Mini Review

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Journal of Zoonotic Diseases and Public Health

2018
Vol.2 No.2:5

Theophylline Use in Animals: A Review

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Received date: July 12, 2018; **Accepted date:** August 20, 2018; **Published date:** August 27, 2018

Citation: Elitok B (2018) Theophylline Use in Animals: A Review. J Zoonotic Dis Public Health. Vol. 2 No.2:5

Abstract

Theophylline is a bronchodilator which is widely using in human and animals and causes an increase in the contraction. So, it gives rise to increasing in the contraction of the diaphragm and effects frequency of the respiratory tract surface elements like cillia, dilation of airways, while has some adverse effects such as nausea, vomiting, headache, and insomnia. This research paper gives an overview of possible effects and using of theophylline in the animals.

Keywords: Theophylline; Animal; Bronchodilator

Introduction

Theophylline has been used in the treatment of respiratory diseases, such as asthma and chronic obstructive pulmonary disease (COPD), for more than 80 years. Although in industrialized countries β-agonists and steroids are the preferred treatment, globally, theophylline remains a widely prescribed drug, particularly in patients with more severe disease, because it is cheap and readily available [1].

Treatment of animal respiratory diseases tends to target bronchodilators [2]. Theophylline is a bronchodilator drug like anticholinergics and β2 agonists. This drug is especially used treatment of people with severe COPD [3,4]. In animals, theophylline is effective bronchodilators in dogs than cattle (and possibly) [5]. Zhou et al. reported that low-dose, slow-release oral theophylline is effective and well-tolerated in the long term treatment of stable COPD, although it does not improve post-bronchodilator lung function [6,7].

A bronchodilatator theophylline has some positive effects on respiratory tract such as increasing contraction potency of the diaphragm and move density of the cilia, and diuretic effect [5,8,9].

Theophylline-related adverse reactions are usually amenable when peak serum theophylline concentrations are <20 mcg/mL and are usually caused by caffeine-like side effects such as nausea, vomiting and insomnia. However, when theophylline concentrations in blood serum exceed 20 mcg/mL, it may be occured persistent vomiting, cardiac arrhythmias, and persistent seizures that can be lethal [10].

High plasma concentrations doses of theophylline inhibiting phosphodiesterases (PDE) and PDE inhibition. These contrptions can not explain the clinical effects of low doses of theophylline, indicating that there must be another mechanism responsible for anti-inflammatory effects Kristen et al. and Barnes 2005 [3,4]. These anti-inflammatory effects are unlikely to require higher concentrations due to phosphodiesterase inhibition or adenosine receptor antagonism. The potency of theophylline over histone deacetylase activity is increased by oxidative stress conditions [3,11,12].

Fat tissues in overweight people are characterized by chronic low-grade inflammation. Theophylline add their diets at dose of 0.1% may cause to reduce corticosterone-induced fasting blood glucose, plasma IL-6 levels and Il6 gene expression in fat tissue. The drug implementation repressed glucocorticoid induced hyperglycaemia and IL-6 production by pressured glucocorticoid receptor activity. Hence, theophylline has got potential therapeutic effect for treating insulin resistance and hyperglycemia [13].

Drug therapy of the respiratory tract in animals is most successful when it is based on a knowledge of normal physiology and disease pathophysiology of respiratory tract diseases [14].

Serum theophylline concentration must be moniorized in point of dosage till it is reached to 10 to 20 µg/ml which is therapeutic range [7]. Loading dose of theophylline with regard to a volume of distribution of 0.5 L/kg (range from 0.3 to 0.7 L/kg) is needed to fast attain maximum bronchodilator effect which is essential high plasma concentrations (10-20 mg/l) during treatment of acute respiratory symptoms [4].

Unlike humans, no side effects are seen until blood levels are enormously out of range so few problems are observed in pets form theophylline administration [15]. When applied per os route, theophylline dose for dogs is 4.5-6.8 mg/kg for 12 hours and 2 mg/kg for cats. However, it should be taken to use the medicine on an empty stomach, one hour before meals or

two hours after meals [16]. If oral applications are to be repeated, theophylline plasma concentrations should be monitored and the dosage should be carefully adjusted according to the patient's condition [17,15]. The results of a study [18] showed that toxicity occurs at higher theophylline plasma concentrations in the dog (37-60 µg/ml) as compared to man (> 20-60 µg/ml) when dosed orally. Since current dosage regimens in dogs are designed to maintain trough-peak theophylline plasma concentrations between 10 and 20-60 µg/ml, the results indicate that the upper limit of this range appears to be safe in the dogs. Daily administration of the brand of theophylline tablets and capsules used in this study at 15 mg/kg (6.8 mg/lb) and 19 mg/kg (8.6 mg/lb), respectively, maintained plasma concentrations within the desired therapeutic range in healthy cats [19,20].

Theophylline was administered to six cats in a three-way cross-over study as a single dose of intravenous aminophylline and oral sustained-release theophylline, between 08.00–09.00 h (Phase I) and 20.00–21.00 h (Phase II). Subjects were maintained on a 12 h light (08.00–20.00 h):12 h dark cycle. Results of the study showed that no single pharmacokinetic parameter could account for the higher plasma concentrations achieved following the evening dose [21].

Aminophylline increased metabolic rate in a dose-dependent manner in the horses as well as other animals [22,23]. The pharmacokinetics of the present drug were detected after a single IV administration of 12 mg of 9.44 mg of theophylline/kg of body weight in healthy horses [24]. Below 59 µmol/litre there was no consistent bronchodilator activity and above 84 µmol/litre excitement and tachycardia limited the usefulness of theophylline in the ponies with recurrent obstructive lung disease [25].

Respiratory stimulants are widely used in asphyxic neonatal calves despite a lack of data about their effectiveness and indications of possible side effects [26].

The suggested oral dose of theophylline for ruminats is 28 mg/kg once daily [27]. In a previous study was reported that theophylline had high healing effects in bovine respiratory efficacy of disease complex such as shipping fever at a dosage of 28 mg/kg of body weight daily for 3 days [28].

The kinetic interaction between theophylline and enrofloxacin could be of clinical significance and may require plasma drug concentration monitoring and adjustment of theophylline dosage in dogs [29]. Remember that quinolone antibiotics such as enrofloxacin, ciprofloxacin something like thyroid hormone applications may cause to rise theophylline levels in the blood. Interaction of erythromycin and other drugs with theophylline resulting from the inhibiting or potentiating its metabolism by CYP1A2 [30]. Given its potential side effects, theophylline may need to be used with care in patients with thea allele at site -2964(G/A) in the CYP1A2 gene, because theophylline metabolism levels are lower in such patients, particularly in young asthmatic individuals in human [31]. Many drugs interact with theophylline by inhibiting or potentiating its metabolism by CYP1A2. CYP2A13 Metabolizes the Substrates of Human CYP1A2, Phenacetin, and Theophylline [32]. Therefore, this toxicity can be anticipated and avoided if careful attention is paid to monitoring the serum theophylline concentrations of such high-risk patients when erythromycin therapy is contemplated as an addition to theophylline therapy [33].

Oppositely, some drugs such as phenobarbitals, ketoconazol, furosemide may be caused to reduce the blood levels of theophylline. The efficacy of beta blockers such as propranolol which use in the treatment of heart diseases may be decreased when used together with theophylline [4,15,34,35].

As a result, bronchodilatator effect of theophylline both human and animal is beneficial property of theophylline, and to be understood-well of its mechanism of action might cause to optimized with some compounds to reduced its potential side effects.

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