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Summary

Bronchopneumonia was diagnosed in a Morgan colt with signs of labored respiration, coughing and bilateral nasal discharge. The diagnosis was confirmed by auscultation, radiology and a tracheal wash. Treatment consisted of antibiotics and nebulization therapy. In this report, nebulization therapy will be reviewed.

Case Report

A six-month-old Morgan colt was presented to the Iowa State Clinics on October 9, 1981. The animal had a history of coughing, labored breathing, and bilateral nasal discharge of two months' duration. He had been treated with gentamicin, chloramphenicol, penicillin, antihistamines, and DMSO with little success.

Upon physical examination, the animal exhibited an expiratory push. The respiratory rate was thirty five; the temperature and pulse were normal. Auscultation revealed increased bronchovesicular sounds over the entire lung field. An expiratory wheeze was heard over the tracheal bifurcation and increased friction and bronchial sounds over the right lower quadrant of the lung field. A bilateral nasal discharge was also present.

Radiographic examination of the guttural pouches appeared normal. In the chest films, the density of the ventral caudal lung field was increased, suggesting some consolidation in the tip of these lobes. The appearance was consistent with an inflammatory response in the lung. There was no evidence of focal abscessation.

A CBC was taken and found to be within normal limits. Fecal flotation revealed *Oxyuris equi, Parascaris equorum* and strongyloid-type eggs.

A tracheal wash was obtained and bacteriology yielded a few colonies of gram negative rods. No significant number of bacteria were seen on direct cytologic examination but many neutrophils, macrophages and debris indicative of a suppurative reaction were present. Mesothelial cells, neutrophils and macrophages were found in the cytological examination of fluid derived from a thoracocentesis.

Bronchopneumonia was the tentative diagnosis and the colt was started on chloramphenicol at a dosage of 25 mg/# B.I.D. Fenbendazole was used to worm the foal. The foal was nebulized 15 minutes twice a day for 10 days and then the treatment was cut back to once a day for 5 more days.

To nebulize the foal, a plastic bag was placed over his head and tubing was placed inside the bag. The tubing was connected to a jet-type nebulizer which was adapted to hook onto an oxygen tank via a Hudson[a] demand value.

The nebulizer ingredients included: 10cc of Mucomyst,[R][b] 20 cc of Bronkosol,[R][c] 10 cc of gentamicin and 50 cc of saline. Two days after the initial treatment, the mucopurulent nasal secretions subsided. By the end of the first week the lung sounds cleared, and 2½ weeks after therapy was initiated, the foal was sent home with no evidence of a respiratory infection.

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[a]Hudson, Hudson Supplies Book Brothers, P.O. Box 834, Fort Dodge, Ia 50501

[b]Mucomyst[R]-(N-acetylcysteine) Mead Johnson & Company, Evansville, Indiana 47721.

[c]Bronkosol[R]-(Isoetharine hydrochloride inhalation, USP, 1.0%) Breon Laboratories Inc., Mfg by Sterling Drug Inc., New York, N.Y. 10016.

Literature Review

The development of aerosol therapy as an approach to the treatment of respiratory disease in veterinary medicine has been a slow process. Inhalants have been used for many years in human medicine as an adjunct to the treatment of respiratory disease. An increased interest in their use has been seen recently due to the fact that pneumonia of gram negative etiology has not been treated successfully by current therapy technique.[17] Furthermore, the discovery that several antibiotics such as kanamycin and gentamicin are poorly absorbed from the lungs suggests that these agents might remain in the lungs for long periods of time following therapy.[11,16] Thus, the frequency of therapy could be reduced, as could the possibility of toxic reactions such as renal damage associated with parenteral administration. These advantages are beginning to catch the attention of veterinary practitioners.

Little is known about aerosol therapy in horses. According to Beech, 95 percent of the aerosol is deposited in the nose of man with nasal breathing and the percentage is even higher in horses because of their anatomy.[3] Extensive turbinates, large surface area, and bends in the nasal passage tend to increase deposition by impact. To bypass the nose and turbinates when nebulizing human patients, mouth breathing or pharyngeal tubes may be used. This increases the probability of particle deposition in the lungs; unfortunately this is not possible in horses.

An aerosol is a suspension of particulate matter in a high speed stream of gas. An aerosol generator produces an unrefined spray of particles of random size. A nebulizer refines the spray by the use of buffers to produce an aerosol of a select size range.[4]

Several factors are important in influencing aerosol distribution and absorption. These include: particle size, method of administration, patency of the airway, duration of contact, and finally, the chemical nature of the drug itself.[5]

The number one factor determining deposition of the inhalant is the droplet size. Larger particles tend to rain out or be deposited in the upper airway; and if the particles are too small and light, the rate of fall is very slow and they enter and leave the lungs without raining out. In human medicine the range for deposition of a drug in the periphery of the lungs is approximately 0.5 microns to 4 microns. Deposition in the bronchioles occurs at about 4 microns to 10 microns; in the larger bronchi, at approximately 10 microns to 20 microns; and finally above 40 microns, most of the deposition occurs in the upper airways.[5,19] In horses, particles less than 3 microns in diameter are expired, and those larger than 8 microns are removed by the nasopharynx.[3,20]

There are 3 basic types of aerosol production methods. The first type is a jet-type nebulizer. According to the laws of physics,[4] gas passing through a constriction will have an increased velocity and a decreased lateral pressure. A capillary tube at a 90 degree angle to the constriction, which has one end submerged in a liquid, will experience a pressure gradient from liquid to airstream. The resultant fluid entrapment produces a coarse spray, which may be directed into a firm surface, or baffle, that reduces the larger particulate output. The second type of aerosol production is via centrifugal aerosol generators.[4] A rapidly spinning disk throws liquid against a baffle at the outer radius of the disk, breaking it into random-size particles. The third and most popular type of aerosol production method is the ultrasonic nebulizer.[4] Ultra high-frequency sound waves are transmitted to a liquid via a piezoelectric transducer. The liquid is fragmented by rapid volumetric change into a relatively constant particulate spray. An outside air source directed across the liquid surface carries away a high density, stable aerosol.

Another important factor is how the aerosol that is generated is delivered to the patient. Humans can breathe through the output circuit of an aerosol generator directly; or aerosol may be delivered by placing the patient in a fog tent, or by using a face hood as a reservoir.[3,5] Members of the equine species are limited to the latter, indirect method. A plastic bag may be placed over the horse's head with tubing directing the aerosol from the nebulizer to the inside of the bag. Alternatively, one could fashion a nose cone out of a variety of equipment: gallon jugs with the bottoms cut away, conical-shaped plastic waste baskets padded with strips of foam, or any other piece of equipment that will deliver the nebulized air in the direction of the nasal passages.[9]

The patency of the airway is a third factor to consider. If there is an upper airway obstruction, it is obvious that the aerosol will be

deposited proximal to the obstruction.[6] Therefore, it is imperative that a patent airway be present for aerosol to be deposited in the periphery of the lung.

Duration of contact also influences aerosol deposition. In human medicine, patients are encouraged to take a slow, deep breath and hold it at the end of inspiration so that maximum deposition of aerosol will occur.[5] If the patient is panting, which is often the case in small animals who are having respiratory difficulty, it is very hard to get an aerosol down into the alveoli. Finally, the chemical nature of the drug itself also influences deposition.[3,6]

It is important to determine where the aerosol should go when treating a specific patient. Bronchodilator drugs are used when one wants the drug to penetrate into smaller bronchioles or toward the alveoli. An aerosol generator should be used that produces a small droplet size. On the other hand, if one wanted rain-out to occur in the upper airways to "superhumidify" secretions, an aerosol generator that produces a larger-sized particle should be used.[6]

The total dose of drug that is actually absorbed is also a factor to consider. Droplet size comes into play here. Although the smaller particles are deposited more peripherally, the larger droplets contain more drug; but the more peripheral the deposition, the greater the percentage of drug that will be absorbed.

Aerosols are used to (1) provide humidification; (2) to provide bronchodilatation; (3) to alter the characteristics of secretions; (4) to treat infections; and (5) to aid in collecting specimens.[6]

Humidity

When the natural upper airway is bypassed, as with a tracheostemy, endotracheal or nasotracheal tube, high density mist or high humidity in the inspired air is needed to prevent mucus impaction. This is because the patient's ability to humidify the gases he breathes is compromised.[6,16] Another danger is that the tracheal mucosa can become dried out and friable with inadequate moisturization. At body temperature, the alveolar gas is completely saturated; a moisture deficit in the large airways is possible if precautions are not taken to add adequate moisture to inhaled gases.

The moisture needed to prevent these complications is supplied as molecular water (high humidity) or as particulate water (aerosol). Many adequate commercial devices are available for providing these forms of moisture.

Bronchodilatation

To provide for bronchodilation a drug must reach the mucosa of the bronchial tree either systemically or topically. A patent airway is imperative if you want to get the drug down to the respiratory bronchiole. The drugs used can be divided into two general categories: specific and nonspecific bronchodilators.[6] In general, the main effects of a bronchodilator are to relax bronchiole circumferential smooth muscles; to relax longitudinal smooth muscle fibers that extend into alveolar ducts and alveolar sacs and therefore increase compliance; and to shrink mucosa and decrease secretory activity through vasomotor effects (decongestant action.)[3,8,13,18]

Epinephrine and isoproterenol are the specific bronchodilators most commonly used in aerosol form. In addition to its bronchodilator action, epinephrine is also a mucosal decongestant. When isoproterenol is used, constrictors such as phenylephrine are occasionally added to produce mucosal decongestion. These sympathomimetics have potent side effects on the cardiovascular system which require individualization of dosage and monitoring of the patient throughout therapy. Sympathomimetics work by increasing phosphorylase activity and they also stimulate the conversion of ATP to 3,5 AMP.[13,18]

Steroids are used as nonspecific bronchodilators. Recent studies have shown that some patients with asthma, especially children, can be maintained on lower total doses of steroids administered by aerosol than might be required if administered parenterally.

Bronkosol^{R} is a sympathomimetic amine with preferential affinity for $Beta_2$ adrenergic receptor sites of bronchial and certain arteriolar musculature, and a lower order of affinity for $Beta_1$ adrenergeic receptors. It has a rapid onset of action and a relatively long duration also. It gives symptomatic relief of bronchospasm and this aids in significantly increasing vital capacity. Drug interactions are important and Bronkosol^{R} should not be administered along with epinephrine or other

sympathomimetic amines since these drugs are direct cardiac stimulants and may cause excessive tachycardia. They may, however, be alternated if desired.

Altering Secretions

Aerosols are also used in an attempt to alter the character of secretions and thus aid in bronchial evacuation. Specifically, saline or mucolytic agents in aerosol form are used to promote bronchial evacuation. The rationale for this type of therapy can be explained by a brief review of mucus production and function in the respiratory tract.

The fluid layer covering most of the respiratory tract epithelium consists of a serous watery liquid in which cilia from the epithelial cells protrude, overlain by the mucus layer.[3] The properties of mucus depend on the glycoproteins around which water is organized and bound.[2,20] The viscosity of mucus, for example, is determined by the intramolecular binding of the glycoproteins. Mucoid sputum, white, adhesive, and gelatinous, is more viscid than is purulent sputum. Mucoid sputum becomes less viscid with the addition of water, and as it dries viscosity increases. With purulence there is increased cross-linkage of glycoproteins by disulfide bonds, and these bonds differ in cleavage properties.[20] Purulent sputum is thick, opaque, and yellow; it is less viscid than is mucoid sputum and contains DNA fibers originating from degenerated white cells. Its vicosity is decreased by pancreatic dornase (streptokinase and deoxyribonuclease).[2,7,20]

Acetylcysteine, pancreatic dornase, ascoxal, trypsin, chymotrypsin, potassium chloride, potassium iodide and buffered L-arginine are common mucolytic agents.[2,10,13,14,15,21] However, bronchospasm and bronchial edema are side effects of mucolytic agents because they can be irritating to mucus membranes.[14,15,20]

Detergents or wetting agents are also used to decrease surface tension and viscosity of sputum. Alevaire,[Rd] a solution with the detergent superinone, is effective in man and has been used in horses.[2] Controlled trials in laboratory animals, however, show that it is no more effective than water.[14,20]

Mucomyst[R] (N-acetylcysteine) works by breaking up the polysaccaride bonds of mucin and therefore is classified as a specific mucolytic agent.[6] Irritation of the airway mucosa is seen in some patients with a history of bronchospastic disease due to this drug, therefore the simultaneous use of a bronchodilating agent is necessary. Acetylcysteine has no effect on blood, fibrin, or pus. A related compound, methylcysteine hydrochloride, decreases bronchial secretions.[2]

Treating Infections

Although most medical personnel feel that antibiotics are best given by injection, aerosols of antibiotics have been used to treat infection. Antibiotic aerosols have been recommended when the antibiotic for the specific organism cultured cannot be given systemically because of its toxicity. Aerosols have also been recommended for use in patients who may have intrapulmonary disease that is walled off from the circulation.[6,12,20]

Antibiotics absorbed poorly or not at all in aerosol form include neomycin, kanamycin, gentamicin, polymixin B, bacitracin, and the antifungal drugs nystatin and amphotericin B.[2] To be effective, these drugs must be deposited over a large area of the lung. This is because their effectiveness depends on the microorganisms being on the surface and the drugs not being inactivated by DNA or other material in the exudate.

Kanamycin is well tolerated but only a small portion is deposited in the lower respiratory tract.[9,11,20] Studies have shown that aerosols of kanamycin can be used effectively to treat pneumonia in rats, mice, and monkeys.[17]. The efficacy of kanamycin aerosols seems to result from persistance of drug in the lung, an observation that may have great importance for patients with impaired kidney function. The use of aerosol therapy seems to almost completely circumvent the problem of renal toxicity associated with kanamycin.

Gentamicin nebulized in laboratory rats results in high concentrations throughout the respiratory tract, but low serum levels.[2]

Carbenicillin and related agents are incompatible with acetylcysteine.[2]

In cattle, nebulization of penicillin, streptomycin, and antihistamine combinations is no more effective than is systemic administration of the same drugs in treating bacterial bronchopneumonia.[1]

Discussion

Familiarity with drugs, their assets and their

[d] Alevaire—Breon Laboratory, 90 Park Avenue, New York, N.Y. 10016.

disadvantages, and the opportunity to medicate the patient properly will play a role in determining how successful nebulization will be as an adjunct to therapy in respiratory disease. When using aerosols one should always think in terms of why the drug is given, how the drug is administered, and what the side effects of aerosol therapy can be.

Aerosols can be a very valuable therapeutic tool. However, as a word of caution, although a little bit is good, a lot is not necessarily twice as good—it may be harmful. An animal can be drowned by the use of an ultrasonic nebulizer.[6] By continual exposure to high flow, high density aerosols, the arterial oxygen tension may progressively decrease as the length of exposure to constant breathing of aerosol increases.[6] This hypoxia is related to an increasing alveolar—arterial oxygen gradient, caused by the deposition of fluid in the alveoli, leading to an intrapulmonary shunt which increases as exposure time progresses.[6] Therefore, hypoxia due to intrapulmonary shunting from the accumulation of fluid is a possible complication with the use of aerosols. Thus, it is important not to routinely use aerosols for hours on end, unless the amount delivered to the patient is constantly monitored and controlled.

Another danger is the possibility of bacterial growth within the nebulizer.[16] Only a sterile nebulizer should be used. When it needs refilling, residual water should be discarded, the container rinsed, and then refilled with sterile water. Tubing that collects condensation should also be cleaned rather than drained back into the reservoir because it may contain contaminating bacteria.

In conclusion, the future of aerosol therapy in veterinary medicine depends on research findings, practicality, availability, early accurate diagnosis, knowledge of disease pathogenesis and the pharmacologic basis of therapy. Aerosol therapy should be used but not abused.[6]

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