Urological Research 8, 1-4 (1980)

Urological Research

ORIGINALS

The Influence of Age and Plasma Glucagon on Renal Clearance of ^{99m}Tc-DTPA (Sn)

W. F. D. Sampson, M. A. Macleod and A. S. Houston

Department of Nuclear Medicine, Royal Naval Hospital, Haslar, Gosport, Great Britain

Accepted: January 19, 1979

Abstract. Using an external arm counting technique and ^{99m}Tc-DTPA(Sn), as previously described (Macleod, Sampson & Houston, 1977), the glomerular filtration rate (GFR) of 120 subjects with normal renal function was measured and found to correlate significantly with age ($r = 0.91$). Using the same technique in the investigation of 260 patients with a variety of diagnoses but who had normal renal function (GFR greater than 86 mls/min), 42 (16%) were found to clear the ^{99m}Tc-DTPA significantly faster. Twelve of these were subsequently found to be diabetic and to have significantly raised plasma glucagon levels. The remaining 30 also had significantly high plasma glucagon levels.

Key words: Glomerular filtration rate, Age, Hyperclearance, Glucagon.

INTRODUCTION

Age related changes have been described in the glomerular structure of the kidney and its vasculature (10) and in the renal glomerular basement membrane in rats (4). These findings suggest that there is a relationship between renal function and age but, to date, there has been no attempt to demonstrate this. Using an arm counting technique already described (6) this paper describes the relationship found between the glomerular filtration rate (GFR) and the age of the individual.

Observations by Levy and Starr (5), Miyazaki et al. (7) and Parving et al. (8) showed that an increase in GFR could be induced by raised plasma pancreatic glucagon levels and in a preliminary study we were able to confirm this (9). The present paper is an extension of this work and is one part of an ongoing study into several metabolic diseases which appear to have as a common factor a disorder of glucagon metabolism.

MATERIALS AND METHODS

During routine measurement of renal dynamic profiles, using a gamma camera and computer to generate activity/time curves of the clearance of ^{99m}Tc-DTPA(Sn), 120 subjects were found to have normal renal function and no clinical evidence of renal disease or metabolic disorder. This was confirmed by conventional clinical, radiological and biochemical examinations. Following the gamma camera studies, the GFR of these 120 subjects was determined by external arm counting using the biological $t_{1/2}$ to measure the renal clearance of the chelate since this is directly related to the glomerular filtration rate and can be simply converted to mls/min if required (6) (Fig. 1).

In the course of measuring the renal dynamic profiles of a series of patients suffering from a variety of diseases including proteinuria, haematuria, urinary infection, urolithiasis and hypertension, 260 were found to have normal dynamic renal function (3). The GFR of these patients was additionally measured using the technique already described.

Free Tc^{99m} and protein bound Tc^{99m}DTPA were estimated by using a Sephadex G-25 medium gel chromatograph with Blue Dextran used as a marker and the column longitudinally scanned with a 2" sodium iodide (T1) crystal and 1 cm slit collimator. Protein binding was found to be between 3% and 4%. Free Tc^{99m} was less than 4%.

0300-5623/80/0008/0001/$01.00

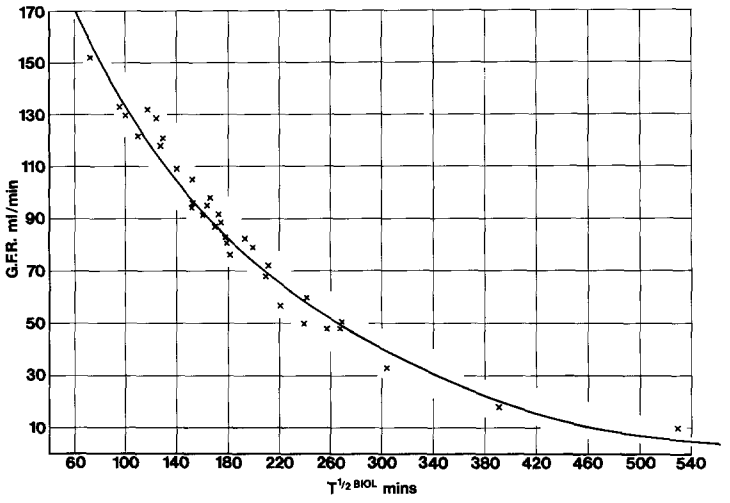

Fig. 1. Relationship of biological $t_{1/2}$ to glomerular filtration rate (6)

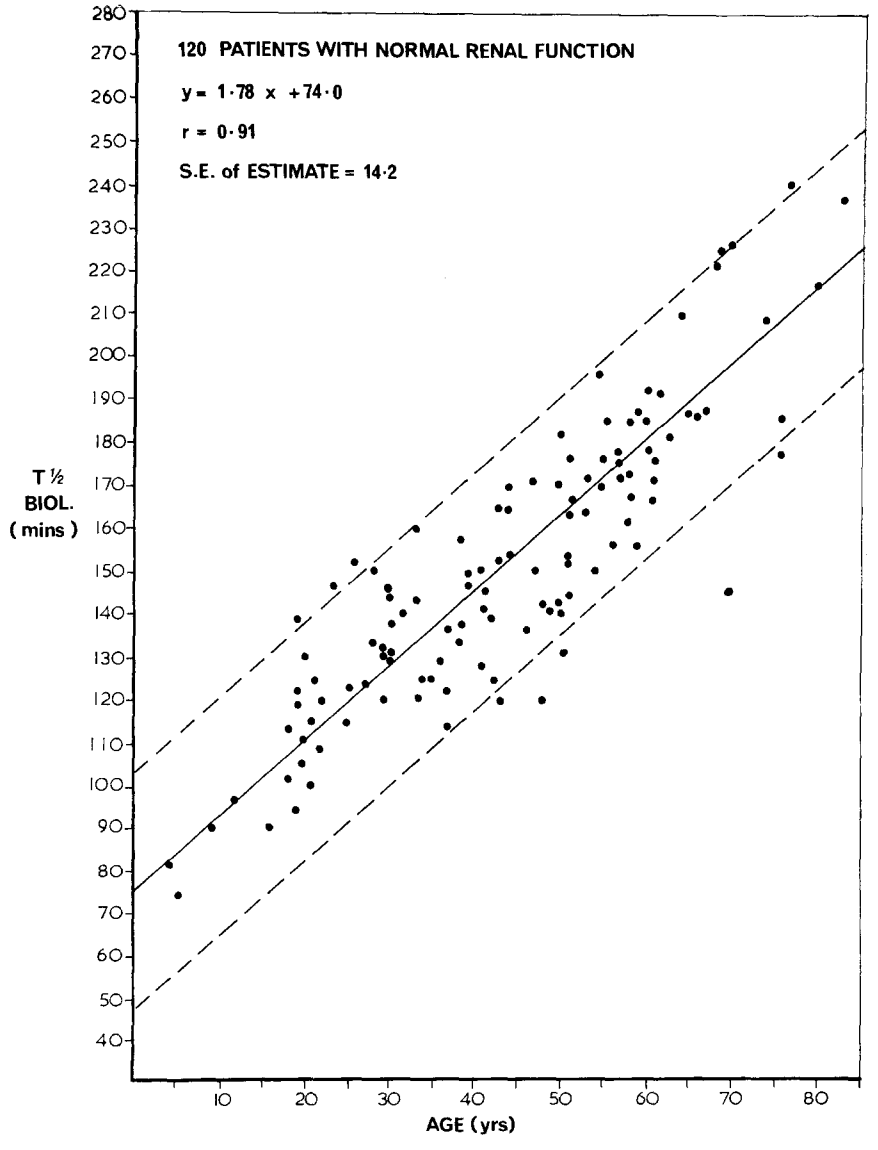

Fig. 2. Regression of $t_{1/2}$ biol. on age with control limits placed at 2 standard errors of estimate on either side of regression line

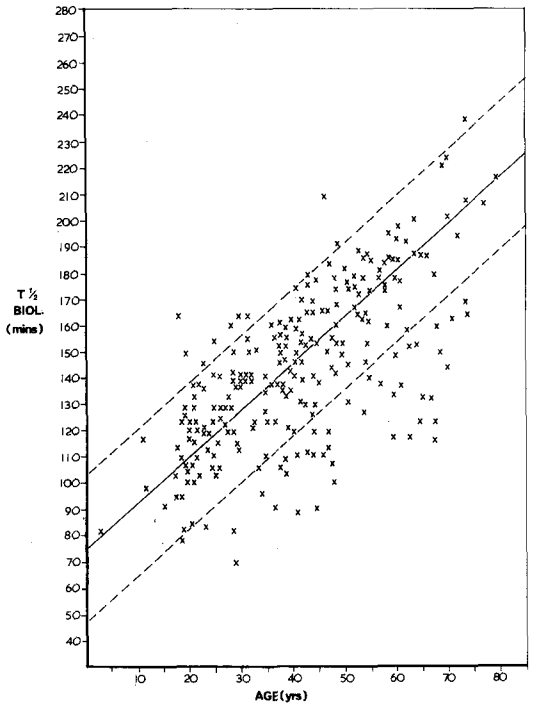

Fig. 3. 260 patients with clinically normal renal function showing 42 (16%) below 2 S. E.' s of estimate from regression line

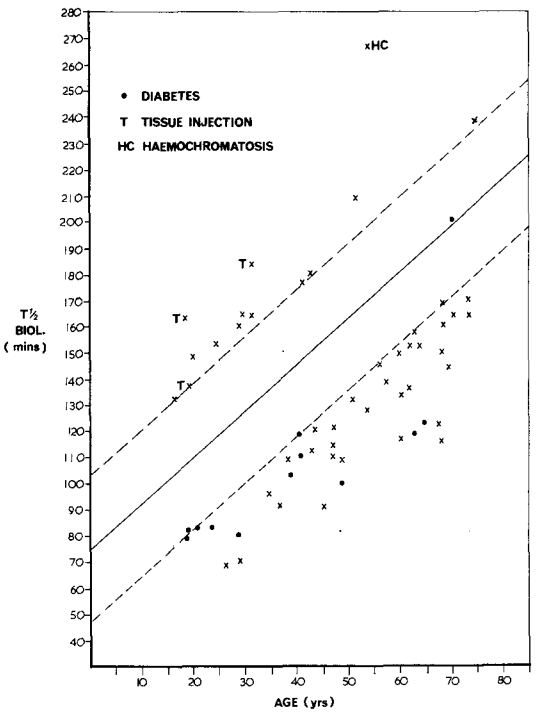

Fig. 4. Breakdown of patients with clinically normal renal function who were above and below 2 S. E.'s of estimate from regression line

Table 1. A comparison of plasma glucose, $t_{1/2}$-biol and plasma glucagon between normal subjects, diabetics and hyperclearers of ^{99m}Tc-DTPA(Sn)

		Plasma Glucose m mol/L	$t_{1/2}$ biol - $t_{1/2}$ Biol (normal for age) min	Plasma Glucagon ng/L
Normal Clearers range (± 1 S.D.) 5 hrs fasting	8	4.8 ± 0.6	± 14	170 ± 100
Diabetics ± 1 S.D. 5 hrs fasting	12 (7 not on treatment) (5 on insulin)	7.4	-36 ± 22	782 ± 378
Hyperclearers 30 ± 1 S.D. 5 hrs fasting	30	5.6 ± 1.5	-49 ± 18	874 ± 405

Venous blood was collected into heparin tubes containing 2, 000 Kallikrein Inactivator Units (KIU) Aprotinin/ml of blood immediately centrifuged and the plasma stored at -10°C.

Plasma immunoreactive glucagon was measured by a single antibody radioimmunoassay technique by Dr. K. J. O' Connor at the Diabetic Research Unit, Wellcome Foundation, Dartford.

RESULTS

The results of these measurements in the 120 normal subjects who had normal renal function showed a close correlation between age and the biological $t_{1/2}$ of ^{99m}Tc-DTPA(Sn). (r = 0.91) (Fig. 2). These results were used to draw a regression line ± 2 Standard Errors of the Estimate (S. E.).

The same measurements in the 260 patients found with normal dynamic renal function were plotted against this regression line and all but 52 were found to lie within 2 S. E.'s of this line.

Forty-two (16%) had renal clearance rates of the chelate faster than 2 S. E.'s from the mean (2.3% predicted) (Fig. 3). Ten of these 42 patients were known to be diabetic and 2 others were

found to be diabetic on further investigation (Fig. 4). Investigation of the remaining 30 patients showed them to have significantly raised plasma glucagon levels and higher fasting blood glucose than 8 of the normal control subjects (Table 1).

Ten of the 260 patients had normal renal function but renal clearance rates ($t_{1/2}$-biol) longer than 2 S. E.'s from the mean and these were subsequently found to have partial tissue localisation of the chelate at the site of the venepuncture when this was routinely monitored with the gamma camera. There was one case of known haemochromatosis and in this case the high serum iron may have stripped the ^{99m}Tc O_4^- from the DTPA-(Sn) by competitive binding (Fig. 4).

CONCLUSIONS

There appears from this investigation to be a clear correlation between the renal clearance of ^{99m}Tc-DTPA and age. Since it has been shown that the measurement of the GFR by arm counting is at least as accurate as creatinine or inulin clearance techniques, the inference from this is that a "normal" GFR can only be interpreted after reference to the age of the patient. For example, the accepted mean normal value of 100 mls/min ($t_{1/2}$-biol of 160 mins) for the creatinine clearance rate whilst being applicable to a 50 year old is well below the 2 S. E. level for a 20 year old (Fig. 2).

The second implication of the results of this study is that clearance rates exceeding 2 S. E.'s from the mean may indicate metabolic abnormality from other pathological processes. Plasma pancreatic glucagon has been found to influence the GFR which may be increased by as much as 40% (5, 7, 8, 9). Diabetics have been found to have raised plasma levels of pancreatic glucagon and increased creatinine clearance rates (1, 2). This correlates with our finding that 12 of 42 patients who showed "hyperclearance" were diabetics. The remainder (30) had raised plasma glucagon and glucose levels and 6 had abnormal glucose tolerance curves (Table 1). These patients can at the moment be described as having a covert disorder of metabolism the significance of which has yet to be defined.

Five of the 12 diabetics were being managed with insulin at the time of the test but only one had a $t_{1/2}$-biol which lay within normal limits. Since Parving et al. (8) noted that only patients who were properly controlled with insulin had a normal GFR, this test which is simple, reliable and reproducible may well be of use in determining the adequacy of insulin therapy.

Finally, this study has shown the error in measurement caused by minor extravasation of the injected bolus of ^{99m}Tc-chelate due to subsequent slow release from the tissues at the injection site. The site of the injection in the arm should therefore be scanned routinely to detect extravasation.

Acknowledgement. We would like to thank Dr. Kevin O'Connor of the Diabetic Research Unit, The Wellcome Foundation, Dartford, Kent for carrying out the measurements of plasma immunoreactive glucagon and for his advice.

REFERENCES

1. Aviram, A., Ben-Ishay, D., Chowers, I., Czaxzkes: Low plasma creatinine in diabetes mellitus. Journal of Laboratory and Clinical Medicine 67, 473 (1966)
2. Ditzel, J., Bang, H. O., Thorsen, N.: Low plasma creatinine in diabetic subjects free of renal disease. Scandinavian Journal of Clinical and Laboratory Investigation 20, 360 (1976)
3. Houston, A. S., Macleod, M. A., Sampson, W. F. D.: Principal components analysis as an aid to classification of renal dynamic studies. European Journal of Nuclear Medicine 4, 295 (1979)
4. Kalant, N., Satomi, S., White, R., Tel, E.: Changes in renal glomerual basement membrane with age and nephritis. Canadian Journal of Biochemistry 55, 1197 (1977)
5. Levy, M., Starr, N. L.: The mechanism of glucagon-induced matriuresis in dogs. Kidney International 2, 76 (1972)
6. Macleod, M. A., Sampson, W. F. D., Houston, A. S.: Urinary clearance of ^{113m}In DTA and ^{99m}Tc(Sn) DTPA measured by External arm counting. Urological Research 5, 71 (1977)
7. Miyazaki, M., Abe, Y., Yamamoto., McNay, J. L.: Comparative study of several vasodilators in glomerular filtration rate and renal blood flow. Proceedings of the 3rd International Symposium on Radionuclides in nephrology, Berlin
8. Parving, H. H., Noer, J., Kehlet, H., Mogensen, C. E., Svendsen, P. Aa., Heding, L.: The effect of short-term glucagon infusion on kidney function in normal man. Diabetologia 13, 323 (1977)
9. Sampson, W. F. D., Macleod, M. A., Houston, A. S.: Glucagon induced hyperclearance of ^{99m}Tc-DTPA(Sn). Proceedings of Eur. Soc. Nuc. Med. 2nd Cong. London 1978 (Abstracts)
10. Sworn, M. J., Fox, M.: Donar kidney selection for transplantation. Relationships between glomerular structure, vascular supply and age. British Journal of Urology 44, 377 (1972)

Mr. W. F. D. Sampson
Department of Nuclear Medicine
Royal Naval Hospital
Haslar, Gosport
Hants
Great Britain