

STUDIES ON INULIN AND p-AMINOHIPPURIC ACID CLEARANCES IN PATIENTS SUFFERING FROM DIABETES MELLITUS*

By

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Since the discovery of insulin diabetic patients hardly die of diabetic coma or acute infection. They live long enough to show degenerative changes in the arteries. Kimmelstiel and Wilson (1936) observed intercapillary glomerulosclerosis in patients suffering from diabetes and other workers observed pyelonephritis, arteriosclerosis, fatty degeneration of tubules as well as intercapillary glomerulo-sclerosis (Barrie et al., 1952). It is evident from the works of Hall (1952) that these renal changes occur commonly in patients in the fourth decade of life whose diabetes is poorly controlled for more than 20 years. The characteristic Kimmelstiel-Wilson lesion in the kidneys cannot be diagnosed during life. It may be possible that before clinical signs and symptoms of the disease appear, there may be functional impairment of the kidney. Therefore assessment of the functions of the kidney would be of importance in diagnosing the early onset of Kimmelstiel-Wilson syndrome. Functions of the kidney may be ascertained by the determination of inulin and p-aminohippuric acid clearances.

In order to find out if the clearance values are normal or otherwise one must have those values for normal subjects to facilitate comparison. Such figures for normal Indians are lacking. In the present investigation, therefore, kidney functions were determined by studying inulin and p-aminohippuric acid clearance in patients suffering from diabetes mellitus and in normal Indians.

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MATERIALS AND METHODS

Selection of subjects. Diabetic patients admitted into the Nilratan Sircar Medical College Hospitals were selected for the study. All the patients showed diabetic type of glucose tolerance curves. Some of the patients were suffering from neuritis, one had cataract, one had carbuncle and another had diabetic retinopathy with microaneurysms in the retina. Patients who were admitted with fractures of long bones, hernia, hydrocele, etc., when recovered and were fit for discharge from the hospital, were selected as normal subjects.

Inulin and p-aminohippuric acid clearance tests. The subjects drank 40 ounces of water one hour before the starting of the test after breakfast. A sterile catheter was passed and retained to drain the urinary bladder continuously. After drawing 5 ml. of blood from the antecubital vein, the bladder was evacuated completely and a portion kept for use as blank. Through the same needle in the antecubital vein a priming solution, containing 30 ml. of a freshly prepared 10 per cent inulin in 0.9 per cent sodium chloride and 4 ml. of 20 per cent p-aminohippuric acid in normal sodium hydroxide, was slowly injected. This was immediately followed by the transfusion of a maintenance solution containing 35 ml. of 10 percent inulin, 10 ml. of 20 percent p-aminohippuric acid and 210 ml. of 0.9 percent sodium chloride. At intervals of 30, 50 and 90 minutes after the injection of the priming solution, 5 ml. of blood was withdrawn and urine samples collected, the bladder being washed each time with 20 ml. saline. Blood samples were collected in vials containing mixed oxalates.

Estimation of inulin. Plasma samples were treated with sodium tungstate and sulphuric acid. 2 ml. of protein free plasma filtrate diluted 1/10, and 2 ml., urine diluted 1/200 were hydrolysed, fructose liberated was made to react with resorcinol and the red colour formed measured in a photoelectric colorimeter according to the method of Roe (1934).

Estimation of p-aminohippuric acid. P-aminohippuric acid was estimated in 2 ml. protein free plasma filtrate and 5 ml. diluted urine by the method of Bratton and Marshall (1939).

Estimation of blood sugar. Blood sugar was determined in the sample collected before the injection of inulin and p-aminohippuric acid in diabetic patients by the method of Hagedorn and Jensen (1923).

From the amount of inulin and p-aminohippuric acid excreted in urine during the two 20 minute periods, amounts excreted in one minute were calculated. From the concentration of plasma inulin and p-aminohippuric acid, the volume of plasma which would contain equivalent amounts of these substances excreted in urine in one minute were determined. This gave the clearances of these substances. The results are given in Tables 1 and 2.

TABLE I
Simultaneous Inulin and p-Aminohippuric Acid (PAHA) Clearances in Diabetic Patients.

Name	Age yrs.	Blood sugar mg. %	Urine flow ml./min.	Plasma inulin mg./cc	Plasma PAHA mg./ml.	Urine inulin mg./ml.	Urine PAHA mg./ml.	Inulin ml./min	Clearances PAHA ml./min	Ratio PAHA/Inulin
J. M.	27	480	1.9	0.31	0.0353	15.20	7.05	93	379	4.07
M. H.	36	160	2.2	0.25	0.0205	14.10	4.70	124	504	4.06
G. B.	35	400	7.2	0.28	0.0375	3.82	2.19	98	420	4.28
H. D.	22	234	7.0	0.27	0.0250	3.40	1.80	88	504	5.72
S. P.	27	429	5.7	0.24	0.0250	5.00	1.96	118	448	3.80
M. R.	25	260	7.3	0.18	0.0200	2.88	1.27	116	459	3.95
B. M.	20	364	11.0	0.24	0.0246	2.36	1.31	108	587	5.43
S. B.	50	444	7.5	0.22	0.0230	3.58	1.54	122	504	4.13
P. G.	52	250	3.9	0.29	0.0327	7.37	3.30	99	393	3.97
M. L.	70	168	5.0	0.37	0.0537	8.00	6.49	108	612	5.66
A. D.	26	375	3.0	0.36	0.0394	13.83	10.68	115	527	4.58
B. K.	18	254	3.0	0.26	0.0250	12.16	3.75	140	450	3.21
A. D.	60	291	9.0	0.22	0.0300	2.60	3.01	108	543	5.02
P. C.	26	278	10.0	0.25	0.0250	3.46	1.32	138	528	3.82
P. C.	32	390	7.0	0.32	0.0180	4.62	1.54	108	600	5.55
N. B.	18	334	3.7	0.19	0.0320	5.37	8.51	105	630	6.00
Average								112±3	505±18	4.58±0.20

The average body surface area of the patients = 1.44 ± 0.06 sq. m.

TABLE 2
Inulin and p-Aminohippuric Acid (PAHA) Clearances in Normal Subjects.

Name	Age yrs.	Urine flow ml./min.	Plasma inulin mg./ml.	Plasma PAHA mg./ml.	Urine inulin mg./ml	Urine PAHA mg./ml.	Inulin ml./min	Clearances PAHA ml./min	Ratio PAHA Inulin
W. A.	29	1.50	0.30	0.0260	30.00	13.73	150	792	5.28
A. C.	40	10.00	0.31	0.0350	3.00	1.66	100	474	4.74
S. R.	23	6.50	0.29	0.0300	4.99	2.16	110	470	4.27
R. D.	21	1.90	0.22	0.0330	11.29	10.00	98	575	5.86
R. S.	30	5.50	0.21	0.0170	4.15	2.04	114	661	5.79
B. K.	22	3.50	0.21	0.0250	6.67	4.82	108	676	6.25
N. D.	25	7.00	0.25	0.0360	4.02	2.32	112	461	4.11
A. M.	26	2.40	0.25	0.0366	9.79	7.54	93	494	5.31
S. S.	39	2.00	0.35	0.0440	16.65	8.82	95	401	4.22
P.	18	2.00	0.21	0.0388	14.82	9.87	141	395	2.80
A. L.	25	2.45	0.31	0.0300	15.22	8.30	120	677	5.64
S. Y.	59	1.75	0.19	0.0500	12.14	12.00	112	420	3.75
B. C.	26	2.00	0.27	0.0437	14.57	14.90	108	682	6.31
Average							112±5	552±35	4.95±0.28

The average body surface area of the subjects = 1.57 ± 0.19 sq. m.

DISCUSSION

The average inulin and p-aminohippuric acid clearances in diabetic patients were 112 ± 3 ml. and 505 ± 18 ml. per minute. The corresponding values in normal subjects were respectively 112 ± 5 ml. and 552 ± 35 ml. The average surface area of the body of normal subjects, calculated according to the formula of DuBois as modified by Banerjee and Sen (1955) was 1.57 sq. m. The same for the diabetic patients was 1.44 sq. m. If the renal clearances of diabetic patients were expressed in terms of the normal body surface area of 1.57 sq. m. the values would be inulin 129 ± 6 ml. and p-aminohippuric acid, 550 ± 31 ml. The glomerular filtration rate (inulin clearance), therefore, is significantly increased in diabetic patients although the renal plasma flow (p-aminohippuric acid clearance) is not altered. The increase in the glomerular filtration rate might be due to increased intra-glomerular pressure as a result of the contraction of the efferent arteries of the glomerulus in diabetic patients. The total renal plasma flow, however, is not altered in diabetes.

The diabetic patients studied suffered from the disease for a short period, varying between 1 and 5 years which was not sufficient for the development of Kimmelstiel-Wilson syndrome. It was, however, not possible to indicate the early onset of the disease by studying the renal clearances.

The inulin and p-aminohippuric acid clearance values observed in normal Indians differed from the values observed by western workers. Thus Brun et al. (1947) in their studies with 10 adult male subjects observed inulin clearance as 125 ± 4 ml. and p-aminohippuric acid, 600 ± 106 ml. per minute. Chapman et al. (1949) observed that the average p-aminohippuric acid clearance values in nine male subjects of ages varying between 21 and 32 years was 613 ± 107 ml. per minute. Smith (1951) reported that the clearance values in male subjects of ages varying between 16 and 49 years were, inulin, 124 ± 26 ml. and p-aminohippuric acid, 654 ± 163 ml. per minute calculated for 1.73 sq. m. of body surface area which was the average surface area of normal men and women of 25 years of age in U. S. A. The average body surface area of normal Indian adults under investigation was 1.57 sq. m. If the clearance values of normal Indians are expressed in terms of 1.73 sq. m. body surface area, the values would be inulin clearance, 123 ml. and p-aminohippuric acid clearance, 608 ml. per minute. These values compare well with the values obtained by Western workers.

SUMMARY

Inulin and p-aminohippuric acid clearance were studied in 16 patients suffering from diabetes mellitus and in 13 normal adults.

In diabetic patients inulin clearance values were 112 ± 3 ml. per minute and p-aminohippuric acid clearance, 505 ± 18 cc per minute. The corresponding values in normal subjects were respectively 112 ± 5 and 552 ± 35 ml.

Average surface area of the body of diabetic patients was 1.44 sq. m. and that of normal subjects was 1.57 sq. m. If the renal clearances are expressed in terms of normal surface area of 1.57 sq. m. the clearance values would be, inulin, 129 ± 6 ml. and p-aminohippuric acid, 550 ± 31 ml.

Renal clearances in normal Indians if expressed per body surface area of 1.73 sq. m., which is the surface area of adult Americans, are comparable with the values obtained by Western workers.

The increased glomerular filtration rate might be due to increased intra-glomerular pressure.

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