Original Article

Evaluation of Phenylephrine Stability in Polyvinyl Chloride Bags

Josiah J. Jansen, PharmD^{*}; Alan R. Oldland, BS RPh[†]; and Tyree H. Kiser, PharmD^{*}

Abstract

Purpose: Phenylephrine hydrochloride (HCl) is commonly used to maintain adequate blood pressure during shock and shocklike states. Phenylephrine is prepared in concentrated stock vials that require further dilution prior to administration. This study evaluated the physical and chemical stability of phenylephrine in extemporaneously prepared polyvinyl chloride (PVC) bags.

Methods: Phenylephrine HCl 10 mg/mL solution was diluted with 0.9% sodium chloride for injection to final concentrations of 200 µg/mL and 400 µg/mL and stored at room temperature (23°C–25°C) exposed to fluorescent light. Stability of phenylephrine HCl was evaluated by high-performance liquid chromatography on days 0, 7, 14, 21, 30, 45, and 60.

Results: Phenylephrine HCl 200 and 400 µg/mL solutions in PVC bags were physically stable during the entire 60-day study period. Phenylephrine HCl retained > 95% of the original concentration.

Conclusion: Phenylephrine HCl diluted to 200 or 400 µg/mL with 0.9% sodium chloride for injection is both physically and chemically stable for a period of 60 days with ≤5% degradation when stored at room temperature and exposed to fluorescent lighting.

Key Words—alpha-1-adrenergic agonist, HPLC, neosynephrine, phenylephrine, stability, vasopressor

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Phenylephrine is a synthetic sympathomimetic agent used to maintain adequate blood pressure during anesthesia as well as treat vascular failure in shock and shocklike states.¹ Phenylephrine can be administered as an intravenous bolus or continuous intravenous infusion. Phenylephrine is prepared in concentrated stock vials that require further dilution prior to administration. Our institution commonly prepares infusions by adding phenylephrine 50 mg, 100 mg, or 200 mg to 250 mL of 0.9% sodium chloride for injection.

Previous stability studies have shown phenylephrine to be stable for 14 days at room temperature when diluted to 100 and 200 µg/mL in sodium chloride 0.9% in polyvinyl chloride (PVC) bags.² However, no studies have evaluated the stability of phenylephrine stored in PVC bags for as long as 60 days.

The purpose of this study was to determine the physical and chemical stability of phenylephrine diluted to 200 and 400 µg/mL in sodium chloride 0.9% PVC bags when stored at room temperature while exposed to normal fluorescent lighting. Stability of the diluted phenylephrine solutions was evaluated over a 60-day period.

METHODS

Sample Preparation

Dilution of phenylephrine hydrochloride^a to 200 and 400 µg/mL was conducted by the University of Colorado Hospital Pharmacy under aseptic technique by adding either 50 or 100 mg of phenylephrine to 250 mL sodium chloride 0.9% PVC bags^b. The bags were then stored at room temperature (23°C–25°C) under normal fluorescent lighting. Three bags for each

^{*}Clinical Specialist, Sterile Compounding, [†]Acute Care Pharmacy Manager, Department of Pharmacy, University of Colorado Hospital, Aurora, Colorado; [‡]Department of Clinical Pharmacy, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, Colorado. Corresponding author: Josiah J. Jansen, PharmD, Clinical Specialist, Sterile Compounding, Department of Pharmacy, University of Colorado Hospital, 12605 E. 16th Avenue, Aurora, CO 80045; phone: 720-848-1389; fax: 720-848-4190; e-mail: josiah.jansen@uchealth.org

concentration were assessed for physical and chemical stability over a total period of 60 days. Stabilities were assessed on days 0, 7, 14, 21, 30, 45, and 60.

Physical Evaluation

Physical stability of phenylephrine was assessed by visual examination. Solutions were evaluated against a black and white background for visible particulate matter, cloudiness, or color change. The pH of the samples was not assessed, as previous studies have not demonstrated appreciable changes in pH.³

High-Performance Liquid Chromatographic Analysis

Phenylephrine concentrations were determined by using high-performance liquid chromatography (HPLC) with ultraviolet detection according to previously published stability-indicating methods with minor modifications.^{2,3} The HPLC system utilized an autosampler^c, delivery pump^d, C-18 column^e, a variable-wavelength ultraviolet light detector set at 273 nm^f, a data integrator^g, and a solvent waste container. The mobile phase consisted of 0.02 M ammonium acetate with 4% (v/v) acetonitrile adjusted with 1 N sodium hydroxide to a pH of 7.2 and was set to a flow rate of 1 mL/min. Analytical-grade phenylephrine^h powder was used for validation and quality control of the HPLC assay. Aliquots of phenylephrine (20 μ L) were then injected into the HPLC system for analysis.

Chromatogram peak heights were utilized for determining phenylephrine concentrations. All samples for each of the storage conditions were assayed in duplicate. Calibration of the HPLC system utilized 8 known concentrations from 100 to 450 μ g/mL of phenylephrine and was conducted twice daily on each of the study days. The accuracy and precision of our assay met standards set for bioanalytical method validation.⁴

Stability Analysis

The percentage of phenylephrine remaining at each time point was determined. The product was deemed stable if there was less than 10% degradation of the initial product.

RESULTS

Phenylephrine diluted to 200 and 400 μ g/mL in 0.9% sodium chloride for injection was physically stable throughout the study. Less than 5% phenylephrine degradation was observed over the 60-day study period (Table 1). Solutions remained clear and no precipitation was observed throughout the study.

DISCUSSION

Previous studies have evaluated the extended stability of phenylephrine diluted in sodium chloride 0.9%.^{2,4} A study by Gupta² evaluated phenylephrine diluted to 100 and 200 mcg/mL in sodium chloride 0.9% PVC bags using stability-indicating HPLC analysis. This study found less than 1% degradation of phenylephrine when stored at room temperature exposed to light over a 14-day period. Kiser et al⁴ utilized stability-indicating HPLC analysis to evaluate the stability of phenylephrine diluted to 100 mcg/mL in sodium chloride 0.9% packaged in polypropylene plastic syringes. Less than 2% degradation of phenylephrine was found over 30 days in syringes stored at room temperature exposed to light, refrigerated in the dark, or frozen in the dark. The present study similarly showed phenylephrine to be stable for at least 60 days when diluted to either 100 or 200 mcg/mL in sodium chloride 0.9% PVC bags and stored at room temperature exposed to light. Although phenylephrine was demonstrated to be stable for 60 days, the manufacturer does not

Table 1. Stability of phenylephrine 200 μ g/mL and 400 μ g/mL repackaged in 250 mL PVC bags and stored at room temperature

Phenylephrine in 0.9% NaCl	Actual initial drug concentration, μ g/mL	% Initial concentration remaining					
		Day 7	Day 14	Day 21	Day 30	Day 45	Day 60
200 μ g/mL	200.5 $\pm$ 1.6	99.7 $\pm$ 0.9	99.8 $\pm$ 1.1	99.3 $\pm$ 1.0	98.3 $\pm$ 1.2	96.9 $\pm$ 1.2	95.2 $\pm$ 1.1
400 μ g/mL	401.3 $\pm$ 2.0	99.9 $\pm$ 0.4	99.7 $\pm$ 0.5	99.6 $\pm$ 0.6	98.9 $\pm$ 0.4	98.0 $\pm$ 0.7	96.6 $\pm$ 0.7

Note: Preparations were exposed to normal fluorescent lighting. Three polyvinyl chloride (PVC) bags were prepared for each concentration. Contents from each of these 6 admixtures were prepared and analyzed in duplicate for high-performance liquid chromatography (HPLC) analysis on the day of assay.

package phenylephrine vials with a preservative, and the sterility of prepared phenylephrine solutions must be assessed according to the standards in chapter 797 of the *United States Pharmacopeia*.⁵ Our institution has utilized this information to implement batching phenylephrine in clinical practice. Twenty-one batches totaling 1,370 admixtures have been prepared and tested for sterility to date, with 100% of batches found to be sterile.

Knowledge of the extended stability of phenylephrine in PVC bags will allow pharmacies to prepare infusions in advance and store them in automated medication dispensing machines on nursing units. This will allow immediate access to the medication and reduce drug delivery time, which is critically important for vasoactive medications. Additionally, extended stability is likely to reduce drug wastage over time.

CONCLUSION

Phenylephrine diluted to 100 and 200 mcg/mL in sodium chloride 0.9% injection was stable for at least 60 days when stored in PVC bags at room temperature.

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APPENDIX

- ^a Phenylephrine hydrochloride injection, USP. 10 mg/mL (1%), 5 mL vial. Manufactured for Sandoz, Inc., Princeton, NJ 08540. Lot 053112.
- ^b 0.9% Sodium Chloride Injection USP. 250 mL Viaflex container. Baxter Healthcare Corporation, Deerfield, IL. Lot C884189.
- ^c Beckman Coulte Model 508 Autosampler. Beckman Coulter, Inc., Fullerton, CA 92834-3100.
- ^d Beckman Coulter Model 118 Delivery Module. Beckman Coulter, Inc., Fullerton, CA 92834-3100.
- ^e *Phenomenex* Luna 5 μ m C-18 150 mm x 4.6 mm column. Phenomenex, Torrance, CA. Serial 80836-8. Batch 5291-32.
- ^f Beckman Coulter Model 166 Detector. Beckman Coulter, Inc., Fullerton, CA 92834-3100.
- ^g 32 Karat software version 8.0. Beckman Coulter, Inc., Fullerton, CA 92834-3100.
- ^h Phenylephrine hydrochloride. Sigma-Aldrich Inc., St. Louis, MO 63103. Lot 055K1677.