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A Simplified Method for Simultaneous Electrolyte Studies in Man Utilizing Potassium-43

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A method is presented which enables the exchangeable sodium, potassium and bromide space to be estimated entirely by gamma counting using sodium-24, potassium-43 and bromine-82. The potassium-43 is a cyclotron produced isotope with a 22-hr half-life. The principal gamma radiation is at 370 keV. Duplicate estimations on nine patients indicate that the error in the estimation in exchangeable sodium, exchangeable potassium and bromide space is 4·6, 2·78 and 2·14 per cent respectively. By using a dual channel automatic gamma counter the assay may be completed in a single counting run. This technique permits a more widespread application of these measurements in clinical research and diagnosis.

UNE METHODE SIMPLIFIEE POUR LES ETUDES SIMULTANEES D'ELECTROLYTE CHEZ L'HOMME UTILISANT LE POTASSIUM-43

On présente une méthode qui permet l'estimation du sodium, du potassium et du bromure échangeables entièrement par comptage de gamma en employant le sodium-24, le potassium-43 et le brome-82. Le potassium-43 est un isotope produit du cyclotron ayant une demi-période de 22 heures. Le principal rayonnement gamma est à 370 keV. Des mesures en duplication sur neuf sujets indiquent que les erreurs d'estimation de sodium échangeable, de potassium échangeable et d'espace de bromure serait de 4,6, 2,78 et 2,14 pour cent. En employant un compteur gamma automatique à deux canaux on peut achever le dosage en une seule série de comptes. Cette méthode permet une application plus répandue de ces mesures dans la recherche clinique et dans la diagnostique.

УПРОЩЕННЫЙ МЕТОД ОДНОВРЕМЕННЫХ ЭЛЕКТРОЛИТИЧЕСКИХ ИССЛЕДОВАНИЙ В ЧЕЛОВЕКЕ С ПРИМЕНЕНИЕМ КАЛИЯ^{43}

Приводится метод, дающий возможность полного определения обменных натрия, калия и брома посредством измерения гамма-активности, применяя натрий^{24}, калий^{43} и бром^{82}. Калий^{43} является изотопом с периодом полураспада в 22 часа, полученным с помощью циклотрона; основные гамма-лучи = 370 килоэлектронвольт.

Дублированные определения на девяти пациентах показывают, что погрешности определения обменного пространства для натрия, калия и брома равны 4,6%, 2,78% и 2,14% соответственно. Применяя автоматический гамма-счетчик с 2-мя каналами, можно производить полное определение в один счетный период. Этот метод дает возможность широкого применения таких измерений в клинических исследованиях и диагностике.

EINE VEREINFACHTE METHODE FÜR GLEI CHZEITIGE ELEKTROLYT-STUDIEN IM MENSCHEN UNTER VERWENDUNG VON KALIUM 43

Es wird ein Verfahren angegeben zur messung des austauschbaren Natrium, Kalium und Brom, lediglich durch Gammazählung unter Verwendung von Natrium 24, Kalium 43 und Brom-82. Kalium 43 ist ein im Zyklotron hergestelltes Isotop mit einer Halbwertzeit von 22 h. Die Hauptgammastrahlung liegt bei 370 keV. Doppelbestimmungen an neun Patienten deuten an, dass der Fehler in der messung des austauschbaren Natrium-, austauschbaren Kalium- und Brom-Raumes 4,6 bezw. 2,78 und 2,14% beträgt. Wenn ein automatischer Doppelkanal-Gammazähler benutzt wird, kann die Analyse in einem einzigen Zählgang beendet werden. Dieses Verfahren kann zu einer grösseren Verwendung dieser Messungen in der klinischen Forschung und Diagnose führen.

1. INTRODUCTION

THE CHIEF problem in assaying mixtures of isotopes used for the simultaneous determination of exchangeable sodium, potassium and chloride for electrolyte studies in man has been the estimation of the radioactive sodium in the presence of radioactive potassium. Several methods of assay of ^{42}K and ^{24}Na have been described, using chemical separation methods,[1–3] physical methods,[4–7] and physical-physiological methods.[8,9] The last method was also used by BOLING[10] using a plastic phosphor for beta detection instead of the more usual Geiger counter. ROVNER and CONN[11] used ^{22}Na instead of ^{24}Na and assayed the mixture of this isotope with ^{42}K by differential decay. However, ^{22}Na, because of its long half-life and radiation characteristics, is undesirable for this purpose.

The method described below utilizes cyclotron-produced ^{43}K instead of ^{42}K and this results not only in improved accuracy over previous methods but a greatly simplified technical procedure, since ^{24}Na and ^{43}K can be assayed by gamma counting alone. A dual channel automatic counter allows the ^{43}K and ^{24}Na to be assayed simultaneously and ^{82}Br is conveniently assayed under the same counting conditions following a resin separation. A single channel automatic counter could also be used, but would require repeated counting.

2. PRODUCTION OF ^{43}K

Carrier free ^{43}K was produced in the external beam of the Medical Research Council cyclotron by irradiating argon-40 with 16·4 MeV α-particles. Details of the method of production are presented elsewhere[12]. ^{43}K is produced by the $^{40}A(\alpha p)^{43}K$ reaction which has a threshold of 3·64 MeV. The argon is circulated at a rate in excess of 100 l/min through the target vessel and the exit gas is passed through a borosilicate fibre filter. Between 50 and 80 per cent of the activity is recovered from the filter. The activity is removed from the filter with 5 ml of 0·001 N hydrochloric acid. The yield is 18 $\mu c/\mu A$ hr and the contamination with ^{42}K is less than 7 per cent. For the present application, 5 mg/ml of KCl carrier is added to prevent glassware adhesion.

2.1. *Physical characteristics of* ^{43}K

The physical characteristics of ^{42}K and ^{43}K are shown in Table 1. The principal differences between the two isotopes are the lower γ and β energies of the ^{43}K, resulting in a lower radiation dose despite its longer half-life.

TABLE 1. Radiation characteristics of potassium-42 and potassium-43

	^{42}K	^{43}K
Half life	12·4 hr	22 hr
Principal γ-energies	1·52 MeV (18%)	0·37 MeV (85%), 0·61 MeV (81%)
k-factor	1·4	5·6
Average β energy (E_β)	1·45 MeV	0·30 MeV
Whole body radiation dose	0·85 mrad/μc	0·6 mrad/μc

3. METHOD

3.1. *Clinical procedure*

50 μc of ^{43}K and 20 μc of ^{24}Na were administered orally at 9 a.m. after an overnight fast of 10 hr. 10 μc of ^{82}Br were given orally 14 hr later. Normal food and fluids were permitted from 9 a.m. up to 9 p.m. Urine was collected in polythene flasks as follows: 0–24 hr, 24–24·5 hr, and 24·5–25 hr. At 24 hr and 25 hr heparinised blood samples were taken.

3.2. *Radioactive assay*

15 ml of each plasma and urine sample were passed through a moist resin column, 6 mm in dia. and 15 cm long, to remove the ^{82}Br. The resin used was Amberlite Tropor Deacidite FFIP, of a calculated exchange capacity of 5·1 mEq. The first 2 ml of the eluent was discarded, and the remainder assayed for radioactivity and for stable sodium and potassium concentration by flame photometry. Plasma was used for the measurement of exchangeable sodium and the bromide space, while urine was used for the exchangeable potassium.

Standards of the radioactive sodium, potassium and bromide were prepared by diluting an additional dose with distilled water up to 1 l. Aliquots of the standard dilution of ^{24}Na and ^{43}K were transferred directly to counting vials. The standard ^{82}Br was passed through an identical resin column as used for the samples. After washing each of the columns with 200 ml deionised water to remove any cations, the resin was transferred into the counting vials. This procedure resulted in identical sample and standard treatment for the ^{82}Br estimation, and produced identical counting geometry.

All the samples were assayed on a dual channel automatic gamma counter. The ^{82}Br was counted under the same conditions as the ^{43}K and ^{24}Na. This enabled all the samples to be counted in a single run on the automatic counter. This practical advantage outweighed the lower counting efficiency which resulted from assaying bromide under these less optimal conditions. Channels 1 and 2 were arranged to accept energies between 0·135 MeV and 0·415 MeV, between 1·05 MeV and 5·6 MeV respectively. The counting efficiencies for ^{24}Na and ^{43}K on channel 1 were 4·5 and 18·8 per cent respectively, whilst in channel 2 the efficiency was 13·4 and 0·1 per cent respectively. The counting efficiency for ^{82}Br (summed in the two channels) was 21 per cent.

4. RESULTS

4.1. In vitro *test of isotope measurement accuracy*

To establish the accuracy of the method, varying amounts of the ^{24}Na, ^{43}K and ^{82}Br were added to each of 6 flasks containing 100 ml of distilled water. Samples were passed through resin columns, and counted to determine the volume of distribution of each isotope. The results obtained are shown in Table 2.

4.2. *Clinical measurements*

Sodium, potassium and bromide spaces were estimated simultaneously in seven patients, and sodium and potassium spaces in a further two patients. These spaces were estimated at both 24 and 25 hr for ^{43}K and ^{24}Na and at 10 and 11 hr for ^{82}Br. The results are shown in Table 3.

5. DISCUSSION

The results presented in Table 2 indicate that no significant systematic error in the laboratory technique is present. The magnitude of the difference between duplicate estimates as seen in Table 3 are comparable or better than similar estimates of other workers.[13–17] The larger error in estimation of exchangeable sodium is associated with the poorer counting statistics of

TABLE 2. *In vitro* test of distribution volume

	^{24}Na (ml)	^{43}K (ml)	^{82}Br (ml)
	99·56	99·49	102·22
	100·12	100·76	99·12
	99·41	99·31	98·44
	99·99	101·34	100·76
	98·04	98·68	100·90
	100·11	100·66	101·80
Mean	99·54	100·04	100·51
coefficient of variation (%)	±0·79	±0·93	±1·48

The actual volume of distribution for each isotope was 100 ml in all six experiments.

TABLE 3. Results of clinical investigations

Patient number	Exchangeable sodium (mEq) Sampling time 24 hr	25 hr	Diff (%)	Exchangeable potassium (mEq) Sampling time 24 hr	25 hr	Diff (%)	Bromide space (l.) Sampling time 10 hr	11 hr	Diff (%)
1	2968	3143	+5·89	3356	3248	−3·2	21·49	21·59	+0·46
2	2086	2089	+0·14	2215	2222	+0·31	16·31	15·85	−2·82
3	1932	2028	+4·96	1850	1951	+5·46	17·31	17·43	+0·69
4	2148	2178	+1·39	2039	2094	+2·69	16·45	15·83	−3·76
5	4350	4480	+2·98	1723	1707	−0·92	28·29	28·71	+1·48
6	2127	1997	−6·11	1962	1952	−0·16	—	—	—
7	4119	4434	+7·6	2832	2859	+0·95	34·11	34·41	+0·88
8	4311	4264	−1·09	3191	3078*	−3·5	35·89	35·00	−2·47
9	2768	2705	−2·27	2021	2047	+1·28	—	—	—
Mean	2978·7	3035·3	+1·50	2354·3	2350·8	+0·32	24·26	24·11	−0·79
Standard deviation of diffs.			4·6			2·78			2·14

* 48 hr value.

the sodium assay. Approximately 3000 counts/400 sec are obtained for ^{24}Na assay in each plasma sample whereas 15,000/400 sec are usually obtained in the potassium assay from the urine sample. The error in the assay of stable sodium and potassium by flame photometry is estimated to be ±2 per cent. The relatively short time (1 hr) between successive samples makes it unlikely that further equilibration would affect the error estimates shown in Table 3.

The considerable saving of time and effort associated with the use of gamma counting only makes the replacement of ^{42}K by ^{43}K for these space estimations very attractive. The longer half-life of ^{43}K and the reduced radiation dose are additional advantages. The problems of calculating the final results are greatly eased by this procedure since all three isotopes are counted in a single run on a dual channel automatic counter. By loading the samples in a predetermined order, a punch tape record obtained from the counter facilitates the use of a computer programme to estimate the individual space values, allowing for physical decay.

6. CONCLUSION

The use of ^{43}K instead of ^{42}K in the simultaneous estimation of exchangeable sodium, potassium and bromide space results in a lower radiation dose and greatly simplifies the practical procedures. The use of a dual channel automatic gamma counter for estimating the three isotopes eases the computational problems associated with this technique and permits a more widespread application in clinical research and diagnosis.

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