SIMPLIFIED METHOD FOR DETERMINING GLOMERULAR FILTRATION RATE WITH ^{131}I-SODIUM IOTHALAMATE

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The use of labeled compounds to measure glomerular filtration rate offers advantages over the common method using inulin (*1–3*). For example, the radioactivity associated with labeled compounds can be detected and quantified easily and with great precision while inulin determinations are tedious and elaborate. Recent publications (*1–3*) make it quite clear that ^{131}I-sodium iothalamate is an excellent inulin substitute for measuring glomerular filtration rate. However, these methods involve rather complex procedures such as the maintenance of intravenous infusions and the introduction of a French Foley catheter into the bladder, which is burdensome to the patient. The purpose of this paper is to present a single-injection method which is practical and accurate.

MATERIALS AND METHODS

The radioactive material used was ^{131}I-sodium iothalamate which was prepared and labeled by the Laboratory of Radiopharmaceuticals of the Mexican Nuclear Energy Commission using the method developed there by Mitta and Alvarez (*4*). In essence, the method consists of labeling the sodium iothalamate through exchange with Na^{131}I. Our material was compared with ^{131}I-sodium iothalamate from Amersham and was found equivalent.

The data presented here cover 23 male medical students with an average age of 23 years and without clinical evidence of renal disease.

Measurements were made with one channel of a Picker dual ratemeter with a 1-in. NaI(Tl) detector crystal. The collimator aperture had a diameter of 5 cm. The ratemeter signal was plotted by a Texas Instruments linear recorder.

The method consisted of having a person seated comfortably with the scintillation probe placed perpendicular to the upper third of the sternum, which was considered the best place to record blood concentrations (*5*). The 30 K scale on the ratemeter was used. Forty to 50 μCi of ^{131}I-sodium iothalamate dissolved in 10 ml saline was injected slowly through a vein in the flexor surface of the elbow until the counting rate reached or slightly surpassed the maximum or 100% reading on the scale (Fig. 1). From this point on the tracing was recorded for 15 or 20 min. Readings were taken every minute and replotted on semilogarithmic paper (Fig. 1). As Fig. 2 shows, two straight exponential decay curves are obtained; it was assumed that the first expresses the mixing of the ^{131}I-sodium iothalamate in the plasma compartment and the second predominantly represents the filtration rate. Our fundamental rea-

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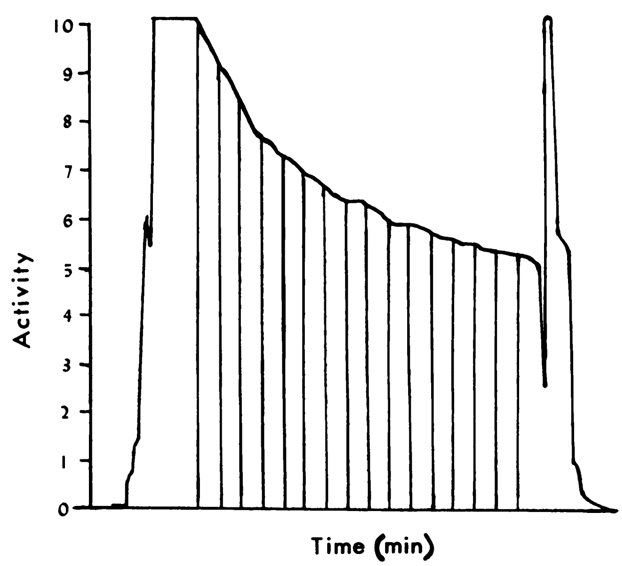

FIG. 1. Tracing obtained from scintillation probe placed perpendicularly in front of upper third of sternum. Vertical lines are drawn from each minute to take readings to be plotted on Fig. 2. Final elevation demonstrates accumulation of radioactive material in bladder.

soning is similar to that recently developed by other authors (*6–8*) but makes simplifying assumptions which render the procedure very practical. We plan to do careful compartmental analysis in the future to settle uncertainties and define the order of magnitude of other minor components.

A constant fraction of the plasma volume is filtered each time interval and cleared of its radioactive content. Theoretically a negative exponential curve is obtained from the equation:

$$Y_t = Y_o e^{-kt}$$

Assuming that Y_t taken after the first minute expresses the decimal fraction of the cleared plasma, this formula is converted to:

$$Y_1 = Y_o e^{-0.698/T_{1/2}} \ .$$

Because direct calculation in each case would be impractical, Table 1 was formulated. To make this table useful, expected $T_{1/2}$ times were introduced into the last formula above to find the corresponding Y_1 values. To use the table, the $T_{1/2}$ values are taken from the semilogarithmic graph obtained from the patient under examination. $T_{1/2}$ is the time necessary for the activity on the second straight line to drop to half its original value (Fig. 2 between arrows). If the initial reading is taken as a 100%, $T_{1/2}$ is the time necessary for it to drop 50%. The corresponding $T_{1/2}$ value is multiplied by the plasma volume of the patient. The plasma volume can be obtained either by direct determination or by estimation since it bears a direct relationship to the weight of the individual. It is generally accepted that there are 45 ml of plasma (*9*) for each kilogram of body weight. On this basis we prepared Table 2. Here the weight of the person examined is multiplied by the $T_{1/2}$ value which can be read in decimal values up to 20 min and from then on at 1-min intervals up to 100 min and then at convenient intervals up to 1,000 min. Table 1, of course, also has these $T_{1/2}$ values.

If we take Case 20 as our example (Figs. 1 and 2), we see that the activity has dropped one half after 22.00 min, and the latter number is the $T_{1/2}$ value that has to be determined in this procedure. The multiplication constant according to Table 2 in this case is 1.395 and the weight is 52.00 kg. Then the filtration constant C_f is:

$$C_f = 52 \times 1.395 = 72.54$$

This value is obtained for the apparent body surface of 1.56 m^2; correcting for 1.73 m^2, a 80.45-ml value is obtained (Table 3). From the tables used on our hospital service, the weight of a 22-year-old male patient 1.65 meters tall should be 60 kg. This

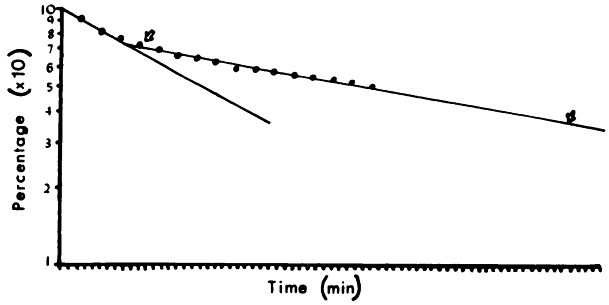

FIG. 2. Plotting of readings obtained from Fig. 1. Second straight line from left to right is exponential to be used to determine $T_{1/2}$ value as can be seen between two arrows.

value is probably more appropriate and nearer to the 45-ml plasma/kg of body weight. For this weight

$$C_f = 60 \times 1.395 = 83.70$$

and for the corresponding 1.73-m^2 body surface constant C_f = 83.22 (Table 3, 12th column). The latter figure should be the most useful for comparative purposes. It must be added that it is more exact, and for that reason preferable, to first determine the true plasma volume and to then use Table 1. However, this is time-consuming and therefore impractical.

RESULTS

The results obtained are presented in Table 3. Twenty-three male medical students were examined. Their age was about 23 years.

The clinical data did not reveal the presence of renal disease. The values obtained for glomerular filtration rate cannot be subjected to a rigorous statistical criterion in normal subjects but are representative of what is found in the student population in the National University of Mexico. The average and standard deviations determined are listed according to the information obtained from height, weight and body surface. The C_f values were studied with the true weight and for the ideal or expected weight according to the Davenport table used in our hospital with the corresponding corrections for the 1.73-m^2 surface generally used for comparison.

DISCUSSION

The theoretical validity of sodium iothalamate as an inulin substitute is mainly based on the results of published work (*1–3*). Some experience gained on prostatectomized patients in whom an in-dwelling catheter is usually used made it possible to establish a direct comparison between the direct method and the one presented in this study. At the beginning a constant drop-by-drop infusion was started, establishing a plateau as registered directly and taking blood and urine samples as required. After completing the study, the infusion was stopped and the curve obtained computed and compared. The results are in accordance to what would be expected, but the observations are not sufficient to allow a definite conclusion.

The sodium iothalamate apparently does not adhere to the erythrocytes since it is an excellent means of determining hematocrit values and, with the aid of a centrifuge hematocrit, of measuring trapped plasma between red blood cells.

The average results are slightly different from those obtained by the classical studies of Homer Smith (*9*). Experience will tell what the reason for this is since the theoretical basis of this procedure is sound. It must not be forgotten that the cases studied were taken from a student population without clinical evidence of kidney malfunction, but that an exhaustive renal study was not undertaken. Some authors (*1,3*) suggest that a correction factor may have to be introduced. The need for such a factor, of course, would not invalidate the usefulness of the procedure presented here.

The iothalamate-to-inulin clearance ratio has varied from 0.74 to 1.23 although a more optimistic study places its average at 1.005 (*1*). The persons

TABLE 1. MULTIPLICATION CONSTANTS FOR DISAPPEARANCE OF RADIONUCLIDES FROM BLOOD STREAM WHEN ELIMINATED BY KIDNEY (TO BE MULTIPLIED BY PLASMA VOLUME IN LITERS)

$T_{1/2}$	0	1	2	3	4	5	6	7	8	9
1	500.0	467.5	421.8	413.3	390.5	370.0	351.7	334.8	319.6	305.7
2	292.9	281.1	270.3	267.2	250.1	242.1	234.0	226.4	219.3	212.6
3	206.3	200.3	194.8	191.3	184.5	179.7	175.1	170.8	166.7	162.8
4	159.1	155.5	152.2	148.9	145.9	142.7	139.9	137.1	134.4	131.9
5	129.5	127.1	124.8	122.6	120.4	118.4	116.2	114.5	112.5	110.9
6	109.1	107.6	105.8	104.2	102.7	101.1	99.7	98.3	96.9	95.6
7	94.4	93.1	91.8	90.6	89.4	88.3	87.2	86.1	85.2	84.0
8	83.0	82.1	81.1	80.1	79.2	78.3	77.4	76.6	75.8	74.9
9	74.2	73.4	72.6	71.8	71.1	70.4	69.7	69.0	68.3	67.6
10	67.0	66.3	65.7	65.1	64.5	63.8	63.3	62.7	62.2	61.6
11	61.0	60.6	60.1	59.5	59.0	58.4	58.0	57.5	57.0	56.5
12	56.2	55.7	55.3	54.7	54.4	53.9	53.8	53.1	52.8	52.3
13	52.0	51.5	51.1	50.8	50.4	50.1	49.7	49.3	49.0	48.6
14	48.3	48.0	47.6	47.3	47.1	46.6	46.3	46.1	45.8	45.4
15	45.2	44.9	44.5	44.3	44.1	43.7	43.4	43.2	42.9	42.6
16	42.4	42.1	41.9	41.7	41.4	41.1	40.9	40.7	40.4	40.1
17	40.0	39.8	39.5	39.3	39.0	38.9	38.6	38.4	38.2	38.0
18	37.7	37.5	37.4	37.2	37.0	36.8	36.6	36.4	36.2	36.1
19	35.8	35.6	35.5	35.3	35.1	34.9	34.8	34.7	34.5	34.3
20	34.0	33.9	33.8	33.5	33.4	33.3	33.1	32.9	32.8	32.7
$T_{1/2}$	21	22	23	24	25	26	27	28	29	30
Value	32.5	31.0	29.7	28.5	27.3	26.3	25.3	24.5	23.6	22.9
$T_{1/2}$	31	32	33	34	35	36	37	38	39	40
Value	22.1	21.4	20.8	20.2	19.6	19.0	18.5	18.1	17.6	17.2
$T_{1/2}$	41	42	43	44	45	46	47	48	49	50
Value	16.7	16.3	16.0	15.7	15.3	15.0	14.7	14.3	14.0	13.7
$T_{1/2}$	51	52	53	54	55	56	57	58	59	60
Value	13.5	13.2	13.0	12.7	12.5	12.3	12.1	11.9	11.7	11.5
$T_{1/2}$	61	62	63	64	65	66	67	68	69	70
Value	11.3	11.1	11.0	10.8	10.6	10.5	10.3	10.2	10.0	9.8
$T_{1/2}$	71	72	73	74	75	76	77	78	79	80
Value	9.7	9.6	9.5	9.3	9.2	9.1	9.0	8.9	8.7	8.6
$T_{1/2}$	81	82	83	84	85	86	87	88	89	90
Value	8.5	8.4	8.3	8.2	8.1	8.0	7.9	7.8	7.7	7.6
$T_{1/2}$	91	92	93	94	95	96	97	98	99	100
Value	7.5	7.5	7.4	7.3	7.2	7.2	7.1	7.0	7.0	6.9
$T_{1/2}$	102	104	106	108	110	115	120	125	130	135
Value	6.8	6.7	6.6	6.5	6.4	6.0	5.8	5.6	5.3	5.2
$T_{1/2}$	140	145	150	160	170	180	190	200	225	250
Value	4.9	4.8	4.6	4.3	4.1	3.9	3.7	3.5	3.0	2.8
$T_{1/2}$	275	300	350	400	500	1000				
Value	2.4	2.2	2.0	1.7	1.4	0.7				

studied in this series had not been hydrated previously. More accurate results and better correlations might be expected with hydration and equilibration. Complementary endeavor in this direction should prove fruitful.

Radioelectrophoretic control indicated great stability of the labeled compound (*4*). After 24 hr the thyroid gland was studied in most of the subjects to see if some free iodine had been taken up. No radioactivity could be found. Furthermore no stable iodine had been administered to reduce a possible uptake.

In a few additional cases, direct blood sampling checked well with the readings from the ratemeter. The readings were always expressed as percentages to some value taken at an arbitrarily selected moment.

The radiation received by the patient is very low and can be estimated for the 50 μCi administered as 1.7 millirems to the whole body (*10*). For this reason the test may be repeated quite frequently without any hazard.

SUMMARY

A single-injection method to determine glomerular filtration rate is presented. Sodium iothalamate

TABLE 2. MULTIPLICATION CONSTANTS FOR DISAPPEARANCE OF RADIONUCLIDES FROM BLOOD STREAM WHEN ELIMINATED BY KIDNEY (TO BE MULTIPLIED BY WEIGHT IN KG)

$T_{1/2}$	0	1	2	3	4	5	6	7	8	9
1	22.500	21.038	18.981	18.599	17.573	16.650	15.827	15.066	14.382	13.757
2	13.181	12.650	12.164	12.024	11.255	10.895	10.530	10.188	*9.8685	9.5670
3	9.2835	9.0135	8.7660	8.6085	8.3025	8.0865	7.8795	7.6860	7.5015	7.3260
4	7.1595	6.9975	6.8490	6.7005	6.5655	6.4215	6.2955	6.1695	6.0480	5.9355
5	5.8275	5.7195	5.6160	5.5170	5.4180	5.3280	5.2290	5.1525	5.0625	4.9905
6	4.9095	4.8420	4.7610	4.6890	4.6215	4.5495	4.4865	4.4235	4.3605	4.3020
7	4.2480	4.1895	4.1310	4.0770	4.0230	3.9735	3.9240	3.8745	3.8340	3.7800
8	3.7350	3.6945	3.6495	3.6045	3.5640	3.5235	3.8430	3.4470	3.4110	3.3705
9	3.3390	3.3030	3.2670	3.2310	3.1995	3.1680	3.1365	3.1050	3.0735	3.0420
10	3.0150	2.9835	2.9565	2.9295	2.9025	2.8710	2.8485	2.8215	2.7990	2.7720
11	2.7450	2.7270	2.7045	2.6775	2.6550	2.6280	2.6100	2.5875	2.5650	2.5425
12	2.5290	2.5065	2.4885	2.4615	2.4480	2.4255	2.4210	2.3895	2.3760	2.3535
13	2.3400	2.3175	2.2995	2.2860	2.2680	2.2545	2.2365	2.2185	2.2050	2.1870
14	2.1735	2.1600	2.1420	2.1285	2.1195	2.0970	2.0835	2.0745	2.0610	2.0430
15	2.0340	2.0205	2.0025	1.9935	1.9845	1.9665	1.9530	1.9440	1.9305	1.9170
16	1.9080	1.8945	1.8855	1.8765	1.8630	1.8495	1.8405	1.8315	1.8180	1.8045
17	1.8000	1.7910	1.7775	1.7685	1.7550	1.7505	1.7370	1.7280	1.7190	1.7100
18	1.6965	1.6875	1.6830	1.6740	1.6650	1.6560	1.6470	1.6380	1.6290	1.6245
19	1.6110	1.6020	1.5975	1.5885	1.5795	1.5705	1.5660	1.5615	1.5525	1.5435
20	1.5300	1.5255	1.5210	1.5075	1.5030	1.4985	1.4895	1.4805	1.4760	1.4715
$T_{1/2}$	21	22	23	24	25	26	27	28	29	30
Value	1.4625	1.3950	1.3365	1.2825	1.2285	1.1835	1.1385	1.1025	1.0620	1.0305
$T_{1/2}$	31	32	33	34	35	36	37	38	39	40
Value	0.9945	0.9630	0.9360	0.9090	0.8820	0.8550	0.8325	0.8145	0.7920	0.7740
$T_{1/2}$	41	42	43	44	45	46	47	48	49	50
Value	0.7515	0.7335	0.7200	0.7065	0.6885	0.6750	0.6615	0.6435	0.6300	0.6165
$T_{1/2}$	51	52	53	54	55	56	57	58	59	60
Value	0.6075	0.5940	0.5850	0.5715	0.5625	0.5535	0.5445	0.5355	0.5265	0.5175
$T_{1/2}$	61	62	63	64	65	66	67	68	69	70
Value	0.5085	0.4995	0.4950	0.4860	0.4770	0.4725	0.4635	0.4590	0.4500	0.4410
$T_{1/2}$	71	72	73	74	75	76	77	78	79	80
Value	0.4365	0.4320	0.4275	0.4185	0.4140	0.4095	0.4050	0.4005	0.3915	0.3870
$T_{1/2}$	81	82	83	84	85	86	87	88	89	90
Value	0.3825	0.3780	0.3735	0.3690	0.3645	0.3600	0.3555	0.3510	0.3465	0.3420
$T_{1/2}$	91	92	93	94	95	96	97	98	99	100
Value	0.3375	0.3375	0.3330	0.3285	0.3240	0.3240	0.3195	0.3150	0.3150	0.3105
$T_{1/2}$	102	104	106	108	110	115	120	125	130	135
Value	0.3060	0.3015	0.2970	0.2925	0.2880	0.2700	0.2610	0.2520	0.2385	0.2340
$T_{1/2}$	140	145	150	160	170	180	190	200	225	250
Value	0.2205	0.2160	0.2070	0.1935	0.1845	0.1755	0.1665	0.1575	0.1350	0.1260
$T_{1/2}$	275	300	350	400	500	1000				
Value	0.1080	0.0990	0.0900	0.0765	0.0630	0.0315				

TABLE 3. GLOMERULAR FILTRATION RATES DETERMINED THROUGH CIRCULATING BLOOD CONCENTRATIONS

Case	No.	Age (yr)	Height (m)	Real weight (kg)	Body surface (m^2)	Expected weight (kg)	Expected surface (m^2)	C_f with real weight (ml/min)	C_f with real weight corr. for 1.73 m^2 (ml/min)	C_f with expected weight (ml/min)	C_f with expected weight corr. for 1.73 m^2 (ml/min)	$T_{1/2}$ (min)
GA	1	22	1.78	74.00	1.92	69.70	1.88	94.91	85.51	89.39	82.26	24.00
GVR	2	22	1.72	68.00	1.84	65.00	1.79	122.40	115.08	117.00	113.08	17.00
EOR	3	22	1.79	70.00	1.88	70.50	1.88	152.15	140.01	153.23	141.00	14.00
FG	4	22	1.71	66.00	1.80	64.30	1.76	84.75	81.36	82.46	81.05	24.00
BV	5	22	1.65	57.00	1.62	67.50	1.78	76.18	81.35	90.21	87.67	22.60
SEA	6	22	1.83	91.00	2.16	73.80	1.97	103.60	82.98	84.02	73.88	27.00
ASM	7	22	1.78	58.00	1.72	69.70	1.88	87.17	87.68	104.76	96.40	20.40
SCF	8	23	1.61	61.50	1.67	57.90	1.62	94.10	97.48	88.59	94.60	20.00
LLM	9	22	1.64	60.00	1.65	61.20	1.66	51.30	53.79	52.29	54.50	36.00
HRA	10	25	1.51	45.00	1.32	52.00	1.49	83.23	109.08	96.17	111.66	16.60
EJF	11	20	1.61	51.00	1.56	57.00	1.60	72.03	79.88	87.21	96.71	20.00
MVM	12	18	1.63	64.00	1.70	56.20	1.60	82.08	83.52	72.03	77.88	24.00
ACJ	13	20	1.72	56.50	1.72	63.40	1.76	86.45	86.95	97.00	95.35	20.00
PGA	14	25	1.69	61.00	1.70	63.90	1.74	52.16	53.08	54.61	54.30	36.00
FUT	15	22	1.89	83.00	2.12	79.00	1.00	149.00	121.59	142.20	100.37	17.00
TRJ	16	30	1.62	52.50	1.58	60.50	1.64	124.70	136.54	143.70	151.64	12.80
CGF	17	22	1.70	52.50	1.60	63.00	1.74	105.13	113.67	126.16	125.43	12.00
MMV	18	21	1.72	75.00	1.88	63.50	1.76	125.55	115.53	106.29	104.48	18.30
AGA	19	18	1.72	65.00	1.76	63.00	1.76	90.68	91.21	87.89	88.40	22.20
AA	20	22	1.65	52.00	1.56	60.00	1.74	72.54	80.45	83.70	83.22	22.00
GEN	21	22	1.75	84.00	2.00	67.00	1.89	107.73	93.19	85.93	78.01	24.00
RFS	22	41	1.60	74.00	1.78	62.50	1.64	157.51	153.09	133.03	140.33	14.30
GGV	23	20	1.65	64.00	1.68	59.80	1.66	137.51	141.60	124.59	129.84	14.60
	$\bar{X}$	22.83	1.69	64.57	1.75	63.93	1.75	100.56	99.33	94.54	98.35	20.82
σ	±		0.09	11.63	0.19	6.03	0.12	29.92	26.73	27.62	25.16	6.29

labeled with ^{131}I was used as an inulin-like substance. The method obviates the use of continuous intravenous infusions for administering the experimental reagent. One need not take blood samples. Furthermore, it is not necessary to insert a catheter into the bladder for urine specimens. We consider that the accuracy and obvious clinical advantages of the method we have presented render it far more useful than other methods now employed.

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