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CORTEX AND MEDULLARY PROTON MAGNETIC RESONANCE IN GENTAMICIN AND GLYCEROL ACUTE RENAL FAILURE IN RATS

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Summary

Acute renal failure was studied in Charles River rats of both sexes. Gentamicin ARF was induced by daily intraperitoneal injections of gentamicin 100mg/kg body weight for eight days and then magnetic resonance was done on day nine. Glycerol acute renal failure was produced by an intramuscular injection of 50% glycerol (10ml/kg body weight). The rats were studied 24 hours later. T1 (spin-lattice) and T2 (spin-spin) relaxation times, in milliseconds, were measured (Bruker PC-20 'Multispec' at 37°C) from renal cortex, medulla, liver and spleen slices. Acute renal failure was confirmed by serum creatinine and blood urea.

Significant medullary, liver and spleen magnetic resonance changes were found in glycerol acute renal failure. The most striking changes were found in gentamicin acute renal failure which is characterized on magnetic resonance by an important prolongation of both cortical and medullary T1 and T2 times ($p<0.025$) compared with normal and glycerol acute renal failure rats ($p<0.05$), without changes in the liver and spleen. It is concluded that renal magnetic resonance properties can differentiate acute renal failure of different aetiologies.

Introduction

Magnetic resonance imaging clearly differentiates normal renal cortex, medulla and the surrounding tissues [1]. Preliminary clinical studies suggest that it would be possible to evaluate renal pathology by magnetic resonance imaging due to the sensitivity of the method in differentiating normal from abnormal tissues [1–5]. This sensitivity is based on the characterization of regional differences in spin-lattice (T1) or spin-spin (T2) relaxation parameters, by both quantitative calculation and by image intensity. The measurement of proton T1 and T2 relaxation times and their translation to image describe the extent to which the hydrogen contained in tissues is 'structured' [6].

The purpose of the present study was to find the differences in the magnetic resonance properties between normal and pathological renal tissue resulting from different experimentally induced acute renal failure (ARF) in rats. Two models of ARF resulting from two different severe insults were studied: injection of gentamicin or glycerol.

Material and methods

All the experiments were performed on Charles River rats of both sexes, weighing 250–300g (Yokneam, Israel). The rats were divided into three experimental groups as follows:

Group A Gentamicin ARF was induced by eight daily gentamicin (100mg/kg body weight) intraperitoneal injections. The relaxation times were measured on day nine.

Group B Glycerol ARF was induced by intramuscular injection, after 16 hours of dehydration, of 50% glycerol solution (10ml/kg body weight). Relaxation times were measured 24 hours after glycerol administration.

Group C Normal control rats.

T1 and T2 relaxation times were measured in renal cortex, medulla, liver and spleen slices, within five to 10 minutes of excision, with a Bruker PC-20 Multispec Spectrometer (Bruker, W Germany Analytische Messtechnik GmbH D-7512 Rheinstetten) operating at 20MHz at 37°C. T1 was determined by the 180– -90 method and a three parameter fit, and T2 by the Carr-Purcell-Meiboom-Gill (CPMG) spin echo sequence method.

Blood samples were taken from all the animals at the end of the experiments for urea and serum creatinine measurements with an autoanalyser.

Mean, standard error of the mean and one way analysis of variance were used to assess statistical significance, $p<0.05$ was considered significant.

Results

The data of T1 and T2 relaxation times in renal cortex, medulla, liver and spleen and blood urea and serum creatinine are given in Table I.

In gentamicin ARF the cortex T1 and T2 relaxation times were 663±50 milliseconds and 93±9 milliseconds respectively, both significantly longer than those of normal rats ($p<0.025$). The T1 and T2 values in the medulla of gentamicin ARF were also significantly different from the normal medulla, T1 720±24 ($p<0.025$) and T2 93±6 ($p<0.025$). The T1 and T2 of the spleen and liver in gentamicin ARF were similar to those found in normal rats. In glycerol ARF the cortex T2 value was 65±4 ($p<0.025$) compared with the normal value. The T1 in the medulla was significantly lower than in the normal tissue, 536±21 ($p<0.025$) and the T2 was prolonged compared with the normal rat, 85±3 ($p<0.025$). In glycerol ARF the liver T1 was 347±10 ($p<0.025$)

TABLE I. T1, T2 and biochemical data in different experimental ARF groups

	Control (n=7)	Gentamicin ARF (n=6)	Glycerol ARF (n=8)
CORTEX			
T1	466±6	663±50*†	458±3
T2	49±2	93±9*†	65±4*
MEDULLA			
T1	636±29	720±24*†	536±21*
T2	73±3	93±6*†	85±3*
LIVER			
T1	284±3	289±3	347±10*
T2	39±1	39±2	44±2
SPLEEN			
T1	613±22	578±26	529±22*
T2	74±4	76±2†	63±2
BLOOD UREA (mg/dl)	37±4	112±19*†	72±17*
SERUM CREATININE (mg/dl)	0.4±0.04	1.3±0.2*†	0.8±0.17*

T1 and T2 in milliseconds Mean ± SE

* $p<0.025$ versus controls

† $p<0.05$ versus glycerol ARF

compared with normal relaxation time, and the T1 of the spleen was shorter 529±22 ($p<0.025$) than in normals. Both cortical and medullary T1 and T2 in gentamicin ARF were significantly different than the respective values in glycerol ARF rats.

Increased serum creatinine and blood urea, and the histology confirmed the development of acute renal failure.

Discussion

This study demonstrates that significant changes occur in renal cortex and medulla magnetic resonance properties in rats with experimentally induced ARF resulting from different insults.

Gentamicin renal toxicity results in significant prolongation of T1 and T2 in both cortex and medulla. In general, as the tissue becomes less solid-like, the T1 and T2 values converge [6]. This is the case in gentamicin ARF, the T1/T2 ratio for the cortex and medulla were 7.1 and 7.7 respectively, compared with 9.5 and 8.7, the corresponding values in the normal kidney.

Results were published in which magnetic resonance analysis differentiates normal rabbit cortex and whole kidney from congested kidney, but the normal kidney could not be differentiated from the ischaemic one [7,8]. T1 decreased

with ischaemia and increased with reperfusion, whereas T2 increased with reperfusion, whereas T2 increased with ischaemia and decreased with reflow. In glycerol ARF, in which haemodynamic changes are definitely involved [9], we found both cortical and medullary T2 prolongation and unchanged or increased T1 relaxation times in the cortical and medullary regions, respectively. Thus 24 hours after glycerol administration, the magnetic resonance cortical and medullary values correspond to those of ischaemia. The significant liver and spleen T1 changes in glycerol ARF suggests a multi-organ pathology in the myohaemoglobinuric ARF.

The fundamental compartmentalization of water in macromolecular solution (such as tissue) can be represented by either a two or three phase model: free water and hydration water or the previous two plus crystalline water [10]. In the three compartment model the T1 of tissue seems to be dominated by the total water content and by the ability of macromolecules to bind water in the hydration layer. T2 is less affected by these parameters, but is affected by the concentration of crystalline water binding sites and by the thickness of the hydration water multilayer. Thus our findings of prolonged T2 in ARF seem to represent important structural water hydrogen changes. The increase in T1 values in gentamicin ARF most probably represents increased plasma volume.

The important hydrogen magnetic resonance changes which are found in experimental ARF in rats may provide information on tissue total water content as well as important modifications in the concentration of the crystalline water binding sites and the thickness of the hydration multilayer. The different insults leading to ARF modify these parameters differently. As a consequence characteristic magnetic resonance properties may provide aetiological functional diagnostic possibilities.

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