CLINICAL INVESTIGATION

Physical Compatibility of Alprostadil with Commonly Used IV Solutions and Medications in the Neonatal Intensive Care Unit

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OBJECTIVE To determine the physical compatibility of alprostadil with intravenous (IV) solutions, a parenteral nutrition (PN) solution, and other intravenous medications commonly used in the neonatal intensive care unit (NICU).

METHODS To simulate y-site administration, each IV solution and the PN solution were slowly mixed 1:1 with alprostadil 15 μg/mL at 25°C. The mixtures were gently shaken and visually examined at 1, 15, 30, 45, and 60 minutes for physical incompatibility (gross precipitation, color change, haze, separation or gas production). In addition, each test tube was touched to assess for gross temperature change. The above mixtures were made a second time and each mixture was slowly mixed 1:1 with each of the test medications at 25°C. The ampicillin-parenteral nutrition and the chlorothiazide-parenteral nutrition solution mixtures were not tested with alprostadil. The mixtures were examined for physical incompatibility as described above.

RESULTS Alprostadil was visually compatible with D5W 0.45% NaCl, D5W 0.45% NaCl with 20 mEq KCl/L, D10W 0.45% NaCl, D10W 0.45% NaCl with 20mEq KCl/L, and a PN solution. Alprostadil was visually compatible with ampicillin, cefazolin, cefotaxime, chlorothiazide, dobutamine, dopamine, fentanyl, furosemide, gentamicin, methylprednisolone, tobramycin, vancomycin and vecuronium when mixed in D5W 0.45% NaCl, D5W 0.45% NaCl with 20mEq KCl/L, D10W 0.45% NaCl, and D10W 0.45% NaCl with 20mEq KCl/L. Alprostadil was visually compatible with cefazolin, cefotaxime, dobutamine, dopamine, fentanyl, furosemide, gentamicin, methylprednisolone, tobramycin, vancomycin and vecuronium when mixed in a PN solution. In addition, no gross temperature change was detected in any mixture.

CONCLUSIONS Based on the results, alprostadil is physically compatible with the tested IV solutions and a PN solution, as well as commonly prescribed IV medications used in the NICU when mixed with the tested IV solutions and a PN solution.

KEYWORDS alprostadil, IV compatibility

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INTRODUCTION

Alprostadil is FDA approved and used as palliative therapy in neonates who have congenital heart disease to temporarily maintain the patency of the ductus arteriosus until corrective or palliative surgery can be performed. The congenital defects include pulmonary atresia, pulmonary stenosis, tricuspid atresia, tetralogy of Fallot, interruption of the aortic arch, coarctation of the aorta, and transposition of the great vessels with or without other defects. The drug is administered as a continuous infusion into a large vein or through the umbilical

ABBREVIATIONS NICU, neonatal intensive care unit; PN, parenteral nutrition

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Table 1. Physical Compatibility of Alprostadil (15 mcg/ml) with IV Solution

IV Solution	Manufacturer	Finding
D5W 0.45% NaCl	Baxter, Deerfield, IL	C
D5W 0.45% NaCl + 20 mEq/L KCl	Baxter, Deerfield, IL	C
D10W 0.45% NaCl	Pharmacy Prepared	C
D10W 0.45% NaCl + 20 mEq/L KCl	Pharmacy Prepared	C
PN Solution*	Pharmacy Prepared	C

**see Table 3 for composition*
C, compatible; PN, parenteral nutrition

artery catheter. The starting dose is 0.05 to 0.1 μg /kg/hr. Generally, it is recommended to start at 0.1 μg /kg/hr, but responses have been reported at 0.05 μg /kg/hr. After a desired effect is achieved, the rate of infusion should be decreased to provide the lowest possible dosage that maintains a response.[1]

Alprostadil, also know as prostaglandin E_1, is one of a group of naturally occurring substances with various pharmacological activities. It is available as an injectable solution of 500 μg /mL in dehydrated alcohol. It is recommended to dilute the drug in either 5% dextrose or 0.9% NaCl in the range of 2 to 20 μg /mL prior to administration. Undiluted alprostadil injection may interact with the plastic sidewall of volumetric infusion chambers causing a change in appearance.[1]

Very little information is available about the compatibility of alprostadil with IV solutions and medications commonly used in neonates with congenital heart disease.[1] This study was undertaken to evaluate the physical compatibility of alprostadil injection with commonly used intravenous (IV) solutions, a parenteral nutrition (PN) solution, and 13 medications commonly used in the NICU.

MATERIALS AND METHODS

The selection of the IV solutions and medications was based on a review of records of infants with congenital heart disease who had received alprostadil (Tables 1 and 2). D5W 0.45% NaCl and D5W 0.45% NaCl with 20 mEq/L of KCl were commercially available solutions (Baxter, Deerfield, IL). D10W 0.45% NaCl and D10W 0.45% NaCl with 20 mEq/L of KCl were prepared by the pharmacy. The 15 μg /mL alprostadil solution was prepared by adding 1.5 mL of the 500 μg /mL commercial alprostadil injection (Bedford, Bedford, OH) to 48.5 mL of D5W (Baxter, Deerfield, IL) in a 60 mL syringe (B-D, Plainfield, NJ). Three syringes were pre-

Table 2. Medications Tested

Drug	Manufacturer	Concentration
Ampicillin	Squibb, Princeton, NJ	100 mg/mL
Cefazolin	Eli Lilly & Co., Indianapolis, IN	100 mg/mL
Cefotaxime	Hoechst, Bridgewater, NJ	100 mg/mL
Chlorothiazide	Merck & Co., White House, NJ	25 mg/mL
Dobutamine	Abbott Labs, Abbott Park, IL	3000 μg/mL
Dopamine	Abbott Labs, Abbott Park, IL	3000 μg/mL
Fentanyl	Janssen Pharmaceutica, Titusville, NJ	10 μg/mL
Furosemide	Abbott Labs, Abbott Park, IL	5 mg/mL
Gentamicin	Elkin-Sinn, Inc., Cherry Hill, NJ	1 mg/mL
Methylprednisolone	Pharmacia Corp., New York, NY	40 mg/mL
Tobramycin	Eli Lilly & Co., Indianapolis, IN	1 mg/mL
Vancomycin	Eli Lilly & Co., Indianapolis, IN	5 mg/mL
Vecuronium	Organon Inc., West Orange, NJ	1 mg/mL

Table 3. Parenteral Nutrition Solution

Component	Concentration
Dextrose %	17.50%
Amino Acids (TrophAmine®)	3.75%
Sodium	25 mEq/L
Potassium	19 mEq/L
Calcium	19 mEq/L
Magnesium	3.8 mEq/L
Phosphates	12.5 mEq/L
Acetate	25 mEq/L
MVI- Ped	52 mL/L
Trace Element Injection 4, Pediatric	2.5 mL/L
Ranitidine	73 mg/L

pared to complete the study. Medications available as lyophilized powders were reconstituted with sterile water for injection (Abbott, North Chicago, IL) or 0.9% saline injection (Abbott, North Chicago, IL) as recommended by the manufacturer. The resulting solutions were allowed to sit for 30 minutes and were visually inspected for complete dissolution of the powder. The reconstituted medications, as well as the medications available as solutions, were diluted with either D5W (Baxter, Deerfield, IL) or 0.9% NaCl (Baxter, Deerfield, IL) to standard concentrations used in our NICU (Table 2). The composition of the PN solution was the same as one being administered to a congenital heart disease patient in the NICU at the time of the study and represents a typical solution used in the NICU (Table 3).

Allen et al. showed that mixing a secondary solution at a 1:1 ratio simulates a medication that is administered via a Y-site injection port of a primary line.[2] Two mL of each of the IV solutions and the PN solution were added to a clean, dry glass test tube. An equal volume of the 15 µg /mL solution of alprostadil was slowly added. Each test tube of alprostadil-IV solution and the alprostadil-PN solution mixture was capped and gently inverted several times to assure adequate mixing.

Using the same technique and method as that previously described for the IV solutions/PN solution study, each medication (i.e., ampicillin, cefazolin, cefotaxime, chlorothiazide, dobutamine, dopamine, fentanyl, furosemide, gentamicin, methylprednisolone, tobramycin, vancomycin, and vecuronium) was slowly added in equal volume to a freshly prepared IV solution/alprostadil mixture and PN solution/alprostadil mixture. Ampicillin and chlorothiazide were not tested with alprostadil in the PN solution, as they are known to be incompatible.

Each resulting mixture was visually examined in fluorescent lighting against a white and black background at 1 minute and thereafter at 15 minute intervals for 60 minutes for physical incompatibility (visible precipitation, color change, haze, separation, or gas production). The examination was done both with the naked eye and with a magnifying glass. In addition, each test tube was touched and assessed for gross temperature change indicating an exothermic or endothermic reaction.

RESULTS AND DISCUSSION

Alprostadil was physically compatible with all the IV solutions tested: D5W 0.45% NaCl, D5W 0.45% NaCl with 20 mEq/L, D10W 0.45% NaCl, D10W 0.45% NaCl with 20 mEq/L and the PN solution (Table 1). Table 4 lists the visual compatibility of all IV solutions, the PN solution and the medications tested together with alprostadil. No medications were found to be visually incompatible when mixed with alprostadil in the tested IV or PN solutions. In addition, no gross temperature change was detected for any admixture.

The compatibility of alprostadil in the IV and PN solutions tested and with the 13 medications tested in these solutions, does not constitute full compatibility, as micro-precipitation and chemical compatibility were not tested. Compatibility with the medications tested at any other concentration than used in this study also cannot be assured. Compatibility is not known with total nutrient solutions (3 in 1 solutions) or with a PN solution with a piggybacked IV fat emulsion, as testing with these solutions or situations was not done.

In conclusion, alprostadil at 15 µg /mL was physically compatible with the IV solutions tested, a PN solution, and 13 medications in these solutions when mixed 1:1 to simulate Y-site administration. Further studies are need to determine chemical stability, if micro-precipitation occurs, stability in total parenteral

Table 4. Compatibility of Alprostadil with Combination of Medication and IV Solution

Medication*	D5W 0.45%NaCl	D5W 0.45%NaCl + 20mEq/L KCl	D10W 0.45%NaCl	D10W 0.45%NaCl + 20 mEq/L KCl	PN Solution
Ampicillin	C	C	C	C	N/A
Cefazolin	C	C	C	C	C
Cefotaxime	C	C	C	C	C
Chlorothiazide	C	C	C	C	N/A
Dobutamine	C	C	C	C	C
Dopamine	C	C	C	C	C
Fentanyl	C	C	C	C	C
Furosemide	C	C	C	C	C
Gentamicin	C	C	C	C	C
Methylprednisolone	C	C	C	C	C
Tobramycin	C	C	C	C	C
Vancomycin	C	C	C	C	C
Vecuronium	C	C	C	C	C

**see Table 2 for manufacturer*
C, compatible; N/A, Not Tested

nutrition solutions, or medications tested at concentrations not used in this study.

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