Sodium nitroprusside (NPS) is a potent vasodilator used in critical care and peri-operative settings for the management of hypertension and metabolic pathways. It has the potential to cause cyanide and thiocyanate toxicity. Protective covering is needed to prevent exposure to ambient light. Concentrations of nitroprusside, thiocyanate and cyanide are substantial in some circumstances. Nitroprusside is used in the treatment of hypertension and for vasospasm, with no adverse events reported.

Materials & Methods

Chemical Stability

Materials

Samples were prepared by adding the contents of a 50 mg vial of sodium nitroprusside (NDC 0491-3204-01). Concentration 50 mg/mL. Hospira, Inc., Lake Forest, IL. Lot number: 76790DD) and 2 mL of a 250 mg/mL sodium thiosulfate pentahydrate (sodium thiosulfate. NDC 0517-5019-01. Concentration 250 mg/mL. American Regent, Shirley, NY. Lot number: 82022DD). Nine sets of each type were stored at ambient conditions and protected from light.

Physical Stability

The appropriateness of the chromatographic method conditions were evaluated by calculating the %RSD of area from triplicate standard injections. The %RSD of triplicate standard curve was prepared by plotting peak area versus standard concentration.

For each compound, a standard mixture was prepared in water at concentrations 0.01 mg/mL to 0.1 mg/mL for nitroprusside, 0.1 mg/mL to 1.0 mg/mL for nitrate, and 0.01 mg/mL to 1.0 mg/mL for thiocyanate. For each compound, a standard curve was prepared by plotting peak area versus standard concentration. The correlation coefficient must be ≥ 0.995.

The %RSD and the linear regression were based on the peak area ratio for the 1:10 admixture. The correlation coefficient must be ≥ 0.995.

For each compound, the reproducibility of the method was assessed by calculating the %RSD of area from triplicate standard injections. The %RSD of triplicate peak area injection must be ≤ 2%.

For each compound, the precision of the method was assessed by calculating the %RSD of area from triplicate standard injections. The %RSD of triplicate standard curve was prepared by plotting peak area versus standard concentration. The correlation coefficient must be ≥ 0.995.

Stability samples were prepared by adding the contents of a 50 mg vial of sodium nitroprusside (NDC 0491-3204-01). Concentration 50 mg/mL. Hospira, Inc., Lake Forest, IL. Lot number: 76790DD) and 2 mL of a 250 mg/mL sodium thiosulfate pentahydrate (sodium thiosulfate. NDC 0517-5019-01. Concentration 250 mg/mL. American Regent, Shirley, NY. Lot number: 82022DD). Nine sets of each type were stored at ambient conditions and protected from light.

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References


Conclusions

Nitroprusside and thiosulfate 1:10 IV admixture is chemically and physically stable for up to 48 hours when stored at room temperature and protected from light. The admixture is an alternative anti-hypertensive agent and provides a more economical option than nicardipine or clevidipine.

Stability of Sodium Nitroprusside and Sodium Thiosulfate 1:10 Intravenous Admixture

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Chemical Stability

The method was verified as linear, repeatable, and accurate. HPLC analysis revealed that chemical stability is retained upon initial mixing of nitroprusside and thiosulfate. Upon mixing, the mean nitroprusside concentration was 0.19 mg/mL and the mean thiocyanate concentration was 0.09 mg/mL. The chemical stability results were compared to the results of conventional dosing of nitroprusside and thiosulfate admixture. Over a period of eight hours, the results showed that the chemical stability was retained.

Physical Stability

Physical stability was assessed using a visual inspection technique previously described and determined to be more reliable than turbidimetric methods. To 250 mL infusion bags were prepared using aseptic technique. The first bag contained 50 mg nitroprusside and 500 mg thiosulfate in D5W; the second contained 50 mg nitroprusside and 250 mg thiosulfate in NS. The bags were then stored at room temperature for 48 hours. After 48 hours of fluorescent light exposure (data not shown). Thiosulfate was not found in a measurable quantity in the admixture. The formation of thiosulfate requires the enzymatic activity of microorganisms, which may be expected.

Results

The combined admixture bags were given a compatible rating at all time points in the study, which demonstrates the physical stability of the nitroprusside/thiosulfate admixture.

Economic Analysis

Results of the economic analysis of hypertension treatment options indicate that a savings can be realized by maintaining the nitroprusside/thiosulfate admixture (Table 1). Based on actual annual drug usage, both nitroprusside and nicardipine were used for antihypertensive treatment. The use of this compounded admixture could result in a projected annual savings of $57,480 compared to nicardipine use.

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