Initial Experience in the Use of Technetium-99 Metastable Hydroxymethylene Diphosphonate as an Alternative Ventilation Agent During Periods of Interim Shortage

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Abstract
Sporadic supply interruptions of select radiopharmaceuticals on the global market require consideration of alternative agents to support continuity of essential nuclear medicine examinations. During an acute shortage of Xenon-133 and technetium-99 metastable (Tc-99m) diethylene-triamine-pentaacetate (DTPA), our institution used aerosolized Tc-99m hydroxymethylene diphosphonate (HDP), a radiopharmaceutical traditionally used in bone scintigraphy, in lieu of traditional ventilation agents, for two cases of suspected pulmonary embolism. Similar to Tc-99m-DTPA, Tc-99m-HDP was readily available and easily compounded in our pharmacy, and tolerated well by patients. Identical delivery equipment was used for administration of Tc-99m-HDP as that used in Tc-99m-DTPA, and thus, there was no requirement for a negative pressure room. Similar to Tc-99m-DTPA and unlike Xenon-133, Tc-99m-HDP allowed direct comparison of all 8 ventilation-perfusion images. In addition, the cost per dose of Tc-99m-HDP proved to be less than Tc-99m-DTPA. Despite these favorable characteristics of Tc-99m-HDP, our experience identified an important challenge in obtaining an optimal flux override ratio of > 3 in a reasonable time frame while obtaining ventilation and perfusion images sequentially despite reversing the imaging order in an attempt to overcome this limitation. Although our experience with Tc-99m-HDP in these two cases was favorable, more clinical experience and investigation are warranted before Tc-99m-HDP can be incorporated as a standard alternative ventilation agent.

Keywords: Hydroxymethylene diphosphonate, pulmonary embolism, radiopharmaceutical, ventilation-perfusion scan

Access this article online
Quick Response Code:
Website: www.wjnm.org
DOI: 10.4103/1450-1147.203063

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How to cite this article: Young CR, Prasad K. Initial experience in the use of technetium-99 metastable hydroxymethylene diphosphonate as an alternative ventilation agent during periods of interim shortage. World J Nucl Med 2017;16:156-9.
Introduction

Recent global shortages of select radiopharmaceuticals have led to consideration of alternative methods by which to conduct essential nuclear medicine examinations. Ventilation-perfusion (VQ) scans for the evaluation of pulmonary embolism (PE) are ordinarily conducted with technetium 99-metastable (Tc-99m) macroaggregated albumin (MAA) as the perfusion agent and Xenon-133 gas or the radioaerosol Tc-99m diethylene-triamine-pentaacetae (DTPA) as the ventilation agent. At our institution, we performed two VQ scans using Tc-99m hydroxymethylene diphosphonate (HDP) during acute shortages of standard ventilation agents using two different protocols on the same day. Ventilation images were performed either before or following perfusion images using a commercially available radioaerosol lung imaging system (Insta/Vent Plus™, Medi/Nuclear Corporation, Baldwin Park, CA, USA).

Case Reports

Case 1
A 53-year-old female with a suspected PE received 79.18 megabecquerels (MBq) of intravenous (IV) Tc-99m-MAA, followed by 2886 MBq of radioaerosolized Tc-99m-HDP, along with a routine chest radiograph (CXR) [Figure 1], as part of a VQ scan. A series of planar VQ images obtained from eight orientations demonstrated no unmatched defects and successfully excluded PE [Figure 2]. Posterior projection images revealed counts of 1973.74 counts/seconds (c/s) in perfusion and 3197.68 c/s in ventilation yielding a flux override ratio of 1.62 with image quality similar to Tc-99m-DTPA.

Case 2
An 81-year-old female with a history of acute on chronic kidney disease and a recently diagnosed right hilar mass [Figure 3] received 2960 MBq of Tc-99m-HDP radioaerosol followed by 301.2 MBq of Tc-99m-MAA IV. A CXR [Figure 4] obtained in conjunction with this examination revealed chronic obstructive pulmonary disease with no acute findings. Anterior planar VQ images [Figure 5] demonstrated matched the absence...
of ventilation and perfusion of the right middle and lower lung with matched nonsegmental defects in the right upper and left lung. Posterior projection images revealed counts of 3408.09 c/s in ventilation and 8257.00 c/s in perfusion yielding a flux override ratio of 2.4 with image quality similar to Tc-99m-DTPA. Tc-99m-HDP allowed the successful exclusion of PE and diagnosis of critical findings of complete middle and lower lobe bronchial obstructing lesion which was not evident on concurrently performed computed tomography imaging.

**Discussion**

During an acute shortage of Xenon-133 and Tc-99m-DTPA, our institution used aerosolized Tc-99m-HDP, a radiopharmaceutical traditionally used in bone scintigraphy, in lieu of traditional ventilation agents, for two cases of suspected PE.

Similar to Tc-99m-DTPA, Tc-99m-HDP was easily available and compounded in our pharmacy, and tolerated well by patients. In addition, since the delivery equipment was identical to that used in Tc-99m-DTPA, there was no requirement for a negative pressure room. Tc-99m-HDP also allowed direct comparison on all 8 ventilation-perfusion images, unlike Xenon-133. Tc-99m-HDP provided addition cost benefit over Tc-99m-DTPA. The two protocols were able to achieve a flux override ratio of 1.6 and 2.4, but we experienced challenges in obtaining an optimal flux override ratio of >3\cite{5} in a reasonable time frame.

Other groups have explored the use of Tc-99m pyrophosphates as ventilation agents with successful outcomes when compared to the accepted standard radioaerosol, Tc-99m-DTPA.\cite{6} Readily available Tc-99m-HDP is currently indicated for bone scans, and we successfully used it off-label as a ventilation agent during an acute shortage.\cite{7} Interestingly, the use of Tc-99m-DTPA as a ventilation agent is also off-label.\cite{8} Furthermore, Tc-99m-HDP is approximately thirty percent less expensive than Tc-99m-DTPA.\cite{9} In some countries, the use of radiopharmaceuticals may be limited to their approved indications which could limit the use of Tc-99m-HDP for lung ventilation imaging.

**Conclusion**

Readily available Tc-99m-HDP enabled adequate VQ imaging over a period of acute shortage and provided continuity of patient care. Further exploration and procedural refinement are needed to overcome our limitations of obtaining an optimal flux override ratio before incorporation of Tc-99m-HDP as a standard alternative ventilation agent.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

**References**
