Assessment of Agreement between Gates Method and Dual Plasma Sample Method for Measurement of Glomerular Filtration Rate

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ABSTRACT

Objectives: Glomerular filtration rate (GFR) is generally considered to be the best index of renal function in both healthy and diseased kidneys. Calculation of GFR plays a vital role in the management of patients having renal diseases. Clinicians can make their final decision regarding the potential need for kidney transplantation and also selection of a potential kidney donor. Many methods have been developed in order to obtain more accurate GFR values. The most popular radionuclide method is camera based Gates method using ^{99m}Tc DTPA (Diethylene triaminepentaacetic acid). This method can provide immediate calculation of individual kidney function as well as of global renal function. But several sources of errors may reduce the reliability of this method. Measurement of multiple blood samples offers almost real values of GFR, which have become the gold standard in clinical research. The aim of this research work was to study the agreement between Gates method and dual plasma sample method for measurement of GFR.

Patients and methods: This cross sectional study was carried out in National Institute of Nuclear Medicine & Allied Sciences (NINMAS), during July 2015 to June 2016. A total of 59 patients were included in this study. GFR was estimated by both the camera based Gates method and dual plasma sample method (DPSM).Statistical analyses were carried out by using the Statistical Package for Social Sciences version 20.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. Categorical data were expressed in percentage and number. Pearson correlation and Bland & Altman (B & A) analyses were applied for assessing correlation and agreement between Gates method and DPSM. Degree of relation between the variables is expressed by r (Pearson's correlation coefficient).

Results: The mean GFR evaluated by Gates method was found 82.2 ± 27.4 mL/min/1.73m^2 and mean GFR by DPSM was found 82.8 ± 24.1 mL/min/1.73m^2. A strong positive correlation (r = 0.833; p = 0.001) was found between the GFR values measured by Gates method and DPSM. With Bland and Altman analysis, it was observed that mean difference of GFR measured by Gates method and DPSM was − 0.6 ± 15.22 mL/min/1.73m^2. The limit of agreement ranged from − 30.44 mL/min/1.73m^2 to 29.24 mL/min/1.73m^2.

Conclusion: There was strong positive correlation between Gates method and DPSM for measurement of GFR. Mean difference between the methods was small. The bias between the methods was considered not significant. The differences within mean ± 1.96 SD are not clinically important. Hence Gates method and DPSM can reflect GFR almost equally and can be used interchangeably.

Key words: Glomerular filtration rate, Gates method, dual plasma sample method.

INTRODUCTION

Glomerular filtration rate (GFR) is an important indicator of the functional status of the kidney and is defined as the volume of fluid filtered from the renal glomerular capillaries into the Bowman's capsule per unit time (1). About 10% of the renal blood flow, which is around 20% of cardiac output at rest (1-1.2 L/min), is filtered and make up the primary urine. The filtration speed of the primary urine is the glomerular filtration rate and is approximately 120 mL/min (2). Increased hydrostatic pressure in the glomerular capillaries increases GFR. On the other hand increased hydrostatic pressure in the Bowman's capsule and increased colloidal osmotic pressure in the glomerular capillaries decrease GFR.

Many methods have been developed in order to obtain more accurate value and simpler procedure for GFR measurement. The commonly used methods are estimated GFR or eGFR, serum cystatin C, camera renogram (Gates method), plasma sampling method and twenty four hours endogenous creatinine clearance. The "gold standard" for GFR estimation

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has been considered to be that of continuous infusion of inulin with urine and plasma sampling; but this method is technically difficult and is rarely performed in a clinical setting (3).

Measurement of GFR, using a radiation emitting agent, is practical as measuring radioactivity is simple and more accurate. [51]Cr EDTA and ^{125}I iothalamate were frequently used for true GFR measurement, but these agents were expensive, the technique were time consuming and highly dependent on the accuracy of urine collection (4,5). On the other hand, ^{99m}Tc DTPA is relatively cheaper and readily available agent, which is completely filtered by glomeruli and not secreted or reabsorbed by renal tubuli (6). Camera-based noninvasive scintigraphic method to evaluate GFR is comparable to standard methods of GFR determination (e.g., inulin clearance and creatinine clearance) (7, 8).

Measurement of multiple blood samples offers almost real values of GFR, which have become the gold standard in clinical research. Their simplification has been achieved by reduction of the number of blood samples to two or even one (9). DPSM using Russell's formula vouched as a reliable method for the valid estimate of true GFR (10).GFR is useful in early detection of renal impairment, for monitoring renal function and also provides guidance in the dosing of naphrotoxic drugs. Moreover the classification of chronic renal disease is dependent on the accurate calculation of GFR (3). Hence it is worthy to establish a procedure for the valid estimation of GFR in routine Nuclear Medicine procedure.

PATIENTS AND METHODS

A total of 59 patients attended in NINMAS at Bangabandhu Sheikh Mujib Medical University (BSMMU) campus, during July 2015 and June 2016, were included in this study. Patients underwent nuclear medicine imaging for ^{99m}Tc DTPA renogram along

with GFR estimation were enrolled in this study. Patients under 18 years of age, severely ill patient, pregnant and lactating mother were excluded. The respondents were briefed about the details of the study procedure and radioisotopes were administered maintaining internationally recommended safe procedures.

Good hydration and voiding were maintained prior to the beginning of study. Approximately 111 MBq to 185 MBq (3 to 5 mCi) of ^{99m}Tc DTPA in equal volume were prepared in two syringes, marked as standard and patient dose.

Routine dynamic renal scan was performed after intravenous injection of patient dose. After scintigraphy, the site of injection on the arm was scanned under the gamma camera. The residual radioactivity at the injection site was less than 0.1% in all subjects.

GFR for each of the patient was measured by modified Gates algorithm automatically by the computer available software (11).

Blood was drawn at 60_{th} and 180_{th} minute post injection from the contra lateral arm and centrifuged at room temperature for 5 minutes. The standard dose was prepared by diluting in normal saline (0.9% NaCl). Equal aliquots of plasma and standard were counted in single well gamma well counter for 1 minute.

GFR was calculated by using the Russell's equation

$$(9): \left[\frac{Q \ln(P_1/P_2)}{T_2 - T_1} \exp \frac{T_1 \ln P_2 - T_2 \ln P_1}{T_2 - T_1} \right]$$

Where, Q = total injected dose counts (cpm), P_1 = activity (cpm/mL) at the time of T1, P_2 = activity (cpm/mL) at the time of T2, T_1 = 60 min and T_2 = 180 min.

GFR was corrected to the standard BSA using the equation (12):

GFRCorr = GFR $\times$ (1.73/BSA m2)

Values of BSA were estimated from the height and weight using the Haycock's formula (13): BSA (m^2) = $0.024265 \times Wt^{0.5378} \times Ht^{0.3964}$

Two different GFR values obtained by Gates method and Russell's DPSM were analyzed to assess the agreement and comparison between the GFR values.

Quality control of all used equipments (gamma camera, dose calibrator, well counter etc.) was performed routinely. The radiochemical purity of ^{99m}Tc DTPA was maintained > 95%.

RESULTS

The study included 59 patients (32 males, 27 females) with mean age 37.9 ± 13.7 years (range, 18-80 years), mean height 157.8 ± 8.4 cm and mean weight 59.2 ± 9.4 kg.

The most common clinical diagnosis was unilateral hydronephrosis (right sided hydronephrosis: 37.3% and left sided hydronephrosis 35.6%) and 72.9% of the patients had serum creatinine level higher than the reference range.

In the present study among 59 patients, more than half (52.5%) patients had GFR level < 90 mL/min/1.73 m2 and mean GFR value was found 82.2 ± 27.4 mL/min/1.73m2 evaluated by Gates method (Table 1). On the other hand, 59.3% of the total patients had GFR level < 90 mL/min/1.73 m2 and the mean GFR value was found 82.8 ± 24.1 mL/min/1.73 m2 evaluated by DPSM (Table 2).

There was a significant strong positive correlation between the GFR level measured by Gates method and DPSM (Figure 1). Bland-Altman plot for Gates method and DPSM for GFR measurement shows the mean difference of GFR measured by Gates method and DPSM was $- 0.6 \pm 15.22$ mL/min/1.73 m2. 95% of differences were found in between $- 30.44$ mL/min/1.73 m2 and 29.24 mL/min/1.73 m2 (Figure 2).

**Table 1: GFR distribution of the studied patients evaluated by Gates method (n = 59)**

Gates GFR (mL/min/1.73m²)	Number of patients	Percentage	Mean ± SD	(min, max)
< 90	31	52.5		
90-120	23	39.0	82.2 ± 27.4	29.3,129.7
> 120	5	8.5		

Table 2: GFR distribution of the studied patients evaluated by DPSM (n = 59)

DPSM GFR (mL/min/1.73m²)	Number of patients	Percentage	Mean ± SD	(min, max)
< 90	35	59.3		
90-120	21	35.6	82.8 ± 24.1	25.3,126.9
> 120	3	5.1		
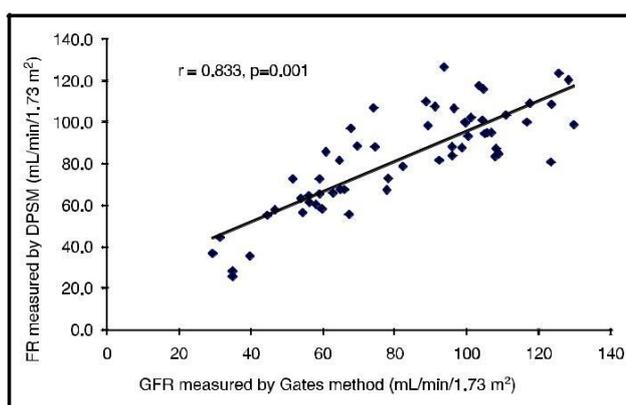
Figure 1: Scatter diagram showing positive correlation (r = 0.833; p = 0.001) between the GFR measured by Gates method and DPSM.
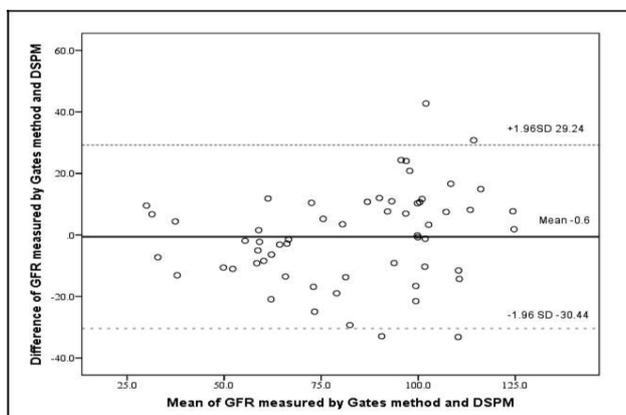
Figure 2: Scatter diagram showing agreement between the GFR measured by Gates method and DPSM

DISCUSSION

In this current study it was observed that more than one third (39.0%) patients belonged to age ≤ 30 years and the mean age was found 37.9 ± 13.7 years. Muammaer et al. found the median age was 34 years with range from 20 to 52 years, which is comparable with the current study (6). Younis et al. and Ayan et al. observed

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similar age ranged from 25 to 70 years and 22 to 65 years respectively (14, 15).

In this present study more than half (54.2%) of the patients were male and 45.8% patients were female. Aydin et al. found 59 males and 25 females in their study (16). Similarly, male predominant also observed by Younis et al. and Itoh (14, 17).

Jackson et al. reported that the Gates method tended to overestimate GFR in comparison to the dual sample in vitro method (18). Itoh also reported overestimated GFR values with the Gates method and indicated that the overestimation might be attributable to insufficient correction for background activity in the kidney (17). In this study, in case of Gates method, it was observed that more than half (52.5%) patients had GFR level of < 90 mL/min/1.73 m2 and the mean GFR was found 82.2 ± 27.4 mL/min/1.73 m2 with ranged from 29.3 to 129.7 mL/min/1.73 m2. Younis et al. found GFR measurement) varied from 42.3 to 98 mL/min/1.73 m2 with mean value 74.1 ± 14.5 mL/min/1.73 m2 by using Gates method (15). Similar findings also reported by Hephzibah et al. (3), which are comparable with the current study. On the other hand Ayan et al. found the mean GFR was 105.25 ± 16.12 mL/min/1.73m2, which is higher than the current study (15).

Zuo et al. reported that the DPSM should be used in order to obtain reliable reference GFR values, when GFR is less than 45 mL/min/1.73m2 (19). In this study, almost two third (59.3%) patients had GFR level < 90 mL/min/1.73m2 and the mean GFR was found 82.8 ± 24.1 mL/min/1.73m2 with range from 25.3 to 126.9 mL/min/1.73m2 measured by DPSM. Younis et al. found GFR by using DPSM with range from 39.2 to 139.6 mL/min/1.73 m2, which is comparable with the current study (14).

In this current study, a strong positive correlation (r = 0.833; p = 0.001) was observed in between the GFRs values, measured Gates method and DPSM, which is closely resembled with several studies (10, 14, 15).

In this present study it was observed that mean difference of GFR measured by Gates method and DPSM was small. Similar findings also observed by Ayan et al. (15).

CONCLUSION

In this study most of the patients had GFR values < 90 mL/min/1.73m2 evaluated by both the Gates method and DPSM. There is strong positive correlation between Gates method with DPSM. With Bland and Altman analysis mean difference between the methods was small. So, Gates method and DPSM can reflect GFR almost equally and can be used interchangeably.

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