Case Report

Application of metoclopramide as gastroprokinetic in koi carp (*Cyprinus carpio*) with positive buoyancy disorders

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Abstract

A two-year-old Koi carp or fancy carp (*Cyprinus carpio*) with a symptom of recurrent positive buoyancy was admitted to the Veterinary Medical Aquatic Animal Research Center of Excellence (VMARCE), Faculty of Veterinary Science, Chulalongkorn University. Radiographic examination with positive contrast media revealed gas accumulation in the gastrointestinal tract without obstruction; subsequently, idiopathic intestinal pseudo-obstruction was suspected. The anti-flatulence drug simethicone was administered, but the fish did not respond to the treatment. Therefore, metoclopramide, as the medical trial at a dosage of 0.5 mg/kg, was intramuscularly injected once daily for four consecutive days. The fish convalesced with neutral buoyancy on day five following initial treatment. The symptom remained in remission for 4 weeks, and the fish required a second metoclopramide treatment to relieve the buoyancy problem. Although the fish was not fully recovering and needed medical treatment every 4 weeks, this is the first report of metoclopramide application as a prokinetic drug for relieving positive buoyancy disorders due to idiopathic intestinal pseudo-obstruction in koi carp.

Keywords: fancy carp, gastroprokinetic drug, metoclopramide, overinflation, intestinal motility disorder

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Introduction

Koi carp (*Cyprinus carpio*) is a popular ornamental fish species belonging to the Cyprinidae family. One of the most common health problems in cyprinid fish is the loss of buoyancy. The fish may remain to sink at the bottom of the tank (negative buoyancy) or float on the water surface (positive buoyancy) (Yasumoto *et al.*, 2021). The etiology of sinking symptoms may be due to fluid overload in the swim bladder or abdominal cavity, neoplasia, or ovarian disorder, which leads to abdominal swelling in fish (Wildgoose, 2007a). The cause of floating symptoms may be infectious or non-infectious causes of swim bladder with gas accumulation (Wildgoose, 2007b). Moreover, positive buoyancy disorder in fish was reported to result from gas accumulation in the gastrointestinal tract with or without obstruction (Weber, 2014; Wildgoose, 2007b).

Metoclopramide is a prokinetic drug that antagonizes dopaminergic (D2) receptors. The drug stimulates gastrointestinal tract motility via increasing muscle contraction and prevents esophageal reflux in humans, dogs, and cats (De Santis *et al.*, 2022; Kalas *et al.*, 2023). The drug is also used as a recombinant gonadotropin-releasing hormone with dopamine antagonists to manipulate spawning in carp (Eslami *et al.*, 2021; Yeganeh *et al.*, 2022). Here, we report the medical trial using metoclopramide to stimulate gut motility, relieve gas, and cure positive buoyancy disorder in suspected idiopathic intestinal pseudo-obstruction in carp.

Case description

A two-year-old Koi carp (5.3 kg body weight), also known as "Karashi koi" in the original Japanese name, visited the Veterinary Medical Aquatic Animal Research Center of Excellence (VMARCE) on 15th February 2023. The diseased carp with clinical signs of positive buoyancy was maintained in a 6 x 1.8 m tank with 8000 L of water with another five fish. The fish maintained normal appetite and defecation. The fish was fed a commercial pellet at 2% body weight daily. For the husbandry management, the tank was connected to a filtration system consisting of a moving base, bio-ball, and oyster shell. Dechlorinate water was used for weekly water exchange at a 30% rate. Water quality, including total ammonia (NH_4), nitrite (NO_2^-), nitrate (NO_3^-), and chlorine (Cl), was maintained within normal ranges.

Clinical examination found that the carp had abnormal swimming behavior, such as floating its head on the water surface or dorsal recumbency with positive buoyancy. Hemorrhagic skin lesions were found at the ventral, dorsal, and operculum of the fish. No ectoparasitic infestation was detected via mucus and gill scraping. The carp was radiography diagnosed as swim bladder disorder, in which the radiolucent region was visualized as the enlarged and displaced posterior chamber swim bladder (Fig. 1). Pneumocystis aspiration was carried out using a sterile 24-gauge needle (1.5 inches). The location and quantity of the air withdrawn were determined and calculated based on radiographic examination. Subsequently, 620 ml of air was aspirated from the swim bladder. Bacterial infection was also considered a potential factor, as it could lead to inflammation of the swim bladder wall or pneumatic duct, thereby causing overinflation of the swim bladder (Britt *et al.*, 2002). Therefore, carp was treated by immersion with 5 ppm enrofloxacin (Baytril®, Bayer, Leverkusen, Germany) to control the bacterial infection for 10 days before discharge. However, the positive buoyancy disorder recurred 20 days after the aspiration was performed, and the fish was then readmitted.

When the fish was resubmitted on 7th March 2023, a plain radiograph was conducted, and gas opacity was visualized in the swim bladder and gastrointestinal tract (Fig. 2A and 2B). Then, a positive contrast radiograph was performed to locate an area of gas accumulation between the swim bladder and gastrointestinal tract. Fish was anesthetized with 100 ppm of anesthetic solution (Aquanes®, Better Pharma, Bangkok, Thailand), and contrast medium (iodine, Xenetix®, Guerbet, Villepinte, France) was given *per os* at 70 g/BW. The findings showed that the enlargement of the radiopaque area situated within the gastrointestinal tract of the fish. The swim bladder was pressed against the spinal cord of the carp (Fig. 2C and 2D). This indicated that gas accumulation in the gastrointestinal tract was more prominent compared to the previous diagnosis. Additionally, the contrast medium persisted in the posterior intestine of the carp for over 18 h, exceeding the typical gut transit time of carp, which ranges from 7.1 to 12.8 h (Opuszynski and Shireman, 1991). Therefore, the floating was likely due to gas accumulation in the gastrointestinal tract rather than swim bladder disorder as in the previous admission.

Firstly, the anti-flatulence drug Simethicone (Air-X®, RX manufacturing, Nakornpathom, Thailand) was used at 80 mg/fish *per os* to eliminate the gas in the gastrointestinal tract. Nevertheless, gas accumulation in the tract did not decrease after 24 h post-treatment. Therefore, metoclopramide at 0.5 mg/kg (Nausil®, Siam Pharmaceutical, Bangkok, Thailand) was intramuscularly injected for 4 consecutive days. During the treatment, fish was immersed in 5 ppm of enrofloxacin (Baytril®, Bayer, Leverkusen, Germany) as a prophylactic treatment to control possible bacterial infection. After metoclopramide treatment, the fish gained balance, and their swimming behavior improved. The fish could control its buoyancy up and down the water column, and the pitch was in a normal position. Plain radiography showed a decrease in gas accumulation in the gastrointestinal tract (Fig. 3). The fish was discharged; however, positive buoyancy symptoms recurred at 4 weeks post-discharge, and the fish had to receive gastroprokinetic treatment to relieve the symptoms. Thus, idiopathic intestinal pseudo-obstruction with gut motility disorder was suspected as the cause of positive buoyancy disorder in the present report.

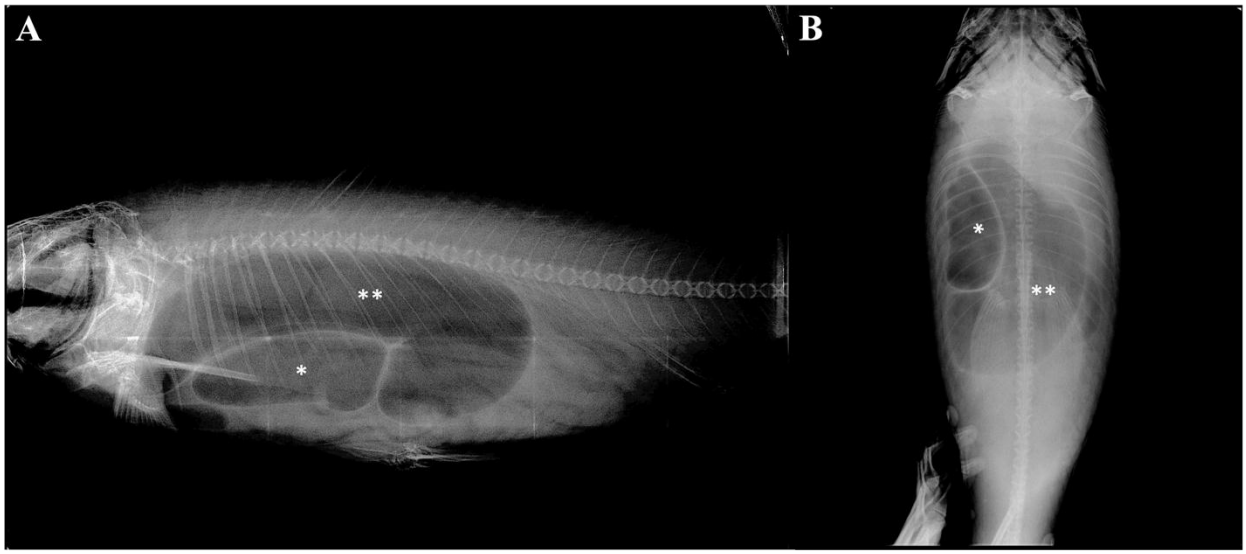


Figure 1 A plain radiograph of the fish with gas accumulation in the swim bladder at lateral (A) and dorsoventral (B) views, respectively. (*) indicates the radiolucent region of the enlarged swim bladder posterior chamber, which is displaced anteriorly. (**) marks the radiolucent area of the swim bladder's anterior chamber.

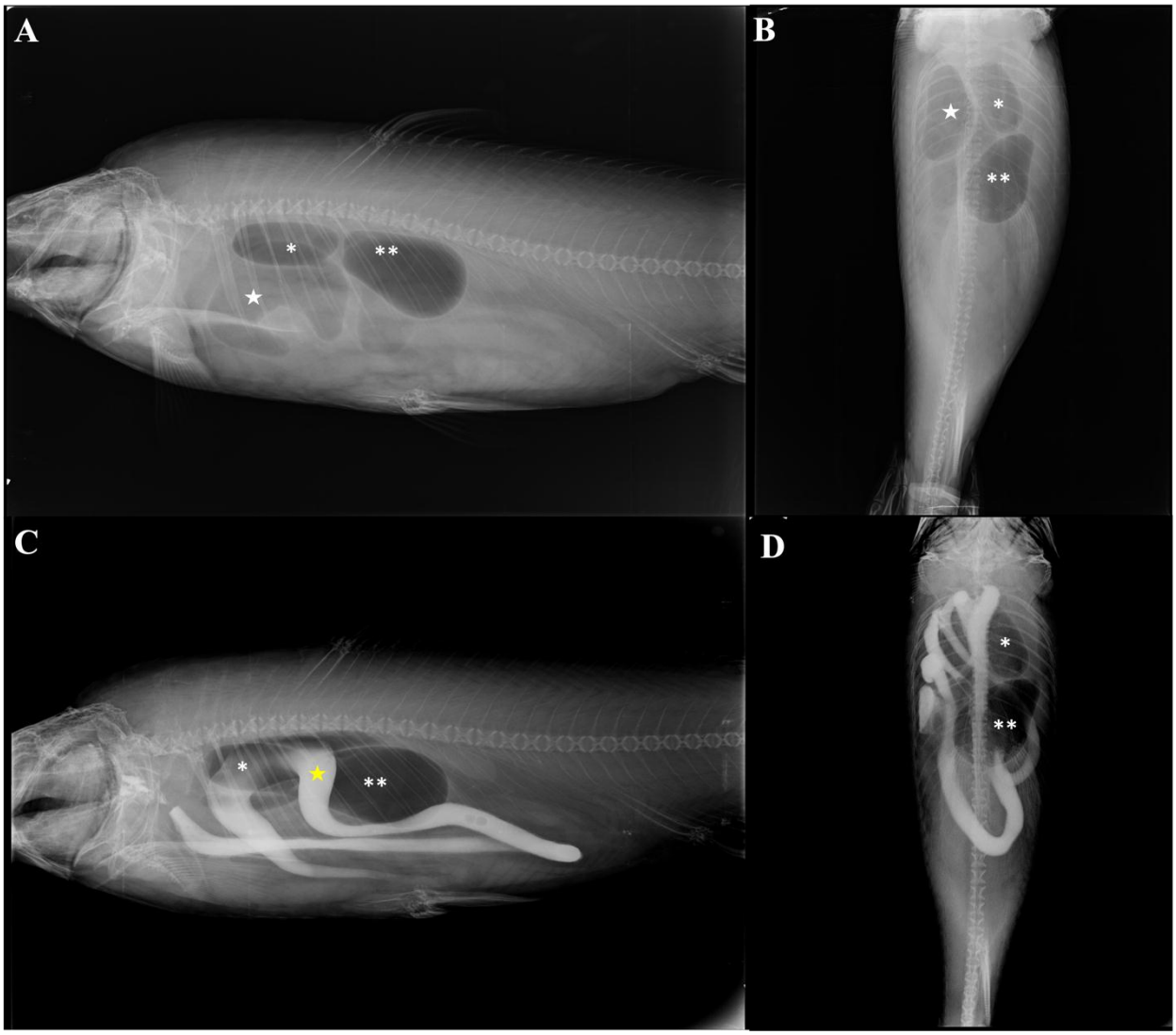


Figure 2 A plain (A and B) and positive contrast (C and D) radiography of the fish with gas accumulation in the gastrointestinal tract at the lateral and dorsoventral view. The white asterisk indicates the swim bladder anterior (*) and posterior (**) chamber, shoved dorsally by the gastrointestinal tract. The white star presents a radiolucent area, and the yellow star displays a positive contrast of gastrointestinal tract enlargement.

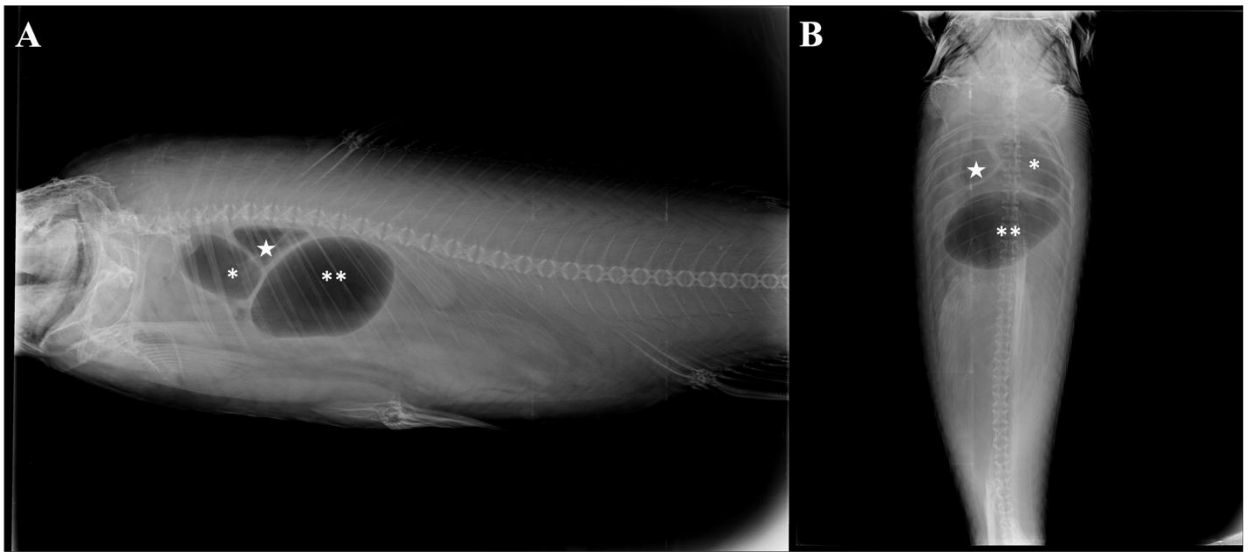


Figure 3 A plain radiograph of the fish after metoclopramide injection at lateral (A) and dorsoventral (B) views, respectively. The white asterisk denotes the swim bladder's anterior (*) and posterior (**) chambers, which are displaced due to diminished gas in the gastrointestinal tract. The white star presents the radiolucent area of the fish's gastrointestinal tract.

Discussion

Loss of neutral buoyancy is a common symptom in ornamental aquatic species. Not only floating on the surface of water or sinking at the bottom of aquaria but also involving abnormal pitch (i.e., head up or head down) and tilting to one side are clinical signs of buoyancy disorder (Wildgoose, 2006). Several primary causes can alter the buoyancy of the fish, such as polycystic disease (Mandrioli *et al.*, 2023; Sales-Ribeiro *et al.*, 2023), abdominal neoplasia (Stilwell *et al.*, 2018), ovarian disorder (Ishikawa and Takayama, 1977), and spondylosis (Boylan *et al.*, 2017). The swim bladder is the organ associated with respiratory and buoyancy functions; therefore, the dysfunction of the swim bladder may lead to positive or negative buoyancy disorder in fish. Infections are a common cause of swim bladder disease (Pees *et al.*, 2010; Pelster, 2021), such as *Aeromonas hydrophila* and *Geotrichum capitatum* infections in goldfish (*Carassius auratus*) (Zoller *et al.*, 2017) and *Sphaerospora dykovae* infection in koi (Chang *et al.*, 2016). Non-infectious factors in swim bladder disease were also reported, such as overinflation (Britt *et al.*, 2002; Doroshev *et al.*, 1981), torsion (Garcês *et al.*, 2020), herniation (Love and Lewbart, 1997), and neoplasia (Lewis *et al.*, 2016; Love and Lewbart, 1997). In the present study, carp was first diagnosed with swim bladder enlargement due to gas accumulation, which might be transferred from the gastrointestinal tract to the swim bladder via a pneumatic duct.

Gas-distended in the gastrointestinal tract can also cause positive buoyancy. This symptom may be caused by intestinal obstruction leading to gas accumulation, but it can also be presented with no obstruction, which is called intestinal pseudo-obstruction (Weber, 2014). Nowadays, the cause of intestinal pseudo-obstruction in fish is still unclear; on the contrary, pseudo-obstruction in other animals may related to immunological disorders (Imai *et al.*, 2014; Zacuto *et al.*, 2016), neurological disorders (Kapur, 2001), etc. In this case report, the swim bladder of the carp was aspirated, but the fish returned with a positive buoyancy problem. Then, readmitted carp were radiographed with positive contrast media, and gas was found to be distended in the gastrointestinal tract. Furthermore, the amount of gas observed in the gastrointestinal tract on the positive contrast radiograph was lower than the normal radiograph. This difference can be attributed to the positive contrast radiograph conducted two days after the fish initially received a radiograph. Nevertheless, simethicone was first used to excrete gas in the canal, but the carp showed no response.

Because of the nonresponsive result of anti-flatulence agents and small motility of excretion positive contrast medium, idiopathic gut motility disorder was suspected. Therefore, metoclopramide was administered to stimulate the intestinal movement of the fish to extrude the gas in the lumen. In the study in elasmobranch, metoclopramide significantly reduced gastric emptying time in white-spotted bamboo sharks (*Chiloscyllium plagiosu*) compared to the control group (Joblon *et al.*, 2020). While in bony fish, zebrafish (*Danio rerio*) found an increase in gut motility in fish receiving domperidone, metoclopramide, mosapride, and magnesium sulfate as human prokinetic drugs (Zhou *et al.*, 2014). Metoclopramide is applied with recombinant gonadotropin-releasing hormone to manipulate fish spawning in koi carp (*C. carpio*) (Eslami *et al.*, 2021; Yeganeh *et al.*, 2022), crucian carp (*C. carassius*) (Cejko and Kucharczyk, 2015), and goldfish (*C. auratus*) (Mohammadzadeh *et al.*, 2021), but there is no report using metoclopramide as a prokinetic drug in the koi carp. Here, we report the application of metoclopramide as a prokinetics drug for the treatment and relief of gut motility disorder in carp.

In conclusion, koi carp with positive buoyancy problems may result from a disorder of the swim bladder or gastrointestinal tract; thus, diagnostic imaging is necessary to identify the cause of the disease. The idiopathic intestinal pseudo-obstruction was suspected in this case because physical obstruction was not found after positive contrast imaging, and the fish responded well to metoclopramide, a prokinetics drug used. Although the fish was not fully recovered,

the present study demonstrates the efficacy of metoclopramide in mitigating positive buoyancy problems caused by gas accumulation in carp.

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