

Digging Deeper

Neonates, Puppies and Drugs – The Reasons for Caution

By Nancy P. Melone, Ph.D.

A seven-week old puppy suffering from watery diarrhea was given a child's dose of loperamide (IMODIUM A-D) by its owner on the telephone instructions of her veterinarian. An additional half dose was administered after another diarrhea episode, as per the instructions on the IMODIUM packaging. Approximately 18 hours later, the puppy was rushed to the veterinarian exhibiting cerebellar and cerebral deficits (vocalization, head pressing, non-reactive pupils and circling).

Case summarized from Staley and Staley, 1994

While many breeders know to use extreme caution when administering drugs, including over-the-counter drugs, to puppies, they might not know the basic pharmacological reasons underlying this advice. Usually, the reasons for caution involve the differences (from adults) in the rates that drugs are absorbed into the neonate's circulation system, distributed to the neonate's tissues or organs or eliminated from the neonate's body.

dog of similar size, the concentration in the puppy is much lower (more dilute) than the concentration in the older dog. This lower concentration can result in drug concentrations outside of the therapeutic range.

Differences in Neonate's Distribution of Drugs to Tissues

The way that drugs are distributed throughout the tissues in young puppies differs from that in older dogs. In animals and humans, the blood-brain barrier serves to protect the brain from certain drugs. In neonates and puppies, this barrier is considerably more permeable than in adult dogs. Drug doses that are at too low a concentration to be therapeutic in adult dogs can result in high concentrations in puppies. Likewise, toxic agents that would not affect an adult dog can produce significant accumulations within the brain of the neonate or puppy, causing developmental damage to the central nervous system. For this reason, too much drug can be distributed to the puppy's tissues, resulting in a drug overdose.

During the first two to three weeks of a puppy's life, plasma protein levels are fairly low. As such, there is less protein available to bind with highly protein-bound drugs, and free drug molecules are available for distribution to tissues. Since there are a larger percentage of drug molecules free to distribute drug to the tissues, doses of drugs that are highly protein bound must be reduced to avoid drug overdose in the puppy.

Deficiencies in the Neonate's Liver that Slow Drug Elimination (Biotransformation)

When a drug is administered to an animal, the drug must also be eliminated from the body at a particular rate or it can accumulate to toxic levels. The kidneys or liver figure prominently in the drug elimination process. Even as late as seven weeks, the neonate's liver is not fully mature. As such, deficiencies in the liver slow the rate at which the drug is eliminated from the neonate's body. Compared to an adult, the neonate eliminates drugs via the immature liver at a much slower rate than the adult dog. Given the slower rate of elimination, drugs accumulate more quickly in the neonate than in an adult dog. This increases the risk of drug overdose to the puppy because the drug can accumulate to toxic levels.

What Happened to the Puppy?

The puppy recovered completely after administration of activated charcoal and two doses of naloxone. Loperamide/IMODIUM should not be used if diarrhea is accompanied by high fever, blood in the stool, risk of liver shunt or other hepatic insufficiency, or if the patient has invasive or toxicogenic intestinal bacterial infections (this can accompany parvovirus).

In addition, veterinarians are cautioned by the authors to use very small doses of loperamide/IMODIUM in puppies. 🐾

Sources:

Bill, R. L. (2006). *Clinical Pharmacology and Therapeutics for the Veterinary Technician* (3rd ed.), St. Louis, MO. Mosby-Elsevier.

Staley E.C., & Staley, E.E. (1994). *Loperamide Intoxication in a Seven-week-old Pup*. *Veterinary Human Toxicology*, 36 (5), 451.



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Differences in Neonate Body Composition that Lower Drug Concentrations

The puppy's body contains a higher ratio of water to fat than an adult dog's body. When a drug (e.g., an injection administered subcutaneously) that typically distributes to extracellular fluid on its way to the circulation system is given to a puppy, the drug is distributed in a larger volume of water than the same amount of drug given to an older dog of identical weight. In addition, drugs are usually not absorbed easily by fat, so concentrations in adults are higher. If we compare the plasma concentration of the drug in the puppy and the older