TAKE A DEEP BREATH
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FOCUS ON

Albuterol Sulfate for Cats

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Albuterol, also known as salbutamol, is a bronchodilator that is indicated as a rescue therapy for acute feline asthma exacerbations. This medication comes in various formulations; the most frequently used is inhaled albuterol delivered using either a metered-dose inhaler or a nebulizer. Albuterol is also available in an oral formulation that is infrequently prescribed in cats.

When albuterol is used in a metered-dose inhaler, it is typically administered with the aid of a facemask and spacer (such as the AeroKat; Trudell Animal Health, trudellanimalhealth.com); therefore, training a cat to accept a facemask and spacer prior to the need for drug administration maximizes success with this modality. When a cat is under general anesthesia and requires bronchodilator therapy, inhaled albuterol can be directly administered into the endotracheal tube using either a metered-dose inhaler or a nebulizer.

MECHANISM OF ACTION

Albuterol is a selective, short-acting β_2 agonist that acts on β_2 adrenergic receptors to relax airway smooth muscle. Binding of albuterol to the β_2 adrenergic receptors on airway smooth muscle cells causes activation of adenylyl cyclase, resulting in increased production of intracellular cyclic 3',5'-adenosine monophosphate (cyclic AMP). Cyclic AMP activates protein kinase A, which inhibits phosphorylation of myosin and results in lower concentrations of intracellular ionic calcium. This results in bronchial, and likely to a lesser extent tracheal, smooth muscle relaxation.[1,2]

EFFICACY

Albuterol is a mainstay of asthma treatment in human medicine with documented efficacy for short-term bronchodilation. In cats, data are limited to studies of experimentally induced asthma. Studies in cats evaluated salbutamol (albuterol) alone or in combination with ipratropium bromide, an acetylcholine antagonist also used as a bronchodilator. Results of these studies were mixed. A study in 2005 evaluating the use of salbutamol and/or ipratropium bromide found reduced bronchoconstriction associated with bronchoalveolar lavage (BAL) when the combination medication was administered.[3] In a group of healthy cats evaluated in 2009, salbutamol appeared to be effective prevention for muscarinic-induced bronchoconstriction.[4] However, a study in 2010 evaluated salbutamol alone and the combination of salbutamol and ipratropium bromide in a group of cats

sensitized to *Ascaris suum* with allergen-induced bronchoconstriction. In this group, salbutamol and the combination product both had limited efficacy in reversing the bronchoconstriction.[5]

Data in clinically affected cats are lacking. In the author's clinical experience, inhaled albuterol is efficacious for rescue therapy delivered with a metered-dose inhaler with a facemask and spacer, as a nebulized treatment, or, in intubated patients, with either a metered-dose inhaler or nebulizer through an endotracheal tube.

CLINICAL APPLICATIONS

As a rescue therapy, bronchodilators are indicated when there is clinical evidence of bronchoconstriction. Bronchoconstriction is a primary feature of feline asthma. It is important to note that bronchodilators do not address the underlying airway inflammation; therefore, they should not be used as a sole therapy but in combination with medications to address the underlying inflammatory airway disease. Clinical signs that support the presence of bronchoconstriction include increased respiratory effort on exhalation and wheezes upon thoracic auscultation. Increased expiratory effort can be noted by looking for increased abdominal effort during exhalation and a slightly prolonged phase of exhalation compared with the inspiratory phase. Suspicion for bronchoconstriction can also be raised on thoracic radiographs when lung hyperinflation and flattening of the diaphragm are noted.

Albuterol is primarily indicated as a rescue inhaler during acute asthma exacerbations. Overuse of albuterol can result in increased airway inflammation and hyperreactivity or paradoxical bronchospasm, a serious, potentially fatal complication described in human medicine. Desensitization to albuterol can also occur with high doses and long-term use. These risks are described further under **Adverse Reactions**. Therefore, it is imperative to directly treat the underlying airway inflammation associated with feline asthma through glucocorticoid administration and reserve albuterol use for rescue therapy.

Administration via a metered-dose inhaler with a facemask and spacer is ideal for at-home use. Nebulized albuterol solution for inhalation is sometimes easier to administer in the hospital setting, particularly to a patient experiencing respiratory distress. It should be noted that while dry powder inhaler formulations are available for human use, they are not suited for use in cats as they cannot be used with a facemask and spacer.

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It is also recommended that cats undergoing bronchoscopy and BAL receive bronchodilator therapy. In the author's hospital, this is included as part of the premedication procedure. Albuterol can be used for this purpose. In 2005, a study described airflow limitation induced by bronchoscopy and BAL in both healthy cats and cats with experimentally induced asthma; airflow limitation was worse in cats with airway inflammation but was noted even in healthy cats.[3] Therefore, bronchodilator therapy is recommended for all cats undergoing this procedure.

RECOMMENDED DOSAGE

Albuterol sulfate is most commonly administered as an inhalant medication. Oral doses are also provided; however, studies evaluating oral efficacy in cats are not available. As noted above, long-term use of inhaled albuterol and use as a sole therapy are not recommended.

Albuterol sulfate metered-dose inhalers typically provide 90 µg/actuation (puff). It is recommended to administer 1 to 3 puffs once every 12 to 24 hours as needed for rescue therapy.[1]

Albuterol sulfate inhalation solution is designed to be delivered via a nebulizer. Several concentrations of this solution are available. The author uses the 0.5% (5 mg/mL) preservative-free solution and dilutes 1.25 mg (0.25 mL) of solution in 2 mL of sterile 0.9% NaCl. This results in a similar concentration, but with lower volume, to that reported by Leemans et al. in 2009.[4] The dose is placed in the nebulizer cup and administered via nebulization. Nebulized salbutamol at

a dose of 3.75 mg in 6 mL saline was evaluated in one study of cats with experimentally induced asthma and found to be efficacious.[4] The author uses the lower volume detailed above as it has been efficacious in a clinical setting.

Oral albuterol can be administered at a dose of 0.02 to 0.05 mg/kg once every 8 to 12 hours.[1] Tablets and a syrup formulation are also available.

PHARMACOKINETICS

The pharmacokinetics of albuterol are largely based on data from human studies. There are no available studies of albuterol pharmacokinetics in cats.

One study has been recently published using a computer model to evaluate distribution of inhaled salbutamol.[6] While the perceived advantage of administering inhaled albuterol is delivery of the drug directly to the target area, there is considerable variation in distribution of the drug. Distribution of inhaled salbutamol (albuterol) in cats was evaluated using computational fluid dynamics. This study demonstrated that when a facemask and spacer was used to deliver albuterol with a metered-dose inhaler, a large amount of the medication was deposited in the device and in the upper airway; only between 5.8% and 25.8% of the medication reached the lungs.[6]

ADVERSE REACTIONS

Albuterol is selective for β_2 receptors, and fewer adverse effects are expected than with nonselective β agonists. Inhaled formulations at therapeutic doses are also thought to be associated with fewer adverse effects than systemic formulations. However, high doses of albuterol may result in hypokalemia, tachycardia, arrhythmias, and hypertension. Hyperglycemia, anxiousness, and muscle tremors are also possible.[7] Diabetic patients receiving albuterol may experience hyperglycemia; therefore, diabetic control should be monitored. Albuterol inhibits uterine contractions at the end of gestation and should be avoided when possible in pregnant animals.[7] Overdose is unlikely in cats receiving therapeutic doses. Recommended monitoring for cats receiving albuterol includes heart rate, heart rhythm, blood pressure, and potassium and blood glucose concentrations.

β_2 receptors are membrane-associated receptors, and with repeated or high dosing, these receptors can internalize. This results in fewer receptors available on the membrane surface to bind with albuterol, leading to desensitization to this medication, or tachyphylaxis. Long-term exposure can eventually result in downregulation of receptor mRNA, also resulting in fewer receptors. Desensitization ultimately results in less bronchodilation in response to albuterol administration, and this decreased efficacy can result in more frequent need for albuterol treatment.[1]

Albuterol is a 50:50 racemic mixture of 2 chemical enantiomers, or 2 molecules that are mirror images of each other in their chemical structure: R-albuterol and S-albuterol. The R-albuterol enantiomer is the more pharmacologically active molecule responsible for the bronchodilatory effects of albuterol, while the S-albuterol enantiomer was long thought to be inert. Further study has revealed that while the S-albuterol enantiomer does not contribute to airway smooth muscle relaxation at therapeutic doses of racemic albuterol, it is not entirely inert. There is evidence in human medicine that the S-albuterol enantiomer is associated with increased airway inflammation and hyperreactivity. Furthermore, the S-albuterol enantiomer has a longer half-life and may accumulate in the airways to a greater extent. It is thought that the potential for accumulation of this enantiomer within the airway may play a role in paradoxical bronchospasm.[8] A 2009 study in healthy cats and cats with experimentally induced feline asthma demonstrated increased airway inflammation in both healthy and asthmatic cats receiving the racemic mixture of albuterol.[9] A pure R-albuterol enantiomer form is available as the medication levalbuterol; however, this medication tends to be more expensive, and in human medicine, controversy exists as to whether it results in a significant difference in clinical outcome compared with racemic albuterol.

CONTRAINDICATIONS

Albuterol is contraindicated in patients with hypersensitivity to albuterol or components of the formulation used.

DRUG INTERACTIONS

Albuterol should not be coadministered with sympathomimetic amines, tricyclic antidepressants, and monoamine inhibitors. Extreme caution should be used in patients also receiving monoamine oxidase inhibitors or tricyclic antidepressants.[10]

Coadministration of albuterol tablets and oral sympathomimetics is not recommended. Coadministration with methylxanthines should be avoided, as reports of cardiac arrhythmias and sudden death have been associated with this combination.[10] Patients receiving diuretic therapy may be at increased risk of hypokalemia; therefore, potassium should be monitored.

SUMMARY

Albuterol is indicated for treatment of bronchoconstriction in cats with feline asthma. It is available in several formulations but is most commonly administered as an inhaled medication using a metered-dose inhaler with a spacer device or a nebulizer. To avoid promoting airway inflammation and potential tachyphylaxis, inhaled formulations should be used only as a rescue therapy. While few direct contraindications to albuterol use exist, significant drug interactions exist and should be avoided. TVP

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