

Unsedated colonoscopy: A neverending story

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Author contributions: Terruzzi V, Paggi S, Amato A, Radaelli F substantially contributed to conception and design; Terruzzi V contributed to data collection, analysis and manuscript draft; Terruzzi V, Paggi S, Amato A and Radaelli F revised and approved the final manuscript.

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Received: March 30, 2011 Revised: August 18, 2011

Accepted: March 1, 2012

Published online: April 16, 2012

Abstract

Although sedation and analgesia for patients undergoing colonoscopy is the standard practice in Western countries, unsedated colonoscopy is still routinely provided in Europe and the Far East. This variation in sedation practice relies on the different cultural attitudes of both patients and endoscopists across these countries. Data from the literature consistently report that, in unsedated patients, the use of alternative techniques, such as warm water irrigation or carbon dioxide insufflation, can allow a high quality and well tolerated examination.

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Key words: Analgesia; Colonoscopy; Endoscopy; Sedation; Unsedated colonoscopy

Peer reviewers: F Douglas Bair, MD, FRCPC, Staff Gastroenterologist, Oakville-Trafalgar Memorial Hospital, Suite 125B -690 Dorval Drive, Oakville, Ontario L6K 3W7, Canada; Shuji Yamamoto, MD, Department of Gastroenterology and Hepatology, Graduate School of Medicine, Kyoto University, 54 Shogoin Kawahara-cho, Sakyo-ku, Kyoto 606-8507, Japan

Terruzzi V, Paggi S, Amato A, Radaelli F. Unsedated colonoscopy: A neverending story. *World J Gastrointest Endosc* 2012; 4(4): 137-141 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v4/i4/137.htm> DOI: <http://dx.doi.org/10.4253/wjge.v4.i4.137>

scopy: A neverending story. *World J Gastrointest Endosc* 2012; 4(4): 137-141 Available from: URL: <http://www.wjgnet.com/1948-5190/full/v4/i4/137.htm> DOI: <http://dx.doi.org/10.4253/wjge.v4.i4.137>

INTRODUCTION

The story begins with the birth of colonoscopy: the examination was described as an invasive and potentially painful procedure, for which either sedation^[1,2] or anesthesia^[3] were recommended. Where are we now? Four decades have passed, and the role of sedation for colonoscopy is still a matter of debate.

Nowadays the sedation of patients undergoing colonoscopy is common practice in the United Kingdom^[4] and in the United States^[5]. Moreover, a trend towards the use of deep sedation by non anesthesiologist- and anesthesiologist-delivered propofol occurs in the United States and France, respectively^[6,7]. Conversely, unsedated or on-demand sedation colonoscopy is routine practice in other European and Eastern countries. In Finland only 6% of colonoscopies are performed with sedation^[8], whereas in Norway the mean sedation rate is 37% (range 6%-97%)^[9]. A recent Italian survey reported that 45% of patients underwent colonoscopy without sedation or analgesia, 44% were sedated by intravenous benzodiazepines with/without narcotics, and only 3% were given propofol^[10]. In a study which included 33 district hospitals in Portugal, sedation was used in 25% of the procedures^[11]. The wide range in sedation practice for colonoscopy in Europe was recently confirmed by the EPAGE study, which included 21 centers from 11 countries; the predominant strategy was conscious sedation in nine centres, deep sedation in four and no sedation in one, respectively. In the remaining seven centres there was no specific predominant sedation strategy^[12]. A large variation in sedation practice was also reported in Asian countries, ranging from 18% in China to 100% in Singapore and Hong Kong^[13]. These differences mainly depend on the different cultural and individual attitudes of both patients

Table 1 Randomized controlled studies comparing CO₂ and air insufflation for colonoscopy: number of enrolled patients, options for sedation, cecal intubation rate and procedure-related pain scores

Study	No. of patients		Sedation	Cecal intubation (%)		Absence of pain (%) or pain score (0-10)					
						During		After 1-6 h		After 24 h	
						Air	CO ₂	Air	CO ₂	Air	CO ₂
Colonoscopy studies	Air	CO ₂		Air	CO ₂	Air	CO ₂	Air	CO ₂	Air	CO ₂
Stevenson <i>et al</i> ^[29] 1992	29	27	No	NR	NR	26%	17%	50%	97%	56%	95%
Bretthauer <i>et al</i> ^[30] 2002	119	121	On demand	90	90	40%	50%	65%	90%	80%	92%
Sumanac <i>et al</i> ^[31] 2002	51	49	Yes	NR	94	67%	85%	55%-69%	93%-91%	82%	85%
Church and Delaney ^[32] 2003	124	123	Yes	98	95	NR	NR	NR	NR	NR	NR
Bretthauer <i>et al</i> ^[33] 2005	52	51	53 yes 48 no	100	100	5%	12%	40%	70%	52%	70%
Wong <i>et al</i> ^[34] 2008	50	46	Yes	98	96	14%	45%	80%	90%	n/r	NR
Yamano <i>et al</i> ^[35] 2010	54	66	No	98	95	45%	80%	65%	85%	97%	95%
Amato A <i>et al</i> ^[36] 2011	113	115	On demand	99.1	95.6	4.6	3.0	NR	n/r	NR	NR

NR: Not reported; NS: Not significant.

and endoscopists across these countries. Indeed, recent literature underlines that unsedated colonoscopy may be feasible in selected subsets of patients^[14-17]. Studies aimed at evaluating patient attitudes towards unsedated colonoscopy helped identify clinical factors associated with a higher probability of accepting and completing the examination without sedation, such as male gender, age over sixty, absence of abdominal pain, high cultural level, and low pre-procedure anxiety level^[16-20]. With this purpose, a recent Norwegian survey indicated that the recommendation to increase the use of sedation and/or analgesia in general practice does not necessarily lead to lower rates of painful colonoscopy^[21].

Bearing in mind that diagnostic accuracy and safety are the main goals in endoscopy procedures and that sedation and analgesia have been reported to accomplish both these goals in colonoscopy^[6], which additional benefits can be provided by unsedated examinations? First, resource consumption required for unsedated colonoscopy is obviously less. Indeed, medication-free endoscopy can make recovery rooms and instruments for post-procedural monitoring unnecessary, it reduces the need for nursing care and escorts and increases the efficiency of endoscopy services^[22]. Second, from the patients' point of view, unsedated colonoscopy decreases recovery time burden and can avoid the risk of unplanned conscious sedation-related cardiopulmonary events, which occur in 1.1% of colonoscopies^[22,23]. Last but not least, the widespread diffusion of colorectal cancer screening programs has increased the proportion of "healthy", young and working subjects undergoing colonoscopy. In this setting, as the interference of sedation and analgesia on patients' daily activities and work has been proven to lower the adherence to screening colonoscopy^[24], unsedated, but well tolerated procedures might play an emerging role.

In order to improve patients' tolerability and to real-

ize their expectations, alternative techniques and "endoscopic tricks" for a painless and high quality sedation-free colonoscopy have been developed.

TECHNIQUES FOR UNSEDATED COLONOSCOPY

In recent years, studies evaluating the effectiveness of technical measures to reduce the dose of sedation during colonoscopy or to perform high quality colonoscopy without sedation have been published^[22,25-27,29-36,38-51]. Although a few studies have reported the benefits of relaxation music, acupuncture and hypnosis, these techniques did not obtain widespread diffusion^[25-27]. Conversely, the use of CO₂ or warm water infusion instead of air have been extensively investigated and subsequently adopted in clinical practice.

Carbon dioxide

The safety of CO₂ insufflation has been tested for colonoscopy since 1974^[28] and during the period from 1992 to 2012 eight randomized controlled trials dealing with this topic were published^[29-36]. Overall 1200 patients were included, 592 of which were randomized to air and 598 to CO₂ insufflation, with or without sedation/analgesia.

In spite of a large heterogeneity among the studies, especially with regards to sedation practice, the incidence and severity of post-procedure pain was consistently lower in CO₂ patients, as summarized in Table 1. Conversely, no significant difference in perceived pain during the procedure and 24 h later was found. Two studies also reported a significantly lower degree of bowel distension in the CO₂ group^[29,31]. Furthermore, the use of CO₂ during colonoscopy allowed faster cecal intubation and lower medication doses^[30,35]. No respiratory adverse events were reported during CO₂ insufflation in these studies.

Due to the positive impact on patient tolerability and

Table 2 Randomized controlled studies comparing the water method and air insufflation for colonoscopy: number of enrolled patients, options for sedation, cecal intubation rate and outcomes (pain, willingness to repeat the procedure, recovery time)

Study	No. of patients		Sedation	Cecal intubation (%)		Outcome measures					
	WW	Air		WW	Air	Pain score (0-10)		Willingness to repeat		Recovery time (min)	
Colonoscopy studies	WW	Air		WW	Air	WW	Air	WW	Air	WW	Air
Leung JW <i>et al</i> ^[45] 2009	28	28	Minimal with increments as needed	100	100	1.3	4.1	96%	96%	13.6	19.8
Radaelli <i>et al</i> ^[48] 2010	116	114	On-demand	94	95	2.8	3.9	90.50%	81.60%	NR	NR
Leung FW <i>et al</i> ^[46] 2010	42	40	unsedated	78	98	3.0	6	93%	78%	NR	NR
Leung CW <i>et al</i> ^[47] 2010	112	114	Minimal sedation	100	100	4.1	5.3	1.41	1.47 ¹	NR	NR
Ransibrahmanakul K <i>et al</i> ^[49] 2010	31	31	Minimal sedation	94	94	3.6	5.5	93.50%	80.6	8.8	10.4
Leung JW <i>et al</i> ^[22] 2011	50	50	On-demand	100	100	2.3	4.9	90%	94%	8.4	12.3
Hsieh YH <i>et al</i> ^[51] 2011	90	89	Minimal sedation	99.9	99.9	2.5	3.4	NR	NR	NR	NR
Pohl J <i>et al</i> ^[50] 2011	58	58	On-demand	82.8	96.5	2.8	4.2	72.40%	67.2%	NR	NR
Amato A <i>et al</i> ^[36] 2011	113	113	On-demand	97.3	99.1	2.8	4.6	90%	79.6%	0-8	0-53

NR = Not reported; ¹Continuous Likert scale (1 = minimal; 7 = maximal); NS: Not significant.

safety, the European guidelines for quality assurance in colorectal cancer screening and diagnosis recommend routine use of CO₂ colonoscopy^[37]. However, the need for a specific CO₂ delivery system, and costs related to this system, may limit its widespread use in clinical practice.

Warm water

Warm water infusion during colonoscopy was initially used as an adjunct to air insufflation in order to deal with colonic spasm and to facilitate the examination in patients with severe diverticular disease^[38-41]. Despite encouraging results from these preliminary studies, the use of warm water to distend the colonic lumen did not have widespread agreement in the international community. However, a renewed interest in this method has been seen in the last few years.

In 2007, Leung and co-authors proposed the use of warm-water irrigation in lieu of air insufflation during the insertion phase of colonoscopy. Their initial and observational studies indicated that warm water infusion could minimize procedure-related discomfort or pain without compromising the technical performance of the examination itself^[42-44]. This technique is based on a switch-off of the air pump and infusion of warm water to distend areas where the lumen is collapsed. Warm water is stored and maintained at 37 °C and infused intermittently using a peristaltic flushing pump through the accessory water channel of the scope. It has been hypothesized that these benefits depend on the decrease in colonic spasm, local distention of the colonic wall and the effect of water weight which straightens the sigmoid colon^[32,39].

To date, the results of nine randomized controlled studies evaluating warm water infusion versus standard air insufflation for the colonoscopy insertion phase have

been published^[22,36,44-50].

In the first study, the authors reported their experience in minimally sedated patients undergoing colorectal cancer screening or surveillance colonoscopy at a single Veterans Medical Center^[45]. This study showed that water infusion could reduce the total doses of sedatives and significantly lower pain scores, without affecting the cecal intubation rate. Two other studies from the same group, carried out in unsedated or minimally sedated subjects, confirmed that the need for medications was reduced, independently of endoscopist expertise^[46,47].

Four studies from the United States^[22], Italy^[36,48] and Deutschland^[50] carried out in unsedated patients with the option of “on-demand” sedation, consistently demonstrated that the warm water method was associated with a decreased request for medications, significantly better patient tolerance of the procedure, and a reduction in patient on-site and at-home recovery-time burdens, as summarized in Table 2. Recently, similar results were obtained using either water infusion or CO₂ insufflation during unsedated colonoscopy^[36]. With regard to performance outcome measures, warm water colonoscopy did not seem to affect the cecal intubation or the adenoma detection rate. Even if the Italian study seemed to demonstrate impaired adenoma detection (although this was not reported for advanced adenomas^[48]), this finding was not confirmed by a subsequent study from the same group^[36] and by other studies, which conversely showed comparable^[47,49-51] or better^[22,52] values in the warm water group.

A recent revision of randomized clinical trials evaluating the water method for colonoscopy showed that pain reduction during insertion was significantly higher when suction of the infused water was performed during the insertion phase (“water exchange”) than during

scope withdrawal (“water immersion”) (56% *vs* 27%)^[53]. The “water exchange” technique has also been reported to be associated with an increase in the adenoma detection rate. It may be speculated that this finding is related to better visualization of the mucosa in patients with suboptimal preparation, due to water infusion and suction during the insertion phase of colonoscopy. Moreover, the reduced need for suction during the withdrawal phase minimizes colonic spasms and helps focus the endoscopist’s attention on mucosal inspection^[52].

These results are encouraging, but require caution, as potential biases can be identified. First, wider external validation is needed, as these results are from a few centers, and in one study only male Veteran subjects were evaluated. Moreover, the non-blindness of the endoscopist to the randomization arm (warm water or air) could have determined the choice to unintentionally delay sedation administration in the study group. Last but not least, warm water colonoscopy is characterized by a longer procedure time^[49], which might affect the cost reduction related to faster recovery time and by the availability of either a peristaltic flushing pump to infuse warm water or a device to maintain water at 37 °C.

Despite these drawbacks, warm water irrigation may represent a valid option for those who do not want or cannot undergo sedated colonoscopy for various reasons (e.g., high risk of sedation-related adverse events, no escort, desire for interaction with the physician during the examination, or the need to work on the endoscopy day).

CONCLUSION

Carey and Sorby^[54] in a 2004 up-to-date review stated that “the scant amount of literature on unsedated colonoscopy makes it difficult to fully assess feasibility and acceptability of this procedure”, now in 2012, in light of published studies, we can assert that colonoscopy without sedation and analgesia is not only technically feasible and reasonable, but sometimes advantageous. Both “endoscopic tricks” proposed above are simple, cheap and potentially available worldwide. Unsedated colonoscopy is fascinating for both physicians and patients, although not for all. It is crucial to identify the subset of subjects most likely to attempt and complete unsedated procedures, who could benefit from being offered one of the above options^[17].

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S- Editor Yang XC L- Editor Webster JR E- Editor Yang XC