Communication from the ASGE Technology Committee

TECHNOLOGY STATUS EVALUATION REPORT

The use of carbon dioxide in gastrointestinal endoscopy

Prepared by: ASGE TECHNOLOGY COMMITTEE

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The American Society for Gastrointestinal Endoscopy (ASGE) Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of gastrointestinal endoscopy. Evidence-based methodology is used by performing a MEDLINE literature search to identify pertinent clinical studies on the topic as well as a MAUDE (U.S. Food and Drug Administration Center for Devices and Radiological Health) database search to identify the reported adverse events of a given technology. Both are supplemented by accessing the "related articles" feature of PubMed and by scrutinizing pertinent references cited by the identified studies. Controlled clinical trials are emphasized, but in many cases, data from randomized, controlled trials are lacking. In such cases, large case series, preliminary clinical studies, and expert opinions are used. Technical data are gathered from traditional and Web-based publications, proprietary publications, and informal communications with pertinent vendors. Technology Status Evaluation Reports are drafted by 1 or 2 members of the ASGE Technology Committee, reviewed and edited by the Committee as a whole, and approved by the Governing Board of the ASGE. When financial guidance is indicated, the most recent coding data and list prices at the time of publication are provided. For this review, the MEDLINE database was searched through December 2014 for relevant articles by using the key words "carbon dioxide" and "gastrointestinal endoscopy," combined with other relevant terms such as "esophagogastroduodenoscopy," "ERCP," "balloon enteroscopy," "colonoscopy," and "complications or adverse events," among others. Technology Status Evaluation Reports are scientific reviews provided solely for educational and informational purposes. Technology Status Evaluation Reports are not rules and should not be construed as establishing a legal standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment or payment for such treatment.

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BACKGROUND

Adequate distension of the GI lumen is required for safe advancement of endoscopes and for careful visualization of the mucosa. Room air, which is widely used for GI luminal distension, possesses the advantages of universal availability and low cost. However, room air is poorly absorbed by the GI tract and is largely evacuated through belching or passage of flatus. To minimize postprocedural abdominal distention, endoscopists commonly suction out as much air as possible after completion of the procedure and immediately before removal of the endoscope. Despite this practice, older studies indicated that 50% of patients reported pain after completion of colonoscopy, with 12% of patients describing the pain as severe, even at 24 hours after the procedure.[1] Despite improvements in endoscope technology and techniques leading to shorter procedure times with lower amounts of air insufflated, some patients still experience postprocedure pain related to distension. Carbon dioxide (CO_2) is rapidly absorbed by the GI mucosa, driving increased interest in its use as an insufflation agent for endoscopic procedures. The ASGE has previously published a Technology Status Evaluation Report on methods of luminal distention, including CO_2, for colonoscopy alone.[2] This document discusses CO_2 as an insufflation agent for all endoscopic procedures within the GI tract.

TECHNOLOGY UNDER REVIEW

CO_2 is absorbed from the GI tract approximately 160 times faster than nitrogen, the major gaseous ingredient of ambient air,[3] and is therefore considered by many to be a superior alternative to room air for insufflation during GI endoscopy.[4,5] It is passively absorbed through the mucosal lining into the bloodstream and eventually exhaled through the lungs. The rapid absorption of CO_2

and the potential associated benefits were initially demonstrated in rat colon model studies, which indicated that CO_2 insufflation was associated with a significantly shorter duration of recovery from luminal distension and elevated intraluminal pressures, compared with room air.[6,7] A human study, evaluating colonoscopy performed with CO_2 insufflation for the localization of colonic lesions during laparoscopic surgery, demonstrated complete colonic decompression over a mean period of 21 minutes.[8]

Randomized studies comparing CO_2 and air insufflation during colonoscopy have indicated no significant differences in the volume of gas insufflated during the procedure.[9,10] Procedure time, dosage of sedation medications, and intraprocedural discomfort experienced by patients were similar between CO_2 and air insufflation groups. However, CO_2 insufflation was associated with less postprocedural pain and distension, indicating that the benefits of CO_2 insufflation predominantly manifest after completion of the endoscopic procedure. The lower pain scores and smaller increases in abdominal girth reported after procedures with CO_2 insufflation compared with air insufflation suggest that the benefits of CO_2 are related to its rapid absorption from the GI tract. This theory is further supported by a randomized controlled study in which 100 patients undergoing colonoscopy were divided into 3 groups: air insufflation only during both colonoscope insertion and withdrawal, air during insertion and CO_2 during withdrawal, and CO_2 only during both colonoscope insertion and withdrawal.[11] Patients in both the CO_2 only and air plus CO_2 combination groups experienced significantly less postprocedural pain than those in the air only group an hour after the procedure (both $P \leq .001$). These results also suggest that residual gaseous distension after completion of endoscopic procedures causes postprocedural pain and that CO_2, which dissipates significantly faster than air, is associated with less postprocedural pain.

Animal studies suggest that an additional potential mechanism for the reduction in pain postprocedure may be the vasodilator effect of CO_2 and its consequent impact on blood flow within a distended colon.[4,7] The mean blood flow within the inferior mesenteric artery of dogs during use of CO_2 as an insufflation agent increased by 109% to 155% above baseline during periods of transiently elevated intraluminal pressure compared with mean blood flows at or below baseline noted with air insufflation.[4] In another study, parietal blood flow in rats decreased after either CO_2 or air insufflation but returned to baseline within 5 minutes in the CO_2 group compared with a persistent decrease for 30 minutes in the air insufflation group.[7] The authors have speculated that the prolonged bowel distension and associated decrease in parietal blood flow seen with air insufflation may contribute to abdominal pain.

CO_2 delivery

Currently, CO_2 delivery during endoscopy is performed by using CO_2 regulators. The primary purpose of the CO_2 regulator is to govern gas flow to rates that are safe for use in endoscopy. A CO_2 source, either a wall-based CO_2 outlet (in endoscopy suites that are equipped with a medical gas pipeline) or a portable CO_2 cylinder is connected by tubing to the CO_2 regulator (Fig. 1). Disposable tubing then delivers CO_2 from the regulator to a dedicated water bottle attached to the endoscopy light source.

CO_2 regulators are commercially available from 3 manufacturers in the United States, including Medivators Inc (Minneapolis, Minn), Bracco Diagnostics Inc (Monroe Township, NJ), and Olympus America Inc (Center Valley, Pa) (Table 1). All of these CO_2 regulators are compact, lightweight units that are easily integrated into standard endoscopy workstations. All are capable of connecting to either a wall-based CO_2 source or a portable CO_2 cylinder. The CO_2 regulators have various flow rate settings and visual or auditory alerts to indicate a low gas reserve and/or inflow pressure. Although all 3 units are compatible with all major endoscopy systems available in the United States, only 2 of the major endoscope manufacturers (Fujifilm Endoscopy, Fujinon Inc, Wayne, NJ) and Pentax (Pentax of America Inc, Montvale, NJ) have endorsed compatibility of the CO_2 regulators with their systems. One CO_2 regulator has an integrated warmer, which allows delivery of CO_2 at body temperature (98.6°F).

Clinical experience

A systematic review of 9 randomized controlled studies (6 colonoscopy studies and 1 study each for sigmoidoscopy, ERCP, and double-balloon endoscopy [DBE]) evaluating CO_2 as an insufflation agent for GI endoscopy demonstrated improved outcomes after use of CO_2 for endoscopic procedures.[12] All studies found that CO_2 was superior to room air, with CO_2 insufflated patients experiencing less postprocedural pain and bowel distention. The review concluded that CO_2 insufflation appeared to be safe. Of note, patients with underlying pulmonary disease were excluded from most studies.

To date, there are 36 published randomized controlled studies, 30 performed in a double-blind fashion, that have compared CO_2 with ambient air or water as insufflation agents during GI endoscopy.[1,9,10,13-45] Most of the studies evaluated insufflation during colonoscopy (23 studies) and ERCP (6 studies). Three studies were designed to compare air with CO_2 as insufflation agents during balloon-assisted enteroscopy, 2 during endoscopic submucosal dissection (ESD), 1 during combined colonoscopy and EGD, and 1 during flexible sigmoidoscopy. CO_2 was

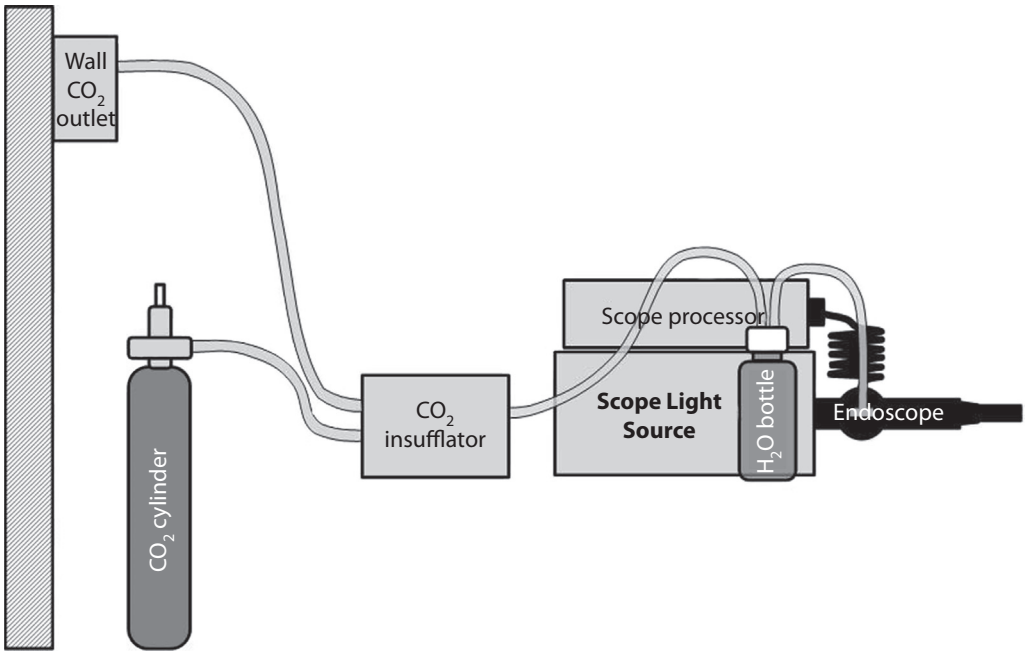

Figure 1. Schematic representation of the setup of a wall or a cylinder carbon dioxide source to the carbon dioxide insufflator and to the water bottle on the endoscopy light source.

TABLE 1. CO_2 regulators currently commercially available in the United States

	Manufacturer		
Features	**Medivators**	**Olympus**	**Bracco Diagnostics**
CO_2 regulator model	EndoStratus	UCR	CO_2 efficient
Compatibility with:	Pentax, Olympus, Fujifilm	Olympus (not tested for other manufacturers)	Pentax, Olympus, Fujifilm
Manufacturer list price	$4310	$7300	$7995
Gas connectivity	Cylinder and wall source compatible	Cylinder and wall source compatible	Cylinder and wall source compatible
Gas reserve indicator or alarm	Visual display for low input pressure	Visual display and audible alarm	Visual display and audible alarm
Over-pressure alarms	No alarm. Has internal pressure relief mechanisms	No	No
CO_2 flow start and/or stop indicator and button	No	No	Yes
Pressure and/or flow regulation, L/minute	High 3.5, medium 2.4, low 1.4	Settings related to tube sizes. Standard 1.8, medium 1.5	Managed flow rate 2. Normal flow rate at 3.4
Safety shutdown	Yes, for low pressure. Heating shut down with excessive temperature	No. Not considered an issue	No
Delivered quantity display	No	No	Yes
CO_2 warmed to 98.6°F	Yes	No	No
CO_2 delivery timer	No	Yes	Auto-timed shutoff
Dimension	7.9″ w × 4.9″ h × 14″ d	5″ w × 6″ × 12″ d	10″ w × 5.5″ h × 10.5″ d
Weight	10.6 pounds	10.8 pounds	9 pounds
Miscellaneous features		Gas-saving air and/or water button	Volume reset display

CO_2, Carbon dioxide.

delivered predominantly by using commercially available CO_2 insufflators, although custom-made devices were used in a few studies. The results of these studies are discussed in the following.

CO_2 use in colonoscopy

CO_2 insufflation has been extensively evaluated during colonoscopy. A recent meta-analysis performed on 21 randomized control trials, including a total of 3607 participants, compared CO_2 with air insufflation during colonoscopy.[46] CO_2 insufflation was associated with significantly less pain during the procedure (9 studies, odds ratio [OR] 0.5; 95% CI, 0.3-0.84), at 1 hour postprocedure (7 studies, OR 0.24; 95% CI, 0.07-0.85), at 6 hours postprocedure (9 studies, OR 0.25; 95% CI, 0.11-0.55), and at 24 hours postprocedure (8 studies, OR 0.42; 95% CI, 0.23-0.77). Although cecal intubation rates were not different between the 2 groups (OR 0.96; 95% CI, 0.63-1.45), the time needed to reach the cecum was significantly shorter in the CO_2 insufflation group (standardized mean difference -0.18; 95% CI, -0.34 to -0.03). The meta-analysis did not include a more recent study of 214 patients undergoing ileocolonoscopy under propofol sedation with either air or CO_2 insufflation. Significantly lower pain scores were noted at 10 minutes, 30 minutes, and 2 hours postprocedure in the CO_2 insufflation group in this study.[39]

Sedation was not used in 9 of these colonoscopy studies,[9,10,14,21,24,32,35,36,38] which evaluated the ability of CO_2 to minimize discomfort related to intestinal distention. In 2 of 3 studies that allowed initially unsedated patients to receive sedative or analgesics if required, CO_2 insufflation was associated with lower sedation requirements.[14,35] In 4 of 6 studies, no difference was noted in intraprocedural pain perception between the CO_2 and air insufflation groups.[14,24,32,36] However, CO_2 insufflation was associated with less pain at 1 hour postprocedure in all 6 studies, compared with air insufflation.[10,14,21,24,32,38] Whereas most of the beneficial effect of CO_2 on pain perception was noted within the first hour after colonoscopy, some benefit was seen for up to 6 hours in most studies, with 3 of 8 studies indicating benefit for up to 24 hours postprocedure in the CO_2 group.[1,14,21] All 8 studies assessing patients' sensations of bloating or fullness after the procedures reported significantly fewer symptoms at 1 hour postprocedure with CO_2 insufflation compared with air.[1,15,26,31-34,38] Two studies reported measurements of abdominal girth before and after the colonoscopies; both demonstrated a smaller increase with CO_2 insufflation compared with air insufflation. Five studies assessed patient satisfaction,[16,20,23,26,31] and 2 studies indicated superior patient satisfaction with the use of CO_2 for insufflation compared with air.[26,31] One study noted that patients undergoing CO_2 insufflation were more likely to be willing to undergo repeat unsedated colonoscopy by using the same insufflation technique compared with those receiving air insufflation (88.6% vs 77.8%; $P = .03$).[35]

Water exchange or water infusion offers an alternative method of colon distension, is considered superior to ambient air insufflation, and may allow colonoscopy to be performed with minimal or no sedation.[47] A recent, randomized, single-blind study compared CO_2 insufflation (n = 226) with water infusion (n = 226) during colonoscope insertion, with all patients undergoing insufflation with CO_2 during colonoscope withdrawal.[45] Colonoscopy was initiated without sedation, but "on demand" sedation was administered as necessary to patients. The study indicated no difference in the eventual need for sedation medications between both groups. Median overall pain scores during colonoscope insertion were higher in the CO_2 insufflation group compared with water insufflation (2.4 vs 2.0; $P = .02$), although the percentage of patients experiencing moderate to severe pain was not different between the CO_2 and water insufflation groups (27% vs 21%; $P = .15$). Water infusion was associated with a higher rate of cecal intubation than CO_2 insufflation (97% vs 92%; $P = .02$). However, time to reach the cecum (15 minutes vs 11 minutes; $P < .001$) and the total procedure time (30 minutes vs 24 minutes, $P < .001$) were longer with water infusion than with CO_2 insufflation. This single study suggests that water may be as good as CO_2 when used as a colon distending modality. However, more studies are needed to address this issue.

CO_2 use in ERCP

Six double-blind studies have been performed, randomizing a total of 654 patients to air or CO_2 insufflation during ERCP.[18,22,25,27,28,40] Four studies evaluated the amount of sedation medications used and found no difference between the air and CO_2 insufflation groups.[18,25,27,40] Only 1 study assessed intraprocedural pain, and no difference was noted between the air and CO_2 insufflation groups.[18] However, compared with room air, CO_2 insufflation was associated with lower levels of postprocedural pain perceived at 1 hour in 3 of 4 studies,[18,22,28] at 3 to 6 hours in 2 of 3 studies,[18,28] and at 24 hours in 1 of 5 studies that evaluated pain at these time points.[18] CO_2 insufflation was associated with significantly less postprocedural distention or a smaller abdominal girth in 3 of 5 studies, with no difference noted in the other 2 studies. The use of CO_2 for insufflation was not associated with shorter procedure times relative to ambient air in any of the 5 studies that addressed this question.[22,25,27,28,40] Overall, these data suggest that CO_2 insufflation during ERCP may be associated with less postprocedural distension and pain compared with air insufflation.

A meta-analysis comparing CO_2 and air insufflation during ERCP evaluated 7 double-blind randomized controlled trials including 1 published in Chinese, enrolling a total of 756 patients.[48] No significant difference was noted between the CO_2 and air insufflation groups in total

procedure time (mean difference, -2.15; 95% CI, -5.15 to 0.85) or in rates of successful cannulation (OR 1.05; 95% CI, 0.3-3.74). CO_2 insufflation was associated with a significantly lower pain perception at 1 hour (mean difference, -9.49; 95% CI, -18.66 to -0.32), 3 hours (mean difference -9.71; 95% CI, -16.95 to -2.48), and 6 hours postprocedure (mean difference, -8.3; 95% CI, -11.59 to -5.01), but no difference was seen at 24 hours after the procedure (mean difference, -2.43; 95% CI, -12.1 - 7.24).

CO_2 in balloon-assisted enteroscopy

Three double-blinded studies randomizing 421 patients compared room air and CO_2 as insufflation agents during balloon-assisted enteroscopy (1 DBE and 2 single-balloon enteroscopies [SBE]).[19,43,44] In the DBE study, the use of CO_2 insufflation was associated with a significantly lower mean propofol dose (290 mg vs 380 mg; $P = .02$).[19] The mean depth of intubation was greater by 30% in the CO_2 insufflation group compared with the air insufflation group (230 cm vs 177 cm; $P = .008$). The significant improvement in the depth of intubation was only observed in antegrade DBE procedures (295 cm vs 224 cm; $P < .001$). CO_2 insufflation was associated with approximately 50% lower mean pain scores compared with air insufflation at 1 hour and 3 hours after DBE. However, mean pain scores were not significantly different between the 2 groups during the procedure and at 6 and 24 hours after the procedure.

Sedation requirements were not different between the CO_2 and air insufflation groups in the single SBE study that evaluated this variable.[43] Total mean intubation extent, antegrade intubation depth, and retrograde intubation depth also were not significantly different between the 2 groups in this study, except in patients with a history of prior abdominal surgery undergoing antegrade SBE. In comparison, the second SBE study found significantly improved intubation depths in the CO_2 insufflation group compared with air, in both the antegrade (323.8 ± 64.2 cm vs 238.3 ± 68.6 cm; $P < .001$) and retrograde (261.6 ± 74.2 cm vs 174.7 ± 62.1 cm; $P < .001$) directions.[44] The diagnostic yield of SBE was not different between the CO_2 and air insufflation groups in both studies. Furthermore, pain scores were not significantly different between the 2 groups at a majority of the time points assessed.

CO_2 for ESD

ESD and per-oral endoscopic myotomy carry a substantial risk for perforation (5%-10%), which may lead to severe pain, subcutaneous emphysema, pneumomediastinum,[49] pneumoperitoneum, or compartment syndrome.[50,51] Sudden escape of insufflation gas from a perforated viscus into the peritoneal cavity and its subsequent accumulation can compromise diaphragmatic action and lead to cardiopulmonary distress caused by development of a tension pneumoperitoneum. Similarly, perforation of the esophagus can result in a tension pneumomediastinum.[52,53] CO_2, by virtue of its rapid absorption, may reduce the secondary deleterious effects of perforation and is therefore commonly used during high-risk endoscopic procedures.[29] Indeed, extraluminal gas may not even be detected on radiography in patients with ESD-induced perforation, when CO_2 has been used as the insufflation agent.[54,55]

A double-blind, randomized, controlled trial comparing CO_2 and air as insufflation agents in 102 patients undergoing gastric ESD found no difference in the mean procedure time, end-tidal CO_2 pressure levels, or minimum oxygen saturation levels.[39] Furthermore, there was no difference in mean pain and abdominal distention scores immediately after ESD and at 1 hour, 3 hours, and 24 hours after the procedure. A crossover trial of CO_2 insufflation during esophageal and gastric ESD cases randomized patients to start with either CO_2 (CO_2 preceding group) or air (air preceding group) insufflation, with crossover to the other insufflation agent after 1 hour.[29] The mean procedure time was significantly lower in the CO_2 preceding group (148 ± 62 minutes vs 190 ± 76 minutes; $P = .026$). The levels of monitored transcutaneous partial pressure CO_2 ($P_{tc}CO_2$) were similar during CO_2 insufflation and air insufflation in both groups.

Although there are no reported randomized control trials on the use of CO_2 during per-oral endoscopic myotomy, direct endoscopic necrosectomy, or natural orifice transluminal endoscopic surgery, CO_2 has been advocated as the insufflation gas of choice for these procedures, which share substantial similarities with laparoscopy.[51,56,57]

CO_2 use in other GI procedures

Two additional randomized controlled studies have compared room air and CO_2 as insufflation agents during flexible sigmoidoscopy[13] and during combined upper and lower GI endoscopy.[41] CO_2 use was associated with improved pain scores at 1 and 6 hours after completion of sigmoidoscopy.[13] In patients undergoing combined EGD and colonoscopy, CO_2 use was associated with lower pain scores and abdominal girth soon after completion of the procedures, compared with room air.[41] CO_2 also has been used as an insufflation agent during cholangioscopy. In a prospective, crossover study evaluating CO_2 versus saline solution infusion for insufflation of the bile duct during peroral cholangioscopy, CO_2 use was associated with a shorter procedure time, without any compromise in the quality of cholangioscopic images.[58]

SAFETY

Safety of CO_2 insufflation during endoscopy

CO_2 is a nonflammable gas and can be used safely while performing electrocautery.[2] It has been widely used for insufflation during laparoscopic surgery, where its safety has been well established.[59] Thirteen randomized studies

comparing air and CO_2 as insufflation agents reported on some form of CO_2 monitoring, performed primarily with $P_{tc}CO_2$, which is considered to be a reliable noninvasive marker of $PaCO_2$ during sedation.[60] Arterial blood gas was used to monitor ventilation in only 1 of these studies.[28] No differences were noted for average or peak values of pCO_2 between ambient air and CO_2 insufflation groups in these studies. Three studies reported on the frequency of PCO_2 values that exceeded 55 mm Hg.[25,28,30] Two of the studies showed comparable incidences, whereas the third found that 16% of patients undergoing CO_2 insufflation had transient PCO_2 values >55 mm Hg compared with none in the room-air insufflation group. End tidal CO_2 was assessed in 6 studies,[13,17,21,28,41,44] with 3 studies indicating a significantly higher value in the CO_2 insufflation groups, either during or at the end of the procedures, whereas 3 studies reported no difference. Twenty-five of 36 of the studies discussed in this review reported no serious adverse events or untoward outcomes related to the use of CO_2 as an insufflation agent. Only 2 studies reported on significant respiratory events, with 1 showing no difference in rates of respiratory depression or apnea (air 3.5%, CO_2 3.9%)[30] and another indicating reversible respiratory depression in 2 patients undergoing ERCP with air insufflation.[25]

There has been some concern regarding the use of CO_2 as an insufflation agent in patients with chronic obstructive pulmonary disease because this patient group may have an increased risk of CO_2 retention. However, few data exist for this patient group because most studies exclude patients with known underlying pulmonary conditions. However, the previously discussed crossover trial in patients undergoing ESD included 20 patients with subclinical pulmonary dysfunction.[29] Underlying diminished pulmonary function, defined as a forced expiratory volume in 1 second of <70%, was not found to be a risk factor for increased transcutaneous PCO_2 ($P_{tc}CO_2$) or CO_2 retention. Two additional studies evaluated the safety of CO_2 insufflation during ESD in patients with known underlying pulmonary disease (forced expiratory volume in 1 second <70%).[60,61] The first study in patients undergoing gastric ESD under moderate sedation compared 127 patients with pulmonary dysfunction with 195 control patients without pulmonary dysfunction.[60] No significant differences were noted in baseline $P_{tc}CO_2$ (41 mm Hg vs 42 mm Hg), peak $P_{tc}CO_2$ during the procedure (both 51 mm Hg), and median $P_{tc}CO_2$ postprocedure (both 50 mm Hg) between the 2 groups. The second study on patients undergoing colorectal ESD compared 77 patients with underlying obstructive pulmonary disease to 294 patients without lung disease.[61] There was no significant difference in the rise in end tidal CO_2 ($ETCO_2$) in those with or without an obstructive pulmonary disorder, with no CO_2 retention observed in either group. Mean procedure time, minimal peripheral capillary oxygen saturation (SpO_2) level during the procedure, and adverse event rates were similar between those with and without underlying pulmonary disease in both studies.

In summary, CO_2 insufflation appears to be well-tolerated even in patients with underlying pulmonary disease and does not seem to induce higher rates of respiratory depression or excessive CO_2 retention compared with insufflation with ambient room air.

CO_2 and gas embolism. Gas embolization is a serious, rare, and potentially under-reported adverse event associated with endoscopic procedures. Most of the reported cases have occurred during ERCP. Details of 26 reported cases of ERCP-related air embolization are summarized in a recent systematic review.[62] Reported risk factors for embolization during ERCP include cholangioscopy by using air insufflation, sphincterotomy, metallic biliary stent placement, prior biliary surgery, transhepatic porto-systemic shunts and pre-existing percutaneous transhepatic drainage catheters.[62] Transmural endoscopic necrosectomy for the management of walled-off pancreatic necrosis after pancreatitis appears to be associated with a particularly high risk of gas embolization. In 4 published series including a total of 254 patients undergoing endoscopic necrosectomy, gas embolization was noted in 4 patients.[63-66] Several cases of gas embolization have been reported in patients undergoing upper GI endoscopy. These have occurred in patients with erosive esophagitis,[67] peptic ulceration with consequent GI tract vascular fistulas,[68,69] in patients who have undergone prior biliary surgery (the Kasai procedure)[70] or who have pre-existing percutaneous transhepatic drainage catheters,[71] and after ablation of duodenal arteriovenous malformations.[72] Air embolization also has been reported after EUS with FNA,[73] small-bowel endoscopy,[74] colonoscopy,[75] and sigmoidoscopy.[76] Several authors recommend the use of CO_2 instead of room air as an insufflation agent during endoscopy because of the rapid tissue absorption of CO_2, in the event that gas embolism takes place.[59,62,69] This recommendation appears to be particularly valid for higher risk interventions including ERCP, cholangioscopy, and endoscopic necrosectomy.

Clinically significant CO_2 embolization has been well-documented during surgery[77] and is estimated to occur in <0.6% of patients undergoing laparoscopic surgery.[78] Subclinical cases of CO_2 embolization may occur far more commonly and appear to be well-tolerated by most patients.[79] The superior tolerance of CO_2 embolization compared with other gases has been confirmed in animal experiments.[80] Although even CO_2 insufflation during endoscopy has been linked to clinically serious embolic outcomes in patients undergoing direct cholangioscopy[81] and endoscopic transgastric pancreatic necrosectomy,[66] overall, CO_2 embolism appears to be reasonably well-tolerated and is therefore the preferred insufflation gas for many endoscopists.[59,62,69]

BARRIERS TO ADOPTION OF CO_2 AS AN INSUFFLATION AGENT

Standard endoscopy systems marketed by all major manufacturers are designed to use room air, which remains the gas predominantly used for insufflation during endoscopy. A survey of European endoscopists found that only 46.5% of respondents were aware of the option of using CO_2 as an insufflation agent, and only 4.2% of respondents actually used CO_2 as an insufflation agent during endoscopy.[82] Technical difficulties in implementing the system (84%) and a lack of perceived significant benefit to patients (49%) were the main cited reasons for not using CO_2 insufflation. Thus, there remain significant technical and perceptual barriers to widespread adoption of CO_2 as an insufflation agent. Development of endoscopy systems with integrated CO_2 insufflators may decrease the barriers to more widespread adoption of CO_2 as an insufflation agent during endoscopy. During the design and construction of new endoscopy units, consideration should be given to including medical gas pipelines for CO_2 delivery to endoscopy procedure rooms.

FINANCIAL CONSIDERATIONS

The list price for a commercially available CO_2 insufflator ranges from $4310 to $7995 (Table 1). The Olympus insufflator comes with reusable CO_2 tubing that costs $230. Other systems use 2 disposable components, including tubing that connects the CO_2 source with the insufflator and a bottle cap that facilitates CO_2 flow from the insufflator to the endoscope (Fig. 1). Several vendors supply these disposable tubes and caps (Medivators Inc, Minneapolis, Minn; Bracco Diagnostics Inc, Monroe Township, NJ; ERBE USA Inc, Marietta, Ga; U.S. Endoscopy, Mentor, Ohio), which cost approximately $10 and $15, respectively. The bottle caps and tubing may be reused within 24 hours. A 6-pound cylinder containing sufficient CO_2 for at least 10 endoscopic procedures can be purchased for approximately $6. Thus the total cost of using CO_2 as an insufflation agent for endoscopy amounts to approximately $3 per procedure, not including the initial capital expense of a CO_2 insufflator for each procedure room.

AREAS FOR FUTURE RESEARCH

There are ample data to support the use of CO_2 for all endoscopic procedures. However, endoscopy companies manufacture and sell equipment designed to use room air as the insufflation agent rather than CO_2. Studies are needed to clarify the barriers to moving to CO_2 insufflation on the part of endoscope manufacturers as well as endoscopy units and endoscopists. Studies assessing the cost effectiveness of CO_2, particularly in outpatient ambulatory surgery center settings may help influence decision making. An important element that may impact the adoption of CO_2 in routine endoscopy practice is evaluation of patient satisfaction, which has not been reported in many prior studies. More studies assessing this parameter are required. Procedures involving trainee and/or fellow participation tend to be longer, with larger volumes of gas used for insufflation and may therefore be associated with increased discomfort. Use of CO_2 as an insufflation agent may potentially improve patient symptoms and satisfaction, although this needs further study. The safety of CO_2 as an insufflation agent in patients with pulmonary diseases also needs to be further investigated. Similarly, the safety and efficacy of CO_2 as an insufflation agent for endoscopy performed on children needs to be further studied.

SUMMARY

There are ample data indicating that use of CO_2 insufflation during many types of endoscopic procedures is associated with less postprocedural pain compared with air insufflation. CO_2 insufflation offers clear benefits to patients undergoing advanced endoscopic procedures, lengthy endoscopic procedures, and unsedated procedures. In addition, CO_2 insufflation offers significant potential benefit to patients undergoing endoscopic procedures associated with higher risks of perforation or of gas embolism. Standard endoscopy systems marketed by all major manufacturers support air insufflation. Development of endoscopy systems with integrated CO_2 insufflators may decrease the barriers to more widespread adoption of CO_2 as an insufflation agent during endoscopy.

DISCLOSURE

R. Pannala is a consultant for Boston Scientific. J. Hwang is a consultant for Covidian and U.S. Endoscopy. All other authors disclosed no financial relationships relevant to this publication.

Abbreviations: ASGE, American Society for Gastrointestinal Endoscopy; CO_2, carbon dioxide; DBE, double-balloon endoscopy; ESD, endoscopic submucosal dissection; SBE, single-balloon enteroscopy.

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