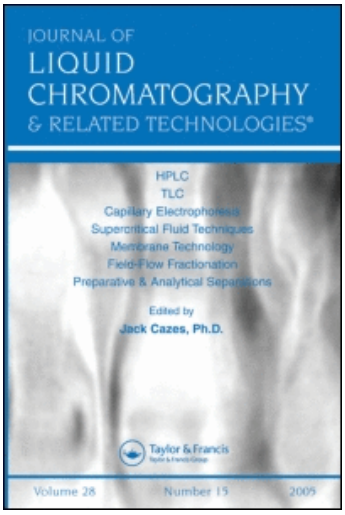

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Measurement of Ceftriaxone in Peritoneal Dialysis Solutions by High-Performance Liquid Chromatography

Milap C. Nahata[a]
[a] Colleges of Pharmacy and Medicine the Ohio State University and Wexner Institute for Pediatric Research Children's Hospital, Columbus, Ohio

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MEASUREMENT OF CEFTRIAXONE IN PERITONEAL DIALYSIS SOLUTIONS BY HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

MILAP C. NAHATA
Colleges of Pharmacy and Medicine
The Ohio State University; and
Wexner Institute for Pediatric Research
Children's Hospital
Columbus, Ohio 43210

ABSTRACT

A simple, rapid, and reproducible reverse phase high-performance liquid chromatographic method for the measurement of ceftriaxone in peritoneal dialysis solutions is described. The mobile phase contained acetonitrile, phosphate buffer, deionized water and an ion pair agent. The samples were injected onto a C18 column and detector was set at 280 nm. The retention time for ceftriaxone and the internal standard was 7.04 and 3.74 min,

Address for correspondence:

Dr. Milap C. Nahata
College of Pharmacy
Ohio State University
500 West 12th Avenue
Columbus, OH 43210

respectively. The standard curves were linear and the coefficient of variation was <3%. The method was used successfully to evaluate the stability of ceftriaxone in the two commercially available dialysis solutions; ceftriaxone was found to be stable for at least 6 hours in each solution at 37°C.

INTRODUCTION

Ceftriaxone is a broad spectrum, third-generation cephalosporin which is effective against a variety of gram-negative and gram-positive bacteria.[1] It has the longest half-life among all cephalosporins which allows less frequent administration of daily doses. The favorable clinical efficacy and safety as well as convenient dosage schedule have made ceftriaxone the most commonly used parenteral third-generation cephalosporin in the hospitals.

Continuous ambulatory peritoneal dialysis (CAPD) is used widely in patients with end-stage renal disease. Bacterial infection is the primary complication of CAPD.[2] Ceftriaxone may be used as an antibiotic in certain patients to treat the infection. Normally, 1) ceftriaxone would be added to the dialysis solutions; 2) the solutions would be warmed to body temperature (37°C) before instillation into the peritoneum to minimize patient discomfort and other complications; and, 3) the dialysis may be carried out for a dwell time of 6 hours per exchange with several exchanges daily. The concentration of ceftriaxone in dialysis solutions may decline under such conditions.

It should be noted that no data are available about the stability of ceftriaxone in dialysis solutions. Because of lack

of a high-performance liquid chrometographic (HPLC) method for ceftriaxone in dialysis solutions, we developed such a method with the intent to use it to conduct its stability studies in two types of peritoneal dialysis solutions. The purpose of this article is to describe a simple, accurate and reproducible reverse-phase HPLC method as well as its application in simulated clinical situations.

Materials and Methods

Equipment

The chromatographic system consisted of a model 110A Beckman pump, chromagabond C18 column (30 cm x 4.6 mm), Varian 2050 detector, and Anspec D 2000 integrator, and a Varian 9090 autosampler.

Chemicals and Reagents

These included ceftriaxone standards (RO-13-9904/001 Lot 4013, Hoffmann-La Roche), 7-chloro-1-ethyl-5-phenyl-3H-1, 4-benzodiazepine-2-one as an internal standard (RO 5-2922/000 Lot 10694-292-A1, Hoffmann-La Roche), acetonitrile (Baker), hexadecyltrimethyl ammonium bromide as anion pair reagent (HDTAB Fisher Scientific), and phosphate buffer.

Commercially available ceftriaxone (Rocephin, Lot 4481, Hoffman La-Roche), and the two dialysis solutions (Travenol) were used to perform the studies. Each of two commercially available dialysis solutions were studied: Dianeal PD-1 1.5% dextrose 500-mL bags (Travenol Labs, Inc., Deerfield, IL 60015, Lot CO94284) and Dianeal PD-1 4.25% dextrose 500-mL bags (Travenol Labs Inc., Deerfield, IL 60015, Lot CO 89953). Each 100 ml of dialysate contained the following: sodium chloride 567 mg, sodium lactate 392 mg, calcium chloride 25.7 mg, and magnesium chloride 15.2 mg.

Mobile phase

Each 1000 mL of mobile phase consisted of acetonitrile 500 mL, deionized water 487.5 mL, phosphate buffer 12.5 mL (pH 7.2), and ion pair HDTAB 6 g.

Standard Curves

The concentrations of ceftriaxone in dialysis solutions is generally 1 mg/ml when treating patients with peritonitis. Thus, the concentrations for the standard curve were 0.25, 0.50, 1.0, 1.5 and 2.0 mg/mL.

Chromatographic procedure

The mobile phase flow rate was maintained at 2.4 mL/min. The detector was set at 280 nm, and the chart speed was 2.5 mm/min. The samples were injected onto the column by an autosampler which withdrew 50 mcL for analysis from each vial.

Application

The samples from two commercially available dialysis solutions containing ceftriaxone 1 mg/mL were processed as the standards. These solutions were then warmed to 37°C and ceftriaxone was measured at 0, 6 and 12 hours to evaluate its stability.

Results and discussion

Each chromatographic run required about 10 minutes. Ceftriaxone eluted at 7.04 minutes, and the internal standard at 3.74 minutes. Typical chromatograms of commercially available dialysis solution without any drug, and with ceftriaxone as well as internal standard are shown in Figure 1.

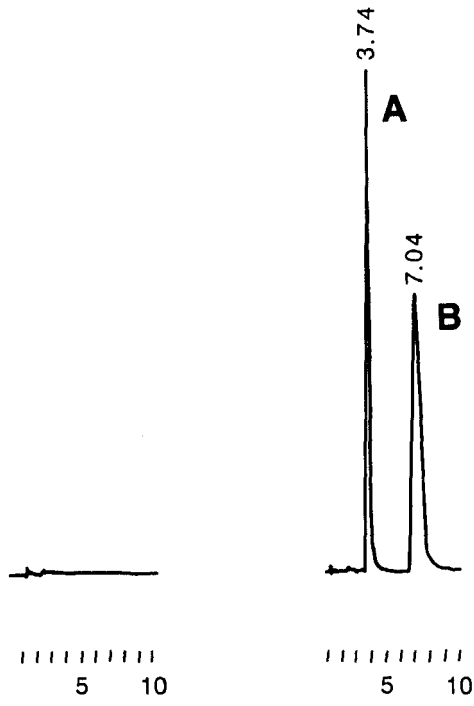

Figure 1. Chromatograms of commercially available dialysis solution without any drug (left) and with ceftriaxone (B) and internal standard (A).

Linearity was determined by linear regression analysis of the data (Table 1). The r value was 0.999. The interday and intraday coeficient of variation was <3%. The accuracy ranged from 99 to 102% (Table 2).

The application of the method showed that ceftriaxone was stable for at least 6 hours in each of two dialysis solutions at 37°C. A loss of >10% of the initial ceftriaxone concentration was considered to be clinically important loss of potency. Thus, the

Table 1. Ratios of peak height for ceftriaxone/internal standard at various ceftriaxone concentrations

Concentration mg/mL	Ratio
0.25	0.293
0.50	0.560
1.0	1.118
1.5	1.761
2.0	2.279

Table 2. Accuracy of ceftriaxone assay

Known concentration mg/mL	Determined concentration (mean, n=5) mg/mL	Percent found
0.5	0.49	99
2.0	2.04	102

Table 3. Stability of ceftriaxone in dialysate solutions at 37°C

	Mean percentage of initial concentration	
Hours in dialysate	1.5% dextrose	4.25% dextrose
0	100	100
6	93.0	95.7
12	68.6*	65.5*

* $P < 0.01$ when compared with initial concentration.

stability of ceftriaxone was <12 hours in each dialysis solution at 37°C (Table 3).

These data suggest that ceftriaxone should be added after warming the dialysis solutions to 37°C and just before starting the dialysis so that its potency can be assured for the 6-hour dwell time for an exchange.

In conclusion, our method was found to be simple, rapid, accurate and reproducible for the measurement of ceftriaxone in peritoneal dialysis solutions. The method was used successfully to evaluate the stability of ceftriaxone in the two commercially available dialysis solutions at 37°C over a 12 hour period.

REFERENCES

1. Nahata MC, Barson WJ. Ceftriaxone: A review. Drug Intell Clin Pharm 1985;19:900-906.

2. Peterson PK, Matzke G, Keane WF. Current concepts in the management of peritonitis in patients undergoing continuous ambulatory peritoneal dialysis. Rev Inf Dis 1987;9:604-612.