COMPARISON BETWEEN ^{131}I-IHSA AND ^{169}Yb-DTPA FOR CISTERNOGRAPHY

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Cisternographic patterns and CSF clearance of ^{169}Yb-DTPA and ^{131}I-IHSA were compared in 12 patients with suspected hydrocephalus. Early cisternographic images were better resolved using ^{169}Yb-DTPA because of the higher counting rate related to the larger permissible doses and the more favorable photon energy for the scintillation camera. In delayed images greater transependymal diffusion of ^{169}Yb-DTPA obscured the cortical architecture. There was a trend toward more rapid CSF clearance of ^{169}Yb-DTPA. However, statistically significant differences were not obtained because of large variations in clearance in the small group of patients reported here. It was concluded on the basis of this limited study that for most cisternography, ^{169}Yb-DTPA is a superior tracer compared with ^{131}I-IHSA.

The increasing importance of radionuclide cisternography and the well-known deficiencies of ^{131}I-IHSA as an intrathecal tracer have stimulated an energetic search for new cisternographic agents. This quest has been given careful definition by Bell, et al (*1*) who summarize the criteria for selecting a tracer and discuss most of the currently available radiopharmaceuticals in terms of their specific properties and the clinical problems to be solved. The ideal properties of a cisternography agent are reproduced with kind permission of the authors in Table 1. By Bell's reckoning, ^{131}I-IHSA merits secondary consideration because of high radiation absorbed dose and prolonged plasma circulation time. Ytterbium-169-DTPA, if it had been considered by Bell, would presumably have ranked high.

Wagner, et al have described the advantages of ^{169}Yb-DTPA over ^{131}I-IHSA for cisternography (*2,4*). These are: (A) more easily collimated ^{169}Yb gamma emissions, (B) lower radiation absorbed dose per microcurie, (C) reduced background because of rapid blood clearance by the kidneys, (D) a quantitative CSF:plasma transfer test by urine collections since DTPA is a glomerular substance analogous to inulin. More recently, ^{111}In-DTPA has been introduced for cisternography (*5*) and is now commercially marketed. The advantages of ^{111}In over ^{169}Yb are principally its physical characteristics since stable binding with DTPA is obtained with both radionuclides.

There are two characteristics of DTPA which are of potential concern when used for cisternography. They relate to Properties 8 and 11 of Table 1.

The first concern is that DTPA may bind Ca^{2+} and Mg^{2+} ions in the CSF, precipitating acute neurologic symptoms (*1*). In the commercial preparation (3M) we have used, calcium ions are added to prevent depleting the CSF of divalent atoms. The second concern is whether labeled DTPA clears the CSF principally through the arachnoid villi, thereby reflecting bulk CSF flow. Hosain, et al (*4*) compared

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TABLE 1. IDEAL PROPERTIES

1. Not metabolized in the CSF
2. Lipid insoluble
3. Easily labeled with a suitable gamma emitter
4. Easily sterilized
5. Nonpyrogenic
6. Nonantigenic
7. Nonirritating
8. Nonreactive
9. High rate of molecular diffusion
10. Rapid blood clearance
11. Main route of egress via the arachnoid villi

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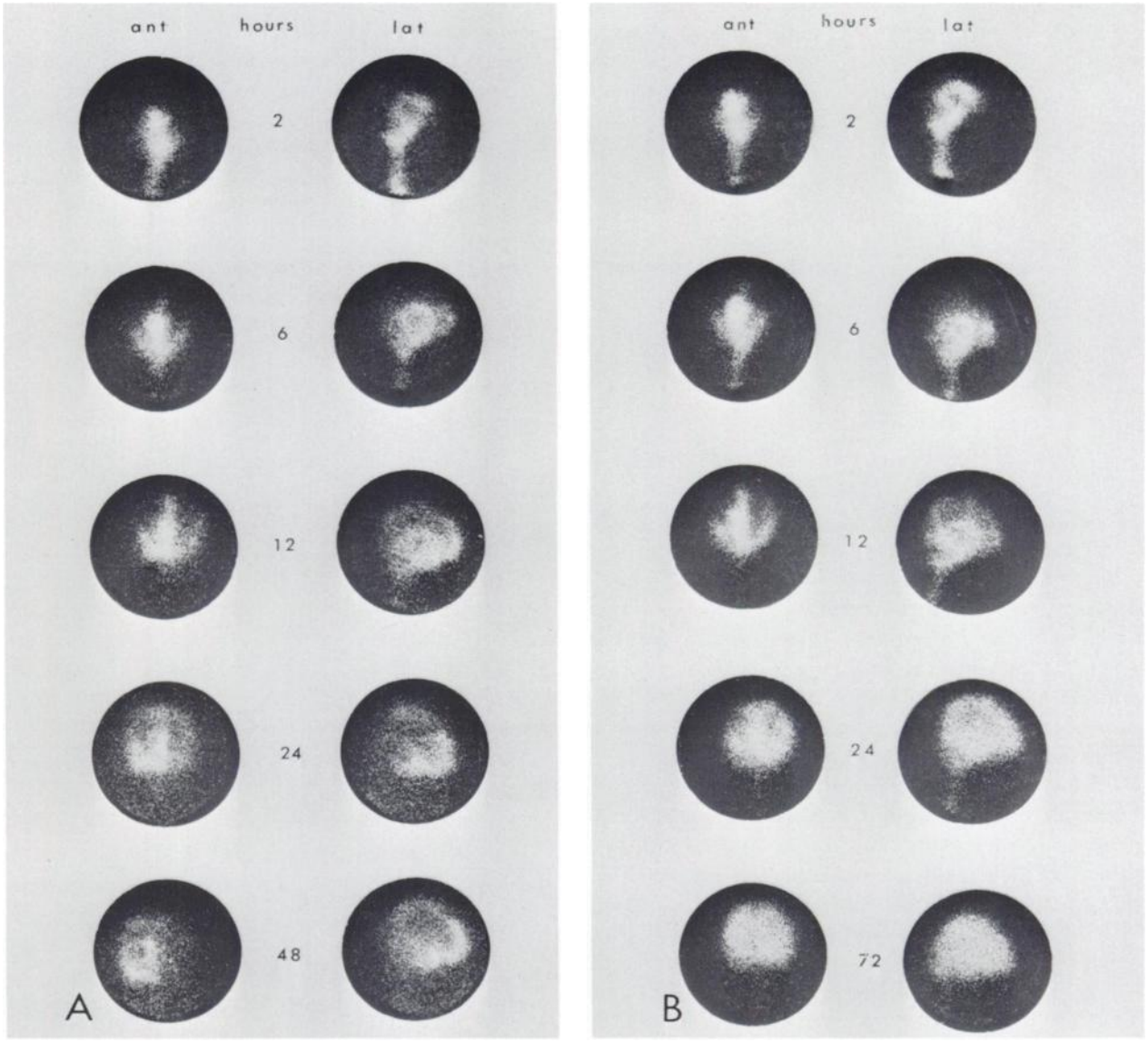

FIG. 1. (A) Patient with hydrocephalus and right frontal porencephaly studied with ^{131}I-IHSA. Porencephaly is best demonstrated at 24 and 48 hr. (B) Same patient studied with ^{169}Yb-DTPA. Early ventricular reflux is more sharply defined with loss of cisternal detail in 24 and 48-hr images because of greater apparent activity in extracellular space.

^{131}I-IHSA and ^{169}Yb-DTPA by serially sampling CSF from the cisterna magna after cisternal injection of the two radiopharmaceuticals. Clearance over 5 hr was similar for the two, leading the authors to conclude that DTPA was cleared in a manner analogous to albumin and probably transferred to the blood by bulk CSF flow. Because transit out of the cisterna magna represents only a short segment of the CSF pathway, we have compared intrathecally injected ^{131}I-IHSA and ^{169}Yb-DTPA in the same patients, thereby evaluating the entire CSF circulatory pathway. In addition, quantitative studies of CSF clearance for the two radiopharmaceuticals were evaluated by external detection in anticipation that this method of study may become increasingly important.

MATERIALS AND METHODS

Twelve adult patients with suspected hydrocephalus were studied by cisternography using 0.5–1.0 mCi ^{169}Yb-DTPA and 3–5 days later, 100–150 μCi ^{131}I-IHSA. Each patient was stable during the period of investigation; all had chronic disease, none had elevated CSF pressure, and none had been shunted. Patients were injected using identical techniques (*6*).

Following lumbar intrathecal injection of the radiopharmaceutical, sequential lateral and anterior scintiphotos of the head were taken with a scintillation camera at 1, 3, 6, 12, 24, and 48 hr. Approximately 20,000 counts/image were obtained. The head position was carefully standardized (*7*), and SSKI was administered to block thyroid uptake of ^{131}I.

The cisternograms were compared according to the pattern of tracer ascent and the rate of tracer clearance from the head. To obtain a measure of clearance, the average head counting rate at each interval was calculated with corrections for room background and, beginning at 12 hr, corrections were applied for vascular activity and physical decay (*7*). The corrected head counting rate at each interval was normalized according to the peak activity obtained and expressed as a percent of this maximum value. This normalizing technique eliminates the calibration for absolute activity and effects of extracranial losses of injected radionuclide. The technique allows a means for direct comparison of one patient study with another.

RESULTS

The cisternogram patterns were all nearly identical with the two radiopharmaceuticals during the first 12 hr. The anatomic detail was generally better with ^{169}Yb-DTPA because of the lower photon energy which resulted in better scintillation camera resolution. Because of higher counting rates, image integration time was reduced with less distortion due to motion. Figure 1 demonstrates these differences. By 24 hr there is a striking difference between the images. Cisternal detail is preserved in the ^{131}I-IHSA images, but greater apparent activity in the extracellular space with ^{169}Yb-DTPA obscures these images so that a cerebral cortical image is seen, and this may persist for several days. This pattern was seen in every case of ^{169}Yb-DTPA as well as in four patients using ^{111}I-DTPA which are not included in this study. Occasionally this phenomenon was found to obscure pathology. Figure 2 shows a patient with a left convexity block secondary to head trauma which is easily seen at 24 and 48 hr in the ^{131}I-IHSA images but not apparent on the ^{169}Yb-DTPA images because of intracerebral activity.

The principal difference seen in the quantitative studies was earlier peak activity with ^{169}Yb-DTPA (Table 2). This was not an inconsistent finding, but on the average the groups were strikingly different. The differences in activity at 24 and 48 hr show a trend toward clearance of ^{169}Yb-DTPA although the differences were not statistically significant ($p = 0.2$ and 0.12 respectively) in this small group of patients.

DISCUSSION

The differences between ^{169}Yb-DTPA and ^{131}I-IHSA in late cisternography images has not been described by Wagner, et al although the essentially cortical images at 24 hr are evident in their illustrations (*2,3*). In cases of ventricular filling and in-

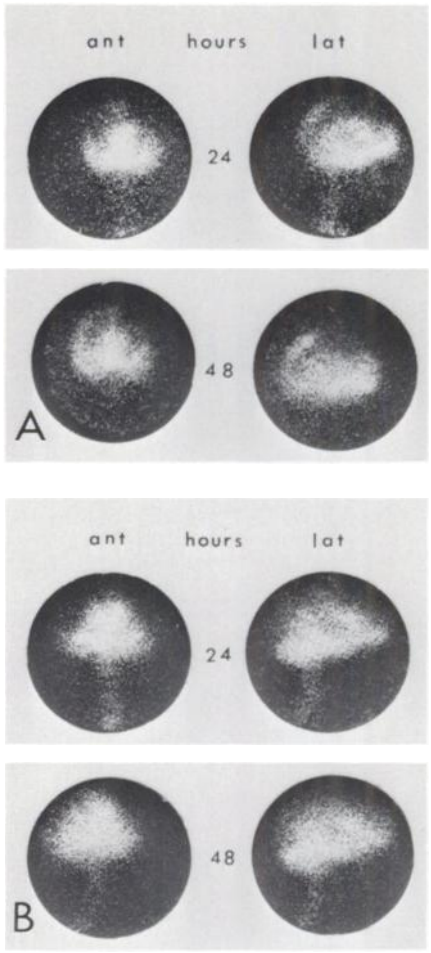

FIG. 2. (A) Patient with hydrocephalus and left convexity block studied with ^{131}I-IHSA. (B) Same patient. Ventricular activity is more apparent but left convexity block is obscured by cortical diffusion.

cisural block, the ventricles appear to grow progressively larger with time. While this apparent ventricular "expansion" is seen with both radiopharmaceuticals, it is much more apparent with ^{169}Yb-DTPA. We attribute the different patterns of delayed cisternogram images to greater diffusion of ^{169}Yb-DTPA into the cerebral ECS than occurs with ^{131}I-IHSA. This hypothesis is supported by several reported tracer-distribution studies. Hochwald, et al (*8*) found that inulin cleared the CSF faster than albumin in cats. Curran, et al (*9*) found greater CSF production rates in monkeys using ventriculocisternal perfusion with inulin than with albumin. Tissue slices from the paraventricular brain in these monkeys demonstrates 2–5 times greater concentration of ^{14}C-inulin than ^{131}I-albumin. Levi (*10*) found that rates of inulin clearance from the CSF varies with the average size of the inulin molecule used. Thus both large and small molecules diffuse across ependyma and pia into cerebral cortex and the rate of diffusion depends on molecular size. In the study by Hosain, et al (*4*) cited above, clearance

TABLE 2. CSF CLEARANCE DATA

Case	Age	Diagnosis	Time (hr) of peak activity		% peak ^{131}I-IHSA activity		% peak ^{169}Yb-DTPA activity		Cisternogram pattern*
			^{131}I-IHSA	^{169}Yb-DTPA	24 hr	48 hr	24 hr	48 hr	
OG	44	NPH	12	6	91	48	71	32	V.R., D.C.
GC	84	NPH	24	6	100	61	78	30	V.R., D.C., C.B.
MC	23	NPH	12	12	70	45	74	36	V.R., D.C., C.B.
RJ	46	NPH	24	6	100	71	94	34	V.R., D.C., C.B.
HB	42	NPH	24	6	100	60	92	67	V.R., D.C., C.B.
EB	58	NPH	4	4	74	45	72	40	V.R., D.C., I.B.
EM	30	NPH	12	12	92	—	79	38	V.R., N.C.
FT	73	Porencephaly	24	24	100	70	100	68	D.C.
CS	44	Atrophy	24	12	100	57	95	38	D.C.
MM	26	Atrophy	12	4	71	25	27	14	N.C.
AB	62	Seizures	6	6	90	34	89	33	V.R., N.C.
			M = 17	7.7	91	53	81	40	
			SD =		±11	±14	±19	±16	

* V.R. = Ventricular reflux; D.C. = Delayed clearance; C.V. = Convexity block; N.C. = Normal clearance; I.B. = Incisural block.

of cisternally injected ^{125}I-IHSA and ^{169}Yb-DTPA were compared by serial samples of CSF formation from the cisterna magna. During the first 2 hr CSF concentrations of the two tracers were nearly identical. However, after this the concentrations diverge showing more rapid clearance of ^{169}Yb-DTPA. The differences are slight, so that large concentration differences would only be expected after several hours which is what our patient studies also suggest. Thus the description of these tracers as "bulk flow" agents is a relative thing. Clearance is primarily by bulk movement of CSF with increasingly greater clearance by ECS diffusion with decreasing molecular size.

What implications do these differences have for selecting a tracer for cisternography? The superior image quality obtained with ^{169}Yb-DTPA on early scan views is the principal advantage of this tracer. Well-resolved images are especially useful in outlining the basal cisterns in the case of infratentorial tumors or for imaging CSF rhinorrhea if ^{99m}Tc-albumin or ^{99m}Tc-inulin is not available. The decreased background attributable to urinary clearance is largely offset in later views by the obscuring effect of ECS diffusion. On the other hand, a high convexity block or variations in cortical anatomy may be obscured by ^{169}Yb-DTPA. In the demonstration of shunt patency, ^{169}Yb-DTPA would be clearly favored because of better image quality and rapid blood clearance. For the majority of studies, which includes the workup of normal pressure hydrocephalus, ^{169}Yb-DTPA is probably preferred because of better image quality. The ventricles are better defined in cases of minimal ventricular reflux and the associated delayed tracer clearance is quite apparent both by inspection of images and by quantitation of intracranial activity although clearance of the smaller molecule is accelerated. Since transependymal diffusion becomes an increasingly important pathway of CSF absorption in hydrocephalus, the tracer clearance difference described here must be borne in mind.

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