ASSESSMENT OF ^{99m}Tc-LABELLED GENTAMICIN IN RENAL FUNCTIONAL IMAGING

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SUMMARY

An aminoglycoside antibiotic, gentamicin is labelled with ^{99m}Tc by the stannous chloride reduction. Scintigraphic studies and organ distribution of this agent in experimental animals showed a selective renal localization. The radioactivity remained for a relatively long period in the kidneys suggesting some tubular reabsorption following filtration at the glomerular level. The concentration of ^{99m}Tc-gentamicin in the kidneys as a function of time has been studied by a gamma camera interfaced to a computer. Renal radioactivity clearance curves were generated from the regions of interests on each kidney. The potential value of ^{99m}Tc-gentamicin in the diagnosis of functional disorders with relation to the glomerular filtration and reabsorption in the proximal nephron is discussed.

Key Words : ^{99m}Tc-gentamicin, renal imaging agent.

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INTRODUCTION

Various ^{99m}Tc labelled antibiotics have been reported in the last decade as diagnostic agents in clinical nuclear medicine. These are penicillamine (1,2), tetracyclines (3,4) and bleomycin (5,6).

Gentamicin is an aminoglycoside antibiotic which is used in the treatment of gram-negative bacillary infections. Labelling conditions of gentamicin with reduced ^{99m}Tc have been described in the former study (7). Gentamicin is excreted almost entirely by glomerular filtration in an unchanged form (8,9).

The present work was undertaken to assess the usefulness of ^{99m}Tc-gentamicin in renal studies. The data concerning the biological behaviour of this compound in experimental animals and the possible significance of the results are discussed in relation to the scintigraphic investigation of renal function and morphology.

EXPERIMENTAL

Gentamicin was provided by Eczacıbaşı Ilaç Sanayi T.A.Ş. (Istanbul, Turkey) and pertechnetate eluate was used from ^{99}Mo generators supplied by several different companies. All reagents were prepared with analytical grade chemicals and pyrogen free water for injection.

Pertechnetate solution (1-2 ml) was administered into the reaction vial containing 10 mg gentamicin and 0.25 mg $SnCl_2.2H_2O$. After 30 min incubation at room temperature the final solution was passed through a 0.22μ millipore filter into a sterile vial.

Chromatographic analysis of ^{99m}Tc-gentamicin was performed using Whatman 3 MM paper developed in n-butanol, acetic acid, water (4:1:1).

^{99m}Tc-gentamicin (0.05 ml / 100 g body weight) were injected into the tail vein of rats. The blood was removed from the heart and tissue samples were dissected out at times ranging from 10 to 60 min. Samples of blood and dissected organs were weighed and counted in a well-type gamma counter in comparison with the radioactivity administered.

Following this, 30 μCi ^{99m}Tc-gentamicin was injected into the rabbits via ear vein. Posterior whole body images of rabbits were obtained by a gamma camera interfaced to a computer (Imac 7300). A dynamic study with a frame rate of 32 sec/image was acquired in a 64 x 64 x 8 matrix over a period of 1 hour following the injection. A frame rate of 95 sec/image was utilized for those studies which lasted over a period of 3 hours. Regions of interest (ROI) were generated on each kidney and time-activity curves were obtained.

RESULTS AND DISCUSSION

Paper chromatography with Whatman 3 MM paper developed in n-butanol, acetic acid, water (4:1:1) was used to assess the overall labelling efficiency of ^{99m}Tc-gentamicin (7). This procedure suggests that unbound ^{99m}Tc-Sn species covered only 3.07 ± 0.71 % of the total radioactivity along the length of the paper strip where the pertechnetate was almost totally eliminated.

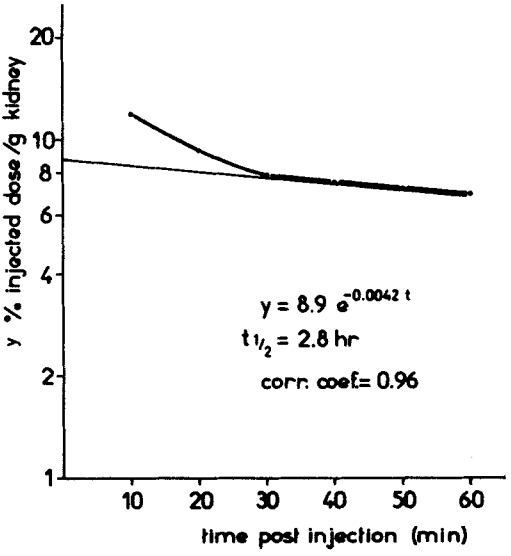

Figure 1. Radioactivity concentration of ^{99m}Tc-gentamicin in the rats kidney as a function of time.

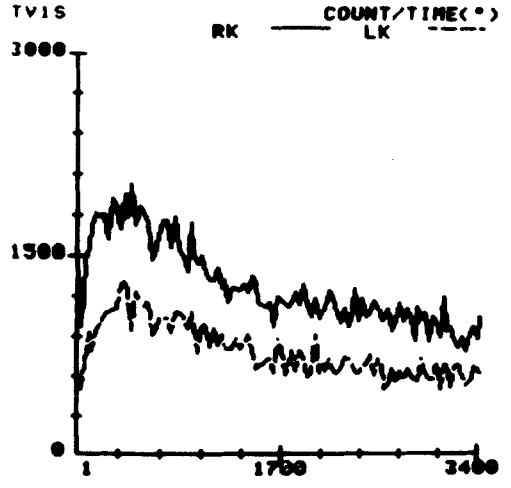

Figure 2. Renal radioactivity clearance curve of rabbits injected with ^{99m}Tc-gentamicin, generated from two ROI's using a gamma camera interfaced to a computer. **The time is in seconds.**

The results of tissue distribution from rats demonstrated that a high percentage of the injected dose was found in the kidneys following IV injection of ^{99m}Tc-gentamicin. Gentamicin is known to be excreted by the glomerular filtration. It was also reported that the great majority of the gentamicin was concentrated in the renal cortex and small amounts in the medulla (8,10). Together with the pattern of blood clearance the rate of clearance by the kidneys was slowed down 30 min after injection (Fig 1). These curves could be expressed as a sum of two exponential components. The mean half-time of the slow component was 2.8 h for renal clearance curve, which was presumably related to the tubular reabsorption following filtration at the glomerular level, while the plasma disapearance curve gave a similar pattern (3.1 h).

The whole body images of rabbits injected with 250 μCi ^{99m}Tc-gentamicin were analysed by a gamma camera interfaced to a computer. Time-activity curves were generated from ROI's on each kidney (Fig 2). There is a flattening of the clearance curve after 30 min. Graphical analysis of this curve was used to study renal function (Fig 3). The mean-half time of the slow component was 3.05.

Organ distribution data as well as gamma camera scintigraphy confirmed that the scintigraphic delineation of kidneys were highly satisfactory (Fig 4). The mean kidney-liver ratio of ^{99m}Tc-gentamicin concentration was 10/1 while a kidney-blood ratio of 6/1 was obtained at 1 h after injection. There is a delay in the elimination of radioactivity due to the contribution of tubular reabsorption mechanism which allows reasonably high target-organ to background ratios.

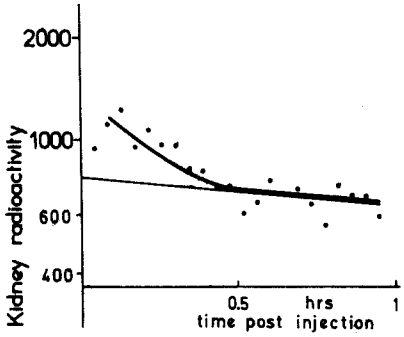

Figure 3. Graphical analysis of the renal radioactivity clearance curve of ^{99m}Tc-gentamicin in the rabbit.

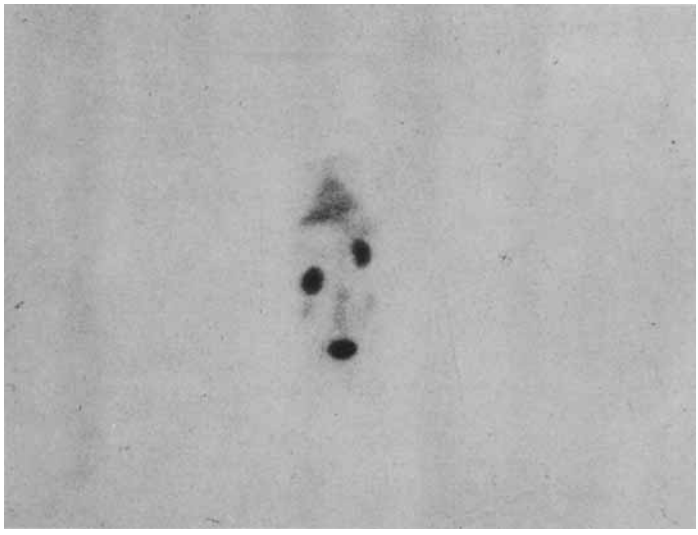

Figure 4. Posterior scintigram of a rabbit, obtained 1 hour post injection of ^{99m}Tc-gentamicin.

CONCLUSION

Many substances are rapidly excreted by glomerular filtration or tubular secretion. Therefore, there are suitable gamma labelled tracers for studying the excretory function of the kidney. On the other hand, there had been no suitable agent for studying tubular

reabsorption together with filtration at the glomerular level. On the basis of biodynamic findings from the animal data it is concluded that ^{99m}Tc-gentamicin may have a potential in the diagnosis of renal disorders with relation to the glomerular filtration and reabsorption in the proximal nephron. Furthermore reasonably longer retention in the kidneys would result in higher target-organ to background ratios allowing more adequate renal scans, supplementary to the simultaneous functional studies.

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