Original Article

Assessment of Abdominal Pain and Abdominal Distension after ERCP with Carbon Dioxide versus Air Insufflations

Prakongwong T
Jearjesdakul J
Opuchar K
Sanprajit T
Piyanirun W
Chuenrattanakul S

ABSTRACT

Background: Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure for diagnosis and treatment of many hepatobilliary tract diseases. Patients may suffer from abdominal pain and distension due to air insufflation during the procedure. Previous studies confirmed the benefit of using carbon dioxide (CO_2) in colonoscopy but still controversial in ERCP. The primary outcome of this study was to compare the difference in pain score after ERCP between using CO_2 and air insufflation. The secondary outcome was the difference of abdominal circumference after ERCP, side effect of CO_2 and ERCP complications between two groups.

Methods: Between April 2012 and February 2013, 77 patients who underwent ERCP were enrolled and randomized to receive CO_2 or air insufflations. ERCP was performed under sedated with midazolam plus pethidine or fentanyl. The abdominal pain was evaluated by 10-point visual analog scales (VAS) before and at 1, 3 and 6 hours after procedure. The waist circumference was measured before and after ERCP, complication of procedure and CO_2 were recorded.

Results: Fifty seven patients (27 in CO_2 group and 30 in air group) were enrolled in the study. The CO_2 and air groups were similar in demographic data, indication for ERCP, duration of ERCP and post ERCP diagnosis. Mean of pain scores at 1 and 3 hours post-ERCP were higher in air insufflation group than in CO_2 insufflation group but no statistical significance (2.17 vs. 1.52, p=0.35 and 1.48 vs. 1.70, p=0.71 respectively). In contrast, patients who received CO_2 had significantly lesser difference in waist circumference after ERCP than those who received air (1.81±1.84 cm vs. 3.52±2.97 cm respectively, p=0.011). There was no significant difference in ERCP complications and no patient reported adverse event of CO_2.

Conclusions: CO_2 insufflation during ERCP was safe and might reduce abdominal distension. Further study should be performed to establish this benefit.

Key words : Carbon dioxide insufflation, air insufflation, endoscopic retrograde cholangiopancreatography, post procedure pain, waist circumference.

[Thai J Gastroenterol 2013; 14(3):164-170.]

Gastroenterology and Hepatology Unit, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand.
Address for Correspondence: *Jindarat Jearjesdakul, M.D., Gastroenterology and Hepatology Unit, Department of Medicine, Phramongkutklao Hospital, Bangkok, Thailand.*

Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure for diagnosis and treatment of many hepatobilliary tract diseases e.g., common bile duct stone, cholangiocarcinoma, bile duct stricture, etc. Known complications of ERCP include pancreatitis, cholangitis, bleeding and perforation. However, patients may suffer from abdominal pain and abdominal distension due to air insufflation during the procedure which can be confused with other complications. Abdominal pain after ERCP is associated with volume of air administration and timing of procedure. Previous studies revealed that carbon dioxide (CO_2) could be absorbed in the bowel faster than nitrogen (150 times) and was rapidly washed out via breath[1,2]. Many randomized controlled trials have confirmed the benefit of CO_2 administration in colonoscopy, sigmoidoscopy, and double contrast barium enema to reduce abdominal pain after procedures[1,3-12]. Especially in colonoscopy, CO_2 insufflation can reduce abdominal pain and diameter of the colon measured on abdominal plain film compared with air insufflation without significant difference in complication rate and side effects.

However, the data of CO_2 administration in ERCP had different results. Two of four studies found that using CO_2 reduced abdominal pain after ERCP while the others showed no significant difference in pain score[13-16]. Abdominal bloating after ERCP is the most common problem occurring in patients undergoing prolonged procedure longer than one hour and often occurred within the first 6 hours after procedure. In most trials, the patients were not admitted and pain score was evaluated via e-mails or telephone calls.

There were approximately 180-200 patients underwent ERCP procedures each year at Phramongkutklao Hospital. All patients were admitted for clinical observation after ERCP. Hence pain score could be accurately assessed by medical personnel. The aim of this study was to compare the difference in post-ERCP pain score between CO_2 and air insufflations.

Materials and Methods

Patients

Patients underwent ERCP at Endoscopy Unit, Phramongkutklao Hospital between April 2012 and February 2013 were included. Midazolam plus pethidine or fentanyl were used for sedation during ERCP. Exclusion criteria including any of the followings: age under18 years old, refusal of consent, baseline abdominal pain score greater than 4 from 10 points of visual analog scale (VAS), neuropsychiatric problem or abnormal level of consciousness, pregnancy, COPD with CO_2 retention, chronic pancreatitis, prior opioid use within 12 hours or long acting opioid use within 45 days before ERCP, critically ill patients i.e. intubation or unstable vital signs, general anesthesia, propofol use, suspected sphincter of Oddi dysfunction and pancreatic duct stone, post ERCP pancreatitis (diagnosed by pain score greater than 5 from 10 points of VAS and serum amylase or lipase greater than 3 times upper limit of normal), using more than 40 mg of hyosine during ERCP, post ERCP cholangitis (diagnosed by pain score greater than 5 from 10 points of VAS, fever and rising of total bilirubin or AST, ALT elevation), bowel perforation (diagnosed by free air from any radiologic images), and patients in whom a duodenoscope could not be inserted into the second part duodenum (because the procedure duration was brief and there was lower risk of post ERCP pain).

Study design

This study was conducted as a prospective, single center, double-blind, randomized, and controlled trial. The study protocol was approved by the InstitMmedicine; clinical research approval number R020h/55)

Patients who met the inclusion criteria had received research information given by a researcher. When patients consented to participate in the research, data were collected including gender, age, weight, height, indications for ERCP, pain score, the American Society of Anesthesiologists (ASA) physical status classification, waist circumference, and base line PCO_2. All the research participants were divided into two groups. They were randomly selected to undergo ERCP with air or CO_2 insufflation by using computer generated blocking. The enveloped code of using air or CO_2 insufflation was open by endoscopy nurses who set the procedure schedule. Both endoscopists and patients did not know the type of gas insufflation.

The pressure of CO_2 was controlled by Olympus UCR Endoscopic CO_2 Regulation Unit (CO_2 regulator designed for use in endoscopy procedures) which was connected to a CO_2 tank and Olympus CLV-180 light source. The flow rate of CO_2 was designed as

same as the flow rate of air when the processor was set on çhighé. In the period of research data collection, CO_2 tank and CO_2 regulation unit were located in the endoscopy room whichever air or CO_2 was used. During ERCP, CO_2 regulator unit and CO_2 tank was covered by veil, therefore the endoscopists did not know which gas was used (Figure 1).

Patients exhaled via a tube connecting to a PCO_2 measuring machine, the Capnocheck Plus. PCO_2 was measured every 15 minutes until the end of the procedure. ERCP procedures were performed in accordance with generally similar in the two groups and by endoscopists who had experience in more than 200 ERCP procedures. The data included type and dosage of medications used for sedation and antispasmodics, type of procedure, post ERCP diagnosis and complications were recorded.

By using 10-point VAS, the severity of pain (pain scores) was assessed by a physician or a nurse prior to ERCP and after the procedure at 1, 3 and 6 hours. Analgesics were prescribed if pain scores were greater than 4 from 10 points. The type and dosage of analgesics to control abdominal pain after ERCP was recorded.

The symptom of bloating was assessed by measuring the waist circumference at the navel while exhaling and marking was done on the skin for precise measurement to compare between pre-and post-ERCP. The post-ERCP waist circumference was measured immediately after the procedure had been finished.

Endpoints

The primary endpoint was abdominal pain after ERCP. The secondary end points were complications of ERCP, side effects of CO_2 and distinction of abdominal circumference before and after ERCP between air and CO_2 groups.

Sample size

A sample size was determined by power calculation. On the basis of previous data, the mean of pain scores in air insufflation group were 22±21 and in CO_2 insufflation group were 10±11. To determine this difference with a power of 0.9 and an alpha 0.05, the number of the sample size were 41 patients in each group.

Statistical analysis

Continuous data were analyzed as mean ± standard deviation (SD). Categorical data were analyzed using Chi-squared test. The pain scores on VAS were compared at each time point using the Student *t*-test. The difference of waist circumference before and after ERCP in each groups were compared by Pair *t*-test. Statistical significance was defined as a *p*-value of less than 0.05. Two-sided tests were used. The statistical analysis was performed using a SPSS software version 19.0.

RESULTS

A total of 64 patients were eligible for inclusion in the study and were randomized to both groups. Seven

Figure 1. The study setup; the CO_2 insufflator was connected to the CO_2 tank (left). For all cases in the study, CO_2 regulator unit and CO_2 tank were covered by veil (right).

patients were excluded from analyses due to pancreatitis and bowel perforation (4 patients from air insufflation group and 3 patients from CO_2 insufflation group). Fifty seven patients were analyzed (Figure 2). Mean age were 63 years in air insufflation group and 60 years in CO_2 insufflation group. Baseline characteristics and comorbidities were shown in Table 1. There was no significant difference in baseline characteristics between each group. The data including type and dosage of sedative drugs, time consumed for cannulation, total duration of the procedure and rate of sphincterotomy and stent insertion were recorded which were not shown to have statistical difference between each group (Table 2).

Prior to ERCP, the mean 10-point VAS were zero in both groups. The mean 10-points VAS at 1, 3 and 6

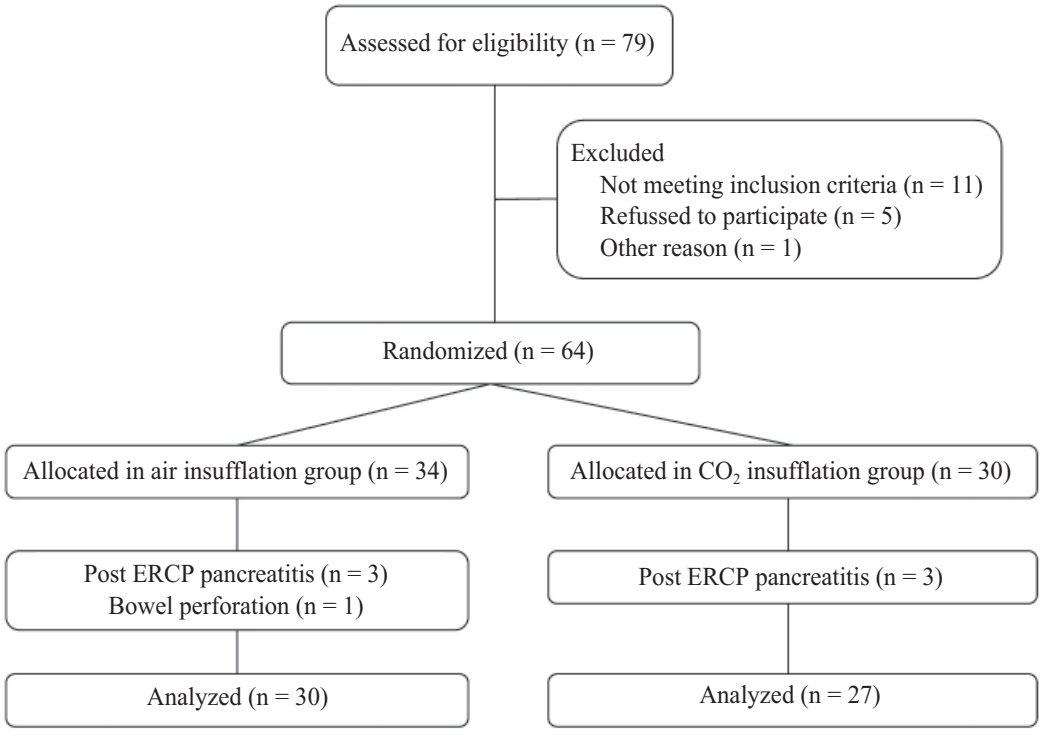

Figure 2. Patient flow diagram.

Table 1. Baseline demographic data of patients in air insufflation group and CO_2 insufflation group.

Characteristics	Air insufflation	CO_2 insufflation	*p*-value
Age, years (mean±SD)	62.60±17.24	60.63±17.6	0.67
Female, n (%)	10 (33.3%)	8 (29.6%)	0.78
BMI, kg/m^2 (mean±SD)	23.48±4.39	23.32±5.21	0.90
Comorbidities, n (%)			
COPD	1 (3.3)	0 (0)	1.00
Coronary artery disease	0 (0)	1 (3.7)	0.47
Hypertension	13 (43.3)	9 (33.3)	0.44
Diabetes	3 (10.0)	2 (7.4)	1.00
Dyslipidemia	8 (26.7)	9 (33.3)	0.58
Cholangiocarcinoma	2 (6.7)	5 (18.5)	0.24
Other malignancies	4 (13.3)	3 (11.1)	1.00
Prior ERCP, n (%)	11 (36.7)	9 (33.3)	0.79
ASA classification (mean±SD)	1.57±0.89	1.67±0.78	0.66

hours were 2.17±2.78, 1.70±1.93, 1.07±1.57 in air insufflation group and 1.52±2.41, 1.48±2.39, 1.04±1.83 in CO_2 insufflation group. Pain scores at 1 and 3 hours after ERCP in air insufflation group were slightly higher than in CO_2 insufflation group, however there was no statistical significance. The waist circumferences were shown in table 3. Patients in air insufflation group had significantly greater difference in waist circumferences between before and after ERCP compared with those in CO_2 insufflation group (3.52±2.97 cm vs. 1.81±1.84 cm respectively, p=0.011). The mean exhaled CO_2 level during procedure in patients who received air was significantly lower than patients who received CO_2 (35.99±4.68 mmHg vs. 39.64±5.99 mmHg respectively, p=0.015). There were no clinically significant CO_2 side effects such as dizziness and drowsiness in both groups. None had exhaled CO_2 level greater than 50 mmHg.

Complications after ERCP occurred in 8 patients. Only one patient in air insufflation group had a serious complication (bowel perforation). The diagnosis was made after detection of free air from abdominal X-ray and computerized tomography. This patient underwent exploratory laparotomy nevertheless the site of perforation was not found. The microperforation of the bowel was then diagnosed. The patient had an uneventful recovery and was discharged from hospital within 7 days. The other 6 patients (3 patients in air insufflation group and 3 patients in CO_2 insufflation group) had mild pancreatitis (BISAP score <3) and were discharged from hospital within 5 days. The remaining one patient in CO_2 insufflation group had transient hypotension during ERCP which was rapidly improved after volume resuscitation with 300 mL of normal saline solution. There was no significant difference in rate of complications in both groups.

Table 2. Characteristics of ERCP performed in air insufflation group and CO_2 insufflation group.

ERCP characteristics	Air insufflation	CO_2 insufflation	p-value
ERCP indication, n (%)			
Choledocholithiasis	13 (43.3)	15 (55.6)	0.43
Pancreatitis	1 (3.3)	1 (3.7)	1
Jaundice	3 (10.0)	1 (3.7)	0.61
Abnormal LFTs	1 (3.3)	0 (0)	1
Mass	4 (13.3)	4 (14.8)	1
Billiary stricture	0 (0)	1 (3.7)	1
Stent exchange	3 (10.0)	1 (3.7)	0.61
Cholangitis	2 (6.7)	3 (11.1)	0.66
Biliary dilatation	1 (3.3)	1 (3.7)	1
Others	2 (6.7)	0 (0)	0.49
Sphincterotomy, n (%)	18 (60)	16 (59.3)	0.96
Stent placement, n (%)	10 (33.3)	5 (18.5)	0.21
Final diagnosis, n (%)			
Normal	8 (26.67)	8 (29.63)	1.00
Mass	9 (30)	4 (14.81)	0.22
Cholangitis	1 (3.3)	1 (3.7)	1.00
Choledocholithiasis	5 (16.67)	7 (25.92)	0.52
Biliary sludge	1 (3.3)	2 (7.40)	0.60
Ampullary stenosis	0 (0)	1 (3.7)	0.47
Biliary dilatation	1 (3.3)	0 (0)	1.00
Bile duct leak	1 (3.3)	0 (0)	1.00
Stent exchange	2 (6.67)	0 (0)	0.49
Others	2 (6.67)	4 (14.81)	0.41
Cannulation success, n (%)	28 (93.3)	23 (85.2)	0.41
Time consumed for cannulation (mean±SD)	15.61±20.13	9.33±11.20	0.18
Total duration (mean±SD)	65.60±44.52	58.81±40.40	0.55

Table 3. Primary and secondary outcomes in air insufflation group and CO_2 insufflation group.

Characteristic	Air insufflation	CO_2 insufflation	*p*-value
Primary outcome			
Abdominal pain scores (mean±SD)			
Prior to procedure	0	0	N/A
Post procedure, hours			
1	2.17±2.78	1.52±2.41	0.35
3	1.70±1.93	1.48±2.39	0.71
6	1.07±1.57	1.04±1.83	0.95
Secondary outcome			
Abdominal circumference, cm (mean±SD)			
Preprocedure	85.56±12.08	79.15±13.53	0.06
Postprocedure	89.08±12.05	80.96±13.40	0.02
Change in abdominal circumference, cm	3.52±2.97	1.81±1.84	0.01
Complications, n (%)			
During ERCP	1 (3.03)	1 (3.70)	0.48
Post ERCP	3 (10)	3 (11.11)	0.70

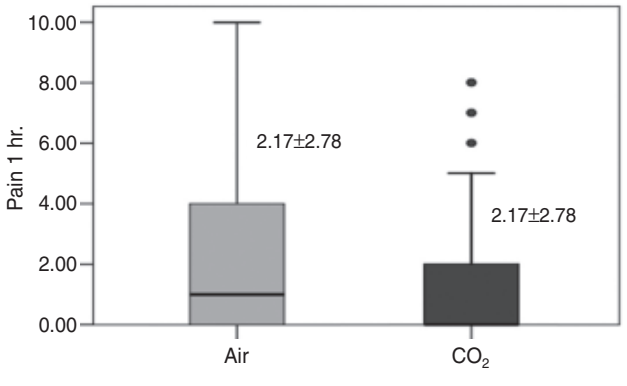

Figure 3. Box plot of pain scores at 1 hour after ERCP between air insufflation and CO_2 insufflation group (values are mean±SD).

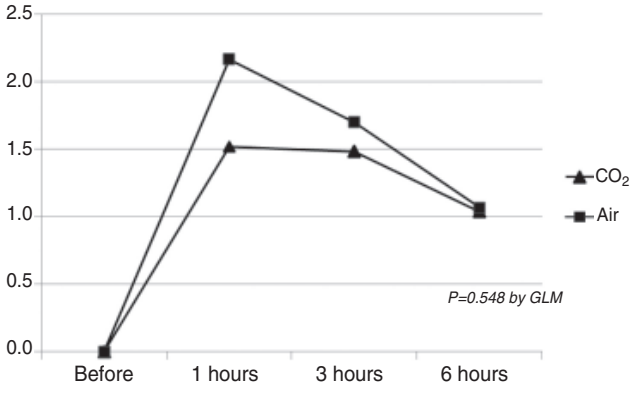

Figure 4. Mean abdominal pain score as measured on a 10-point visual analogue scale pre-ERCP and at 1, 3, 6 hours post ERCP. As measured by generalized linear model (GLM), there was no difference between pain scores over the time course of the study.

DISCUSSION

In this study, we performed a randomized, double-blind, controlled trial to assess the ability of CO_2 insufflation during ERCP to reduce abdominal pain and distension after ERCP. Our results showed that the increment in waist circumference after ERCP in CO_2 insufflation group was significantly less than in the air insufflation group. However there was not statistically different in post procedural abdominal pain.

There were four randomized controlled trial that compared between using CO_2 or air insufflations for ERCP[13-16]. Dellon et al randomized 74 patients, and Kuwatani et al randomized 80 patients to either air or CO_2 insufflations for ERCP. The results from both studies revealed that there was no significant difference neither in post procedural abdominal pain or changing of waist circumference before and after ERCP. However data from Kuwatani et al showed that gas volume score after ERCP (measured from abdominal plain film) in CO_2 insufflation group was significantly lower than in air insufflation group.

In contrast, the results from the studies of Bretthauer et al (randomized 118 patients) and Maple et al (randomized 100 patients) showed that there was significant decrease in abdominal pain after ERCP in CO_2 insufflation group compared with air insufflation group. Abdominal distension was less in CO_2 insufflation group as measured by gas volume in the study of Bretthauer and by waist circumference in the study of Maple.

Our study showed the differences in pain score in the group using CO_2 insufflation. This could be due to the effect of CO_2 during the first 1-3 hours after ERCP. The results had demonstrated the trend of decreasing in pain scores in CO_2 insufflation group than air insufflation group although the difference did not reach the statistical significance. However, two previous studies showed results that using CO_2 was able to reduce abdominal pain after ERCP significantly. Our study might be underpowered due to small number of patients in each group. Similar to four previous studies, our study showed no significant difference in rate of complication after ERCP and adverse effect due to using CO_2. Our data suggested that CO_2 was safe to use.

This study was the first study of which the data of pain score was recorded by medical personnel so the assessment was more precise than in the other previous studies which reported by patients themselves. Furthermore we admitted all patients into the hospital after ERCP, so the complication after ERCP could be evaluated accurately.

There were some limitations in this study. It was a small, single center study. We could not include the number of patients as we expected within the limited period of time. Assessment of the abdominal distension by measuring waist circumference might be less accurate than measuring from radiography.

In conclusion, the use of CO_2 in ERCP was safe and might reduce abdominal distension after ERCP compared with conventional technique. A larger study should be performed to establish this benefit of CO_2 insufflation for ERCP.

REFERENCES

1. Hussein AM, Bartram CI, Williams CB. Carbon dioxide insufflation for more comfortable colonoscopy. Gastrointest Endosc 1984; 30:68-70.
2. Coblentz CL, Frost RA, Molinaro V, *et al.* Pain after barium enema: effect of CO_2 and air on double-contrast study. Radiology 1985; 157:35-6.
3. Stevenson GW, Wilson JA, Wilkinson J, *et al.* Pain following colonoscopy: elimination with carbon dioxide. Gastrointest Endosc 1992; 38:564-7.
4. Bretthauer M, Thiis-Evensen E, Huppertz-Hauss G, *et al.* NORCCAP (Norwegian colorectal cancer prevention): a randomised trial to assess the safety and efficacy of carbon dioxide versus air insufflation in colonoscopy. Gut 2002; 50:604-7.
5. Bretthauer M, Hoff G, Thiis-Evensen E, *et al.* Carbon dioxide insufflation reduces discomfort due to flexible sigmoidoscopy in colorectal cancer screening. Scand J Gastroenterol 2002; 37:1103-7.
6. Sumanac K, Zealley I, Fox BM, *et al.* Minimizing post-colonoscopy abdominal pain by using CO(2) insufflation: a prospective, randomized, double blind, controlled trial evaluating a new commercially available CO(2) delivery system. Gastrointest Endosc 2002; 56:190-4.
7. Church J, Delaney C. Randomized, controlled trial of carbon dioxide insufflation during colonoscopy. Dis Colon Rectum 2003; 46:322-6.
8. Bretthauer M, Lynge AB, Thiis-Evensen E, *et al.* Carbon dioxide insufflation in colonoscopy: safe and effective in sedated patients. Endoscopy 2005; 37:706-9.
9. Phaosawasdi K, Cooley W, Wheeler J, *et al.* Carbon dioxide-insufflated colonoscopy: an ignored superior technique. Gastrointest Endosc 1986; 32:330-3.
10. Silva A, Ho HS, Mathiesen KA, *et al.* Endoscopy during laparoscopy. Reduced postprocedural bowel distention with intraluminal CO2 insufflation. Surg Endosc 1999; 13:662-7.
11. Nakajima K, Lee SW, Sonoda T, *et al.* Intraoperative carbon dioxide colonoscopy: a safe insufflation alternative for locating colonic lesions during laparoscopic surgery. Surg Endosc 2005; 19:321-5.
12. Lowe AS, Chapman AH, Wilson D, *et al.* A double-blind randomised, placebo-controlled trial evaluating the influence of oral long-acting muscle relaxant (Mebeverine MR), and insufflation with CO(2) on pain associated with barium enema. Eur Radiol 2003; 13:1664-8.
13. Bretthauer M, Seip B, Aasen S, *et al.* Carbon dioxide insufflation for more comfortable endoscopic retrograde cholangiopancreatography: a randomized, controlled, double-blind trial. Endoscopy 2007; 39:58-64.
14. Maple JT, Keswani RN, Hovis RM, *et al.* Carbon dioxide insufflation during ERCP for reduction of postprocedure pain: a randomized, double-blind, controlled trial. Gastrointest Endosc 2009; 70:278-83.
15. Dellon ES, Velayudham A, Clarke BW, *et al.* A randomized, controlled, double-blind trial of air insufflation versus carbon dioxide insufflation during ERCP. Gastrointest Endosc 2010; 72:68-77.
16. Kuwatani M, Kawakami H, Hayashi T, *et al.* Carbon dioxide insufflation during endoscopic retrograde cholangiopancreatography reduces bowel gas volume but does not affect visual analogue scale scores of suffering: a prospective, double-blind, randomized, controlled trial. Surg Endosc 2011; 25:3784-90.