J* 1972; 2 : 13-19.
2. Wiseman MJ, Saunders AJ, Keen H and Viberti GC. The effect of blood glucose control on increased glomerular filtration rate and kidney size in insulin dependent diabetes. *N Engl J Med* 1985; 312 : 617-621.
3. Uusitupa M, Siitonen O, Pyorala K, Arro A and Penttiala I. Occurance of clinical proteinuria and microproteinuria in newly diagnosed maturity onset, non-insulin dependent (Type II) diabetics. *Acta Endocrinologica* 1984; 106 (Supplement 263) : 42.
4. Bahl AL, Chugh RN and Lal HB. Diabetes nephropathy. *J Ind Med Assoc* 1967; 48 : 530-534.
5. Vaishnava H, Dixit NS, Aga V and Gulati PD. A clinico-pathological study of renal involvement in Indian diabetics. *J Ass Phys Ind.* 1971; 19 : 5-11.
6. Ahuja MMS, ed. *Practice of diabetes mellitus*, New Delhi : Vikas Publishing House Pvt Ltd. 1983; 122-143.
7. Shah CP, Shah BR, Sanghavi NG, Shah JB, Trivedi PM and Venugopal K. Creatinine clearance rate in diabetes mellitus. *J Ind Med Assoc* 1973; 61 : 33-36.
8. Mohan V, Ekoe JM, Ramachandran A, Snehalatha C and Viswanathan M. Diabetes in the tropics. Differences from diabetes in the West. *Acta Diabet Latina* 1986; 23 : 91-98.
9. Adithan C, Shashindran CH, Gandhi IS and Balachander J. The creatinine clearance rate in malnutrition and in cirrhosis of the liver. *Ind J Med Sci* 1981; 35 : 233-236.
10. Wiseman MJ, Bognetti E, Dodds R, Keen H and Viberti GC. Changes in renal function in response to protein restricted diet in Type I (insulin dependent) diabetic patients. *Diabetologia* 1987; 30 : 154-159.
11. Varley H, ed. *Practical clinical biochemistry*, London : The English Language Book Society and William Heineman Medical Books Ltd. 1969; 197-201.
12. Bergstorm S, Ahlberg M and Alvestrand A. Influence of protein intake on renal haemodynamics and plasma hormone concentration in normal subjects. *Acta Med Scand* 1985; 217 : 189-196.
13. Pullman TN, Alving AS, Dean RJ and Landonne M. The influence of dietary protein intake on specific renal functions in normal man. *J Lab Clin Med* 1954; 44 : 320-332.
14. Zatz R, Meyer TW, Rennke HG and Brenner BM. Predominance of haemodynamic rather than metabolic factors in the pathogenesis of diabetic glomerulopathy. *Proc Natl Acad Sci (USA)*. 1985; 82 : 5963-5967.
15. Brenner BM, Meyer TW and Hostetter TH. Dietary protein intake and the progressive nature of kidney disease : The role of haemodynamically mediated glomerular injury in the pathogenesis of progressive glomerular sclerosis in aging, renal ablation and intrinsic renal disease. *N Engl J Med* 1982; 307 : 652-659.
16. Dworkin LD, Ichikawa I and Brenner BM. Hormonal modulation of glomerular function. *Am J Physiol* 1983; 244 : F95-F104.
17. Rowe JW, Andres R, Tobin JD, Norris AH and Shock NW. The effect of age on creatinine clearance in man : a cross sectional and longitudinal study. *J Gerontol* 1971; 31 : 155-163.