Clinical experience with $^{99m}$Tc-MAG3, mercaptoacetyltriglycine, and a comparison with $^{99m}$Tc-DTPA

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Abstract. The preparation, application and clinical usage of $^{99m}$Tc-mercaptoacetyltriglycine, MAG3, a tubular secreted compound, is described in the first 225 patients in a phase III study. Image quality, relative renal function, and renal transit times were compared with a 4 fold greater administered activity of $^{99m}$Tc-DTPA in 11 patients. Correlation coefficients of 0.94 for relative function, 0.83 for parenchymal transit time index and 0.82 for whole kidney transit time index were found. Frusemide responses were similar. $^{99m}$Tc-MAG3 is an efficacious radiopharmaceutical for routine renal radionuclide studies, giving excellent image quality in patients with hypertension, poor renal function, obstructive nephropathy or a renal transplant.

Key words: $^{99m}$Tc-MAG3 - $^{99m}$Tc-DTPA

Since its introduction into clinical use in 1970 (Hauser et al. 1970), technetium labelled diethylenetriamine penta-acetic acid ($^{99m}$Tc-DTPA) has played an unchallenged role as the main radiopharmaceutical for detecting functional abnormalities in the urinary tract in routine clinical use. $^{99m}$Tc-DTPA is cleared by glomerular filtration and provides an excellent alternative to iodine labelled orthoiodhippurate, OIH, because of its physical properties and reduced radiation exposure (Taylor et al. 1980; Barbour et al. 1976). Disadvantages, however, stem from the fact that its low extraction efficiency (20%) gives rise to a proportionately low target to background ratio, a fact that should be taken into account when interpreting results in cases of reduced renal function. A high extraction efficiency, up to 87% (Britton and Brown 1971), can be achieved with orthoiodohippurate, OIH, labelled with $^{131}$I or $^{125}$I, but the disadvantages of the former include a high radiation dose, especially in the presence of outflow obstruction (Elliott and Britton 1978) and poor spatial resolution and sensitivity of images, while the higher cost and reduced availability of the latter precludes its use as a routine renal imaging agent.

Recently, a new and promising series of technetium complexes were synthesized as potential replacements of OIH in kidney function studies (Davison et al. 1981). The new chelating agents were based on an amide nitrogen and thiolate sulphur donor groups.

A preliminary member of the series, $^{99m}$Tc-N, $\text{N'}$-bis (mercaptoacetyl) ethylenediamine ($^{99m}$Tc-DADS) showed rapid extraction and clearance by the kidney but was inferior to OIH as regards to its biological properties (Fritzberg et al. 1981; Fritzberg et al. 1982; Klingensmith et al. 1982, 1983).

Efforts to avoid stereoisomer formation resulted in the development of a new (N3-S) ligand, $^{99m}$Tc-mercaptoacetylglycylglycylglycine ($^{99m}$Tc-MAG3) which was shown to be a potential replacement of OIH in animals (Fritzberg et al. 1986). Preliminary studies with volunteers (Taylor et al. 1986) and patients (Taylor et al. 1987; Jafri et al. 1988) has shown $^{99m}$Tc-MAG3 to be a single radiochemical agent with fast renal excretion.

As outlined in recent work from this department (Jafri et al. 1988), phase I and II studies were done to compare the simultaneous clearance of $^{99m}$Tc-MAG3 and $^{131}$I-OIH and to compare renal handling of $^{99m}$Tc-MAG3 with $^{125}$I-OIH. In this work (phase III), a clinical evaluation of $^{99m}$Tc-MAG3 involving 225 patients has been undertaken. In a sub group, the results obtained in 11 patients with $^{99m}$Tc-MAG3 have been compared with those obtained within 4 weeks with $^{99m}$Tc-DTPA. This work is undertaken to evaluate whether $^{99m}$Tc-MAG3 meets the requirements of the ultimate renal radiopharmaceutical which should be safe, cheap, readily available, easy to prepare and clinically useful.

Materials and methods

A total of 225 patients referred to the Nuclear Medicine Department for routine radionuclide renography were selected for this study (males 135, females 90 mean age: 47 years range 9 to 75 years). The majority of patients came from either the hypertension clinic or the Urology Department at St. Bartholomew's Hospital, London. The causes for referral were hypertension (94), assessment of a renal transplant (42), possible urinary tract obstruction (75) and (14) for various other reasons, Table 1, 33 of these studies were follow-up tests in the same set of patients.

The studies with MAG3, being approved by the City and Hackney District Ethical Committee for routine use, were carried out with a thorough explanation given before each routine procedure and most patients were willing to try a new imaging agent in preference to the existing one.
The study was approved by the Governmental Administration of Radioactive Substances Advisory Committee.

Preparation of $^{99m}$Tc-MAG3. MAG3 was supplied by Mallinkrodt Diagnostica, Holland, as a freeze dried white powder in multidose vials (Code MP600). Under aspetic conditions, when required 925 MBq (25 mCi) $^{99m}$Tc eluate, from an Ultratechneknow FM generator, in a volume less than 1 ml was added to the vial. Before addition, the activity was diluted with saline to 4 ml and attention was paid