289

RADIOIODINATED ROSE BENGAL KINETICS IN EXTRAHEPATIC BILIARY OBSTRUCTION AND HEPATIC HOMOGRAFT REJECTION IN THE DOG

BERNARD LAUNOIS, MD, JACQUES L. CORMAN, MD,
KEN A. PORTER, MD, THOMAS RYERSON, MD,
STEPHEN BOSTROM, MT, AKE GUSTAFSSON, MD,
CARL G. GROTH, MD, AND
THOMAS E. STARZL, MD, PHD, FACS

IN HUMAN RECIPIENTS of orthotopic hepatic homografts, rejection and extrahepatic biliary duct obstruction are accompanied by indistinguishable abnormalities in standard liver function tests (1). In a search for a simple and atraumatic method that could aid in the differentiation between these two conditions, the kinetics of rose bengal sodium I 131 (2,3) were studied in the dog.

METHODS

Three groups of animals were studied: group 1, six normal control dogs; group 2, six dogs that had ligation of the common bile duct; group 3, six dogs that had received orthotopic hepatic homografts. The dogs in the last group received postoperative immunosuppression with azathioprine 1–8 mg/kg/day. The radioisotope studies were carried out one–three times weekly, for one month in the animals of group 2 and until death of the animal of rejection or other causes in group 3.

Following intravenous injection of 200 microcuries of the rose bengal I 131, the intravascular retention was assessed by monitoring radioactivity over the heart with a scintillation camera and data storage system. Liver uptake and bowel appearance of the radioisotope was followed by serial scintiphotos. Intravascular retention was expressed in percentage as the ratio between the activity at 20 vs 5 min after the isotope injection. Standard biochemical liver function tests were performed frequently, and postmortem liver specimens were studied with light microscopy.

RESULTS

Group 1: In the normal dogs the maximum intravascular retention varied between 28% and 58% (mean 45.5%). The liver uptake of

From the Department of Surgery and the Division of Nuclear Medicine, University of Colorado School of Medicine and VA Hospital, Denver, and the Department of Pathology, St. Mary's Hospital and Medical School, London.
Supported by research grants from the Veterans Administration, Division of Research Resources grants RR-00051 and RR-00069, and US Public Health Service grants AI-10176-01, AI-AM-08898, AM-07772, and HE-09110.

the isotope was good, and bowel excretion invariably occurred within 24 hr.

Group 2: In the dogs with extrahepatic biliary obstruction, the intravascular retention value increased for one week and then leveled off. Maximum values in the individual dogs were 75, 80, 82, 84, 86, and 87% (mean 82.3%). Liver uptake was good, but in no instance did excretion of the isotope to the bowel occur. All dogs showed an increase in bilirubin (max 5.9 to 17.3 mg/100 ml) and alkaline phosphatase (max 9.5 to 148 Bodansky units).

Group 3: Among the immunosuppressed homograft recipients, four died after 5 to 18 days with biochemical or morphological evidence of rejection. In two more dogs, azathioprine was stopped after 9 and 15 days, following which rejection occurred. During the development of the rejection, the intravascular retention rose to values in the 70%–85% range. Liver uptake was good and excretion into the bowel occurred. When end-stage rejection had developed, the maximum intravascular retention values were 88, 90, 91, 93, 95, and 97% (mean 92.5%). At this time the liver uptake was fair and bowel excretion was usually not seen.

DISCUSSION

The present data suggest that differentiation between homograft rejection and total extrahepatic biliary obstruction can be aided by studying the kinetics of radioactive rose bengal. In dogs with moderate rejection as well as in dogs with obstruction, the intravascular retention values and the radiographic liver picture were very similar, but only the former animals had excretion of the dye into the bowel. When rejection became advanced, bowel excretion was inconsistent, presumably due to severe intrahepatic cholestasis, but at this stage the retention values were higher than those recorded after obstruction. Data from seven human recipients of orthotopic hepatic homografts are consistent with the findings in the dogs.

REFERENCES

1. Martineau G, Porter KA, Corman J, et al: Delayed biliary duct obstruction after orthotopic liver transplantation. Surgery (in press)

2. Nordyke RA, Blahd WH: Surgical vs nonsurgical jaundice: Differentiation by a combination of Rose Bengal I^{131} and standard liver-function tests. JAMA 194:949, 1965

3. Rosenthal L: The Application of Radioiodinated Rose Bengal and Colloidal Radiogold in the Detection of Hepatobiliary Disease. St. Louis, Warren H Green Inc, 1969