

## **A case of acquired idiopathic megaesophagus in a dog: the use of sildenafil as treatment**

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### *Abstract*

Acquired idiopathic megaesophagus in dogs is rarely found in Indonesia. In this case report, a dachshund dog was presented with a history of vomiting after eating. Clinical examination, complete blood count, kidney, and liver tests identified only minor dehydration. On observation of the dog after eating, the sign reported as vomiting was confirmed as regurgitation. Radiography and contrast studies identified a significantly dilated oesophagus. With an absence of other clinical abnormalities, the dog was diagnosed with idiopathic megaesophagus and prescribed treatment with sildenafil twice daily at 0.75mg/kg for five days, along with postural management of feeding. Treatment resulted in cessation of regurgitation and improvement in the dog's condition. This result suggests that sildenafil could be a useful alternative treatment for acquired idiopathic megaesophagus in dogs.

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**Keywords:** Megaesophagus, dog, regurgitation, dilated oesophagus, sildenafil

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## Introduction

Megaesophagus is a disease of the oesophagus resulting from abnormal motility, leading to dilation (Hall *et al.*, 2005). Megaesophagus is more common in dogs, rarely occurring in cats. It may be congenital idiopathic, acquired idiopathic, or secondary. Congenital megaesophagus is a dilatation of megaesophagus that occurs in puppies 10-weeks or younger (Quintavalla *et al.*, 2017). Acquired idiopathic megaesophagus occurs in adult dogs and the cause is unknown (Hall *et al.*, 2005). Secondary megaesophagus is associated with other diseases, such as myasthenia gravis, hypothyroidism and oesophageal cancer (Nakagawa *et al.*, 2019).

In addition to weight loss, the main symptom of megaesophagus is regurgitation (Nakagawa *et al.*, 2019). This may be mistaken with vomiting by the owner and the vet, subsequently, misleading the diagnosis (Quintavalla *et al.*, 2017). As megaesophagus is often concurrently associated with aspiration pneumonia and may be fatal (Hall *et al.*, 2005; Kanemoto *et al.*, 2017), dogs presenting with megaesophagus are usually given a guarded prognosis for survival.

Thoracic radiography may be reliable in diagnosing megaesophagus (Hall *et al.*, 2005). Consistently effective treatments for megaesophagus are still unavailable (Quintavalla *et al.*, 2017). Surgical approaches to the lower oesophageal sphincter (LOS) have given unsatisfactory treatment results (Diamant *et al.*, 1974).

Relaxing the LOS is important an important therapeutic aim, allowing the oesophagus to empty (Quintavalla *et al.*, 2017). Megaesophagus may develop when the LOS fails to relax in response to the accumulation of ingesta in oesophagus. According to Quintavalla *et al.* (2017), administering sildenafil can relax the LOS and improve the condition of dogs with

congenital idiopathic megaesophagus. Therefore, sildenafil was used to treat a dog patient with acquired idiopathic megaesophagus in this case report.

## Clinical description

A 14-month-old, 6,7 kg neutered male dachshund dog named Douglas was referred to the Bali Vet Clinic with a two week history of persistent vomiting after eating. The dog had been appropriately vaccinated and dewormed. The dog showed active, good appetite, and no indication of infection during examination. Initially the dog was hospitalised with conservative therapy, including bland diet (Hills Prescription Diet® A/D Urgent Care - Chicken), cefotaxime (22 mg/kg IV BID), dexamethasone (0.1 mg/kg SC once), vitamin B complex injection (0.1 mg/kg IV once), ondansetron (0.5 mg/kg IV BID) and sucralfate (500 mg PO BID). After three days the dog presented with no signs of improvement. On re-examination the dog was found to be bright, alert and clinically normal apart from mild dehydration (<5%). Evaluation of a complete blood count and serum biochemistry revealed no abnormalities. Approximately 15 minutes after beginning to eat the dog was seen to passively bring up food that was still in the form that had been ingested, confirming that what the owner had called vomiting was actually regurgitation.

Lateral (figure 1a) and ventrodorsal (figure 1b) thoracic radiographs suggested dilatation of the oesophagus, with no evidence of aspiration pneumonia. Contrast radiography was performed after the administration of a barium meal, confirming oesophageal dilatation. Considering the absence of other clinical signs and laboratory abnormalities, megaesophagus secondary to other disease was considered unlikely. Therefore, according to physical examination and laboratory results, the diagnosis in this case was acquired idiopathic megaesophagus.



**Figure 1** Thoracic radiograph of the oesophagus.  
 a, ventral view of the radiograph showed the accumulation of barium (radiopaque) in the lower oesophagus (white arrow).  
 b, lateral view of the radiograph showed the accumulation of barium in the middle and lower oesophagus (arrow).

After finding the dilatation of the oesophagus, the treatment were an intravenous infusion of lactated ringer solution was administered at 3 mL/kg/hr to correct hydration status and the dog was fed A/D diet using postural management twice daily and hospitalized for the three days.

Prior to discharge, postural management of feeding was demonstrated to the owner, feeding the dog in an elevated manner and maintaining the dog in an upright position for 30 minutes after eating and drinking.

Five days after discharge, the owner informed that the dog still had regurgitation even though in lower frequency than before. Therefore, the owner was suggested to do a trial of sildenafil administration. The owner agreed and then was instructed to administer his dog 0.75 mg/kg sildenafil 1 hour before feeding twice daily for the next 5 days. On follow-up discussion with the owner seven days after administering sildenafil and continuing postural management of feeding, the owner reported no further regurgitation after eating. Post-treatment radiographic examination was not undertaken because the owner was satisfied with the result and thought that his dog did not need further examination. A year later the dog was brought to the clinic for vaccination and the owner informed that the dog never showed regurgitation anymore.

### Discussion

Generally, megaesophagus is characterized by persistent regurgitation and weight loss. The occurrence of those symptoms and thoracic radiograph showing a dilated oesophagus underlies the diagnosis of megaesophagus. Unlike secondary megaesophagus, where treatment of the primary disease will often resolve the megaesophagus, treatment of congenital and idiopathic megaesophagus is not usually curative and mostly aimed at symptomatic treatment (Simpson, 1994).

Several drugs have been used to investigated for idiopathic megaesophagus in dogs, such as metoclopramide and cisapride. These drugs mainly act to increase the contraction of oesophageal muscle, with the aim to move food into the stomach. However, these prokinetic agents work on smooth muscles, and are therefore ineffective in dogs as the muscle of the oesophagus is striated (Washabau, 2003). Moreover, metoclopramide and cisapride may stimulate LOS contraction which contain smooth muscle, worsening the megaesophagus (Quintavalla *et al.*, 2017).

Besides promoting oesophagus contraction, another therapeutic strategy that may apply is to relax LOS tone. The goal is to facilitate the emptying of the oesophagus by opening LOS so the ingesta will move into the stomach. Sildenafil is proven can relax the LOS in human, cats, and dogs (Quintavalla *et al.*, 2017). This drug indirectly enhances the action of nitric oxide (NO) as a neurotransmitter, stimulating the relaxation of LOS. Endogenous NO can induce LOS smooth muscles to relax through the synthesis of cyclic guanosine monophosphate (cGMP). Sildenafil is a selective phosphodiesterase-type 5 (PDE-5) inhibitor. PDE-5 reduces the synthesis of cGMP, therefore, inhibition of

PDE-5 facilitates endogenous NO accumulation and LOS relaxation (Zhu *et al.*, 2007). As the canine oesophageal muscle, excluding the LOS, is striated, sildenafil may not hinder oesophageal peristalsis in dogs (Quintavalla *et al.*, 2017). In humans, sildenafil did not induce gastroesophageal reflux (Kim *et al.*, 2006). This may also be the case in dogs.

This is the first published case report of successful treatment of acquired idiopathic megaesophagus with sildenafil alongside feeding management. The decision to utilise sildenafil in this case was prompted by a recently published study (Quintavalla *et al.*, 2017) of sildenafil (1 mg/kg BID) as a treatment for congenital megaesophagus. The dosage of Sildenafil in this case was 0,75 mg/kg BID, which is still following the recommended dosage, 0,5 - 2,7 mg/kg PO q8-24h (Ramsey, 2017). the dose of Sildenafil, in this case, did not follow the dose from Quintavalla *et al.* (2017) at the beginning because it was thought that the smaller dose would be sufficient to prevent regurgitation when the dog was also held upright for a while after eating and drinking. This dose 0,75 mg/kg was simply the median of the minimum dose (0,5 mg/kg) recommended by Ramsey (2017) and the dose used in the study (1 mg/kg) of Quintavalla *et al.* (2017). If there were no improvement, the next dosage used would be 1 mg/kg BID, following Quintavalla *et al.* (2017). Evidently, this first dose, 0,75 mg/kg, has been able to improve the dog condition. It showed that the dosage of Sildenafil in this case, 0,75 mg/kg BID, can be used as a megaesophagus treatment alongside feeding management.

The most frequent side effects of Sildenafil in humans is cardiac arrhythmia (Shinlapawittayathorn, 2005). On the contrary, to date, no study was published about the adverse effects of Sildenafil over time in dogs. Based on the study from Quintavalla *et al.* (2017), it is safe to use Sildenafil twice a day for 14 days in dogs. Kellum and Stepien (2007) stated that 4 of 22 dogs (18%) in their study showed side effects, which are lethargy, somnolence, clear nasal discharge, and erect ears after Sildenafil treatment. However, due to the use of other multiple medications alongside Sildenafil in the study, it becomes debatable whether the Sildenafil alone can cause those side effects. A research study (Saetang and Surachetpong, 2020) found no significant difference in routine hematological and blood chemical results between the placebo and sildenafil groups on day 7 and from day 0 to day 7 in the sildenafil group. Therefore, Sildenafil is safe as a treatment for dogs, particularly in the short term. Feeding and holding the dog upright for a while after eating and drinking is still necessary to prevent regurgitation due to megaesophagus (Quintavalla *et al.*, 2017).

In conclusion, sildenafil (0,75 mg/kg, BID) may be an effective drug for symptomatic regurgitation in dogs with idiopathic megaesophagus, decreasing the LOS tone and allowing food to move into the stomach. Sildenafil is considered to have no side effects, particularly for a short term treatment in dog. As idiopathic megaesophagus is an uncommon presentation for dogs in Indonesia veterinary clinics, it will be difficult to investigate this further, however a prospective randomized controlled trial would be

indicated to confirm safety and efficacy of the treatment.

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