PERCHLORATE BLOCKING OF $^{99m}TcO_4^-$ UPTAKE BY SIMULTANEOUS INTRAVENOUS INJECTION IN DOGS

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It is current practice in many nuclear medicine laboratories to administer potassium perchlorate ($KClO_4$) orally 2 hr before the intravenous administration of ^{99m}Tc-pertechnetate ($^{99m}TcO_4^-$) when performing brain scans. The oral administration of $KClO_4$ is useful in blocking the uptake of $^{99m}TcO_4^-$ in the thyroid, salivary glands, and choroid plexus (*1–3*). In this report, concentrated solutions of $^{99m}TcO_4^-$ containing perchlorate ions (ClO_4^-) present either as perchloric acid ($HClO_4$) or sodium perchlorate ($NaClO_4$) were administered intravenously to dogs. The blocking effect produced by the simultaneous intravenous administration of the $^{99m}TcO_4^-$-ClO_4 solutions was compared both qualitatively and quantitatively with that produced by the oral administration of $KClO_4$.

MATERIALS AND METHODS

The solutions of $^{99m}TcO_4^-$ containing ClO_4^- ions used in this study were prepared by first eluting a commercially available ^{99m}Tc generator* with 20 ml of 0.9% sodium chloride (NaCl) solution. The resulting solutions of $^{99m}TcO_4^-$ were subsequently passed through an ion exchange column containing 25 mg of a strongly basic anion exchange resin†. The $^{99m}TcO_4^-$ was adsorbed onto the strongly basic anion exchange resin and was subsequently removed from the column by eluting with 4 ml of a 1.68 *N* $HClO_4$ solution or a solution containing 204 mg of $NaClO_4$/ml, both solutions have the same ClO_4^- concentration. The solutions were passed through the ion exchange column at a rate of approximately 1–2 ml/min. This method of preparing $^{99m}TcO_4^-$ solutions containing ClO_4^- ions resulted in concentrations that were greater than four and one half times that obtained from the ^{99m}Tc generators.

These solutions of $^{99m}TcO_4^-$ containing ClO_4^- ions were evaluated both qualitatively and quantitatively in dogs. To qualitatively evaluate these solutions three dogs having an average weight of 18.3 kg were given an intravenous injection of each of ten solutions in varying sequence, either 48 or 120 hr apart. The dogs were first anesthetized with a 7% sodium pentobarbital solution at a dose of 35 mg/kg. Each of the solutions to be evaluated was then injected rapidly into the right saphenous vein and photographs made at 10, 30, 60, and 120 min postinjection with the Anger gamma camera.

Three groups of three dogs were used in the quantitative study. A control group with an average weight of 22.6 kg was given 5 mCi of $^{99m}TcO_4^-$ in 0.9% NaCl solution intravenously. A second group with an average weight of 22.9 kg was given 5 mCi of $^{99m}TcO_4^-$ in 0.9% NaCl solution intravenously 2 hr after the oral administration of a 100-mg capsule of $KClO_4$. The third group with an average weight of 23.2 kg was given 5 mCi of $^{99m}TcO_4^-$ in a $NaClO_4$ solution containing approximately 100 mg of $NaClO_4$ intravenously.

The dogs were first anesthetized with a 7% sodium pentobarbital solution at a dose of 35 mg/kg. The dogs were then given the solution of $^{99m}TcO_4^-$ to be evaluated and were sacrificed 30 min later by the intracardiac injection of 10 ml of a saturated solution of potassium chloride. Immediately after death, the animals were dissected. A parotid gland, a portion of skeletal muscle from the neck, one lobe of the thyroid gland, a portion of brain tissue from the cerebral cortex, and the choroid plexus were removed, weighed on an analytical balance, and placed in test tubes containing 1 ml of 0.9% NaCl solution. The dissection required approximately 45 min. To

* New England Nuclear, North Billerica, Mass. 01862.

† Supplied courtesy of Rohm and Haas, Philadelphia, Pa., 19105, CG-400 (C1) AR Type II, 200-400 mesh.

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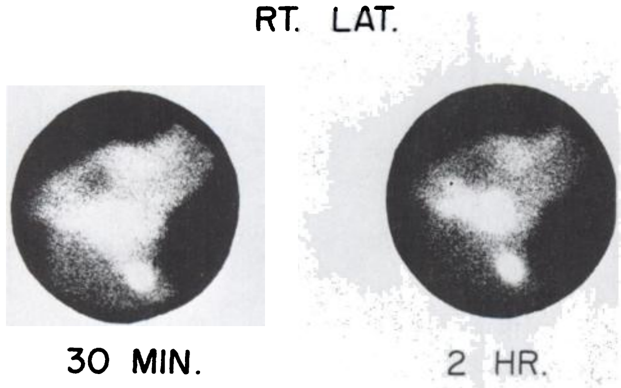

FIG. 1. Scintiphotographs of Dog 294, 30 and 120 min after 5 mCi $^{99m}TcO_4^-$ in 0.9% NaCl solution i.v.

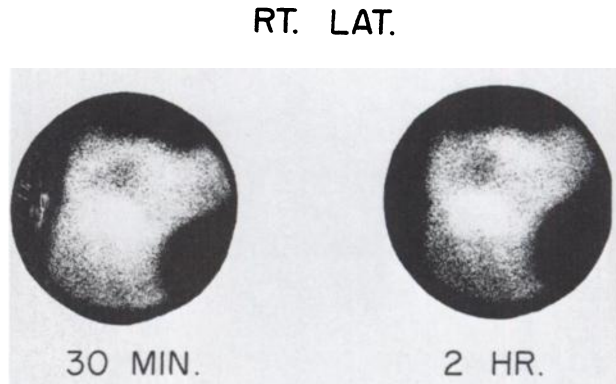

FIG. 2. Scintiphotographs of same dog as in Fig. 1, 2 hr after administration of 100 mg $KClO_4$.

maintain consistency, the tissues were taken in the above order each time and assayed for radioactivity for 2 min in a Nuclear-Chicago gamma well counter approximately 1.5 hr postinjection. Immediately after the first assay, the tissues were assayed a second time, and an average of the two computed. The counts per minute per milligram of tissue were calculated and the ratios of parotid to skeletal muscle, thyroid to skeletal muscle, choroid plexus to skeletal muscle, and choroid plexus to brain tissue were computed.

RESULTS

Physicochemical. Experimental studies were performed to determine optimum conditions for removal of $^{99m}TcO_4^-$ from the 20 ml of eluate obtained from the generator. A yield of 96% of $^{99m}TcO_4^-$ was obtained with 25 mg of the anion exchange resin. The smallest amount of 1.68 *N* $HClO_4$ (or 204 mg of $NaClO_4$/ml) solution which eluted more than 95% of the $^{99m}TcO_4^-$ from the anion exchange resin was 4 ml.

Using this second elution column it was possible to concentrate the ^{99m}Tc activity by a factor of 4.5. The increased specific activity of a subsequently injected bolus would improve the quality of flow studies using this eluate.

Qualitative. Ten $^{99m}TcO_4^-$ solutions were injected in the qualitative study. After the administration of 5 mCi of $^{99m}TcO_4^-$ in 0.9% NaCl solution, there was substantial localization of the $^{99m}TcO_4^-$ ion in the parotid and thyroid gland. This may be clearly seen in Fig. 1. The photographs of Dog 294 are representative of all the results obtained. The choroid plexus did not appear on the scans performed in this study. When 100 mg of $KClO_4$ was administered orally 2 hr before the i.v. injection of 5 mCi of $^{99m}TcO_4^-$ in 0.9% NaCl, this localization of the $^{99m}TcO_4^-$ ion was substantially blocked as shown in the photographs in Fig. 2. Similar results were obtained when 5 mCi of $^{99m}TcO_4^-$ eluted from the anion exchange column with $HClO_4$ were injected, thereby simultaneously administering the $^{99m}TcO_4^-$ and the ClO_4^- ions. The results are shown in the photographs in Fig. 3.

Adjusting the pH of the $^{99m}TcO_4^-$-$HClO_4$ solutions between <1 and 8 did not appear to change blocking produced by these solutions. However, by varying the ClO_4^- ion content of the $^{99m}TcO_4^-$ solutions, it was found that the ClO_4^- ion content was directly related to the degree of blockage achieved. $NaClO_4$ solutions were used in this portion of the study because the pH of the solutions was closer to that of the blood. The photographs in Fig. 4 show that with a dose of approximately 100 mg of $NaClO_4$ there is minimal localization of the $^{99m}TcO_4^-$ ion in the parotid and thyroid glands. Doses of approximately 75 and 50 mg of $NaClO_4$ reduced the uptake of $^{99m}TcO_4^-$ ion but not to the same degree as the 100-mg dose. This was particularly true in the parotid gland at 2 hr postinjection. The uptake of the $^{99m}TcO_4^-$ ion in the thyroid gland was prevented with all doses of $NaClO_4$ used except for the 12.5-mg dose. At this dose, the thyroid gland shows a slight uptake of the $^{99m}TcO_4^-$ ion, as seen in Fig. 5.

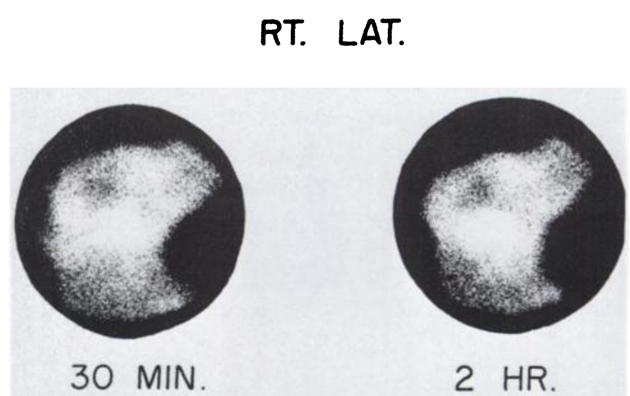

FIG. 3. Scintiphotographs of Dog 294, 30 and 120 min after 5 mCi $^{99m}TcO_4^-$-$HClO_4$ with pH <1 i.v.

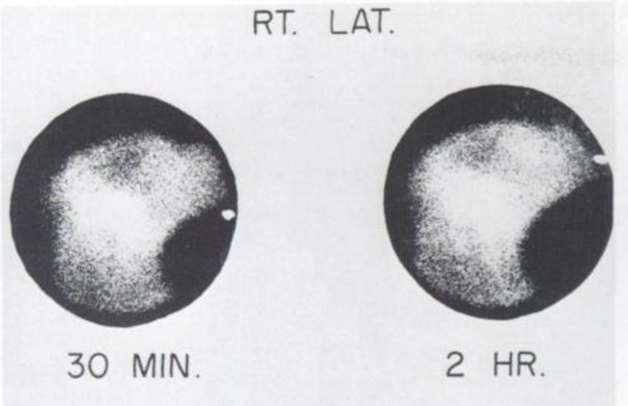

FIG. 4. Scintiphotographs of Dog 294, 30 and 120 min after $^{99m}TcO_4^-$-$NaClO_4$ i.v. containing approximately 100 mg $NaClO_4$.

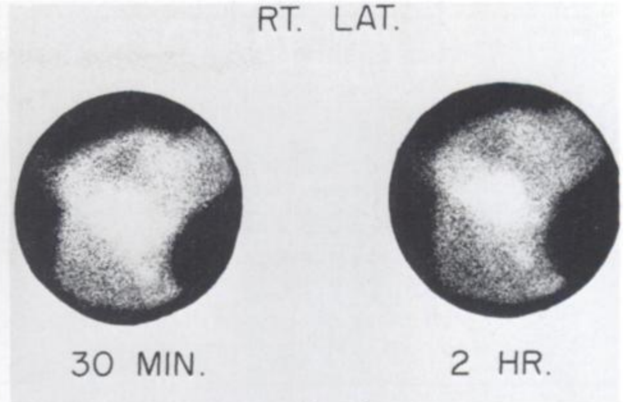

FIG. 5. Scintiphotographs of Dog 294, 30 and 120 min after $^{99m}TcO_4^-$-$NaClO_4$ i.v. containing approximately 12.5 mg $NaClO_4$.

Quantitative. Table 1 presents the average tissue concentration measured as cpm/mg of $^{99m}TcO_4^-$ ion following the i.v. injection of 5 mCi of various $^{99m}TcO_4^-$ solutions in three groups of dogs. The animal group receiving only $^{99m}TcO_4^-$ in 0.9% NaCl solution showed the highest degree of localization of the $^{99m}TcO_4^-$ ion in the parotid (751 cpm/mg), thyroid (929 cpm/mg), and choroid plexus (385 cpm/mg). With the oral administration of 100 mg of $KClO_4$ 2 hr before the injection of $^{99m}TcO_4^-$ in 0.9% NaCl solution, the average tissue concentrations of $^{99m}TcO_4^-$ ion in the parotid, thyroid, and choroid plexus were 478, 425, and 150 cpm/mg, respectively. When the $^{99m}TcO_4^-$-$NaClO_4$ solution containing approximately 100 mg of $NaClO_4$ was administered, the average tissue concentrations of the $^{99m}TcO_4^-$ ion were 329 cpm/mg for parotid, 176 cpm/mg for thyroid, and 150 cpm/mg for the choroid plexus. Therefore, it is apparent that there was substantial reduction in the localization of $^{99m}TcO_4^-$ in these three tissues in the presence of both $KClO_4$ and $NaClO_4$.

The tissue concentration ratios, rounded to the nearest whole number and computed from the data in Table 1, are reported in Table 2. The control group, receiving only 5 mCi of $^{99m}TcO_4^-$ in 0.9% NaCl solution, was found to have tissue ratios of 16:1 for parotid to skeletal muscle, 19:1 for thyroid to skeletal muscle, 8:1 for choroid plexus to skeletal muscle, and 55:1 for choroid plexus to brain tissue. By administering 100 mg of $KClO_4$ orally 2 hr before the radiopharmaceutical, these ratios were reduced to 8:1, 7:1, 3:1, and 19:1, respectively. The simultaneous administration of the $^{99m}TcO_4^-$-$NaClO_4$ solution containing 100 mg of $NaClO_4$ reduced these ratios to 5:1 for parotid to skeletal muscle, 3:1 for thyroid to skeletal muscle, 2:1 for choroid plexus to skeletal muscle, and 12:1 for choroid plexus to brain tissue.

DISCUSSION

Concentrating effects on $^{99m}TcO_4^-$ can be achieved that are 4.5 times that initially obtained from the nuclide generators by using a second eluting column containing an anion exchange resin. Over 90% of the $^{99m}TcO_4^-$ adsorbed on the resin from the first eluate can be recovered.

In these studies, the animals given $^{99m}TcO_4^-$ in 0.9% NaCl solution exhibited a high degree of uptake of the $^{99m}TcO_4^-$ ion in the parotid, thyroid, and choroid plexus. However, when the $^{99m}TcO_4^-$ solution from the anion exchange resin column was administered intravenously in the dogs, this uptake of the $^{99m}TcO_4^-$ ion was diminished. The prevention

TABLE 1. AVERAGE* TISSUE CONCENTRATION OF $^{99m}TcO_4^-$ ION FOLLOWING I.V. INJECTION OF THREE DIFFERENT $^{99m}TcO_4^-$ SOLUTIONS IN DOGS

$^{99m}TcO_4^-$ solution administered (5 mCi)	cpm/mg				
	Parotid	Skeletal muscle	Thyroid	Brain tissue	Choroid plexus
$^{99m}TcO_4^-$ in 0.9% NaCl solution	751	48	929	7	385
$^{99m}TcO_4^-$ in 0.9% NaCl solution after oral $KClO_4$ (100 mg)	478	60	425	8	150
$^{99m}TcO_4^-$-$NaClO_4$ (100 mg) solution administered simultaneously	329	65	176	13	150

* Average of samples from three dogs measured in cpm 1½ hr postinjection.

TABLE 2. COMPARISON OF CONCENTRATION RATIOS* OF $^{99m}TcO_4^-$ FOLLOWING I.V. INJECTION OF $^{99m}TcO_4^-$ SOLUTIONS IN DOGS

$^{99m}TcO_4^-$ solution administered (5 mCi)	Ratios†			
	Parotid: skeletal muscle	Thyroid: skeletal muscle	Choroid plexus: skeletal muscle	Choroid plexus: brain tissue
$^{99m}TcO_4^-$ in 0.9% NaCl solution	16:1	19:1	8:1	55:1
$^{99m}TcO_4^-$ in 0.9% NaCl solution after oral $KClO_4$ (100 mg)	8:1	7:1	3:1	19:1
$^{99m}TcO_4^-$-$NaClO_4$ (100 mg) administered simultaneously	5:1	3:1	2:1	12:1

* Tissue ratios rounded to the nearest whole number and computed from data in Table 2.
† Ratio = (cpm/mg of tissue)/(cpm/mg of tissue).

of this uptake was found to be directly related to the ClO_4^- ion content of the solution.

The dogs were also administered $KClO_4$ orally 2 hr before the i.v. administration of $^{99m}TcO_4^-$. From a comparison of the photographs in Figs. 2 and 4 taken in the qualitative experiments, it appears that the simultaneous intravenous administration of $^{99m}TcO_4^-$-$NaClO_4$ produced a block of the uptake of the $^{99m}TcO_4^-$ ion of the same quality as the oral $KClO_4$ at the doses used. The duration of block also appeared to be equal. Following the administration of ClO_4^- ion by both methods, there was slight appearance of the $^{99m}TcO_4^-$ ion in the parotid at 2 hr postinjection.

The quantitative experiments further substantiated the finding that the $^{99m}TcO_4^-$-$NaClO_4$ solution produced a block of the uptake of the $^{99m}TcO_4^-$ ion of as good or better quality than the oral $KClO_4$ at the doses used. The tissue concentration ratios presented in Table 2 show that these ratios are lower when the $^{99m}TcO_4^-$-$NaClO_4$ solutions were administered than when the oral $KClO_4$ was used as the blocking agent.

From this study, the $^{99m}TcO_4^-$ solutions containing ClO_4^- ions appear to offer the advantage of substantially reducing the localization of the $^{99m}TcO_4^-$ ion in the parotid, thyroid, and choroid plexus. The simultaneous administration of ^{99m}Tc and the ClO_4^- ion would appear to make it possible to consider elimination of the prior administration of oral $KClO_4$ and its associated 2-hr waiting period. Further studies are needed in animals and human patients to substantiate the reported findings.

The use of a second ion exchange column with the need for guaranteeing sterility, nonpyrogenicity, and safety of the intravenous solution increases the complexity of radiopharmaceutical preparation. However, it seems feasible to easily adapt this technique to a prefabricated closed system.

SUMMARY

A strongly basic anion exchange resin has been found to remove the $^{99m}TcO_4^-$ from a saline eluate. Subsequently, sodium perchlorate may be used as the eluant to remove the radionuclide from the resin, concurrently achieving a concentrating effect of 4.5 times.

The preliminary biological evaluation of these solutions indicates that they are useful in greatly reducing the localization of the $^{99m}TcO_4^-$ ion in the parotid, thyroid, and choroid plexus. Should subsequent studies confirm that these solutions are satisfactory for human use, their administration will eliminate the 2-hr delay in brain scanning when $KClO_4$ is used as the blocking agent. These solutions will also eliminate the need for premedication, thereby simplifying a now cumbersome technique. However, additional studies are needed to further substantiate this work and to determine whether or not there is toxicity from the intravenously administered ClO_4^- ion.

ACKNOWLEDGMENT

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