Double-balloon enteroscopy in two dogs

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It is difficult to insert a flexible endoscope deep into the small intestine. A new method, double-balloon enteroscopy, has been developed to improve access to the small intestine, and the aim of this study was to evaluate its usefulness for examination of the small intestine of dogs. The method uses two balloons, one attached to the tip of the endoscope and another attached to the tip of an overtube. The double-balloon endoscope is advanced through the intestine by being held alternately by the balloon on the endoscope and the balloon on the overtube. The technique was applied in two dogs of medium size, using both oral and anal approaches, and it was possible to examine the whole surface of the mucosa of their small intestines.

ADVANCES in endoscopic techniques have made endoscopy an indispensable method for the diagnosis and treatment of disease of the oesophagus, stomach, duodenum and colon in human and veterinary medicine. However, the mid-small intestine has been comparatively neglected because it is difficult to gain access to it with an endoscope (Yamamoto and Kita 2005a). The length of the small intestine, its intraperitoneal location with multiple overlying loops, and its active contractile movements often make conventional endoscopic and radiographic examinations inadequate for diagnosis and therapeutic intervention. Video push enteroscopy, with endoscopes up to 250 cm in length, was introduced in human gastroenterology in the 1990s. An endoscope is inserted forcibly by straightening the stomach and the duodenum; it takes a long time to reach the small intestine, and the portion that can be visualised is limited to 50 to 150 cm of the proximal jejunum (Gerson 2005). Intraoperative enteroscopy, which involves insertion of an endoscope through an incision in the mid-small intestine (enterotomy), was the only technique available to view lesions endoscopically in the mid to distal small intestine before the advent of capsule endoscopy and double-balloon enteroscopy.

Double-balloon enteroscopy, first described by Yamamoto and others (2001), is an endoscopic technique that allows the whole of the small intestine to be visualised by taking advantage of its free mobility (Yamamoto and Kita 2005b). The diagnostic value of double-balloon enteroscopy is greater than that of other imaging modalities and potentially allows therapeutic intervention. Preliminary tests in human beings in Japan (Yamamoto and others 2001) and Germany (May and others 2003) showed that it could be used to perform total small intestine enteroscopy, with a good safety profile and patient tolerance, by using a combination of oral and anal approaches. The advantages of the technique are that the entire length of the small intestine can be examined and treated, high-quality images can be visualised, and the endoscope is as manoeuvrable as conventional videoendoscopes (Yamamoto and Kita 2005a). High-quality videoendoscopic images have made it possible to detect lesions that had previously been poorly visualised in human beings, small intestinal tumours, bleeding polyps and inflammatory fibroid polyps (Yamamoto and Kita 2005a); ulcers and erosions, and angiodysplasia (May and other 2005a); lymphoma, stenoses of the small intestine, and strictures due to tumours or from extrinsic causes (Kita and others 2005); and arteriovenous malformations that can be treated by endoscopic argon plasma coagulation (Gerson 2005). Small intestinal diseases have also been described in dogs: bacterial diseases due to *Salmonella* or *Campylobacter* species, idiopathic inflammatory bowel diseases, lymphangiectasia, lymphoma, histoplasmosis and neoplasia (Tams 2003). However, endoscopic examinations of the whole small intestine in dogs with these disorders have not been reported. Small intestinal disorders in dogs have been investigated by endoscopic biopsy with conventional endoscopes, but they are limited to the descending duodenum and terminal ileum. Enteroscopy is most likely to be of value in identifying focal small intestinal diseases. Although many gastrointestinal diseases involve diffuse lesions, focal changes are also possible; for example, focal areas of lymphoma in the jejunum or ileum may be missed because conventional endoscopes are too short (Tams 2003), and the degree of inflammatory infiltrates is occasionally significantly more intense in certain segments of the small intestine than in the colon (Tams 2003).

This paper describes the use of the new double-balloon enteroscopy technique in two dogs.

MATERIALS AND METHODS

The endoscope used was the EN-450P5 (Fujinon) (Fig 1). It consists of an endoscope that can carry a balloon at its distal end, with a working length of 200 cm, an external diameter of 8·5 mm, and a working channel diameter of 2·2 mm. It is equipped with a 145 cm long flexible overtube, with an external diameter of 12·2 mm and an internal diameter of 10 mm, which also has a balloon at its tip. The two balloons attached at the tips of the enteroscope and the overtube are made of 0·1 mm thick latex and are very soft. Both are inflated and deflated with air from a one-touch pressure-controlled pump system. The lowest balloon inflation pressure sufficient to grip the intestinal wall in human beings, and that avoids pain or damage, is 45 mmHg. This pressure was used in the dogs.

The endoscope advances through the intestine by being held alternately by the balloon on the endoscope and the balloon on the overtube, with a push and pull technique. During the insertion process, the endoscope is first inserted until it reaches the stomach, and the overtube is then advanced over the endoscope. The endoscope is then inserted further, through the pylorus, and its balloon is inflated to maintain a stable position within the intestinal lumen. The overtube is then advanced along the endoscope and its balloon is inflated (Fig 2a). When both balloons are inflated, the tips of the endoscope and the overtube are pulled slowly together, to gather and shorten the intestine between them on the overtube and to simplify the shape of the intestine ahead, avoiding the formation of redundant loops (Fig 2b). The balloon of the endoscope is then deflated, and the endoscope is advanced while the system is fixed by the balloon on the tip of the overtube. When the endoscope is stable again, with its balloon inflated, the balloon of the overtube is deflated and advanced to reach the tip of the endoscope. These procedures are repeated further and further into the small intestine. By this process, the working length of the endoscope can be used most effectively, and the endoscope can be advanced distally after the intestine has been shortened and its shape simplified. The procedure is possible because of the flexibility of the small intestine, which is loosely attached in the abdominal cavity by a long mesentery to the dorsal body wall. An endoscopist and an assistant are necessary to perform the procedure; the assistant is cru-

Veterinary Record (2007)
161, 587-591

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FIG 1: Double-balloon endoscope (EN-450P5; Fujinon)

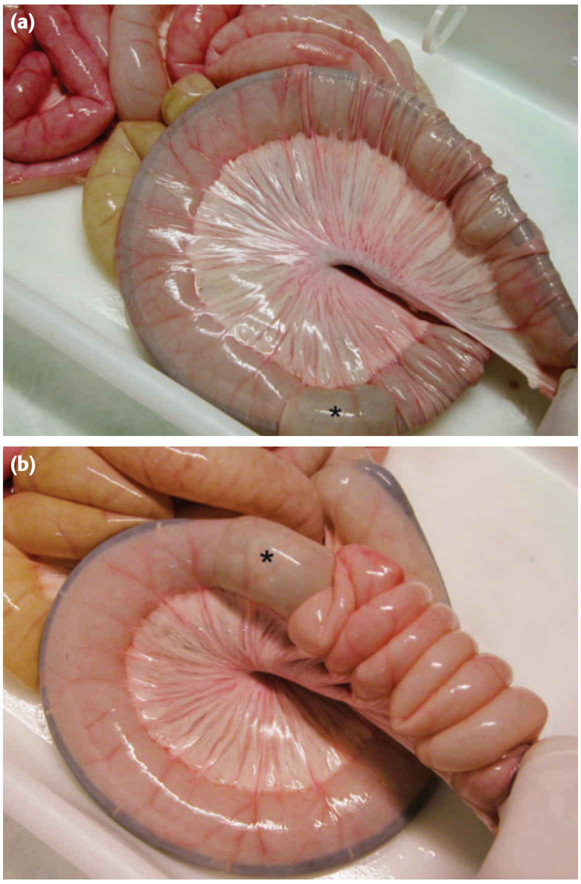

FIG 2: External view of an anatomical specimen from a dog during an oral double-balloon enteroscopy, showing (a) the push procedure, forming a loop, and (b) pulling the endoscope and overtube back to reduce the previously formed loop. The asterisks indicate the position of the overtube's balloon

cial for holding the instrument, and alternately advancing the endoscope and the overtube, for inserting and withdrawing the system, and for controlling the balloons.

During the double-balloon enteroscopy, a specially developed method (May and others 2005b) was used to measure the depth of insertion of the endoscope and record the time of each push and pull movement during the exploration on a standardised documentation sheet on which the advancement (cm) during each movement was recorded. After each push and pull procedure the endoscopist judged whether the advancement was 0, 10, 20, 30 or 40 cm.

In vitro procedure

The gastrointestinal tracts of four dogs, weighing 11, 18, 24 and 30 kg, whose cause of death were unrelated to gastrointestinal disorders, were obtained from postmortem examinations at the Veterinary Hospital, University of Murcia. They were flushed with saline solution until all the contents were removed. The stomach and the complete small intestine were kept with their mesentery. After flushing and before the exploration was performed, the mesentery was tied down to prevent it moving during the enteroscopy. The intestines were explored with the double-balloon endoscope within two hours of the dogs having been euthanased, to test whether the pressure in the balloons was optimal for dogs, and to obtain Fig 2.

In vivo procedure

Two laboratory dogs with no known small intestinal disorders were used for the enteroscopy exploration. They were four and six years old and weighed 23 and 26 kg, respectively. The animal facility at Murcia University follows animal care and use guidelines according to the European Convention for the Protection of Vertebrate Animals used for the Experimental and other Scientific Purposes (Council Directive 86/609/EEC), and the animals were treated in accordance with these guidelines.

Enteroscopy in the two dogs was performed after 24 hours' fasting (solid food) and after an oral laxative (X-Prep R; Viatris Pharmaceuticals) had been administered. Before colonoscopy, the dogs received an anal electrolyte lavage preparation; two to four warm water enemas, with a volume of approximately 33ml/kg, were administered to them 12 to 18 hours before the endoscopy. The last enema was administered two hours before the procedure and resulted in the return of clean fluid without faecal material. The animals were given a continuous intravenous fluid infusion during the procedure and were examined under general anaesthesia. They were premedicated with a combination of 0·05 mg/kg acepromazine and 0·01 mg/kg buprenorphine administered intramuscularly. Anaesthesia was induced with a dose of 5mg/kg propofol, administered intravenously to effect, and after orotracheal intubation, the animals were maintained with isoflurane (1 to 1·2 x minimum alveolar concentration) and 100 per cent oxygen using an anaesthetic breathing system adapted to their size. During the enteroscopy, the dogs' blood pressure and oxygen saturation were monitored. The enteroscopies were carried out by one of the authors (E. P-C.). When necessary, the endoscope was advanced under fluoroscopy and a plain abdominal radiograph was obtained with the animal in dorsal recumbency (Fig 3). The pylorus and the papilla ilealis were intubated first with the endoscope and the overtube was then advanced over the endoscope. At 0 (duodenum), 1, 2, 3 and 4 m depth of insertion during the oral endoscopy, the small intestinal mucosa was marked with a tattoo by submucosal injection of sterilised ink through an injection catheter (Fig 4). After the exploration and while the endoscope and overtube were being pulled back out, these submucosal landmarks were found and biopsy specimens were obtained with biopsy forceps. The biopsies were fixed in formalin, embedded in paraffin, and 4 µm thick sections were cut and stained with haematoxylin and eosin. Both the fluoroscopic and the endoscopic images obtained during the procedure were recorded on DVD, and the times for the insertion of the endoscope and the examinations were recorded.

RESULTS

The total time taken for the oral examination was two hours and 10 minutes. The estimated depth to which the enteroscope was inserted was 4·95 m. The first metre of small intestine was reached in the first 15 minutes, with four advancing manoeuvres. The second metre was reached during the next

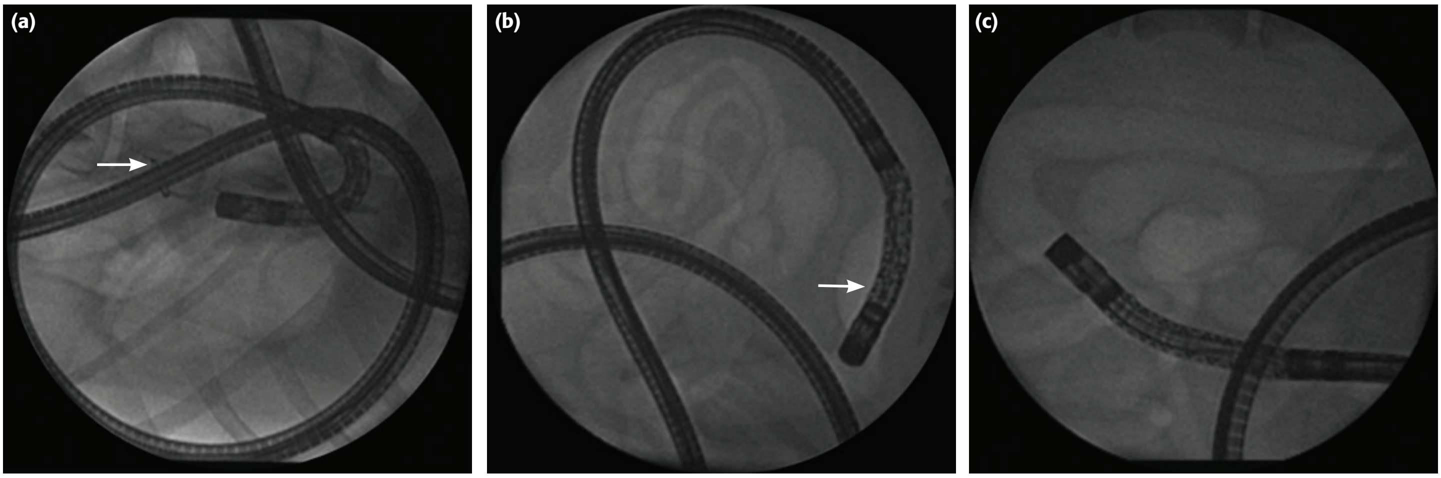

FIG 3: Fluoroscopic checking during oral double-balloon enteroscopy in a dog. (a) Push procedure forming a loop; the arrow indicates the hip of the overtube. (b) Pulling the enteroscope back through the overtube: the depth of the insertion of the enteroscope is measured as 1·90 m from the pylorus. The arrow indicates the position of the endoscope's balloon. (c) The enteroscope's position is approximately 4·90 m from the pylorus and close to the ilecolic valve

20 minutes with five more advancing manoeuvres. The third metre was reached after a further 15 minutes and five more advances; the fourth metre was reached during the next 26 minutes, after seven more advancing manoeuvres; and the endoscope reached its deepest insertion (4·95 m) during the last 20 minutes of exploration after five more manoeuvres. In total, 26 advancing movements were performed during the oral insertion process. At the beginning of the investigation each advance was often up to 30 cm, but by the end of the investigation 10 cm advances were more common. The submucosal ink marks were neither difficult to make nor difficult to locate and biopsy. In the opinion of the pathologists, the biopsy specimens were acceptable for routine histological evaluation; no lesions were found.

The per anal exploration had a total examination time of 15 minutes; the estimated depth of insertion of the endoscope into the small intestine was 95 cm in a total of four advancing manoeuvres.

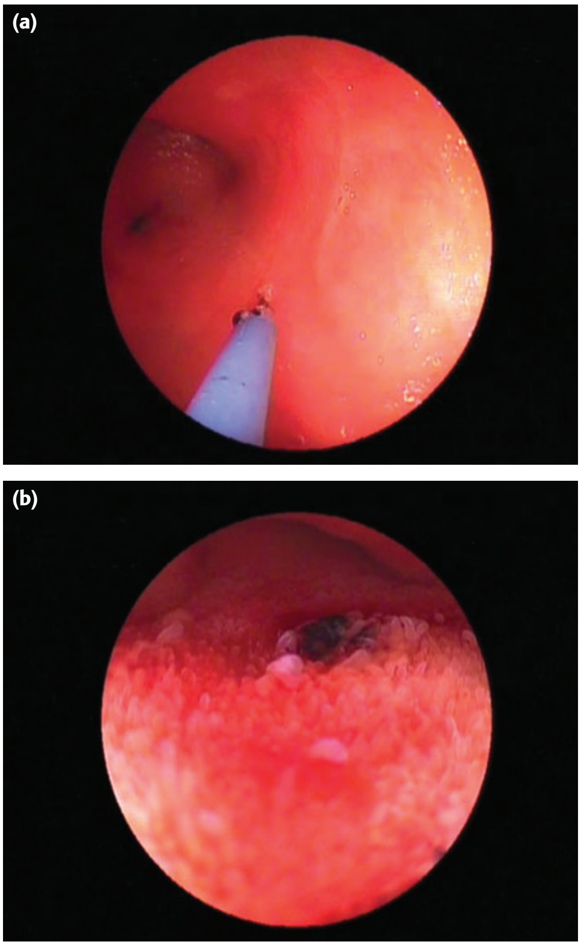

FIG 4: Endoscopic images obtained during oral double-balloon enteroscopy in a dog. (a) Endoscopic placement of a tattoo in the small intestine by injection of sterilised ink into the submucosal layer. (b) Endoscopic view of the ileum, showing the sterilised ink injected into the submucosal layer

DISCUSSION

The protocol used in this study was similar to that used in human double-balloon endoscopy and it was not difficult to perform in the dogs. The small intestine can move freely in the abdominal cavity, and there was no problem in shortening its length. The method made it possible to introduce the endoscope safely into the whole of the small intestine. In human beings, the method is valuable not only for diagnosis but also for treatment, for example, endoscopic haemostasis, polypectomy, endoscopic mucosal resection, balloon dilation and the placement of stents in the small intestine (Yamamoto and Kita 2005a). The disadvantages of the technique in human medicine include the long examination time and requirement for sedative medication, the need for additional nursing staff, and the need for fluoroscopy to control the loop reduction and to aid the ileal intubation during the retrograde approach (Gerson 2005). In the two dogs, fluoroscopy was not necessary for ileal intubation because the relatively short colon made the procedure easy.

The balloons used in the study were inflated to 45 mmHg, which is the lowest pressure needed to hold the human intestine for endoscope insertion and is designed not to cause pain or discomfort. There are no references about the pressure required for use in dogs, but the results obtained with the anatomical specimens showed that 45 mmHg was satisfactory.

In dogs, the double-balloon endoscope can be inserted by either the oral or the anal approach, depending upon the location of any suspected lesions. When the position of the lesion is predictable, the shorter route can be chosen, because up to two-thirds of the small intestine can be examined by either approach (Yamamoto and Kita 2005a). It is likely that the whole small intestine could be observed by using a combination of the two routes. The main cause of difficulty in inserting the double-balloon endoscope in dogs is likely to be adhesions following abdominal surgery, as has been reported in human beings (Yamamoto and Kita 2005a).

When the small intestine is being bent on to the overtube by means of repeated push-and-pull manoeuvres it is virtually impossible to be certain of the enteroscope's depth of insertion or to estimate the length of the small intestine that has been visualised or to determine the location of any pathological changes (May and others 2005b). This difficulty may explain the substantial differences in the lengths of the small intestine reported to have been explored in human beings. Gerson (2005) reported results ranging from 44 to 665 cm, Di Caro and others (2005), Ell and others (2005) and May and others (2005a) reported mean distances from 220 to 320 cm, and Matsumoto and others (2005b) reported mean distances between 100 and 144 cm. Fluoroscopy has been used to evaluate the performance of double-balloon enteroscopy (Matsumoto and others 2005a), but May and others (2005b) showed that radiographic control of the enteroscope's position does not help to determine its depth of insertion, because even in the best circumstances the repeated push-and-pull procedures always create similar radiographic images. The measurement technique used in this work has been used by Yamamoto and Kita (2005a), and the authors think that it is very useful. With this system it was estimated that 4·95 m of small intestine was explored in the two dogs. As the normal length of the small intestine in medium-sized dogs is considered to be 2 to 4·8 m (Nickel 1986), this estimation appears reasonable.

The double-balloon enteroscope can be inserted easily, but there are substantial differences between the percentages of the small intestine that have been reported to have been examined; Yamamoto and others (2004) and Yamamoto and Kita (2005a) reported 86 per cent, Di Caro and others (2005) reported 16·2 per cent, and May and others (2005a) reported 45 per cent. Yamamoto and Kita (2005a) described good endoscope manoeuvrability even when the enteroscope was inserted distally; however, they found it difficult to advance the endoscope into the distal part of the small intestine during per oral exploration. In the fresh specimens that were examined in the present study, a large volume of air collected in this part of the small intestine as it was being bent on to the overtube by repeated push-and-pull manoeuvres, and this may be an important reason for the difficulty in advancing the endoscope during the last part of the exploration. No references to this problem were found in the literature. Most authors consider that a time limit should be imposed on the length of the examination, but opinions differ about the time; Gerson (2005) suggested up to 240 minutes as the maximum examination time, but Di Caro and others (2005), Ell and others (2005) and May and others (2005a) suggested that an examination should take no longer than 100 minutes, to avoid complications such as perforation. In the two dogs there were no complications after 130 minutes' exploration.

Double-balloon endoscopy is considered to be safe (May and others 2003, Di Caro and others 2005, Gerson 2005, Yamamoto and Kita 2005a), and only two cases of complications have been reported in human beings (Yamamoto and others 2004). One patient suffered a perforation after endoscopic examination of a small intestinal malignant lymphoma, probably because chemotherapy had caused necrosis in the tumour. The other patient was diagnosed as having Crohn's disease of the small intestine, and after double-balloon endoscopy the subject suffered abdominal pain and fever, although laparotomy was not necessary. When fragile lesions are observed in the small intestine, the endoscope should not be inserted across the lesion, to avoid the risk of a perforation (Yamamoto and Kita 2005a).

This preliminary study shows that the double-balloon method can be used safely to introduce an endoscope into the depth of the small intestine of dogs, by either the oral or the anal approach, depending upon the suspected location of any lesion. Double-balloon enteroscopy may be an effective tool for the diagnosis of small intestinal disorders in dogs and possible therapeutic intervention for conditions including tumours, bleeding polyps, inflammatory fibroid polyps, ulcers and erosions, lymphoma, strictures due to tumours or extrinsic causes and arteriovenous malformations. Further study is needed to determine the range of size of dogs that can be examined by the method, and its diagnostic utility and safety.

ACKNOWLEDGEMENTS

The authors tank Dr Robert W. Henry (University of Tennessee, USA), Dr Paloma Peinado and Mr Mickel Tomlinson for their assistance with translation into English. They also thank ST Endoscopia for their technical support, time and patience throughout the enteroscopy explorations.

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