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The use of creatinine clearance in evaluation of glomerular filtration rate (GFR) has many disadvantages. Alternatively, GFR can be determined by more reliable methods such as plasma clearance of Cr-51 ethylenediamine tetraacetic acid (Cr-51 EDTA) or Tc-99m diethylenetriamine pentaacetic acid (Tc-99m DTPA). Cr-51 EDTA, which gives a more accurate GFR result, is very expensive and has to be imported. On the other hand, Tc-99m DTPA is cheaper and can be prepared in any nuclear medicine laboratory. To evaluate the quality of DTPA that was prepared at our laboratory, the plasma clearance of Tc-99m DTPA was compared with that of imported Cr-51 EDTA in 40 patients with various diseases. Using a double compartmental multiple blood samples method, the correlation coefficient(r) of the two radiopharmaceuticals was 0.93 with a standard error of estimation (Sx.y) of 12.1 ml/min. The p value of a paired t-test was 0.65. We conclude that our in-house Tc-99m DTPA has a comparable quality to that of imported Cr-51 EDTA in the measurement of glomerular filtration rate.

Key words : *Tc-99m DTPA, Cr-51 EDTA, Glomerular filtration rate, Plasma clearance, Radionuclide study.*

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ธวัชชัย ชัยวัฒนรัตน์, มาคุ้มครอง โปษยะจินดา, นุ้ย แซ่โซว. เปรียบเทียบประสิทธิภาพของเท็คนีเซี่ยม - 99 เอ็ม ดีทีพีเอ ที่ผลิตขึ้นเองกับโครเมี่ยม - 51 อีดีทีเอ ที่ซื้อจากต่างประเทศในการวัดอัตราการกรองของไตในผู้ป่วย. จุฬาลงกรณ์เวชสาร 2538 มิถุนายน; 39(6): 437-442

เป็นที่ทราบกันดีแล้วว่าการใช้ค่า creatinine clearance ในการประเมินอัตราการกรองของ glomeruli มีข้อเสียหลายประการ วิธีที่ดีกว่าก็คือการคำนวนหาค่า plasma clearance ของ Cr-51 ethylenediamine tetraacetic acid (Cr-51 EDTA) หรือ Tc-99m diethylenetriamine pentaacetic acid (Tc-99m DTPA) อย่างไรก็ตาม Cr-51 EDTA ซึ่งให้ค่าที่ถูกต้องกว่านั้น มีราคาแพงและต้องสั่งซื้อจากต่างประเทศ ส่วน Tc-99m DTPA นั้นสามารถผลิตขึ้นได้ในห้องปฏิบัติการเวชศาสตร์นิวเคลียร์ทุกแห่ง ในราคาที่ถูกกว่ามาก ดังนั้นเพื่อประเมินถึงประสิทธิภาพของ DTPA ที่ผลิตขึ้นเองในห้องปฏิบัติการเวชศาสตร์นิวเคลียร์ของโรงพยาบาลจุฬาลงกรณ์ ผู้ศึกษาจึงศึกษาเปรียบเทียบ plasma clearance ของ Tc-99m DTPA ดังกล่าว กับ Cr-51 EDTA ซึ่งสั่งซื้อโดยตรงจากต่างประเทศ ในผู้ป่วยด้วยโรคต่าง ๆ 40 ราย ค่า plasma clearance คำนวณโดยวิธีการเจาะเลือดหลายครั้ง และใช้ double compartmental model พบว่าค่า plasma clearance ของเภสัชรังสีทั้งสองมีค่าสัมประสิทธิ์ความสัมพันธ์(r) เท่ากับ 0.93 มีค่าความผิดพลาดมาตรฐาน (Sx.y) เท่ากับ 12.1 มล./นาที มีค่า p value จากการเปรียบเทียบความแตกต่างระหว่างคู่ (paired t-test) เท่ากับ 0.65 ซึ่งไม่มีความสำคัญทางสถิติ ผู้ศึกษาสรุปว่า Tc-99m DTPA ที่เตรียมขึ้นใช้เองในโรงพยาบาลจุฬาลงกรณ์ มีประสิทธิภาพดี เทียบเท่ากับ Cr-51 EDTA ในการคำนวณหาค่าอัตราการกรองของ glomeruli

Creatinine clearance (CCr) is most commonly used as an indicator of glomerular filtration rate (GFR) in the assessment of renal function. However, it is known that CCr is merely the estimated value of GFR because the rate of creatinine formation is not constant.[1] Creatinine is partly excreted[2] and reabsorbed via tubular cells[3] and complete urine collection is usually very difficult.

The more precise method of GFR estimation is a calculation of plasma clearance of a radiopharmaceutical, especially ethylenediamine tetra acetic acid labeled with chromium-51 (Cr-51 EDTA). This method is easier to use and gives clearance values very close to inulin clearance,[4-6] however, Cr-51 EDTA is very costly because it has to be imported.

It has been shown that diethylene triamine penta acetic acid labeled with technetium-99m (Tc-99m DTPA) is a radiopharmaceutical that can be used to evaluate renal function and give plasma clearance values close to that for Cr-51 EDTA clearance.[7] The advantage of Tc-99m DTPA is that DTPA can be prepared in any laboratory without the need of sophisticated instrumentation. DTPA can then be easily labelled with Tc-99m and be ready to use. The aim of this study is to evaluate the efficacy of Tc-99m DTPA prepared in the Nuclear Medicine Laboratory of Chulalongkorn Hospital by comparing the plasma clearance of Tc-99m DTPA to that of imported Cr-51 EDTA.

Materials and methods

Subjects

Forty patients who were referred to the Nuclear Medicine Division for renal function examination were included in this study. Twenty-four were male and sixteen were female. The patients afflictions were : 12 chronic renal failure, 7 head and neck carcinoma, 5 nephrotic syndrome, 5 Systemic Lupus Erythematosus, 3 carcinoma of the cervix, 2 hypertension, 2 carcinoma of the central nervous system, 2 acute renal failure, 1 multiple myeloma, and 1 lymphoma. The edematous patients were excluded from the study because plasma clearance value estimation was unreliable in this condition.[8]

Methods

Cr-51 EDTA, approximately 100 microCuries, and Tc-99m DTPA, approximately 1.5 milliCuries, were intravenously administered simultaneously via the anticubital vein. Before injection, quality control (for radiopharmaceutical impurity) of the Tc-99m DTPA was done using Gelman instant thin layer silica gel chromatography (ITLC-SG). The heparin locked scalp vein needle was inserted into the anticubital vein on the other arm. Five-ml blood samples were taken at 10, 20, 30, 50, 60, 90, 120, 180 and 240 minutes after radiopharmaceutical injection. Each blood sample was put into the heparinized test tube and was centrifuged, and then 1 ml of plasma from each tube was drawn and counted for the radioactivity of both Cr-51 and Tc-99m.

The count rate of Cr-51 EDTA and Tc-99m DTPA for all of the plasma samples were then plotted on the semilogarithmic graph. The plasma clearance of both Cr-51 EDTA and Tc-99m DTPA were then calculated in the same manner by the double exponential model[9] using the curve peeling technique. The plasma clearance was then calculated using equation 1:

$$\text{Clearance} = (Q \times B_1 \times B_2)/\{(A_1 \times B_2) + (A_2 \times B_1)\} \quad \ldots\ldots 1$$

where Q = count rate of the injected radiopharmaceutical

B_1, B_2 = slopes of the 1st and 2nd exponential function respectively

A_1, A_2 = intercepts of the 1st and 2nd exponential function respectively

The preparation of stock solution of DTPA

The detail method of preparation of DTPA stock solution was reported by Eckelman[10]. In brief the preparation for about 40 vials is as follow:

To 1 ml of $CaNa_3DTPA$ solution (100 mg/ml):

1. Add 5 mg $SnCl_2 2H_2O$ and heat at 100° C under N_2 for 15 min.
2. Dilute to 18 ml with sterile H_2O.
3. Adjust pH to 4.0 with HCl.
4. Dilute to 20 ml with sterile H_2O.
5. Purge solution with N2 for 15 min.
6. Filter solution through a sterile 0.22-micron filter into evacuated vials, 1 ml of solution per vial.
7. Keep frozen in the refrigerator.

To prepare solution of Tc-99m DTPA solution, add Tc-99m pertechnetate saline solution to the defrozed DTPA solution and mix for 1 minute.

Statistics used

1) The correlation coefficient (r) and standard error of estimation (Sy.x) of Cr-51 EDTA and Tc-99m DTPA plasma clearance were calculated using the least square fit method.

2) The paired t-test was used to test the difference of Cr-51 EDTA and Tc-99m DTPA plasma clearance.

Results

The age of the patients ranged from 15-77 years with the mean ± s.d. of 41.85 ± 16.35 years. Creatinine clearance values of the patients were between 2.0 and 112.4 ml/min with the mean ± s.d. of 45.5 ± 31.7 ml/min. The plasma clearance of Cr-51 EDTA was between 7.8 and 111.9 ml/min with the mean ± s.d. of 47.1 ± 30.7 ml/min. The plasma clearance of Tc-99m DTPA was between 5.3 and 116.5 ml/min with mean ± s.d. of 46.2 ± 31.9 ml/min. Plasma clearance of Cr-51 EDTA and Tc-99m DTPA in a patient with hypertension are demonstrated in Fig.1. The regression equation of Cr-51 EDTA and Tc-99m DTPA plasma clearance was Y = 0.858 + 0.963 X with correlation coefficient (r) of 0.9278 and the standard error of estimation of 12.1 ml/min (Fig.2). The paired t-test of the two plasma clearances had p value of 0.65.

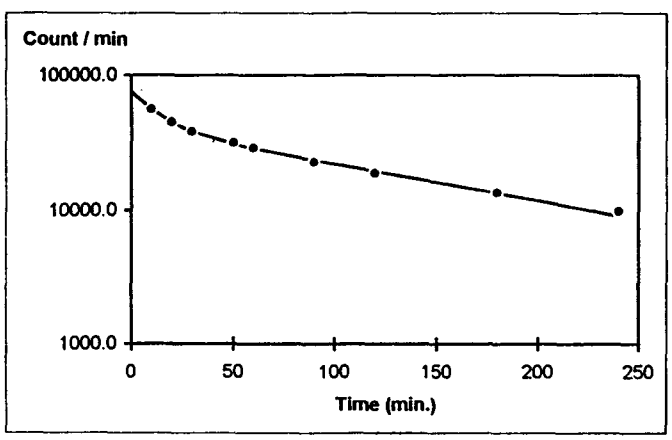

Figure 1. Plasma clearance curve of Cr-51 EDTA or Tc-99c DTPA in a patient with hypertension

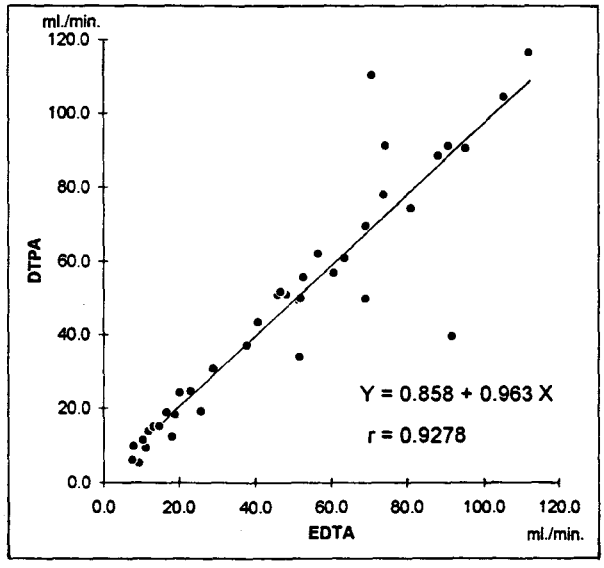

Figure 2. Linear regression of Tc-99m DTPA and Cr-51 EDTA plasma clearance

Discussion

Tc-99m DTPA is widely used as a radiopharmaceutical for renal scintigraphy. DTPA is excreted via glomerular filtration hence it can be used to calculate the glomerular filtration rate. Usually, Cr-51 EDTA is used as a reference test, but the high cost and scarcity, limit the use of Cr-51 EDTA in our country. In addition, it results in a higher radiation dose being absorbed as compared to Tc-99m DTPA. The advantages of Tc-99m DTPA include suitable gamma energy of Tc-99m for the gamma camera to produce kidney images while Cr-51 EDTA could not do so. It has been reported that some degree of binding of DTPA to the plasma protein may occur which might result in a low GFR.[7,11] Therefore, before using locally made Tc-99m DTPA as a GFR agent, it's efficacy has to be tested.

In the present study, the plasma clearance of our in-house Tc-99m DTPA was comparable to that of imported Cr-51 EDTA with the correlation coefficient (r) of 0.9278, and the paired t-test showed that there was no significant difference between the plasma clearance valves of these two agents.

There have been many studies attempting to find easier ways to calculate GFR, such as obtaining only 1 or 2 blood samples[12,13] or no blood sample taking at all,[14-17] and the results seemed to be promising, but these methods gave only estimated values which can be used only to roughly evaluate renal function.[18] Therefore if the exact values of GFR need to be known, our present method would be very useful.

Conclusion

The Tc-99m DTPA produced at the Nuclear Medicine Laboratory, of Chulalongkorn hospital can be accurately and reliably used for GFR measurement using the multiple blood samples model as compared to the standard agent, Cr-51 EDTA. It provides not only renal function information but also renal anatomical information, and at a very low cost.

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