Radiopharmaceutical Fractionation as a Crisis Management Strategy: Experience with ^{99m}Tc-DTPA

[1]Sanjida Islam, [1]Md Ariful Islam, [1]Sanchoy Chandra Biswasarma, [1]Afifa Khatun, [2]Mohammad Anwar-Ul Azim, [1]Md. Saiful Islam, [1]Most. Layla Saroware Banu

[1]National Institute of Nuclear Medicine and Allied Sciences (NINMAS)
[2]Planning & Development Division, Bangladesh Atomic Energy Commission (BAEC)

Correspondence Address : Sanjida Islam, Scientific Officer, NINMAS, Block-D, BMU campus, Shahbag, Dhaka-1000. Email: sanjida.ru@outlook.com

ABSTRACT

Imaging with ^{99m}Tc-DTPA is a standard technique for assessing renal function. A single vial of DTPA cold kit contains sufficient amount of ligand for multiple dose preparation. This study was conducted to optimize kit utilization during a nationwide supply shortage by adapting kit fractionation approach. In this study a full vial of DTPA kit was aseptically divided into three aliquots using 0.9% and preserved at 4°C. Then the fraction was used over multiple days, with each fraction radiolabeled using freshly eluted ^{99m}Tc. Radiochemical purity (RCP) was assessed by ITLC-SG and consistently remained ≥ 95% in all fractions. The average of % RCP of DTPA fractions 96.77%. All clinical studies produced satisfactory image quality without the need for repeat imaging. This approach of kit fractionation led to reduced kit consumption, minimized waste, and improved operational efficiency. Additionally, this method can be considered as annual cost reduction method.

Keywords: Kit Fraction, 99mTc-DTPA, Renal Scintigraphy

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INTRODUCTION

In nuclear medicine (NM) practice, dynamic renal scintigraphy utilizing Technetium-99m DTPA (^{99m}Tc-DTPA) is one of the most widely used diagnostic procedures for the evaluation of renal function. DTPA (Diethylenetriamine pentaacetic acid) with ^{99m}Tc acts as an ideal agent as it produces a complex that is primarily cleared from the body through glomerular filtration without significant tubular secretion or reabsorption. Renal scintigraphy with ^{99m}Tc-DTPA is considered a standard functional imaging technique due to its favorable physical characteristics, including optimal gamma emission, short half-life, and low radiation dose to patients (1,2).

Conventionally the preparation of ^{99m}Tc-DTPA typically involves reconstitution of commercially available full lyophilized cold kit vial followed by radiolabeling with freshly eluted sodium pertechnetate obtained from a ^{99m}Tc-generator. As a result, unused portions are often discarded, leading to unnecessary wastage and increased operational costs (3).

During recent periods of nationwide disruption in the supply chain of DTPA cold kits, many nuclear medicine centers faced significant challenges in maintaining uninterrupted renal scintigraphy services. Limited kit availability resulted in increased patient waiting time and potential delays in clinical decision-making. Under such circumstances, radiopharmacy practices may adopt alternative resource-optimization strategies to sustain clinical services. Radiopharmaceutical kit fractionation is one of the such method where the cold kit is aseptically divided into multiple sterile aliquots using 0.9% NaCl. Later the fraction can be labeled separately with ^{99m}Tc. Previous studies have demonstrated that cold kits often contain excess ligand relative to the essential radiolabeling activity, allowing successful fractionation while maintaining acceptable radiochemical purity and diagnostic image quality (4).

The adoption of fractionation approach of DTPA cold kit preparation during a nationwide DTPA kit scarcity is described in this paper, which also assesses its feasibility as an affordable way to maintain nuclear medicine practice.

MATERIALS AND METHODS

Study Design:

This study was conducted as a prospective observational implementation in the radiopharmacy unit of National Institute of Nuclear Medicine & Allied Sciences during a

period of nationwide shortage of DTPA cold kits. The goal was to assess the actual condition of radiopharmaceutical fractionation for the preparation of ^{99m}Tc-DTPA used in routine dynamic renal scintigraphy diagnostic procedure. The study focused on maintaining uninterrupted diagnostic services while minimizing kit wastage and operational costs.

Radiopharmaceutical preparation:

The commercial lyophilized DTPA cold kits contain Diethylenetriamine pentaacetic acid 35 gm, Tin (II) chloride dehydrate 2 gm. For fractionation, 0.6 ml of sterile saline was added to the mother vial of DTPA. After complete dissolution, the vial was aseptically divided into 3 sterile fractions having 0.2 ml in each vial and labelled as vial 1, 2 and 3. The vial 1 was used the same day of fraction. Then the vial 2 and 3 were stored at 4°C until use. For radiolabeling, an appropriate volume of freshly eluted sodium pertechnetate containing ^{99m}Tc was added to each fraction. The mixture was gently mixed and incubated at room temperature for 15 minutes as specified by the manufacturer. This procedure allowed multiple doses of ^{99m}Tc-DTPA to be prepared from a single cold kit while maintaining appropriate labeling conditions (5).

Radiochemical purity of the prepared ^{99m}Tc-DTPA was evaluated using Instant Thin Layer Chromatography technique (ITLC-SG). The chromatography strips were developed using two different solvent systems methyl ethyl ketone and 0.9% saline to separate free pertechnetate and hydrolyzed reduced technetium from the labeled complex.1µl of sample was placed into two different strips and placed into the solvent tank. After development the strips are air dried and cut into two pieces. The activity of both strips was measured using dose calibrator (6).

Patients referred to scintigraphy division for dynamic renal scintigraphy were received reconstituted ^{99m}Tc-DTPA fraction kit on 1st, 2nd and 5th day of fractionation. In order to examine renal perfusion, function, and drainage, imaging was carried out utilizing a gamma camera system in accordance with standard renal scintigraphy protocols, including dynamic acquisition and time–activity curve analysis.

Finally, all images were assessed independently by two professional nuclear medicine physician following institutional protocol. To create time-activity curves and evaluate renal function and drainage, regions of interest (ROI) were drawn manually over the kidneys and background. Visual evaluation of the image quality revealed that all studies were diagnostically satisfactory and did not require repeat imaging (7).

RESULTS

Radiochemical Purity:

The percentages of RCP of 21 DTPA cold kit fractions prepared from 7 mother DTPA vials after reconstitution with freshly eluted ^{99m}Tc from generator were analyzed. All fraction preparations consistently achieved acceptable radiochemical purity (RCP ≥ 95%) as determined by ITLC-SG analysis (Figure 1). The mean radiochemical purity (%RCP) was 96.77±1.12% (n=21), indicating consistent radiolabeling quality of the fractionated DTPA kits.

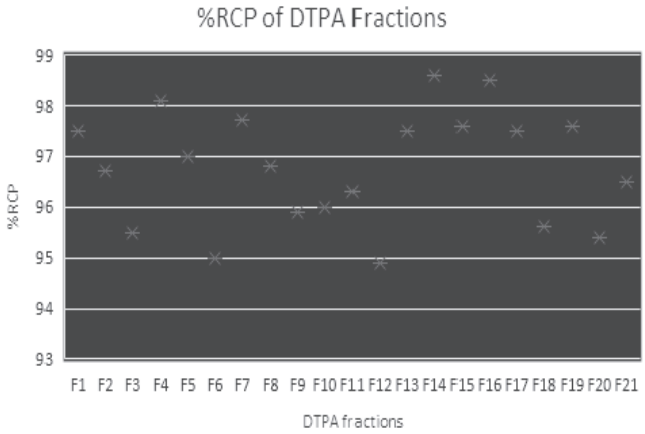

Figure 1: Percentage of radiochemical purity (% RCP) of twenty-one (21) fractionated vials of ^{99m}Tc-DTPA radiopharmaceuticals obtained from seven (7) mother vials.

Calculation of Radiochemical Purity:

For each system, RCP and impurities were calculated using the following equations:

In Saline (0.9% NaCl): In this system, ^{99m}Tc-DTPA remains at the solvent front, where the ^{99m}Tc hydrolyzed and reduced from remains in the bottom.

$$\% \text{ of } {}^{99m}\text{Tc HR} = \frac{A}{Total} \ 100$$

In MEK: In this system, ^{99}Tc-DTPA remains at the origin, where the free TcO_4- from remains in the solvent front.

$$\% \text{ free } TcO_4\text{-} = \frac{A}{Total} \ 100$$

$$\text{RCP } (\%) = 100 - (\% \text{ of } {}^{99m}\text{Tc HR} + \% \text{ free } TcO_4^-)$$

Kit utilization:

A substantial reduction in DTPA kit consumption was observed following the implementation of the fractionation strategy. Under the conventional practice, a full vial of the DTPA kit was utilized for a single scheduled day, irrespective of the number of patients, leading to inefficient use of resources. In contrast, the fractionation approach allows a single vial to be divided into three aliquots, enabling its use over three separate days. This facilitates more flexible patient scheduling while ensuring optimal utilization of the radiopharmaceutical.

As a result, the total number of DTPA kits required annually can be significantly reduced, making this approach a practical and cost-effective strategy for resource-limited settings. Furthermore, this method contributes to minimizing both radiopharmaceutical wastage and unnecessary radiation exposure, thereby enhancing overall operational efficiency and safety in nuclear medicine practice.

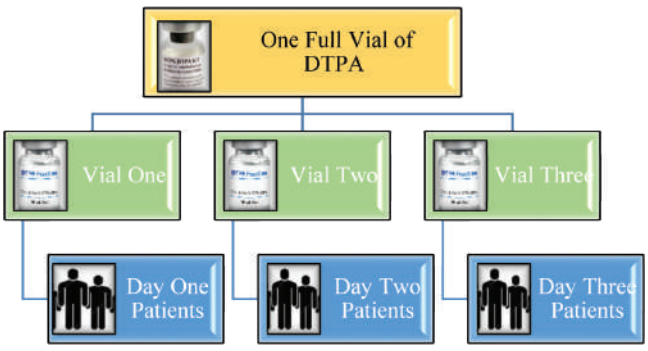

Figure 2: Fractionation of a single DTPA vial for multi-day clinical use

Clinical Performance:

All the renal scintigraphy images were acceptable for clinical interpretation. No repeat imaging was done due to suboptimal quality of radiopharmaceutical.

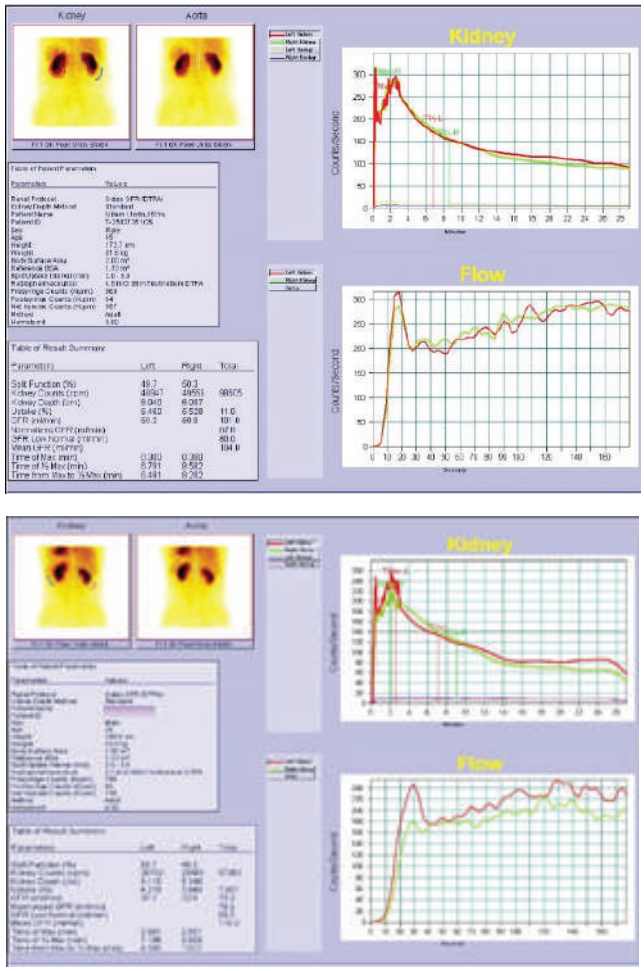

Figure 3: Renal scintigraphy images of two adult patients administering reconstituted ^{99m}Tc-DTPA fractions.

DISCUSSION

This study validates that fractionation approach of a single DTPA kit into multiple aliquots is a practical and cost-effective strategy for optimizing radiopharmaceutical utilization in routine nuclear medicine practice. In usual practice a full vial of ^{99}Tc-DTPA is used for a single scheduled day patient. This often leads wastage of the total available activity. In contrast, the fractionation approach allows division of the vial into smaller aliquots in aseptic manner that can be used over multiple days, thereby improving resource efficiency.

The maintenance of radiochemical purity (RCP) and sterility over time are the main challenges in implementing kit fractionation approach. In this

investigation, RCP was assessed using Instant Thin Layer Chromatography–Silica Gel (ITLC-SG), and acceptable purity levels were maintained throughout the fractionated usage period. This finding is consistent with established guidelines that emphasize the importance of routine quality control to ensure the safety and efficacy of radiopharmaceuticals (8).

Fractionation allows for more flexible patient scheduling over several days which is especially useful in facilities with fluctuating patient loads or a limited supply of radiopharmaceuticals. This strategy is particularly relevant in environments with limited resources, because annual operational expenses can be significantly decreased by reducing the frequency of kit purchases without sacrificing diagnostic accuracy.

Another important advantage of the fractionation method is the reduction of radioactive waste. By utilizing a greater proportion of the prepared radiopharmaceutical, both chemical and radioactive waste generation can be minimized. This method allows to follow radiation safety principles ALARA as it minimizes unnecessary radiation exposure to both staff and the environment (9).

However, certain limitations must be considered. It is recommended to use the fractions within one week. The extended use of a reconstituted vial requires strict adherence to aseptic handling techniques to prevent microbial contamination.

Overall, the findings suggest that fractionation of DTPA kit is a feasible and cost-effective strategy. This approach helped us to continue renal scintgraphy during DTPA cold kit supply disruption. Again, fractionation of DTPA cold kit opens a footpath to reduce costs, minimize wastage, and improve workflow efficiency in nuclear medicine departments. With appropriate quality control and radiation safety measures, this approach can be adopted as a standard practice, particularly in settings having low patients load and also facing supply limitations.

CONCLUSION

The present study was an attempt to compensate the supply shortage with the limited inventory of DTPA cold kit to continue renal scintigraphy procedure at our center.

The observations revealed that if fractionated with highest care all the three fractions from a single full DTPA cold kit produced almost similar results. Although the present study reported the feasibility of cold kit fractionation. However, for each fractionation quality tests must be conducted before the administration of the radiopharmaceutical. In future this method can be widely implemented in centers with nonuniform patients' number, low availability of ^{99m}Tc. Again, the adaptation of fraction method can also be considered during annual cold kit requirement calculation which can contribute to national profit.

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