

Colonoscopy, pain and fears: Is it an indissoluble trinomial?

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Abstract

Colonoscopy is the reference method in the secondary prevention, diagnosis and, in some cases, treatment of colorectal cancer. It can often cause pain associated with embarrassment, anxiety, and physical and emotional discomfort. Pain intensity is influenced by a lot of factors, and there is a strict relationship among pain, pain perception, and mind. Several methods can be used to break the trinomial colonoscopy, pain and fear. Sedoanalgesia is recommended by several guidelines. If no sedation is offered, the patient must accept a higher chance of unacceptable discomfort and the endoscopist a lower chance of completing the procedure because of patient discomfort. Other non-pharmacologic methods such as acupuncture, music, and hydrocolonoscopy can be used as alternatives to pharmacologic sedoanalgesia. Furthermore, new endoscopic technologies such as variable-stiffness colonoscopes and ultrathin colonoscopes, or the use of carbon dioxide instead of air for colon insufflation, can reduce the pain caused by colonoscopy. In the future, technical improvements such as wireless capsules or robotic probes, will probably enable to overcome the present concept of colonoscopy, avoiding the use of traditional endoscopes. However, at present the poor attention paid by endoscopists to the pain and discomfort caused by colonoscopy can not be justified. There are several methods to reduce pain and anxiety and to break the trinomial colonoscopy, pain

and fear. We must use them.

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Key words: Colonoscopy; Pain; Fear; Anxiety; Discomfort; Conscious sedation

Core tip: Colonoscopy can often cause pain associated with embarrassment, anxiety, and physical and emotional discomfort. Control of discomfort and pain during colonoscopy is considered to be a high priority by patients. This review of the literature encompasses the main methods for reducing pain and anxiety, to break the trinomial colonoscopy, pain and fear.

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INTRODUCTION

At present, colonoscopy is the reference method in the secondary prevention, diagnosis and, in some cases, treatment of colorectal cancer^[1,2]. For this reason, and as a consequence of the improvement of both imaging techniques (for instance, magnification) and interventional procedures (ESD), and the screening programs for the colon cancer prevention that are ongoing in many countries, the annual number of colonoscopies is strongly increasing. However, colonoscopy is considered highly invasive and is usually assumed to be an uncomfortable and often painful procedure. These concerns can result in anxiety that unfavourably decreases patient cooperation and satisfaction with the procedure^[3]. Therefore, analgesia and sedation are frequently used. The decision to use premedication and the kind of premedication are influenced by national and cultural differences among

countries^[4,5]. Moreover, there is a wide variation in colonoscopy practice also among centers in the same country^[6], probably caused by the poor attention paid to the pain control during invasive procedures^[7].

However, the fear of experiencing pain during colonoscopy can cause the patient refusal to undergo the examination, with possible negative implications on both diagnosis and treatment. Several studies showed that fear of being embarrassed or fear of pain during colonoscopy were positively associated with unwillingness to participate in colorectal cancer screening^[8,9].

Therefore, it is quite evident that colonoscopy, pain and fear (of being embarrassed during colonoscopy, of experiencing pain, of having cancer, *etc.*) are strictly linked together, and only reducing the procedure-related patient discomfort can break such a trinomial, making colonoscopy more accepted with increase of the diagnostic yield.

In this review, we will discuss the relationship among fear, anxiety, and pain, as well as the ways of breaking the trinomial colonoscopy, pain, and fear.

RELATIONSHIP AMONG PAIN, FEAR, AND ANXIETY

All invasive procedures can cause pain associated with embarrassment, anxiety, and fear. Such a situation was defined by Morrison as “discomfort”^[10]. Discomfort can be physical (malaise and trouble due to the duration of the procedure, need to maintain an uncomfortable position, or need to remain motionless for a long time); or emotional (embarrassment of showing the body, anxiety and fear of experiencing pain, anxiety and fear of an unfavorable diagnosis). Pain intensity during an invasive procedure varies according to patient compliance, and is influenced by a lot of factors, such as previous experience, pre-existing pain and/or chronic pain, presence of fear or anxiety, type and duration of the procedure, and related expectation of pain^[10,11]. There is a strict relationship among pain, pain perception, and mind, and mind-body medicine can examine interactions as they occur among the brain, mind, body, and behavior^[12]. Mind can be defined as “conscious and unconscious thought patterns, including images, perceptions and intentions, generated by a functional network of distributed neural centers in the brain and body, including homeostatic representations that provide the context for human self awareness and emotional experience”^[12]. An expanding evidence base reveals that the limbic system (in particular the amygdala) has the capacity to up- or down-regulate pain’s emotional response^[13].

Fear represents a normal emotional response to a threat that is true, or is recognized as true by the individual (*i.e.*, fear of colonoscopy and related pain). Conversely, anxiety is an irrational state of mind, characterized by a sensation of uncertainty and inadequacy and often associated with neurovegetative symptoms (such as tachycardia, hypertension, tachypnea, shakes, and so on), and can

become a pathological and distressing condition^[14].

Pain can cause both immediate and long-term harmful effects. The effects of acute procedural pain consist of a variety of physical, emotional, behavioral, cognitive, and psychological manifestations, including fear, anxiety, anger, aggressive behavior, inability to concentrate, embarrassment, refusal to consent to further procedures, and distrust of the health care team, and may effect overall economic, social, and spiritual well-being^[15-17]. For these reasons, a recent position statement on the procedural pain management recommends the use of anxiolytic drugs associated with analgesics to manage the pain related to medical procedures. Furthermore, methods of non-pharmacologic management are also recommended during all phases of the procedures^[18].

Patient experience is a critical aspect of medical procedures, in particular of endoscopic procedures. Patients with favorable endoscopy experience are more likely to comply with medical advice, adhere to screening and use medical service in the future, whereas patients with poor experience are more likely to leave their care provider and be less compliant^[19].

A systematic review of literature showed that the control of discomfort and pain during the colonoscopy was considered to be a high priority by patients^[20].

Given the mind’s ability to influence the pain perceived during colonoscopy, acting on the pain and/or patient’s discomfort is mandatory to break the trinomial “colonoscopy, pain and fears”.

SEDOANALGESIA AND OTHER METHODS TO REDUCE PAIN

Sedoanalgesia practices

The use of sedoanalgesia by administering *iv* drugs for lower gastrointestinal endoscopic procedures is strongly recommended by several guidelines. If no sedation is offered, the patient must accept a higher chance of unacceptable discomfort and the endoscopist a lower chance of completing the procedure because of patient discomfort^[21]. However, the use of sedation for lower gastrointestinal endoscopic procedures is considerably influenced by the cultural differences among countries and the rules which regulate the drugs use^[4,5].

Propofol deep sedation is frequently used in some countries, whereas in other ones conscious sedation induced by means of a combination of a benzodiazepine and an opioid is more frequently used^[22-24]. Recently, a new option for sedation has been approved by the Food and Drug Administration. It is a Computer Assisted Personalized Sedation system called the SEDASYS[®] System (Ethicon Endo-Surgery, Inc., Cincinnati, OH, United States), that is indicated for the intravenous administration of Propofol for the initiation and maintenance of minimal to moderate sedation for ASA I or II patients undergoing endoscopic examination. Although the intention of this approval is to cut the anesthesia related

expenses, at present this system is scarcely used. Consequently, in many countries—such as Italy—moderate sedation using benzodiazepine (like Midazolam) and an opioid (like Pethidine), is the most popular method of sedation, although the use of Propofol is progressively increasing, because the satisfaction of both patients and endoscopists is greater. Moreover, recovery and discharge times are shorter with the use of Propofol^[25,26].

Several other drugs can be used for colonoscopy sedation, such as Alfentanil, Fospropofol, Remifentanil, Remimazolam^[5]. However, some of these drugs are still scarcely used, because they have been marketed quite recently, and can be only used by anaesthetists.

The optimal sedative for colonoscopy should be short acting, safe, easy to administer, and with minimal side effects, but this sedative is yet to be found. In this perspective, the use of nitrous oxide gas as an alternative method to *iv* sedoanalgesia for colonoscopy appears quite interesting and promising. Two systematic reviews suggest that nitrous oxide gas provides comparable analgesia with the advantage of a shorter recovery time and greater safety than *iv* analgesia-sedation methods used during colonoscopy^[27,28].

However, all sedoanalgesia methods can cause adverse cardio-respiratory events, even though the incidence of serious adverse events is low with all currently available agents^[29]. Some other methods that do not require the *iv* administration or the inhalation of drugs are reported in the literature to reduce patient's discomfort and to increase the acceptability of the examination.

Acupuncture

The use of this ancient technique displayed several effects on gastrointestinal tract, and a United States National Institute of Health consensus statement published in 1998 indicated that acupuncture might be useful for the treatment of certain pain conditions^[30].

In 2003, Fanti *et al*^[31] conducted a randomized placebo-controlled study to evaluate the analgesic effect of electro-acupuncture in a group of patients who were undergoing colonoscopy. They found that patients in the acupuncture group reported not significantly reduced pain during the procedure. Some years later, Ni *et al*^[32] reported a randomized study on two groups of 40 patients undergoing colonoscopy. In the first group, acupuncture was performed in the traditional points ST 36, ST 37, SP 9, SP 6, LI 4 from 30 min before colonoscopy to the end of the procedure; in the latter group no treatment was performed. Cecum was reached significantly more frequently, and discomfort resulted less marked, in the patients who underwent acupuncture. The same authors reported similar results in a subsequent study, in which they also observed lower plasma concentrations of beta-endorphin in the patients treated with electro-acupuncture, confirming a meaning attenuation of the patients' stress response during colonoscopy after electro-acupuncture^[33].

However, on the basis of these data and some few other studies with conflicting results, currently available

data do not support the use of acupuncture as an analgesic adjuvant during colonoscopy^[34].

Audio distraction

Listening relaxing music during pain-invoking experience is considered to have a therapeutic effect, as it promotes relaxing responses, triggers positive associations, and diverts attention from anxiety^[35]. For this reason, music has been used to decrease anxiety levels in patients in a variety of scenarios, such as digestive and bronchial endoscopy^[36,37]. However, the studies published in the literature are very heterogeneous as concerns either the type and design of the study, or the type of music used (classical, easy-listening, relaxing, Turkish classical music, *etc.*). Moreover, also the results are often conflicting.

From 2007 to 2009 three meta-analyses were published on this topic. The first of them included six randomized controlled trials that involved 641 patients undergoing esophagogastroduodenoscopy, flexible sigmoidoscopy or colonoscopy, with or without intervention through music therapy. This meta-analysis yielded significantly lower anxiety levels, reduction in analgesia requirements, reduction in sedation requirements, and procedure times in patients receiving music therapy in comparison with controls^[38].

The second meta-analysis dealt with the effect of music on procedure time and sedation during colonoscopy. Eight randomized controlled trials for a total of 722 patients enrolled were included into the meta-analysis, that concluded that music is effective in reducing procedure time and sedative requirement during endoscopic examination^[39].

Also the third meta-analysis dealt with the effect of music during colonoscopy^[40]. One hundred and seven articles were examined, but just 8 randomized controlled trials for a total of 712 patients enrolled met the inclusion criteria. Music played during colonoscopy was shown to improve patients' overall experience, but it did not alter other parameters, such as sedative pain medication requirements, procedure times, patients' pain, and patients' willingness to repeat the same procedure in the future.

Finally, Lee *et al*^[41] designed a prospective randomized controlled trial to test the hypotheses that visual distractions could reduce the requirement for sedatives during colonoscopy, and that the combination of audio and visual distractions could have additive beneficial effects. One hundred and sixty-five patients were randomly allocated into three groups to receive different modes of sedation: visual distraction plus sedation, audio-visual distraction plus sedation, sedation alone. Visual distraction alone did not decrease the dose of sedative medication required for colonoscopy. When audio distraction was added, both the dose of sedative medication required and the pain score decreased significantly.

Hydro-colonoscopy and other substances instilled into the colon

Historically, air insufflation was used to advance the

colonoscope through the colon. In 1984, Falchuk and Griffin^[42] described a water technique that facilitated colonoscopy in patients with severe diverticular disease. Fifteen years later, a prospective randomized study on 100 unselected patients undergoing colonoscopy showed that the passage through the left colon was significantly faster with the water intubation method than with the traditional method^[43]. Afterwards, several studies investigated the usefulness of this technique, based on the assumption that the instillation of water at 37 °C into the colic lumen could minimize colon spasms, reducing pain and maintaining the same efficacy of air in reaching the cecum. The water weight would enable to enlarge the lumen without stretching the colon walls. However, this technique requires a thorough colon cleansing to allow a good visualization of the lumen.

In 2012, a systematic review and meta-analysis of randomized controlled trials on hydro-colonoscopy examined nine studies for a total of 1283 patients enrolled. Warm water infusion resulted less painful than standard air insufflation, reducing the need for sedation/analgesia, and improving patient acceptance of colonoscopy^[44].

Some authors proposed also the corn seed oil assistance in colonoscopy. Theoretically, warm water is thought to decrease spasm of the colon and straighten the sigmoid colon due to the gravity of water when the patient is in the left decubitus. On the other hand, oil lubrication decreases the friction between the colonic mucosa and the shaft of the scope, but it is devoid of the aforementioned effects by warm water. Brocchi *et al*^[45] performed two prospective, randomized and controlled studies comparing the oil method with a standard technique in one^[46] and with a warm water technique in the other. The results of the two studies were similar and consistent with a favorable effect of the oil technique on successful intubation to the cecum, level of patient pain, and degree of difficulty during colonoscopy.

Beside warm water and corn seed oil, other substances have been instilled into the colon to reduce spasms. Peppermint oil has a satisfactory spasmolytic effect on the smooth musculature of colon. Asao *et al*^[47] instilled a solution of peppermint oil through the accessory channel of the colonoscope in 409 patients undergoing colonoscopy. About twenty seconds later, they documented a relaxation of the musculature that lasted about twenty minutes. Finally, Ai *et al*^[48] evaluated the antispasmodic effect of the Chinese herbal medicine Shakuyaku-kanzo (TJ-68) on the colonic wall by direct spraying during colonoscopy. TJ-68 is an extract powder composed of Shakuyaku (*Paeoniae radix*) and Kanzo (*Glycyrrhizae radix*) combined at a ratio of 1:1, and inhibits acetylcholine-induced contraction and the contractile machinery of the smooth muscle.

The authors conducted a randomized study on 101 patients, and concluded that direct spraying of TJ-68 on the colonic mucosa suppressed colonic spasm. However, the effectiveness use of TJ-68 has been evaluated in just few studies, and there are no systematic reviews and

meta-analyses supporting its actual clinical usefulness.

NEW ENDOSCOPIC TECHNOLOGIES FOR COLON EXAMINATION

Fixed, angulated sigmoid colons or long, floppy colons are the main causes of both the difficulty of reaching the cecum and the pain experienced by the patient. Several studies have been designed to evaluate the use of pediatric colonoscope for colonoscopy in adults, based on the assumption that the pediatric colonoscope could provide greater comfort in adult patients, because of its smaller diameter and greater flexibility. The results of these studies showed that the pediatric colonoscope is suitable for colonoscopy in adult, and is also useful in patients in whom colonoscopy with the adult colonoscope is unsuccessful in reaching the cecum^[49]. Furthermore, ultrathin colonoscopes (diameter 9.2 mm) are available today, and theoretically they should allow for a further reduction of the pain experienced by the patient. However, at present there is no evidence about such an assumption. Moreover, an initial “learning curve” is needed in using these colonoscopes for endoscopists used to an adult colonoscope, because the ultrathin tool is quite less stiff, and more pull-back maneuvers are required during the examination.

The need of flexibility must often be balanced with the need of stiffness, to avoid the risk of creating loops in the mobile tracts of the colon. In the last years, variable-stiffness colonoscopes have become available in both adult and pediatric classes. These new tools have a stiffness control ring that allows to modify the flexibility during the examination, reducing the risk of creating loops in the left tract of the colon, and allowing for a higher cecal intubation rate with less abdominal pain, according to the conclusion of a meta-analysis of randomized controlled trials published in 2009^[50]. However, the results of the comparison between variable-stiffness colonoscope and standard adult colonoscope are conflicting. In another meta-analysis, Xie *et al*^[51] concluded that variable-stiffness colonoscope significantly improved the cecal intubation, but cecal intubation time was similar for the two colonoscope types (standard and variable-stiffness colonoscopes). Moreover, the sedation dose used with the two types of instrument resulted similar; and no difference in pain scores for patients could be demonstrated, because of the differences in the scale used in the selected studies.

Insufflation of the bowel is necessary to improve visualization during colonoscopy, but it is one of the main causes of the abdominal pain experienced by the patient. It is common practice to use ambient atmospheric air, also termed “room air”, to insufflate the lumen. However, the safety of carbon dioxide (CO₂) insufflation during colonoscopy is well known starting from 1974^[52]. CO₂ is more rapidly absorbed from the bowel than room air, allowing for a more rapid intestinal decompression

and potentially decreasing intraprocedural and postprocedural pain. Many studies evaluated the safety and efficacy of CO₂ insufflation for gastrointestinal endoscopy. Two recent systematic reviews and meta-analysis showed that CO₂ insufflation is safe in patients without severe pulmonary disease, and is associated with decreased bowel distension and postprocedural pain^[53,54]. Furthermore, one of them showed that insufflation with CO₂ in colonoscopy could also decrease abdominal pain during colonoscopy^[54]. For these reasons, the use of carbon dioxide insufflation, instead of air, is currently a quality standard to maximize comfort during colonoscopy^[55]. Nevertheless, the use of CO₂ for insufflation has not been widely adopted in practice for various reasons (cultural prejudices, lack of knowledge, costs, *etc.*).

In the last years, the traditional concept of colonoscopy and colon examination is changing, as new tools are going to be available. The wireless capsule colonoscopy, with the second generation of PillCam[®] Colon, is becoming available in routine clinical practice^[56]. Likewise, the Endotics[®] system, that consists of a robotic probe moving forward with an inchworm locomotion, allows for the painless progression into the colon, because it does not create loops, nor cause stretching of the colon walls^[57]. The applicability of the Endotics[®] system in clinical practice has already been proven^[58], and in 2014 its second version will be marketed with an operative channel of 3 mm in diameter, that will enable to take biopsies and will open the way to perform also other operative maneuvers.

CONCLUSION

Fifty years after the introduction of flexible colonoscopy in clinical practice, psychological and religious barriers due to the indignity of the procedure, fear of the procedure related to either the procedure-related pain or possible unfavorable diagnosis, are still working to make colonoscopy, pain, and fear an apparently indissoluble trinomial.

In the future, technical improvements will probably enable to overcome the present concept of colonoscopy, avoiding the use of traditional endoscopes. However, the next availability of such technical improvements can not justify the poor attention paid by endoscopists to the pain and discomfort caused by colonoscopy, as highlighted by the variability in the use of sedoanalgesia, either among countries, or in the same country. There are several valid methods to reduce pain and anxiety and to break the trinomial colonoscopy, pain and fear. We must use them.

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