REMOVAL OF GADOTERIC ACID (DOTAREM®) BY HEMODIALYSIS AND SAFETY IN DIALYSED PATIENTS

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OBJECTIVES

Gadoteric acid, a safely used ionic, macrocyclic gadolinium-based contrast agent (GBCA) (1), is cleared from the blood by glomerular filtration only, as this is the case for most GBCAs (2). A prolonged exposure to gadolinium is considered as a risk factor for developing nephrogenic systemic fibrosis (NSF) after administration of some of these contrast agents in patients with chronic kidney disease (CKD) (3,4).The aim of this study was to evaluate the dialysability of gadoteric acid in patients with end-stage renal disease (ESRD), requiring hemodialysis.

METHODS

Phase I, monocentric, non-comparative, non-randomized, open-label clinical trial, including 10 evaluable patients (adults male or female), presenting with ESRD who required hemodialysis for 4 hours, 3 times per week. Gadoteric acid (Dotarem®) was injected intravenously at a dose of 0.1 mmol/kg.

The primary evaluation criterion was the decrease in serum gadoteric acid concentration after each hemodialysis session. To calculate the dialysability, blood samples were drawn simultaneously from the inflow and outflow lines of the circuit during the first hemodialysis session, and from the vascular access just before and after each of the three hemodialysis sessions. The 3 hemodialysis sessions started 1 to 2 hours, 2 days (i.e., 48 2h) and 4 days (i.e., 96 4h), respectively, following the gadoteric acid injection. The total gadolinium concentration was measured in the serum by inductively coupled plasma mass spectrometry (ICP-MS). The secondary evaluation criteria were the clinical safety (vital signs, injection-site tolerance) and laboratory assessments which were evaluated during a 4-day follow-up after gadoteric acid injection. Adverse events (AEs) and serious AEs were evaluated through a 3 week and 3-month post-injection period, respectively.

Table 1

Baseline and demographic characteristics	Subjects N = 10	Baseline and demographic characteristics	Subjects N = 10
Age, years [Median (range)]	64.0 (31-79)	Urine output n (%)	
Weight, kg [Median (range)]	70.6 (61-116)	Anuria	6 (60)
Male, n (%)	5 (50)	Oliguria	2 (20)
Caucasian, n (%)	10 (100)	Residual diuresis	2 (20)
Renal disease, n (%)		Mean baseline serum creatinine, µmol/l [Median (range)]	779 (371-1467)
Glomerulopathy	5 (50)	Vascular access	
Uropathy	3 (30)	Arteriovenous fistula	6
Polycystic kidney disease	1 (10)	Double lumen, central venous catheter	4
Renal artery stenosis	1 (10)	Years [Median (range)] since first dialysis	5.50 (1.0-13.0)
Renal transplant, n (%)	3 (30)	Days [Median (range)] from last dialysis prior study entry to first gadoteric acid injection	4.0 (3- 4)

Table 2

Hemodialysis sessions	Time Point	Blood gadolinium concentration		Percent decrease in gadolinium concentration versus corresponding pre session value		Percent decrease in gadolinium concentration compared to the pre-dialysis values of first session (geometric mean)
		N	Geometric mean (µmol/L)	Geometric mean	95% Confidence Interval	
First session	Pre-session	10	519.3	NA	NA	
	0.5 h	10	59.9	88.1	86.4; 90.0	
	1.5 h	10	33.5	93.4	92.2; 94.6	
	4 h	10	12.0	97.1	95.3; 98.9	97.1
Second session	Pre-session	10	41.6	NA	NA	
	4 h	7	2.5	94.8	33.5; 99.3	99.5
		3	<LLQ	100	NA	
Third session	Pre-session	9	108	NA	NA	
	4 h	2	0.3	89.9	-9.2; 15.2	99.7
		7	<LLQ	100	NA	

LLQ: Lower Limit of Quantification

RESULTS

Demographic characteristics are summarized in Table 1. During the first hemodialysis session, gadolinium was efficiently eliminated, with a clearance (mL/min; geometric mean [95%CI]) of 224.6 [216.0; 233.9] at 0.5h and of 225.9 [215.6; 237.2] at 1.5h. This was reflected by a decrease in gadolinium serum concentration (geometric mean) of 88% at 0.5 h, of 93% at 1.5 h and 97% 4 hours after the start of dialysis (Table 2).

The decrease of gadolinium concentrations (geometric mean) after a 4-hour session (versus the corresponding pre-dialysis values) was more than 95% for the second session, and more than 90% for the third session (Table 2). If the values post 2nd and 3rd sessions are compared to the pre-dialysis values of the first session, the decrease was at least 99.5% and 99.7%, respectively.

No AEs at least possibly related to gadoteric acid were reported. No AEs occurred at the injection site during the observation period. There were no clinically relevant changes in mean laboratory values and vital signs. No cases of NSF have been reported so far.

CONCLUSIONS

The results of the study indicate that gadoteric acid was effectively removed by 3 hemodialysis sessions in patients with ESRD. The good general safety profile of gadoteric acid was also confirmed.

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