Application of pharmacokinetics local model to evaluate renal function

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Abstract The pharmacokinetics local model was used to evaluate renal function. Some typical kinds of renal function cases, normal or disorder, were selected to be imaged with SPECT and those data measured were treated by the pharmacokinetics local model computer program (PLM). The results indicated that parameters, including peak value, peak time, inflexion time, half-excretion time, and kinetic equation played and important role in judging renal function. The fact confirms that local model is very useful in evaluating renal function.
Keywords Renal function, Pharmacokinetics, Local model, SPECT

1 Introduction

In evaluating patient's renal function by SPECT. we generally judge whether renal function normal or not with CPMs of imaging agent accumulated in the kidney at different time and the curve lined straightly one by with these CPMs. Why not use pharmacokinetic equation and parameters much more accurate to judge renal function? The reason is that previous pharmacokinetic models, such as the compartment model, can not describe radiopharmaceuticals' kinetic action in the specific organ such as heart, liver, kidney or other tissues.[1,2] Previously, we put forward our pharmacokinetics local model that can perfectly describe radiopharmaceuticals' kinetic action in specific organ.[3] In this paper we use the model to evaluate the renal function in SPECT imaging.

2 Patients and method

2.1 Patients

One health volunteer man aged 35 years no urinary system disease. 7 patients of confirmation of renal disorders, including 5 men and 2 woman in age from 22 to 56 years. All patients were confirmed by case history. biochemical test and B-supersonic detector.

2.2 Radiopharmaceutical and imaging

Technetium-99m-Ethylenedicysteine kit (^{99m}Tc-EC), 97% radiochemical purity, was provided the pharmaceutical factory of Jiangsu Institute of Nuclear Medicine. Before experiment, all patients urinated at half an hour after drinking 500 mL of water. Imaging was performed with the patient in the supine position in the posterior projection using a SPECT (Diacam, Siemens Co.). Region of interest was drawn over the whole kidney. After 185 MBq ^{99m}Tc-EC intravenous bolus injection, two groups of images with 32 frames of 2 s/frame and 30 frames of 60 s/frame were collected. Meanwhile, corresponding CPMs for region of interest were also obtained.

2.3 Calculation with local model

We have complied a local computer program called PLM.[3] Being inputted CPMs at different times, it can evaluated pharmacokinetic equation and parameters, such as the peak value (C_m), the peak time (T_m), the half-excretion time ($T_{1/2}$) and the area below the CPM-time curve (AUC). With the equation we can conveniently draw the CPM-time curve and calculate the value of CPM at any time. These parameters, equation and curve are very useful in evaluating renal function.

2.4 Application of pharmacokinetic parameters

Pharmacokinetic parameters play an important role in evaluating renal function. For normal renal function, in general, T_m is 3.69±0.75 min and $T_{1/2}$ 9.29±3.31 min.[4]

The elimination ratio at 20 min (Re_{20}) af-

The Project Supported by Natural Foundation of Jiangsu Province China
Manuscript received date: 1998-08-24

ter injection is defined as

$$Re_{20} = (C_m - \text{Value of CPM at } 20\,\text{min})/C_m$$

The value of CPM at 20 min can easily be calculated with the pharmacokinetic equation. Re_{20} for normal renal function is 71±17.89%.[4]

Pharmacokinetic equation has another important application in evaluating renal function. We can find out the inflexion of curve by calculating its second derivative and define T_i as the time when the second derivative equals to zero.

In comparing right and left renal function, both kidneys' AUCs within the same range of time can be used as judging standard. In comparing normal and disorder renal function, AUC within any range of time can also be evaluated with the pharmacokinetic equation.

3 Results and discussion

Using SPECT, we collected CPMs at different times, and these data were inputted into the computer program PLM to evaluate equations, parameters and curves. The results were listed in Table 1. We only focus on the object 1,2,3,4 for discussion because these four objects are the most typical kinds of renal function. The data collected by SPECT and curve fitted by PLM were showed in Fig.1.

Table 1 Calculated results by PLM for evaluating renal function*

Object	Sex	C_m /$\times 10^3$ min^{-1}	T_m /min	$T_{1/2}$ /min	T_i /min	CPM_{20} /$\times 10^3$ min^{-1}	Re_{20} /%	Renal function
1	Male	97	4	10	6	24	75.3	Normal
2	Female	123	10	50	25	111	9.8	Disorder
3	Male	–	–	–	–	61	–	Disorder
4	Male	59	12	40	28	53	10.2	Disorder
5	Male	110	6	19	9	56	49.1	Disorder
6	Female	178	6	31	10	115	35.4	Disorder
7	Male	51	3	17	–	24	52.9	Disorder
8	Male	73	6	15	8	30	58.9	Disorder

*The value of CPM at 20 min after injection

As a normal renal function, it must have short peak time, short half-excretion time, short inflexion time, high peak value and rapid excretion. The results of the volunteer, object 1, indicate that T_m (4 min), $T_{1/2}$(10 min), T_i(6 min) and Re_{20}(75.3%) are located in normal ranges, respectively. Fig.1a shows experimental data collected by SPECT and fitting curve calculated by PLM. Obviously, the accumulation and excretion of ^{99m}Tc-EC in the volunteer's kidney expresses the normal renal function.

Object 2, on the other hand, is a patient with renal disorder. Her T_m, $T_{1/2}$, T_i and Re_{20} are 10 min, 50 min, 25 min and 9.8%, respectively. Fig.1b show that the peak time is delayed, the excretive section of curve goes down very show and T_i is much larger than that of the normal. All these indicate that the patient's renal excretion is slow and renal function disorder. It means that the patient is suffered from upper urinary passage incomplete obstruction.

Object 3 is a typical upper urinary passage obstruction example. The results indicate that curve is gradually upward and keeps at high level, as shown in Fig.1c. There is no peak, peak time, inflexion time or half-excretion time at all. If the obstruction could be removed, the patient's renal function would recovered.

Object 4 is patient suffered from chronic incomplete renal function disease. It has a delayed peak time and low peak value in Fig.1d, which shows that accumulation of ^{99m}Tc-EC in kidney is slow and somewhat difficult. Besides these, excretion is also very slow. It is undoubted that the situation is resulting from a long-term renal function injured.

It is a new concept that inflexion of curve is used to evaluate renal function. Calculation of the inflexion is very easy by the pharmacokinetic equation. It was impossible to establish the equation describing radiopharmaceuticals kinetics in the specific organ with the other pharmacokinetics model in the past. In Table 1, the difference of T_i between normal and disorder renal function is much larger than that of T_m. In judging whether renal function normal

or not, therefore, T_i is a perfect parameter.

In spite of that we did not discuss the use of AUC in judging renal function, it is obvious that AUC is very useful. As we know, AUC is function of time and increase with increasing time. When the time is near to the T_m, the AUC of normal renal function in general is larger than that of disorder renal function. Another application of AUC is in comparing the right renal function with the left, which we did not discuss in detail here.

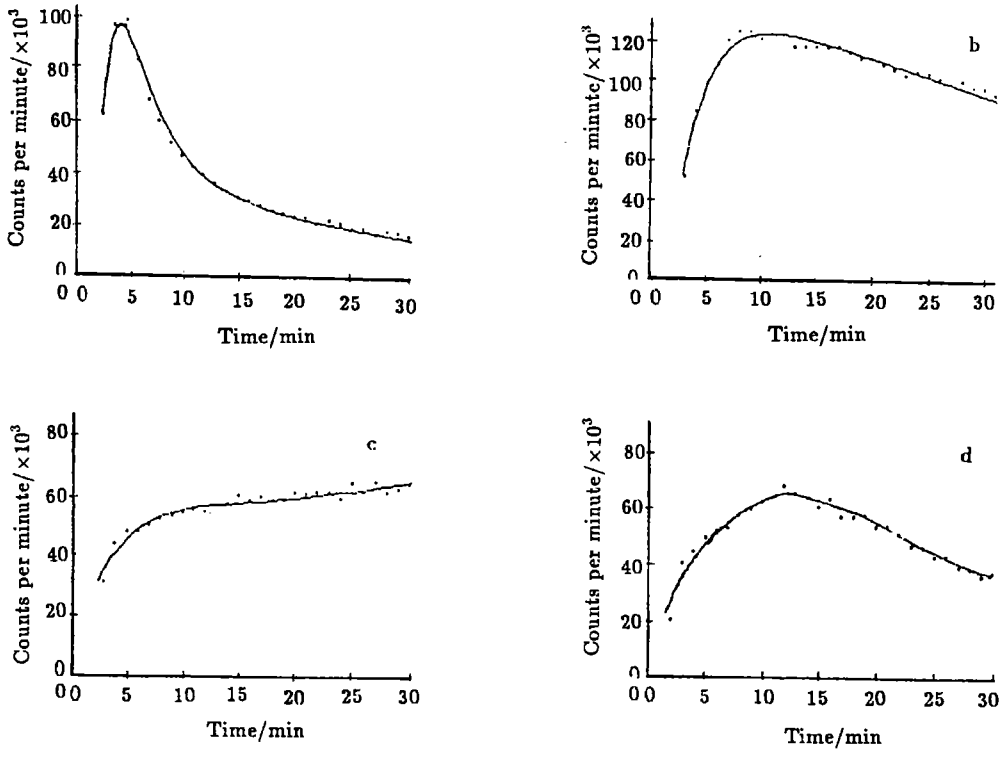

Fig.1 CPM-time curve and experimental data
+ Experimental data collected by SPECT; — Fitting curve calculated by PLM; 1a, 1b, 1c, 1d are corresponding to object 1, 2, 3, 4, respectively

4 Conclusion

We selected four objects to demonstrate the application of pharmacokinetics local model in evaluating renal function. Renal function, especially function disorder, has various situation, but the four objects are the most typical, and the other situation can be discussed in similar way.

It could be indicated that the curve calculated by local model is exactly conformed with those experimental data collected by SPECT. It strongly confirms that local model may correctly describe the pharmacokinetic action of radiopharmaceuticals in the special organ.

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