Effect of Solvent Flow Rate in Mini-Column Testing of ^{99m}Tc-Mertiatide

James A. Ponto, MS

Department of Radiology, University of Iowa Hospitals and Clinics and University of Iowa College of Pharmacy, Iowa City, Iowa

Objective: The recommended method for radiochemical purity testing of ^{99m}Tc-mertiatide involves the use of a C-18 solid-phase mini-column cartridge. The mertiatide package insert states that the solvents should be "pushed through the cartridge slowly," but a flow rate is not specified. The mini-column cartridge instruction sheet recommends flow rates of 5–10 and 2–10 mL/min for conditioning and for elution, respectively, of the cartridge. The purpose of this study was to evaluate the effect of different flow rates on determining the radiochemical purity of ^{99m}Tc-mertiatide.

Methods: Radiochemical purity was tested on 10 consecutive vials of ^{99m}Tc-mertiatide prepared for routine clinical use and on 4 vials of ^{99m}Tc-mertiatide spiked with 6%–15% free pertechnetate using 3 different flow rates: slow drip (5 mL/min for conditioning and 2 mL/min for elution), fast drip (10 mL/min for conditioning and 10 mL/min for elution), and very fast drip (about 15–20 mL/min for conditioning and about 15–20 mL/min for elution). An infusion pump was used to provide constant flow rates for the first 2 conditions, whereas manual handling, reflecting real-life practice, was used for the third condition.

Results: All 3 flow rates yielded essentially identical radiochemical purities for each vial tested (agreement was always within 0.3% for a given vial). The elapsed times for mini-column conditioning, loading, and elution were approximately 15, 5, and 3 min for the slow drip, fast drip, and very fast drip, respectively.

Conclusion: Faster flow rates for mini-column testing of ^{99m}Tc-mertiatide save time (and correspondingly reduce radiation exposure to the worker) without adversely affecting the results of radiochemical purity determinations.

Key Words: ^{99m}Tc-mertiatide; radiochemical purity; quality control testing

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For correspondence or reprints contact: James A. Ponto, MS, Nuclear Medicine, 3832 JPP, University of Iowa Hospitals and Clinics, 200 Hawkins Dr., Iowa City, IA 52242.

E-mail: james-ponto@uiowa.edu

The renal tubular secretion agent ^{99m}Tc-mertiatide (mercaptoacetyltriglycine, or MAG3) was introduced by Fritzberg et al. in 1986 (*1*). It has since become a standard, and often preferred, radiopharmaceutical for a variety of renal imaging procedures including renal blood flow, renal function, diuresis renography, and evaluation of renovascular hypertension (*2–4*).

The manufacturer's package insert recommends the use of a C-18 solid-phase mini-column cartridge (WAT051910; Waters Corp.) for testing the radiochemical purity of ^{99m}Tc-mertiatide (*4*). The instructions in the package insert are vague regarding the flow rates to be used when conditioning the cartridge, describing the process simply as "push" and "flush." For sample analysis, the insert states that the solvents are to be "pushed through the cartridge slowly so that the elution occurs in a dropwise manner," but a flow rate is not specified (*4*). The instruction sheet supplied with the mini-column cartridges recommends flow rates of 5–10 and 2–10 mL/min for conditioning and for elution, respectively, of the cartridge (*5*). Because of the lack of specific flow rate recommendations in the mertiatide package insert and the rather broad range of flow rates recommended in the mini-column cartridge instructions, this study was undertaken to evaluate the effect of different flow rates on determining the radiochemical purity of ^{99m}Tc-mertiatide.

MATERIALS AND METHODS

Radiochemical purity testing was performed on 10 consecutive vials of ^{99m}Tc-mertiatide prepared for routine clinical use and on 4 vials of ^{99m}Tc-mertiatide spiked with 6%–15% free pertechnetate. The testing was performed following package insert instructions for materials and procedures. Samples from each vial were tested using 3 different flow rates. The first, slow drip, used the slowest flow rates recommended in the mini-column cartridge instruction sheet: 5 mL/min for conditioning and 2 mL/min for elution. The second, fast drip, used the fastest flow rates recommended in the mini-column cartridge instruction sheet: 10 mL/min for conditioning and 10 mL/min for elution. The third, very fast drip, used a very fast flow rate of approximately 15–20 mL/min for conditioning and approximately 15–20 mL/min for elution. An infusion pump (model 351; Sage Instruments) provided constant and specific flow rates for the first 2 conditions, whereas manual handling, reflecting real-life practice, was used for the third condition.

RESULTS

Figures 1 and 2 show the results for radiochemical purity in the ^{99m}Tc-mertiatide vials prepared for routine clinical use and in the vials of ^{99m}Tc-mertiatide vials spiked with ^{99m}Tc-pertechnetate for the 3 flow rates. All 3 flow rates yielded essentially identical radiochemical purities for each vial tested (agreement was always within 0.3% for a given vial). Elapsed times for mini-column conditioning, loading, and elution were approximately 15, 5, and 3 min for the slow drip, fast drip, and very fast drip, respectively.

DISCUSSION

The instruction sheet for the mini-column cartridge warns that separation efficiency may vary with flow rate (*6*). Specifically, if the flow rate is too high, components may not interact sufficiently with the sorbent (i.e., they may pass through the column when they should be retained on the column), resulting in loss of resolution. For example, Hammes et al. found that reliable radiochemical purity determinations for ^{99m}Tc-tetrofosmin using a silica mini-column cartridge require flow rates to be no greater than 5 mL/min (*7*). Hence, the effect of different flow rates for each compound to be tested should be evaluated to establish acceptability—the primary purpose of this study.

The relatively high radiochemical purity in the 10 ^{99m}Tc-mertiatide vials prepared for routine clinical use limited the evaluation of flow rate effects on the separation of radiochemical impurities. Therefore, several vials were spiked

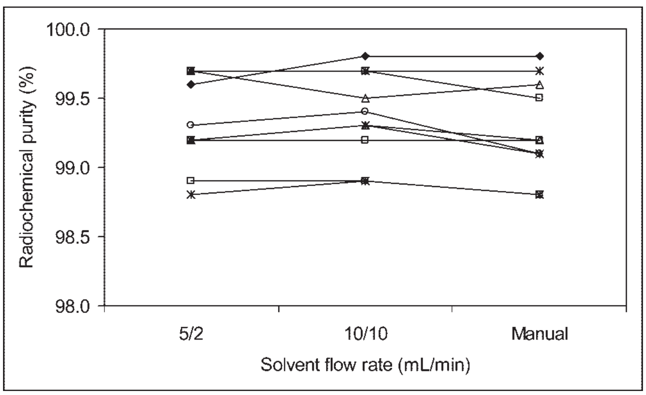

FIGURE 1. Radiochemical purity results on 10 vials of ^{99m}Tc-mertiatide prepared for routine clinical application using 3 flow-rate conditions.

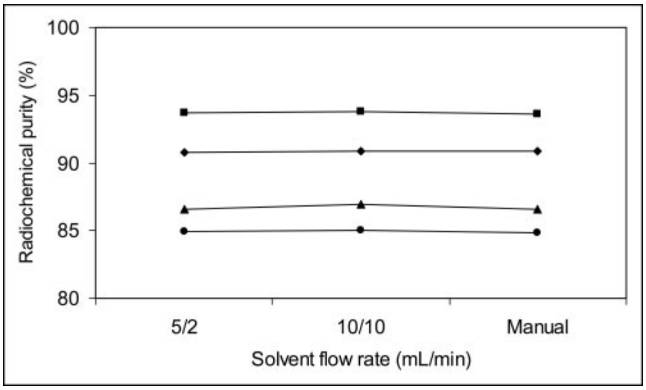

FIGURE 2. Radiochemical purity results on 4 vials of ^{99m}Tc-mertiatide spiked with 6%, 9%, 13%, and 15% ^{99m}Tc-pertechnetate using 3 flow-rate conditions.

with ^{99m}Tc-pertechnetate, the radiochemical impurity most likely to occur and of greatest concern. At radiochemical purity levels slightly above and below the acceptability limit of 90% (*5*), the 3 flow rates used in this study did not affect the results (Fig. 2).

The time required for analysis using each flow rate was also recorded. As expected, faster flow rates allowed completion in shorter times. The time savings for faster flow rates, although modest, may be appreciated in busy practice settings. An additional benefit of using faster flow rates is that shorter times yield a proportional reduction in radiation exposure.

CONCLUSION

Radiochemical purity testing of ^{99m}Tc-mertiatide can be successful using various flow rates through the mini-column cartridge. Faster flow rates save time (and correspondingly reduce radiation exposure to the worker) without adversely affecting the results of radiochemical purity determinations.

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