BIO-DISTRIBUTION AND DOSIMETRY OF A RENAL AGENT IN NORMAL BANGLADESHI SUBJECTS

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ABSTRACT: Radiation absorbed dose estimation was performed on eleven normal patients who were in a process of routine diagnostic investigation of the renal function. Bio-kinetics and bio-distribution of ^{99m}Tc-DTPA in patients was evaluated by dual-head gamma camera imaging and blood-plasma sample counting method. Radiation dose estimations were performed using standard MIRD techniques and bio-distribution of different organ was estimated by drawing region of interest (ROI) according to MIRD phantom model [1]. From the time-activity curves, cumulative activities and residence times of ^{99m}Tc-DTPA in the kidneys, brain, upper large intestine (ULI), small intestine (SI), lower large intestine (LLI), stomach, heart, liver, lung and remainder of the body was calculated. Using the information of residence times of the total body and urinary bladder voiding at 2.4 hours on MIRD 12 absorbed dose for the ^{99m}Tc-DTPA in different target organs of the body was measured [2]. The estimated average absorbed dose to the kidneys as a target organ in normal Bangladeshis are 5.71E-03 mGy/MBq of ^{99m}Tc-DTPA which is closer to the ICRP 53 and other recent published data. The calculated effective dose equivalent and effective dose was found 5.72E-03 mSv/MBq and 4.89E-03 mSv/MBq respectively.

Keywords: Bio-Kinetics, Bio-Distribution; Absorbed Dose; ^{99m}Tc-DTPA, Effective Dose Equivalent, Effective Dose.

1. INTRODUCTION

^{99m}Tc Diethylene Triamine Pentaacetic Acid (DTPA) is a biological renal agent is completely eliminated by glomerular filtration after intravenous administration and no tubular secretion is occurred when blood enters the glomerulus of the kidneys through afferent arteriole [3]. It is also a soluble molecule and a chelate with a molecular weight of 500, and its binding to the protein is less and are nearly in between 3% to 5% [3]. ^{99m}Tc-DTPA used in this study is formed by addition of ^{99m}Tc as pertechnetate to a lyophilized mixture of $CaNa_3DTPA$ and $SnCl_2$. The drug meets requirement for measuring glomerular filtration rate (GFR) i.e.; renal functions of the biological system. After intravenous injection it rapidly penetrates capillary walls entering extra-cellular fluid by 3.8 minutes, and does not enter cells because of lipid insolubility and negative charge [3]. Before the intravenous administration measured chromatographic radiochemical purity was $\geq$ 95%. The aim of this study is to find more accurate and specific results of radiation absorbed dose, for ^{99m}Tc-DTPA, for the kidneys as a target organ subject to normal Bangladeshis.

2. MATERIAL AND METHODS

Eleven normal patients received 185 MBq of ^{99m}Tc DTPA by twice at an interval of at least four days as single intravenous injections of the radiopharmaceuticals. At first administration of the drug bio-kinetics was determined through dual-head gamma camera images acquired posterior position over the kidneys and the data was stored in the gamma camera computer at 3 sec per frame intervals for 3 min plus 60 sec per frame intervals for 27 min, for a total time of 30 min. The activity in both kidneys as a function of time was estimated from drawing region of interest (ROI) on the kidneys. Blood or plasma samples were taken at about 5 min intervals for the first half hour and at about 60, 90, 120, 150 and 180 min. Plasma samples were analyzed to see the initial whole body retention of the radiopharmaceuticals, because DTPA are not incorporated into red cells to any significant of degree [4, 5].

In the second administration whole body images was taken from both anterior and posterior position after immediate administration of ^{99m}Tc DTPA. Drawing region of interest (ROI) the bio-distribution of the drug in the source organs the kidneys, brain, upper large intestine (ULI), small intestine (SI), lower large intestine (LLI), stomach, heart, liver, lung and other tissues are measured in term of percentage uptake. For dose calculation it is assumed that the source organs are kidneys, bladder contents and the remainder of the body as described in the MIRD 12. The remaining body activity is assumed to be distributed uniformly and its residence time is estimated by subtracting kidney residence time from that of total body less bladder content. For this purpose we have used the MIRD 12 values of residence times for total body and the bladder content at 2.4 hour. Effective dose equivalent [6] has been calculated as the weighted sum of the dose equivalent to the appropriate tissues at risk using risk weighting factors as defined in ICRP 30 and effective dose [7] is calculated according to data of the publication of ICRP 60.
The methodology used for internal dose calculations is actually provided by the Medical Internal Radiation Dose Committee (MIRD) of the Society of Nuclear Medicine (SNM) in the United States and its many collaborators and consultants and is referred to as the "MIRD schema" is as below.

2.1 The MIRD Schema

The conventional method of calculating absorbed dose delivered internally is known as the MIRD schema [8]. The first step in applying the MIRD schema is to identify all the source and target organs. The average dose $\overline{D}$ (in Gy) delivered to a target of mass m (in kg) is given by

$$\overline{D} = \frac{\tilde{A}}{m}\sum_i \phi_i \Delta_i \qquad \ldots\ldots\ldots (1)$$

Where $\tilde{A}$ is the cumulative activity in the source (in Bq s); ϕ_i is the absorbed fraction for a given energy E_i, and Δ_i is the equilibrium dose constant for radiation of type i (in Gy kg/Bq/s). Values of ϕ_i and Δ_i derived from Monte Carlo calculations, can be found from MIRD tables [1, 9].

2.2 Cumulative Activity

The cumulative activity $\tilde{A}$ is the total number of radioactive disintegrations, which occur in the source organ, and depends on: the administered activity; the uptake of, retention by and excretion from the organ; and the physical decay of the radionuclide.

$\tilde{A}$ is equal to the time integral of the activity in the source organ:

$$\tilde{A} = \int_0^{\alpha} A(t)dt \qquad \ldots\ldots\ldots (2)$$

Where A(t) is the area under the time-activity curve .

For ^{99m}Tc-DTPA, the tracer uptake is instantaneous but clearance by both physical and biological decay is significant. Therefore the cumulated activity in the source organ for ^{99m}Tc-DTPA can be written as:

$$\tilde{A} \approx 1.44\, T_e A_0 \qquad \ldots\ldots\ldots (3)$$

Where T_e is the effective half life of the radiotracer and A_0 is the activity initially present in the source organ [10]. There is more than one component to the biological excretion curve, and each component has an effective half-life given by equation-(3) for that component.

2.3 Residence Time (τ)

The residence time τ which is defined as the average time that the administered activity spends in the source organ, and is given by

$$\tau = \frac{\tilde{A}}{A_a} \qquad \ldots\ldots\ldots \quad (4)$$

Where A_a is the administered activity.

2.4 S-Factors

We can write the equation (1) as follows:

$$\bar{D} = \tilde{A}S \qquad \ldots\ldots\ldots (5)$$

Where the mean dose per unit cumulated activity is,

$$S = \frac{1}{m}\sum_i \phi_i \Delta_i \qquad \ldots\ldots\ldots (6)$$

S-factors have been tabulated for a variety of radionuclides and for different source/target configurations in both standard men [11] and children. Finally, these cumulated activities were converted into residence time and using equation-(6) absorbed doses was calculated.

3. RESULTS & DISCUSSION

We performed internal dosimetry on eleven normal adults who were in a procedure of routine diagnostic investigation of renal function with ^{99m}Tc-DTPA. To ensure the patient has normal renal function, clinical investigations e.g. blood for urea, creatinine, and ultrasonogram of kidneys with physical investigations were done for each patient. Bio-distribution for ^{99m}Tc-DTPA in source organs at different times is evaluated from whole body images of Dual Head ECAM gamma camera. The bio-kinetics of both kidneys as a function of time was estimated from drawing region of interest (ROI). For the simplicity of dose calculation; only kidneys, bladder contents and the remainder of the body are assumed that the source organs as in MIRD 12. The remaining body activity is assumed to be distributed uniformly and its residence time is estimated by subtracting kidney residence time from that of total body less bladder content. For this purpose we have used the MIRD 12 value of total body and the bladder content at 2.4 hour. The average absorbed dose to kidneys as a target organ was found 5.71E-03 mGy/MBq for ^{99m}Tc-DTPA in normal Bangladeshis which is closer to the published ICRP 53 data's. Calculated effective dose equivalent and effective dose was respectively 5.72E-03 mSv/MBq and 4.89E-03 mSv/MBq. Effective dose equivalent and effective dose has been calculated as the weighted sum of the dose equivalent to the appropriate tissues at risk using risk weighting factors as defined in ICRP 30 and according to data of the publication of ICRP 60, respectively. The dosimetric data in this study was tabulated in Table-II may be different from the published reported data in ICRP-53 due to different metabolic rate, biological excretion and absorbed dose of Bangladeshis from other countries.

Most of the dosimetric data published in ICRP-53 have been summarized based on the bio-kinetic model or extrapolation from animal data, in which lots of assumptions are considered [12]. Therefore direct measurements can provide more accurate bio-kinetic data of activity as well as the absorbed doses. NCRP also recommended about the direct measurements of the activity and absorb doses [13]. In this study we have demonstrated a direct method to obtain bio-distribution and the bio-kinetics of ^{99m}Tc-DTPA in normal Bangladeshis. Then with using the residence times of total body and urinary bladder at 2.4 hour

on MIRD 12, absorbed dose at different target organs are calculated. However, to obtain accurate bio-kinetic data of organ activities and absorbed doses for gamma photon, MIRD schema may provide better accuracy.

4. **CONCLUSION**

Radiation absorbed dose determines the amount of radiation energy deposited in tissue by radio-nuclides within the body. Bio-kinetics and bio-distribution of ^{99m}Tc-DTPA in the patients can be evaluated by dual-head gamma camera imaging and blood-plasma sample counting. ^{99m}Tc-DTPA gamma camera based, absorbed dose determination is feasible and calculation of the absorbed dose in the target organ with the use of MIRD schema is adequate. In this study the absorbed doses per unit of activity of ^{99m}Tc-DTPA in the kidneys as a target organ are found comparable to the most of the published data.

Table I(A): Cumulated Activities for different Source Organs in unit of (μCi.hr.).

Patient	Kidneys	Brain	ULI	SI	LLI
1.	452.63	477.82	290.33	605.41	332.53
2.	427.59	492.20	315.89	607.97	379.61
3.	456.45	600.63	273.81	628.00	352.07
4.	439.24	567.77	299.90	632.01	372.45
5.	426.67	528.60	325.87	661.64	384.46
6.	463.55	587.58	314.37	623.51	356.20
7.	459.16	507.14	305.12	650.44	344.27
8.	395.72	518.67	292.93	700.72	375.69
9.	468.95	523.76	311.08	616.50	363.32
10.	463.84	506.13	321.05	664.38	383.94
11.	441.52	513.76	317.65	606.88	366.42
Average $\tilde{A}$	445.03	529.46	306.18	636.13	364.63

Table I(B): Cumulated Activities for different Source Organs in unit of (μCi.hr.).

Patient	Stomach	Heart Wall	Lung	Liver	Remainder of the body
1.	239.24	160.49	433.62	912.81	1872.05
2.	242.34	154.92	400.06	994.09	1856.77
3.	255.25	143.54	443.31	965.75	1927.28
4.	240.46	146.58	429.30	1025.14	1912.06
5.	237.60	151.55	407.81	974.62	1941.04
6.	257.06	152.26	439.06	967.89	1965.62
7.	237.84	140.38	422.41	1018.71	1848.11
8.	276.33	171.53	416.57	1000.61	1940.66
9.	250.69	148.36	445.95	1030.21	1942.08
10.	268.03	156.46	437.66	975.83	1914.65
11.	256.97	163.75	428.11	1031.16	1907.31
Average $\tilde{A}$	251.07	153.62	427.62	990.62	1911.60

Table-II: Estimated Absorbed doses from an I.V. administration of ^{99m}Tc DTPA.

Target Organs	Estimated Radiation Dose	
	mGy/MBq	rad/mCi
Adrenal	1.71E-03	6.32E-03
Brain	1.30E-03	4.80E-03
Breast	1.10E-03	4.07E-03
Gallbladder Wall	2.19E-03	8.09E-03
LLI Wall	4.60E-03	1.70E-02
Small Intestine	2.78E-03	1.03E-02
Stomach	1.85E-03	6.83E-03
ULI Wall	2.46E-03	9.10E-03
Heart Wall	1.69E-03	6.25E-03
kidneys	5.71E-03	2.11E-02
Liver	1.80E-03	6.68E-03
Lungs	1.49E-03	5.50E-03
Muscle	1.11E-03	4.12E-03
Ovaries	5.54E-03	2.05E-02
Pancreas	1.76E-03	6.51E-02
Red Marrow	1.94E-03	7.18E-03
Bone Surface	2.49E-03	9.21E-03
Spleen	1.80E-03	6.68E-03
Testes	3.98E-03	1.47E-02
Thymus	1.51E-03	5.58E-03
Thyroid	1.52E-03	5.64E-03
Urinary Bladder Wall	3.82E-02	1.41E-01
Uterus	9.27E-03	3.43E-02
Effective Dose Equivalent (mSv/MBq or rem/mCi)	5.72E-03	2.12E-02
Effective Dose (mSv/MBq or rem/mCi)	4.89E-03	1.81E-02

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