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^{99m}Tc Sn COLLOID SCANS IN THE DIAGNOSIS OF RENAL GRAFT REJECTION

F X Sundram, **R P S Edmondson**, E S Ang

Singapore General Hospital, Singapore

Summary

^{99m}Tc SN colloid uptake was studied (131 scans) in 50 patients with suspected renal graft rejection. Normal scans were obtained in 14 scans in 13 patients with normal graft function. Clinical, biochemical, radiological and histological evidence was used to confirm the results. Percentage uptake of the initial dose was compared to the 15min/initial uptake ratio as an index of rejection. Fifteen minute uptake ratio was superior (84% correct) to initial uptake (78% correct). Most (85%) of the false negative scans were in patients with chronic rejection. The method is useful in the diagnosis of acute but not chronic rejection.

Introduction

The diagnosis of renal allograft rejection can be difficult especially when it coexists with acute tubular necrosis. A variety of radionuclide techniques have been used in an attempt to facilitate the diagnosis. The most promising seems to be the uptake of labelled sulphur colloid (S-colloid) [1,2]. The site of uptake of colloid in rejecting kidneys is not entirely clear but it probably adheres to aggregating platelets and polymerising fibrin which occur in areas of vasculitis in the rejecting kidney [3,4].

In essence the technique consists of either comparing the intensity of radioactivity in the graft at least 15 minutes after IV injection with the radioactivity in the adjacent iliac crest or determining the percentage of the initial dose taken up by the graft at 15 minutes [1]. However the first technique suffers from the disadvantage that bone marrow extraction of the colloid may vary with changes in the patient's immune status e.g. after steroid pulse therapy resulting in false positive results and the second method may be affected by changes in renal graft blood flow such as may occur in vascular rejection, sepsis and acute tubular necrosis, again giving rise to spurious results [1].

To overcome these objections it has been proposed that the ratio of uptake of radioactivity at 15 minutes to initial uptake may give better results than the

absolute percentage uptake at 15 minutes or comparison with bone marrow uptake [1]. Furthermore, the preparation of S-colloid may be troublesome and lengthy compared to ^{99m}Tc Sn colloid (Sn-colloid) which has a similar particle size.

This study investigates the sensitivity, specificity and accuracy of ^{99m}Tc Sn colloid uptake in diagnosing renal graft rejection and to compare the use of the ratio of 15 minutes to initial uptake with the conventional absolute percentage 15 minute uptake.

Methods

One hundred and thirty-one scans were performed in 50 patients clinically suspected of undergoing graft rejection, 14 scans were performed in 13 patients with stable normal graft function to establish normal values for colloid uptake. Rejection was diagnosed as follows: 1) clinical symptoms and signs, e.g. fever, graft tenderness, fluid retention; 2) 25 per cent rise above the baseline serum creatinine; 3) exclusion of other causes of deterioration in graft function such as obstruction or vascular occlusion by ultrasound examination, DTPA renography and, where indicated, arteriography; 4) percutaneous or open renal biopsy (18 patients).

Scanning was performed in the supine position using a computer linked Anger Scintigraphic Camera (GE 400 A/T) placed over the graft covering the whole pelvic region. A low energy all purpose parallel hole collimeter with a 20 per cent window centered on a 140 keV Tc peak was used.

Two to three mCi of ^{99m}Tc Sn colloid (Amersham) was given by intravenous bolus injection at time zero. Data acquisition was started immediately and two static images in 128x128 matrix word mode obtained at 0–5 minutes and 15–20 minutes post injection. Data were stored in a digital computer (Star). The radioactivity of the syringe and its contents was counted pre- and post-injection and the net administered counts calculated by subtraction.

At the end of the study an irregular region of interest was drawn over the transplanted kidney to obtain the total counts at 0–5 minutes and 15–20 minutes. The background counts were subtracted by creating a mirror image of the region of interest over the contralateral pelvis.

The counts were corrected by applying a tissue attenuation coefficient based on an average kidney depth of 5cm.

The absolute uptake of radioactivity in the transplanted kidney at 15–20 minutes expressed as the percentage of the administered dose was calculated together with the ratio of the counts at 15–20 minutes and 0–5 minutes, also expressed as a percentage. The sensitivity (S), specificity (SP) and accuracy (AC) were calculated as follows:

$$S = \frac{TP}{TP+FN} \qquad SP = \frac{TN}{TN+FP} \qquad AC = \frac{TP+TN}{TP+TN+FP+FN}$$

where TP=true positive; TN=true negative; FP=false positive; FN=false negative.

Results

Normal values

The mean ± SD initial uptake and 15 minute uptake ratio for the control group were 0.56±0.2 per cent and 48.5±9.0 per cent respectively. For the purpose of interpreting the scans in the patient group, those with an initial uptake >0.9 per cent and/or 15 minute uptake ratio >60 per cent were considered as positive for rejection.

Using clinical and biochemical parameters it was impossible to confirm the results of 12 scans. These were mainly in patients in the immediate post-operative period who were oliguric and requiring dialysis. Vascular integrity and lack of obstruction were confirmed by isotope renography and ultrasound examination and they received routine pulse therapy with methylprednisolone on post-operative days 6–8. Thus subsequent onset of function could have been due either to resolving rejection or recovering acute tubular necrosis.

Of the remaining 119 scans, using initial uptake, there were 62 true positive, 26 true negative, 13 false positive and 18 false negative scans, giving a sensitivity, specificity and accuracy of 77.5 per cent, 66.6 per cent and 73.9 per cent respectively.

Using 15 minute uptake ratio and initial uptake together five false negative results were converted to true positive and two false positive to true negative giving a sensitivity, specificity and accuracy of 83.8 per cent, 71.8 per cent and 79.9 per cent respectively.

Seventeen scans could be directly related to renal histology. Of these (using 15 minute uptake ratio) there were 12 true positive, three true negative, one false positive and one false negative, giving a sensitivity, specificity and accuracy of 92 per cent, 75 per cent and 88 per cent respectively.

Discussion

The sensitivity, specificity and accuracy of this method compare favourably to the S-colloid method [2,6]. The use of the ratio of 15–20 minute uptake to initial uptake appeared to improve the sensitivity, specificity and accuracy compared to our own conventional method using the absolute percentage uptake. However, a significant number of false positive and negative results persisted. There are a number of possible reasons for this. Firm histological evidence for the presence or absence of rejection was only available in 15 per cent of the scans but when only those cases were considered the results improved even more, thus the independent clinical and biochemical confirmation of the scan diagnosis may have been inaccurate in some of the cases. Of the 13 false negative scans, 11 were in patients of whom seven had clinical and four had histological evidence of chronic rejection; these latter patients had virtually no thrombosis or fibrin deposition, thus little colloid uptake would be expected. Of the 11 false positive scans, three could be explained by the presence of sepsis [2] or lymphomatous tissue surrounding the kidney and two had concomitant renal artery stenosis proven on arteriography. The deterioration in function in those

two patients was attributed to the stenosis but it is possible that this lesion was in fact part of the rejection process [5]. There was no obvious explanation in six patients, none of them had a transplant biopsy, thus it remains possible that at least some of them were undergoing subclinical rejection.

In conclusion, ^{99m}Tc Sn colloid scans appear to be a useful method for the diagnosis of acute renal graft rejection, but are unhelpful in chronic rejection. The ratio of 15–20 minutes to initial uptake of radioactivity in combination with absolute percentage uptake is superior to the absolute percentage uptake alone as the criterion for rejection. Further studies with histological confirmation are being carried out to establish the usefulness of this method in the early oliguric post-operative period and whether it can give an early warning of impending clinical rejection.

References

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