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PHARM PROFILE

Desmopressin Acetate

- **Used to diagnose and treat central diabetes insipidus**
- **Used to treat von Willebrand's disease**

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Desmopressin acetate (1-deamino-8-D-arginine vasopressin; DDAVP) is a synthetic analogue of the antidiuretic hormone vasopressin.[1] It is useful for treating bleeding disorders, such as von Willebrand's disease, and polyuria related to central diabetes insipidus (DI) in small animals.

PHARMACOLOGY

DDAVP differs in structure from endogenous vasopressin in two places. The amino terminal is absent at position 1, and the D isomer replaces the L isomer at position 8.[2] These differences give DDAVP more antidiuretic potential and fewer vasopressor properties than vasopressin.[2] They also prolong the actions of DDAVP two- to threefold.[2]

The specific mechanism of action of DDAVP is to increase reabsorption of water in the collecting ducts of the kidneys.[1] DDAVP binds to V2 antidiuretic receptors on tubule cells in the kidneys and stimulates an increase in adenylate cyclase activity, leading to increases in cAMP concentrations,[3] which in turn increase renal tubule permeability and free water reabsorption.[3] This results in a decrease in net urine production and an increase in urine osmolality.[1] At therapeutic doses, DDAVP does not interfere with sodium or potassium excretion into the urine.[1]

In addition, DDAVP has a higher capacity compared with vasopressin to increase plasma coagulation factor VIII and von Willebrand's factor (vWF) on a dose-dependent basis.[2] The increases occur rapidly and appear to result from stimulation and release of endogenous stores of factor VIII and vWF as opposed to increased synthesis of these agents.[4] Thus when repeated doses of DDAVP are given, the response tends to lessen.[4] DDAVP cannot be administered orally because it is destroyed by the gastrointestinal tract.[1] In dogs, the antidiuretic activities of DDAVP typically begin within 1 hour after administration.[1] The action peaks in 2 to 8 hours and can last up to 24 hours.[1] The distribution and metabolism of DDAVP are not well understood. In humans, intravenous DDAVP has a terminal half-life ranging from 0.4 to 4 hours.[1]

INDICATIONS

DDAVP is used to diagnose and treat central DI in small animals. DDAVP coupled with a water deprivation test can be used to differentiate central DI, nephrogenic DI, and psychogenic polydipsia in animals presenting with polyuria and polydipsia.[2] The purpose of the water deprivation test is to assess the appropriate release of endogenous vasopressin during dehydration and the kidneys' response to vasopressin.[2] After this test, DDAVP is given (either 2 µg SC or IV or 20 µg intranasally or conjunctivally) if the animal cannot concentrate urine after losing at least 5% of its body weight.[2] Urine osmolality is then measured every 2 hours for 6 to 10 hours. If osmolality increases by at least 10%, central DI is strongly suspected.[2]

Animals with psychogenic polydipsia should have a urine concentration of greater than 1.035 with water deprivation alone. Animals with nephrogenic DI show no response to DDAVP, whereas animals with central DI have a urine concentration of greater than 1.035.[2] Once a diagnosis of central DI is made, DDAVP is a mainstay of treatment. Administration of DDAVP completely corrects

vasopressin deficiency and eliminates polyuria and polydipsia both short and long term.[2]

DDAVP is also used to treat von Willebrand's disease in breeds of dogs in which there is a high prevalence, such as Doberman pinschers, Shetland sheepdogs, Scottish terriers, golden retrievers, and poodles.[2] Although the hemostatic properties of DDAVP in cats are not well studied, when administered to normal dogs DDAVP increased plasma concentrations of coagulation factor VIII and vWF two- to fourfold in some studies.[2,5] Other studies have found more modest increases in factor VIII and vWF in dogs, but evidence suggests that DDAVP corrects bleeding time independently of increasing vWF levels.[2,4] Thus DDAVP can be used to increase hemostatic function in patients with abnormal bleeding times even if the vWF concentrations do not increase dramatically.[6] DDAVP is most useful when pet owners are taught to administer it at the first sign of hemorrhage, such as epistaxis or hematuria.[2] DDAVP increases levels of vWF more than factor VIII.[2] Factor VIII is important in the pathogenesis of hemophilia A, and the effects of DDAVP in the rare cases of dogs with hemophilia A are unknown.[2] DDAVP could also be given to a blood-donor dog 30 minutes before drawing blood to increase the concentration of vWF and factor VIII in the transfused blood if the recipient is deficient in these factors.[2]

CAUTIONS

Side effects of DDAVP are uncommon in small animals. Caution should be used when administering DDAVP to German shorthaired pointers.[2] Type II von Willebrand's disease is common in this breed, and DDAVP administration could result in thrombocytopenia when given to a patient with type II disease.[2] Caution is also needed when administering DDAVP to patients at risk for thrombotic events.[1] DDAVP is safe to use in dogs with central DI. Possible water intoxication, induced by a dysfunctional inhibitory thirst mechanism, is the major complication of DDAVP use in patients with central DI, but this problem is uncommon.[2] Likewise, hypersensitivity reactions are possible but uncommon.[1]

The safety of DDAVP for use in canine pregnancy has not been established.[1] However, no harmful fetal effects were seen when 125 times normal human doses were administered to rats and rabbits.[1]

Client Counseling Information

- DDAVP is a lifelong treatment, not a cure.
- DDAVP should be administered at the first sign of hemorrhage in von Willebrand's disease.
- Both the nasal solution and injectable product should be refrigerated.
- Monitor your pet for swelling.

ACUTE TOXICITY

Overdose may result in fluid retention or overload and subsequent hyponatremia.[1] If this occurs, appropriate treatment includes dose reduction and fluid restriction.[1] Monitoring of electrolytes is recommended.[1]

DRUG INTERACTIONS

Concomitant administration of chlorpropamide, carbamazepine, clofibrate, fludrocortisone, or urea has the potential to increase the antidiuretic effects of DDAVP and put the patient at risk for water overload.[1] The antidiuretic effect of DDAVP may be decreased with concomitant administration of lithium, epinephrine, demeclocycline, heparin, or alcohol.[1]

DOSAGE AND ADMINISTRATION

In small animals, DDAVP can be administered intravenously, subcutaneously, intranasally, or intraconjuctivally. The intraconjunctival route is preferred for animals with central DI because of ease of administration.[2] Parenteral use is recommended for patients with von Willebrand's disease because of the need for higher concentrations.[1,2] For treating central DI in dogs, the recommended dose is one to four drops of intranasal solution once or twice daily applied to the conjunctiva indefinitely.[2] The dose should be adjusted to control signs of polyuria and polydipsia.[1] Parenteral dosing is reserved for patients not responding to or tolerating DDAVP intraconjunctivally or intranasally.[2] The intranasal formulation is safe for parenteral use, and the dose is 0.5 to 2 µg IV or SC q12–24h.[2] Appropriate dosing for cats with central DI is one to two drops of the intranasal preparation intraconjunctivally q12–24h.[1]

For von Willebrand's disease, the appropriate canine dosage is 1 µg/kg SC, and the effect lasts 3 to 4 hours. Subsequent doses within 24 hours do not add benefit.[1] DDAVP can also be used intravenously in these patients but must be diluted in 0.9% normal saline and given over 20 to 30 minutes.[2]

PREPARATIONS

DDAVP is available as a nasal solution containing 10 µg/0.1 ml or 1.5 mg/ml.[1] The former is available in 2.5- and 5-ml bottles and comes with either two calibrated rhinal tube applicators (1.5 to 4 µg per drop) or a nasal compression pump that delivers 10 µg of DDAVP in each spray.[2] The 1.5-mg/ml concentration is manufactured only in 2.5-ml bottles.[1]

DDAVP as a parenteral injection

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is available in 1-ml ampules and 10-ml multiple-dose vials at a concentration of 4 µg/ml.[1] DDAVP tablets (0.1 and 0.2 mg) are also available but are not recommended because they are destroyed in the gastrointestinal tract.[1]

STORAGE AND HANDLING

Refrigeration is recommended for both nasal and parenteral DDAVP solutions.[1] However, an unopened bottle of nasal solution is stable for 3 weeks at room temperature.[1] DDAVP should not be frozen. Tablets should be stored at room temperature.

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