Methods of luminal distention for colonoscopy

The ASGE Technology Committee provides reviews of existing, new, or emerging endoscopic technologies that have an impact on the practice of GI endoscopy. Evidence-based methodology is used, performing a MEDLINE literature search to identify pertinent clinical studies on the topic and 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 February 2012 for relevant articles by using the key words "colonoscopy," "insufflation," "air," "carbon dioxide," and "water." 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.

BACKGROUND

More than 14 million colonoscopies are performed annually in the United States, with approximately half of these examinations for colorectal cancer screening.[1] An ASGE/ACG Taskforce on Quality in Endoscopy proposed that effective endoscopists should achieve cecal intubation in 90% or more of all cases and 95% or more of screening colonoscopies.[2] During the insertion phase of colonoscopy, at least partial distention of the lumen is needed to allow adequate visualization to safely direct the instrument to the cecum. During withdrawal, a greater degree of luminal distention is desired to allow optimal inspection of the colonic mucosa. Several gaseous and liquid agents have been used for colonic luminal expansion. The ideal agent for colonic luminal expansion would facilitate cecal intubation, provide excellent mucosal visualization, limit intra- and postprocedure pain, and would be safe and inexpensive.

TECHNOLOGY UNDER REVIEW

Air insufflation

Commercially available endoscopic light sources contain an integrated air pump, and air insufflation has remained the most commonly used technique for luminal distention since the advent of colonoscopy in the late 1960s.[3,4] Occluding the top of the air-water valve with a fingertip shunts air to the tip of the endoscope via the endoscope air channel. The maximal pressures generated by endoscopic light source air pumps range from approximately 300 to 375 mm Hg. However, air pressures at the endoscope tip are typically 30% to 40% less because of air leakage through the air channel itself or through the endoscope-light source connection.[5,6] This corresponds to flow rates of 1.8 to 2.7 L/min at ambient pressure, with flow rates decreasing as pressure external to the endoscope increases (eg, within the distended colon).[6] Several newer integrated air pumps have variable settings for air flow regulation (eg, off, low, medium, high). In a study of 34 patients undergoing routine diagnostic colonoscopy with air insufflation, the mean sustained intraluminal air pressure was 22 mm Hg (range 9-57 mm Hg).[5] The mean amount of air insufflated at routine colonoscopy has ranged from 8.2 to 17.8 L.[7,8]

CO_2 insufflation

The use of CO_2 as an insufflating agent for the large bowel was initially proposed in 1953 as a method to prevent gas explosions during the electrosurgical removal of polyps at rigid proctoscopy.[9] In addition to being nonflammable, CO_2 is absorbed across the intestines 160 times more rapidly than nitrogen and 13 times more rapidly than oxygen, which are the principal gas components of air.[10] Animal studies have also demonstrated that CO_2 insufflation attenuates the reduced parietal blood flow seen with colonic distention, both caused by more rapid resolution of bowel distention, but also

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Table 1. Operating characteristics for endoscopic CO_2 regulators available in the United States

Vendor	Model	CO_2 sources accepted	Maximum gas pressure	Variable gas flow	Gas flow rates	Safety features	Price
Bracco Diagonistics, Inc. Princeton, NJ	CO_2EFFICIENT	gas cylinder	375 mmHg	No	3.4 L/min - "Managed flow" setting reduces gas flow from 3.4 L/min to <1 L/min after 10 seconds if air/water button is not touched	Mechanical pressure relief valve, electronic pressure relief valve, timed shut-off, volume shut-off, hydrophobic filter in gas tubing	$7995
	CO_2MPACT	gas cylinder or gas line	375 mmHg	Yes - 3 level flow - automated switch	High - 3.4 L/min Medium - 2.9 L/min Low - 2.0 L/min	Mechanical pressure relief valve, mandatory variable timed shut-off, hydrophobic filter in gas tubing	$4995
Olympus America, Inc, Center Valley, PA	UCR	gas cylinder or gas line	338 mmHg	Yes - 3 levels of flow - achieved by using different gas tubing kits	Standard gas tube - 1.5 L/min Low flow gas tube - 1.2 L/min Extra low flow gas tube - <1.2 L/min	Optional variable timed shut-off	$6200

by a direct vasodilating effect of CO_2.[11,12] In the 1980s, endoscopists began to evaluate CO_2 insufflation as a potential method to reduce postcolonoscopy pain and bloating.[13] More recently, CO_2 insufflation has been evaluated in upper endoscopic procedures including ERCP and balloon-assisted enteroscopy. Outcomes data from these upper endoscopic applications are only briefly summarized here; a more complete discussion is beyond the scope of this colonoscopy-focused document.

There are 3 CO_2 regulators designed for use with GI endoscopes that are approved by the U.S. Food and Drug Administration in the United States. These regulators all require a CO_2 source, most commonly a medical gas cylinder, although some operative or endoscopy suites may be equipped with a medical gas pipeline for CO_2. A specialty water bottle is required, as well as gas tubing that transmits CO_2 into the water bottle. The air button on the endoscopic light source must be turned off for CO_2 to be used. The primary purpose of the regulator is to govern the gas flow to levels that are safe for use in endoscopy, although additional features are available on various models. Operating characteristics for endoscopic CO_2 regulators available in the United States are shown in Table 1. The mean volumes of CO_2 used at colonoscopy are similar to those used for air, reported at 8.3 L to 14.0 L.[7,8]

Water instillation

Reports as early as 1984 described the use of water instillation into the sigmoid colon as a method to facilitate passage of the colonoscope.[14,15] Potential benefits of this method include straightening and/or opening the sigmoid colon, reducing spasm, avoiding air-induced distention and elongation of the colon, and reducing patient discomfort. A large number of studies have recently emerged that evaluate water-assisted colonoscopy, although with variation in some technical aspects.[16] Some studies have allowed limited use of air insufflation, whereas others prohibited air insufflation until the cecum was reached by turning the air button on the light source to "off." Water volumes instilled have ranged substantially (from 200 mL to 2 L), and water temperature has varied from room temperature to 42°C, although most have used 37°C. Last, a potentially relevant dichotomy in technique is whether the instilled water is suctioned back during insertion or on withdrawal.[16] Typically, once cecal intubation is achieved with water-assisted methods, standard air or CO_2 insufflation is used during withdrawal.

Other agents

Helium, argon, nitrogen, and xenon have all been evaluated as insufflation gases for laparoscopy.[17] However, various issues related to absorbability, availability, and expense significantly limit their application to colonoscopy, and they have not been used in this setting. Intraluminal administration of 90 mL of corn oil in 3 aliquots for lubrication has been associated with a higher cecal intubation rate than with standard technique in 2 randomized, controlled trials (RCTs).[18,19] Intraluminal administration of 200 mL of a dilute peppermint oil solution was associated with an effective spasmolytic effect in an RCT that used a placebo saline solution.[20] However, because the use of these agents was not primarily for colonic luminal expansion, they are not discussed further.

EASE OF USE

Air pumps used for endoscopic insufflation do not require any gas cylinder or gas lines for use. As previously mentioned, CO_2 may be supplied by either a medical gas pipeline or, more commonly, by medical gas cylinders. Typically size E gas cylinders are used in this setting, and these cylinders contain approximately 1600 L of compressed CO_2. In practice, the number of colonoscopies that may be performed by using a single tank depends on a number of factors, including the duration of the examinations, endoscopist insufflation behaviors, and use of regulator functions that may save CO_2 such as "managed flow" and variable flow settings. All available CO_2 regulators have a warning mechanism when the residual CO_2 supply is low. Although no data directly address endoscopist ease of use for colonoscopy, multiple RCTs that compared air and CO_2 insufflation at colonoscopy have measured total examination time.[21] In these studies, there was no difference in total examination time between air and CO_2, although a strong trend toward shorter examination time with CO_2 was seen in 1 study.[8]

The ease of use of water-assisted methods is variable because of the heterogeneity of the methods used and their intended patient population. Because these methods have primarily been evaluated as techniques to facilitate colonoscopy with no, minimal, or on-demand only sedation, comparison with colonoscopy by using moderate or deep sedation is difficult and likely not valid. For instance, differences in cecal intubation times in RCTs of water-assisted versus air insufflation colonoscopies in which the primary outcome was completing the examination without sedation are not applicable to sedated colonoscopy. Very few data exist regarding water-assisted techniques in sedated patients.[22]

Data suggest that the more stringent use of water-assisted insertion technique (ie, air insufflation prohibited) is associated with a learning curve of at least 100 cases, as determined by continued improvement in cecal intubation time.[23] Expert endoscopists with a moderate amount of experience with water-assisted insertion (40 practice cases) experienced a prolongation of cecal intubation times from approximately 6 to 8 minutes and a reduced cecal intubation rate (83%) with the water-assisted technique compared with standard air insufflation (97%).[24] Instilling water will bring any uncleansed stool into suspension, and the resulting turbidity interferes with luminal visualization. Suctioning turbid water and replacing it with clean water overcomes this issue, but at the expense of added time. However, most studies have reported cecal intubation times of 5 to 13 minutes with water-assisted techniques, and in many of these studies, this was not different from times in the air insufflation arm.[16] Practically, 1 to 2 L of warm water (tap or sterile) must be prepared before colonoscopy. Use of an auxillary peristaltic flushing pump is simpler and faster than manual water instillation with 60-mL syringes.

SAFETY

Perforation

The rate of perforation at colonoscopy has ranged from 0.05% to 0.3% in large studies.[25-28] Perforation can result from thermal or mechanical injury, but may also result from barotrauma from insufflated air. As intraluminal pressure increases, the diameter of the right colon increases more than the left colon.[5] As such, the right side of the colon (particularly the cecum) is the more susceptible segment to barotrauma-induced perforation, in accordance with the law of Laplace. Potential risks for barotrauma relate to those factors that may impair the decompression of gas from the colon proximally (eg, obstructive ileal disease, overly competent ileocecal valve) or distally (eg, floppy and/or deformed sigmoid colon).[5]

Data derived from human cadaveric colon studies and measured pressures at barium enema examinations suggest that approximately 80 mm Hg represents the upper limit of safety for sustained intraluminal pressure.[5,6,25] During initial phases of insufflation, the gas primarily expands the volume of the colon without significant increases in pressure.[6] However, after some volume of gas has sufficiently expanded the colon, the compliance of the colon changes, and further insufflation more rapidly increases the intraluminal pressure and thus wall tension. Although the gas flow rates at the colonoscope tip decrease as intraluminal pressure increases, it has long been recognized that endoscopic light source air pumps are still capable of delivering air flow rates that are potentially damaging to the colon.[5,6,26] This issue has been acknowledged with the development of pressure release valves[27] and variable flow rates on light source air pumps, measures that, when used, likely reduce, but do not eliminate, the risk of colonic barotrauma injury.

Perforation at colonoscopy with CO_2 insufflation has not been reported. However, there have been several reports of perforation with colonic insufflation of CO_2 for CT colonography, including both manual insufflation systems and, theoretically, safer automated delivery systems that insufflate to a specified intraluminal pressure (eg, 25 mm Hg).[28,29] Thus, although the rapid absorption of CO_2

may reduce the risk of barotrauma injury at colonoscopy, this has not been conclusively demonstrated, and some risk undoubtedly remains. Perforation has not been reported with use of the water-assisted insertion techniques.

Colonic explosion

Colonic explosion is a serious, but fortunately rare adverse event of colonoscopy with electrosurgery (eg, polypectomy or argon plasma coagulation).[30] For explosion to occur, there must be a combustible gas (either hydrogen or methane) at potentially explosive levels, sufficient oxygen, and the presence of a heat source. Hydrogen and methane are produced by fermentation of nonabsorbable (eg, lactulose, mannitol) or incompletely absorbed (eg, lactose, fructose, sorbitol) carbohydrates by the colonic flora and are potentially explosive at levels of 4% (hydrogen) and 5% (methane).[31] Adequate bowel preparation with polyethylene glycol has been associated with very low levels of hydrogen and methane, and colonic insufflation and suction during colonoscope advancement will also serve to dilute or remove any pockets of these gases.[32] Mannitol preparations have been associated with a higher frequency of potentially explosive levels of hydrogen and methane.[33,34] Because oxygen is a requirement for explosion and CO_2 is nonflammable, the use of CO_2 as an insufflating gas virtually eliminates the risk of colonic explosion.[9,35]

Hypercapnia

CO_2 absorbed as a result of colonic insufflation is primarily eliminated by an increase in minute ventilation. RCTs of CO_2 and air insufflation at colonoscopy by using no sedation,[8,36] moderate sedation,[37] and deep sedation[38,39] that have used either end-tidal or transcutaneous CO_2 monitoring have all demonstrated no significant difference in the increase in CO_2 levels between the air and CO_2 groups. Most studies that used sedation demonstrated a small intraprocedure increase in CO_2 levels for both air- and CO_2-insufflated patients.[8,41,43] Although not directly compared, small studies that performed pre-and postcolonoscopy arterial blood gas measurements saw clinically insignificant increases in mean P_{CO_2}, with no change in pH, both in patients insufflated with CO_2[39] and air.[40] Patients with chronic obstructive lung disease are at theoretically higher risk of hypercapnia with CO_2 insufflation. Although no adverse events have been reported in this patient subset, this issue has not been adequately studied.

Hyponatremia

The use of fluid irrigation during transurethral surgical procedures is occasionally complicated by the development of iatrogenic water intoxication (transurethral resection syndrome), characterized by cardiovascular, central nervous system, and metabolic disturbances including hyponatremia.[41] Analogous syndromes have been seen in other procedures using irrigation including transcervical gynecologic procedures, percutaneous nephrolitotomy, and arthroscopy.[42] Symptomatic hyponatremia has been reported with overzealous tap water colostomy irrigation[43] and with colonic irrigation as an alternative medicine treatment.[44] In a study that measured pre- and post-colonoscopy serum sodium values, 3 of 40 (7.5%) patients were found to have a post-procedure sodium level less than 130 mmol/L, whereas all patients had normal preprocedure sodium levels.[45] The study used a standard colonoscopy technique, but did not report water irrigation behaviors. Thus, although metabolic alterations such as hyponatremia have not been reported with the use of water-assisted colonoscopy, these potential disturbances have not been formally evaluated and remain a theoretical concern.

Hypothermia

Significant decreases in body temperature caused by colonic irrigation were seen in 7 of 54 (13%) patients in a surgical study that used on-table anterograde lavage during urgent surgery for left-sided colonic disease (eg, diverticulitis).[46] However, although not well studied, this issue should be obviated in water-assisted colonoscopy with the use of warm water that approximates body temperature.

OUTCOMES DATA AND COMPARATIVE STUDIES

Air versus CO_2

A number of fully published RCTs have compared air and CO_2 as insufflating gases at colonoscopy; the results of 9 RCTs were recently summarized in a meta-analysis.[21] This meta-analysis found that a smaller proportion of patients who received CO_2 as the insufflating gas reported any abdominal pain (intraprocedurally and at 1, 6, and 24 hours post-colonoscopy) compared with air. The strongest effect was at 1 hour post-procedure, when the use of CO_2 was associated with a relative risk of 0.26 (95% CI, 0.16-0.43) for the presence of any abdominal pain; this was associated with a number needed to treat of 2 patients. The reduction in procedure-related pain was consistent across all of the individual trials, which included trials using moderate sedation, deep sedation, and no sedation. Self-reported flatus at 1 and 6 hours post-procedure was also reduced in patients who received CO_2. There was no difference in cecal intubation rates, cecal intubation times, total examination times, or adverse events between air- and CO_2-insufflated patients in this meta-analysis. Trials that have also included abdominal radiography 30 minutes to 6 hours after colonoscopy have uniformly found less intestinal gas with CO_2-insufflated patients.[13,47,48]

Five RCTs compared air and CO_2 as insufflating gases at ERCP.[49–50] Compared with patients who received air, patients who received CO_2 had less post-procedure abdominal distention in 4 of the 5 RCTs,[53-57] and less post-procedure abdominal pain in 3 of the 5 RCTs.[53,54,57] No differences in adverse events or any other relevant outcomes were seen in any of these studies. In 2 RCTs that compared air and CO_2 insufflation during double-balloon enteroscopy,[51,52] patients receiving CO_2 experienced less post-procedure abdominal pain in both trials, and in 1 of the studies, greater intubation depth was also attained in the CO_2 arm.[58]

Air versus water assisted

A number of RCTs evaluated water-assisted insertion versus a standard air insufflation technique at colonoscopy using no,[53,54] minimal,[55–65] on-demand,[19,24,66,67] or moderate sedation.[22] Nine trials assessed pain associated with colonoscopy by using a visual analogue scale, assessing the patient's pain either during or immediately after the procedure or both.[19,24,60-67] Eight of these 9 studies reported a significant decrease in patient-reported pain scores with the use of water-assisted insertion. Of the 4 trials using on-demand sedation, 3 of the 4 reported using significantly less sedation with the water-assisted technique,[19,24,67] with a trend toward this outcome in the fourth trial.[66]

Two of 3 trials of unsedated colonoscopy had higher final cecal intubation rates by using water-assisted insertion compared with air insufflation.[60,61] No difference in final cecal intubation rates was seen in RCTs that used minimal, on-demand, or moderate sedation. However, cecal intubation rates by intention-to-treat analysis tend to be lower than "final" rates both for water-assisted and air insufflation techniques, as breaks in study protocol (eg, allowing air insufflation for a case randomized to water instillation or administering sedation) typically facilitated completion of the examination in these trials. Differences in cecal intubation times have been varied, with 2 trials reporting longer insertion times with air insufflation,[19,64] 5 trials reporting no difference in insertion times between the 2 techniques,[60-63,66] and 4 trials reporting longer insertion times with water instillation,[22,24,65] including the only trial that used moderate sedation.[22]

Of the 10 RCTs that reported adenoma detection rates (ADR), it was no different in 8 studies,[19,24,60-62,64,65,67] whereas 1 study reported a higher ADR in the air insufflation arm,[66] and another reported a higher ADR in the water instillation arm.[22]

CO_2 versus water assisted

Data comparing CO_2 insufflation with water-assisted insertion limited to a single RCT is currently available only in abstract form. In this trial, more than 300 patients undergoing unsedated colonoscopy were randomized to air insufflation, CO_2 insufflation, or warm water instillation.[68] Median pain scores and need for on-demand analgesia were similar in the CO_2 and water-assisted arms, and in each case were significantly lower than in the air insufflation arm. No differences in cecal intubation rates or ADR were seen.

FINANCIAL CONSIDERATIONS

With regard to capital purchasing, there are no additional costs associated with air insufflation because air pumps are an integral part of modern endoscopic light source units. Costs associated with water instillation methods are minor if syringes and tap water are used; available peristaltic flushing pumps range in price from $1430 to $2212. Some facilities may require the use of sterile water rather than tap water for instillation, which will increase the cost of this method. Prices for CO_2 regulators are shown in Table 1. A specialty water bottle with an additional input on its cap for connecting CO_2 tubing costs approximately $450. The ongoing costs for endoscopic CO_2 insufflation relate to purchase of the gas itself, and 2 of the 3 available systems use disposable tubing that carries CO_2 from the regulator to the water bottle (daily change recommended). Both the actual CO_2 and the disposable tubing are very inexpensive; the cost per case for the CO_2 has been estimated to be less than 1 € (equivalent to ~$1.35) and the daily cost for a tubing set is approximately $9.[3]

There are no data that formally analyze the cost-effectiveness of CO_2 insufflation for colonoscopy. Techniques that facilitate unsedated colonoscopy such as water-assisted methods have the potential for cost savings as they obviate the need for an intravenous line, medications, and long recovery periods and may also favorably affect indirect societal costs such as absenteeism from work. However, challenges remain with regard to widespread use of unsedated colonoscopy, including patient acceptance as well as practical issues that may arise (eg, does the patient have a driver, so that on-demand sedation can be used, if needed?).

AREAS FOR FUTURE RESEARCH

Further studies may be useful in determining whether the use of reduced air flow settings on newer light sources during insertion is associated with less abdominal pain and mucosal barotrauma. The technical methods for water-assisted insertion are still evolving, and comparative studies (eg, water instillation alone vs water exchange) would be useful to refine optimal technique. Whether water-assisted techniques have a role in colonoscopy performed with moderate or deep sedation remains uncertain. Although the clinical utility of CO_2 insufflation is well established, a thorough, well-conducted cost-effectiveness analysis is still needed. The inclusion of patients with chronic obstructive lung disease in studies of CO_2 insufflation would help to establish the safety profile of CO_2 in this subset. Additional studies comparing CO_2 insufflation and water-assisted techniques (or a combination of these methods) in unsedated colonoscopy would be useful.

SUMMARY

Several options are available for luminal expansion at colonoscopy. Air insufflation remains the most common method used. The use of CO_2 insufflation has been associated with a reduction in abdominal pain intra- and post-procedurally up to 24 hours compared with air insufflation, and CO_2 also appears to benefit patients undergoing some lengthier upper endoscopic procedures with respect to less postprocedure pain. CO_2 insufflation is safe in unsedated and sedated patients. Water-assisted insertion methods have been shown to facilitate unsedated and minimally-sedated colonoscopy and have been associated with a reduction in intra- and post-procedure abdominal pain. Water-assisted insertion methods require some technical skill and are associated with a learning curve to master these techniques. The role of water-assisted insertion techniques in patients undergoing colonoscopy with moderate or deep sedation is unclear.

DISCLOSURE

All authors disclosed no financial relationships relevant to this publication.

Abbreviations: ADR, adenoma detection rate; RCT, randomized, controlled trial.

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