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Pharmacokinetics of Atenolol in Patients Treated With Chronic Hemodialysis or Peritoneal Dialysis

Vito M. Campese, MD, Eben I. Feinstein, MD, Victor Gura, MD,
William D. Mason, MD, and Shaul G. Massry MD

Atenolol is a relatively selective beta₁-adrenoceptor blocking agent devoid of partial agonist or membrane stabilizing properties.^{1,2} The drug is not significantly bound to plasma proteins and it is excreted in the urine unchanged.^{3,4} The elimination half-life in subjects with normal renal function is six to seven hours.^{3,5} However, since the elimination of the drug is closely related to glomerular filtration rate (GFR), its half-life is prolonged in subjects with impaired renal function proportionately to the decrease in GFR.⁶ In dialysis patients, there is very little elimination of the drug during the interdialytic period. The apparent plasma half-life of atenolol in these patients ranges between 42 and 73 hours.⁷⁻¹⁰ However, during a standard hemodialysis procedure of four hours, plasma concentration decreases by approximately 50%.¹⁰ No data are available on the effects of peritoneal dialysis on the elimination half-life of this drug. The purpose of this study was to determine the plasma half-life of this drug in patients treated with chronic peritoneal dialysis or chronic hemodialysis.

METHODS

A total of 21 patients, 11 men and ten women, with end-stage renal disease were studied. Fifteen were Hispanic, three black, two white, and one Oriental. Their ages ranged between 24 and 63 (mean, 41 ± 2.6) years. Ten patients were managed with maintenance

hemodialysis, three times weekly; 11 patients were treated with chronic in-center peritoneal dialysis. All patients on hemodialysis were dialyzed for five hours with hollow-fiber dialyzers (Cordis-Dow 1.3 m²). Patients receiving peritoneal dialysis were dialyzed for 12 hours with a PDS 300 machine (Physio-Control) using a flow rate of 400 mL/min/5 min, a dwell time of 12 minutes and an outflow of 13 minutes.

After the nature of the study was explained to all participants, written informed consent was obtained. All patients were admitted to the Clinical Research Center on the morning of the day before they were to receive dialysis therapy. They were given a dose of 100 mg of atenolol orally. A blood sample was drawn before and five hours after dosing. The following day, patients underwent regular dialysis. Plasma atenolol levels were determined before and 2, 3, 4, and 5 hours during dialysis in patients undergoing hemodialysis. In those treated with peritoneal dialysis, vital signs and plasma atenolol levels were determined before and 0.5, 1, 3, 6, 9, and 12 hours during dialysis.

Blood samples were collected in prechilled tubes, centrifuged at 4°C, and the plasma was stored at -20°C until analysis. Atenolol concentrations were assayed with the high pressure liquid chromatography method.¹¹ The data were evaluated statistically by Student's *t* test and are expressed as the mean ± standard error of the mean.

RESULTS

Plasma levels of atenolol before and during hemodialysis or peritoneal dialysis are summarized in the Table. The elimination half-life of atenolol during hemodialysis was 7.3 ± 0.51 hours, corresponding to a reduction of about 34% in the plasma concentration. Plots of the logarithm of plasma atenolol levels during peritoneal dialysis versus time on dialysis (Figure) yielded a relatively linear relationship. However,

From the Division of Nephrology and Department of Medicine, University of Southern California School of Medicine, Los Angeles, CA. This work was supported in part by grant GCRG-RR-43 from the General Clinical Research Centers Program of the Division of Research Services of the National Institutes of Health and by a grant from Stuart Pharmaceuticals, Division of ICI Americas, Inc. Address for reprints: Vito M. Campese, MD, Division of Nephrology, USC School of Medicine, 2025 Zonal Ave, Los Angeles, CA 90033.

TABLE

Plasma Atenolol Concentrations

Patients	Day 1		Day 2 (dialysis)			
Hemodialysis						
Time (hrs)	5*	0†	2	3	4	5
Plasma atenolol (ng/mL)	486 ± 94.3	378 ± 55.6	268 ± 38.3	244 ± 37.8	236 ± 37.0	229 ± 34.5
Peritoneal Dialysis						
Time (hrs)	5*	0†	3	6	9	12
Plasma atenolol (ng/mL)	588 ± 79.0	456 ± 57.1	410 ± 52.7	367 ± 47.1	348 ± 45.1	307 ± 43.9

*Hours after dosing.

†Approximately 24 hours after dosing.

Values are expressed as mean ± standard error of the mean.

plots of the logarithm of plasma atenolol levels during hemodialysis versus time on dialysis yielded a biexponential curve. Estimation of atenolol elimination gave half-life values of 4.2 ± 0.32 hours during zero to two hours and 17.3 ± 2.4 hours during three to five hours of hemodialysis.

DISCUSSION

We found an average reduction of 22% in plasma atenolol levels during the dialysis-free intervals, both in patients on chronic hemodialysis and in patients on chronic intermittent peritoneal dialysis. However, Seiler and associates¹² found no decrease in plasma levels during the interdialytic period in six patients on chronic hemodialysis.

Dialysis removes a substantial amount of this drug from the blood. In the present study, we have shown that the elimination half-life during five hours of hemodialysis is approximately 7.3 hours corresponding to a reduction in blood levels of 34%. This value is not markedly different from the value of 7.5 ± 3.7 hours obtained by Flouvat and associates,¹⁰ but higher than the five hours obtained by Seiler and colleagues.¹² During peritoneal dialysis, the elimination half-life is approximately 23 hours, and a 12-hour peritoneal dialysis reduces plasma levels by 26%.

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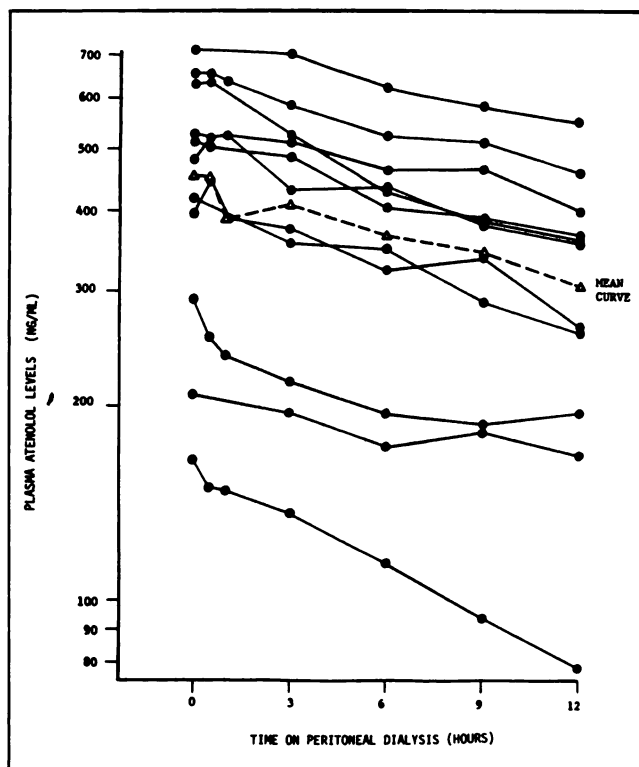


Figure. Plasma atenolol levels (ng/mL) during peritoneal dialysis in 11 patients with chronic renal failure treated with chronic peritoneal dialysis.

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