Chapter 6

Special Considerations in Pediatric Compounding

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Introduction

The number of new medications marketed in the United States is constantly on the rise. In most cases, however, despite their unique needs, these new medications are not specifically approved by the U.S. Food and Drug Administration (FDA) for pediatric use and are typically not available in a suitable dosage form for pediatric patients. Approximately 20% of currently available medications are specifically approved for use in the pediatric population.[1] Despite not being labeled for use in children, there is often a very real need for these therapies. The off-label use of medications is common in pediatric patients. Compounded formulations have an important role, especially in the treatment of infants and young children (those <6 years of age) or those patients who require tailored doses based on body size and weight and access. The fixed doses and concentrations intended for adults are often not appropriate for use in younger patients. Because these formulations are typically more suitable for adults, additional manipulations are needed. In fact, The Joint Commission suggests that the pharmacy prepare patient-specific, unit-dose pediatric medications instead of using a commercially available adult concentration so as to reduce the risk of pediatric medication errors and adverse events.[2] This chapter will focus on the issues surrounding the provision of parenteral medications to the neonatal, infant, and pediatric patient, with special emphasis on the neonate. In addition to specific compounding considerations, other aspects, such as standardization, product selection, and drug delivery systems will also be addressed.

Challenges in Drug Delivery

Concentration Considerations

Intravenous (IV) medications not approved for infants and young children are often not available in low concentrations that allow for accurate and precise measurement of small doses. For example, enoxaparin is commercially available at a lowest concentration of

100 mg/mL. If the dosing in an infant is 1.7 mg/kg, the volume of medication to be given to a 1-kg neonate is 0.017 mL, which is not possible to measure even when using a 1-mL tuberculin syringe. It is well known that there is great risk of errors occurring when measuring doses whose final volume is <0.1 mL. Such measuring errors with potent medications like morphine and digoxin have led to fatal outcomes in pediatric patients.[3,4]

One common approach to more accurately measure these small doses is to dilute the more concentrated medications intended for adults. There are numerous pitfalls associated with altering an adult formulation for use in infants and children. Often there are insufficient data to support the assigned beyond-use dating of compounded formulations, and there is the inherent risk of error whenever such compounding is done. The diluted drug's stability and sterility may not be known. Furthermore, diluted medications may be stable for varying periods of time, and dilutions derived from multidose vials can lead to lower than desired concentrations of any preservatives present. Although not practical, sterility and pyrogen tests should be done to ensure the quality of the modified extemporaneous formulation if extended dating is desired.

Routes of Delivery

Intravenous

Although the IV route is the preferred method of drug delivery in critically ill neonates (i.e., birth to 1 month), special attention must be paid to avoiding excessive fluid. In comparison to the 100 mL/hour infusion rates used in adults, full-term infants (gestational age ≥38 weeks) may only receive 10–20 mL/hr, and premature infants (gestational age <37 weeks) receive only 3–5 mL/hr.[5] A typical term infant has a total blood volume of approximately 250 mL with preterm infants having even less (e.g., 60 mL for a 600-g preterm infant).[6]

Obtaining vascular access in infants (1 month to 2 years) and children (2–12 years) is often a complicated process. Infants have poor integrity of their vascular system, reduced vascular diameter, and decreased perfusion, all of which can lead to endothelial damage during catheter insertion.[7] For these reasons, it is often difficult to find veins viable for IV access, especially in the critically ill child. In active children, peripheral catheters are more likely to become dislodged, resulting in the IV being replaced more frequently. In comparison to adults, infants and small children have smaller peripheral veins, more subcutaneous (sub-Q) fat, are prone to vasoconstriction, and are much less likely to remain still during a painful procedure or infusion of acidic medications (e.g., potassium, lidocaine). Multiple attempts at placing an IV catheter is harmful to pediatric patients for many reasons, including pain, stress, disruption of the skin's integrity, and increased risk of infection.

Scalp Vein Catheters

In addition to the more traditional peripheral and central venous catheters used in adults and older children, several other access routes are available for the small child and infant. Scalp veins should only be used once other alternative access routes are exhausted. The scalp veins provide a secondary option for peripheral intravascular access in small children and infants because of minimal sub-Q fat and the lack of a flexible joint for less movement. These differences reduce the chance of catheter dislodgement, which is a common occurrence with IV catheters placed in the arms or legs. Cannulation of the scalp vein is indicated in any patient who requires intravascular access for the administration of medications or fluids and helps preserve the vessels of the arms and legs for peripherally inserted central catheters.[8] When inserting the catheter, care must be taken to avoid placing the scalp vein catheter near sites of superficial skin injury or infection. In most cases, at least partial shaving of the infant's head is necessary. It may take 6–12 months for hair to grow back properly, which may be upsetting to the parents. Hematoma is the most common complication.[9] One of the most limiting factors associated with scalp vein catheters is the risk of infiltration of the sub-Q tissue with IV medication or fluids as it may cause superficial blistering, deep tissue necrosis, or tissue calcification, especially if calcium-containing fluids are used.[10] For these reasons, many centers do not allow the administration of vesicants or irritants (including parenteral nutrition [PN] or calcium containing fluids) through scalp catheters.