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Prospective study of the factors associated with poor tolerance to ambulatory colonoscopy under conscious sedation

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ABSTRACT

Background: conscious sedation with benzodiazepines and opiates for colonoscopy is a widespread clinical practice.

Objective: to determine the patient's tolerance to colonoscopy and identify the factors associated with lower tolerance.

Methods: a prospective, single-center, descriptive study of patients undergoing ambulatory colonoscopy under conscious sedation. The pain was assessed using a visual analogue scale with a score of 0 to 100 and also qualitatively.

Results: three hundred patients with a median age of 54 years completed the study (p25-75: 45-64); 138 were men (46%). Tolerance was good in 273 cases (91%). The median value of tolerance was 13 (p25-p75: 4-33). Pain was considered as mild in 215 (71.7%), moderate in 57 (19%) and intense in 28 (9.3%). In the univariate study, greater pain was associated with females, anxiety, the indication for the procedure, the length of time and difficulty of the examination, and the doses of sedatives. In the multivariate study, both the indication (OR 2.92, 95% CI = 1.03-8.2, $p < 0.05$) and the difficulty of the examination (OR 4.68, 95% CI = 1.6-13.6, $p < 0.01$) were significant. Complications were found in 16 patients (5.3%), although all of them were insignificant.

Conclusions: tolerance of patients undergoing ambulatory colonoscopy under conscious sedation is good in most cases and complications are infrequent and minor. A worse tolerance to the test is associated with women patients, individuals with anxiety prior to colonoscopy, indication, difficult and longer exploration and lower doses of sedatives.

Key words: Colonoscopy. Tolerance. Benzodiazepines. Opiates. Sedation.

INTRODUCTION

Colonoscopy is a diagnostic and therapeutic method used throughout the world. As colorectal cancer screening (CRC) is becoming more widespread, the frequency of its indication is increasing (1).

Colonoscopy is a potentially painful exploration. The pain experienced during the procedure is one of the factors which determines the satisfaction of the patient and it is of paramount importance in terms of adherence to screening programs (2,3). In addition, good tolerance plays a key role in allowing the endoscopist to carry out the exploration properly. Therefore, significant efforts have been made to improve tolerance by making improvements in colonoscopes, using conscious or deep sedation as well as CO_2 or water for the insufflation of the colon and even employing robotic support (4).

In terms of sedation, the use of benzodiazepines alone or in combination with opiates has been considered as the standard method of choice for digestive endoscopy for many years (5-7). However, this combination is being replaced by the use of propofol in many countries, including Spain (6,8). However, the absence of clear legislation about the use of this sedative by endoscopists and the high cost associated with its administration by anesthetists clearly limits its use in other countries (5,6). Even in those countries where the use of propofol is more accessible, the benzodiazepines and opiates combination is still recommended by clinical guidelines in low complexity procedures such as diagnostic colonoscopies or simple therapy (9,10). Therefore, learning about the results of this type of sedation remains of interest in current clinical practice, especially where propofol sedation guided by an endoscopist is not possible.

In the context mentioned above, it would be useful to determine the factors which are related to poor tolerance to colonoscopy under conscious sedation since it could permit an *a priori* selection of patients who might require deep

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sedation with propofol. This would contribute to improving patient satisfaction and reducing costs whilst making repetition of explorations due to poor tolerance unnecessary and reducing the number of examinations where an anesthetist might be required to administer sedation.

Several previous studies have associated worse tolerance with different factors, including patient characteristics, such as being female, younger, having pre-procedure anxiety, low body mass index (BMI) and smoking, as well as previous use of benzodiazepines, opiates or psychotropic drugs. Others have associated poor tolerance with aspects related to both the exploration and the diagnostic procedure itself, including the reason for the procedure as well as the duration and difficulty of the colonoscopy. However, the methodology used in these studies varies considerably since many of them analyze oral endoscopy and colonoscopy together, whilst others include unsedated patients or assess tolerance through indirect methods such as the use of higher doses of sedatives (11-20). Furthermore, no studies with these characteristics have been found in our context.

As such, we concluded that it would be relevant to conduct a study to analyze the tolerance of patients to ambulatory colonoscopy under conscious sedation with benzodiazepines and opiates and identify the factors associated with lower tolerance.

MATERIAL AND METHODS

Patients

This is a prospective study which included patients who had undergone an ambulatory colonoscopy under conscious sedation with benzodiazepines and/or opiates. The study was conducted over a period of a year in the Hospital de Alta Resolución in Écija (Seville, Spain), which serves a population of 56,000 people. In order to participate, patients were required to sign a written consent form. The study was approved by the ethical committee of the Hospital Universitario Virgen del Rocío under code number CEI 2013PI/008.

Inclusion criteria were patients aged 18 years and over, with indication for ambulatory colonoscopy by the Digestive Diseases Unit, who had signed the consent form for the study and underwent the procedure under sedation with opiates and/or benzodiazepines.

Exclusion criteria were: patients who underwent colonoscopy without sedation or with deep sedation and those whose indication was not a complete colonoscopy. Patients with severe hearing or cognitive disorders which would not allow evaluation by means of a visual analogue scale (VAS) were also excluded.

Technique

The colonoscopies were performed by three Digestive Diseases specialists from our hospital who devoted 40% of their time to endoscopy and the rest to consultation. The length of experience of the endoscopists, following their specialist training period, was between two and seven years.

A Fujinon® ST 250 WL5 model video-colonoscope, with no variable tube rigidity and ambient air insufflation, was used with a 2200 Fuji System video-processor. The insertion of the colonoscope was performed by the endoscopists themselves, aided by nursing staff for the attachment process. The endoscopist decided the necessary postural changes, as well as the manual abdominal pressure required to perform cecal intubation.

Pain evaluation

Patients' general variables (age, gender, weight, height, BMI, comorbidity and reason for examination) were recorded. If a colonoscopy had been previously performed, the pain experienced by the patient was assessed quantitatively by means of a 0 to 100 mm VAS, as well as qualitatively as "bad" or "good". Patients were informed verbally and in writing of the risks and benefits of colonoscopy. They were also informed that the procedure was to be performed under conscious sedation, although patients who did not tolerate the test were offered the option of deep sedation under the supervision of an anesthetist or, alternatively, suspension of the test.

On the day of the endoscopy, before the examination itself, a nurse asked the patient to indicate their degree of anxiety through a 0 to 100 mm VAS. After the colonoscopy was performed, the endoscopist filled in a form with aspects related to the exploration such as duration, cecal intubation, subjective difficulty of the colonoscopy, drugs and doses used, and preparation of the colon. In addition, they also indicated in a 0 to 100 mm VAS how they perceived the pain being suffered by the patient during the examination and, in a qualitative way, judged it as "good" or "bad". This assessment of tolerance was then carried out by the nurse. In all cases the scale was completed "blindly", without knowing the response of the others.

Once they had recovered from sedation, the nurse required the patient to indicate the degree of pain suffered during the examination using a VAS whilst also making a qualitative judgment of it being "good" or "bad". The pain was assessed as mild, moderate or intense according to values of 1-29, 30-79 and 80-100, respectively.

Conscious sedation using opiates and benzodiazepines

For conscious sedation, midazolam, and sometimes pethidine, was applied by the nurse using intravenous boluses at the indication of the endoscopist. The unit had a sedation protocol based on the Spanish Society of Digestive Endoscopy (SEED) guidelines which was applied according to the endoscopist's criteria (9). This protocol established three risk groups defined by age and underlying pathology. Initial doses were 2 mg of midazolam and 50 mg of pethidine, with lower doses for higher risk groups. It also established the possibility of performing successive administrations in boluses every 2-5 minutes, with doses of 1 mg of midazolam and 25 mg of pethidine in the lower risk group and smaller doses in those of greater risk.

The patient was monitored using pulse oximetry to record the heart rate and oxygen saturation. The patients received

systematic oxygen supplementation through nasal cannulas at a constant flow of 2 liters/minute.

Statistical analysis

Continuous variables are expressed by means or medians according to their symmetric or asymmetric distribution. The categorical variables are presented as numerical and as a percentage. Comparisons between categorical variables were performed using the Chi-squared or Fisher's tests. The Student's t-test was used for continuous variables which were found to be homogenous and have normal distribution. When this was not the case, the Mann-Whitney U test was used. The correlation between the variables was studied using the Spearman's correlation coefficient. A multivariate study was performed using the logistic regression method, with the enter method, to examine the relationship between the independent variable and the dependent variables, calculating the odds ratio with a confidence interval of 95%. The study data were analyzed using the SPSS statistical package (SSPS Inc. Chicago IL, 15.0).

RESULTS

All patients who met the criteria agreed to take part in the study. A total of 343 patients were included, of which 337 had a full colonoscopy indication. Of these, 319 were performed under conscious sedation, and finally 300 colonoscopies (94%) were deemed valid for the study. The reasons why some were not included were either lack of data because they could not fill out the VAS or because it was not properly registered after the colonoscopy. No differences were observed in the general characteristics of the patients who completed or did not complete the study.

One hundred and thirty-eight men (46%) and 162 women (54%) took part, with a median age of 54 years (p25-75: 45-64). The most frequent indications for the exploration were CRC family screening in 115 (38.3%) cases and monitoring of polyps in 48 (16%), both together amounting to more than 50% of patients. Other indications were anemia, positive fecal occult blood (FOB) test or rectal bleeding in 64 (21.3%) cases, diarrhea in 31 (10.3%), constipation in nine (3%), abdominal pain in eleven (3.7%), revision of inflammatory bowel disease in eleven (3.7%) and other indications in eleven (3.7%) patients (Table 1).

The patient assessed tolerance to the examination as good in 273 (91%) of colonoscopies; the nurse, in 268 (89.3%); and the physician, in 260 (86.7%) ($p < 0.01$). The median value on the VAS pain scale as assessed by the patients was 13 (p25-75: 4-33), by the nurse 10 (p25-75: 3-26) and by the doctor 11.5 (p25-p75: 4-28). There was a significant and clear correlation between patient and nurse assessments ($r = 0.61$, $p < 0.01$) and a somewhat lower correlation between the patient and the doctor ($r = 0.54$, $p < 0.01$). The highest correlation was obtained between the doctor and the nurse ($r = 0.77$, $p < 0.01$). In terms of the evaluation of pain by the patient according to the VAS scale, it was considered as mild in 215 (71.7%) cases, of which 27 (9%) rated it as 0, 57 as moderate (19%) and 28 as intense (9.3%).

Table 1. *Sample characteristics*

Sample characteristics	n = 300
Characteristics of the patients	
Gender (male/female)	138/162
Median age (median, p25-p75)	54 (45-64)
Weight (median kg, p25-p75)	77.5 (66-89)
Height (median m, p25-p75)	1.64 (1.57-1.70)
BMI (median kg/m^2, p25-p75)	28.39 (25.08-32.52)
History of previous abdominal surgery (n, %)	134 (44.7)
Previous colonoscopy (n, %)	115 (38.3)
Previous or suspected IBS (n, %)	28 (9.3)
Results of the colonoscopy	
Duration of procedure (median min, p25-p75)	23 (18-30)
Procedures which do not reach cecum (n, %)	40 (13.3)
Due to pain	14 (4.7)
Due to bad preparation	9 (3)
Due to technical difficulties	13 (4.3)
Due to stenosis	2 (0.7)
Use of sedatives (n, %)	
Midazolam (mg)	297 (99)
Pethidine (mg)	271 (90.3)
Fentanyl (mcg)	19 (6.3)
Dose of sedatives (median, p25-75)	
Midazolam	2.06 (2-2)
Pethidine	38.48 (25-50)
Fentanyl	23 (7)
Intervention by anesthetist (n, %)	5 (1.7)
Complications associated with sedation-tolerance (n, %)	16 (5.3)
Bradycardia	13 (4.3)
Excessive somnolence	2 (0.6)
Nausea	1 (0.33)

Cecal intubation was achieved in 86.7% of cases. It was not possible to complete the exploration of the cecum due to pain in 14 (4.7%) patients. In five (1.7%) cases, deep sedation by an anesthetist was required, and exploration of the cecum was completed in four of them. Females were associated with a worse tolerance as expressed in a higher score on the VAS scale, 15 (p25-75: 4-43) as opposed to 10.5 for males (p25-75: 3-25, $p < 0.01$). The same was true when the exploration was considered to be difficult by the endoscopist 34.5 (p25-75: 13-73) *vs* 10 (p25-75: 3-22; $p < 0.01$). There was a clear correlation between worse tolerance and a longer exploration time ($r = 0.14$, $p < 0.05$), with greater anxiety prior to exploration ($r = 0.17$, $p < 0.01$), and lower doses of midazolam ($r = -0.13$, $p < 0.05$) and pethidine ($r = -0.16$, $p < 0.01$) (Fig. 1). No association was found with a history of abdominal surgery, the diagnosis of irritable bowel syndrome or colon preparation.

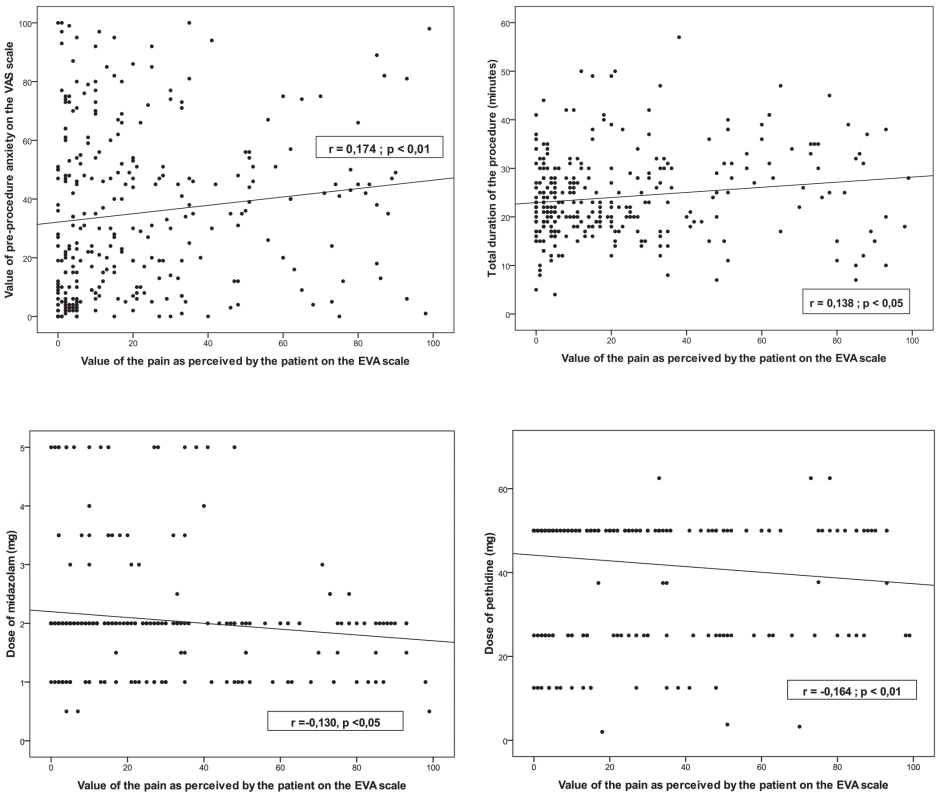

Fig. 1. *Correlation of the values on the VAS scale of the pain as perceived by a patient with pre-colonoscopy anxiety, the duration of exploration and the doses of midazolam and pethidine.*

When the analysis was made taking into account the qualitative assessment of the patient's exploration as good or bad, we observed in the univariate study that women were associated with worse tolerance (20 [12.3%] *vs* 7 [5, 1%], $p < 0.05$). This was reflected in height differences (1.59 *vs* 1.64 m, $p < 0.05$), doses of midazolam (1.63 *vs* 2 mg, $p < 0.05$) and pethidine (36.9 *vs* 43.1 mg, $p < 0.05$), the time of examination (30 *vs* 22 min, $p < 0.05$), the difficulty of colonoscopy (16 [59.3%] *vs* 54 [19.8%], $p < 0.01$) and with the indication for colonoscopy (CRC screening-polyps *vs* other; 9 [5.5%] *vs* 18 [13.1%], $p < 0.05$). There was no relation, however, in terms of weight, BMI, colon cleansing or the degree of anxiety prior to colonoscopy (Table 2). The findings were similar when the result of the patient's VAS was dichotomized at ≤ 30 or > 30. In the multivariate study, including the variables prior to performing the colonoscopy, such as gender, indication for colonoscopy and anxiety prior to exploration, only the indication for the exploration was associated with a poor tolerance (OR 2.78, 1.16-6.68, $p < 0.05$). If we add to this model the variables obtained after the exploration, such as the difficulty of the examination as determined by the endoscopist, the length of time of the examination and the doses of midazolam and pethidine used, it can be observed that the indication (OR 2.92, 95% CI = 1.03-8.2, $p < 0.05$) and the difficulty of the examination (OR 4.68, 95% CI = 1.6-13.6; $p < 0.01$) were the key variables associated with a poor tolerance to colonoscopy (Table 3).

There were certain adverse effects that could be related to excessive or insufficient sedation in 16 (5.3%) cases, all of them mild (Table 1). Among them, 13 cases of bradycardia were detected which were resolved by the use of intravenous atropine or physiological saline infusion. Intense somnolence which required the use of intravenous flumazenil to reverse the effect of benzodiazepine was only observed in two cases. In both instances the doses used were the usual ones according to the established protocol and the patients were not of extreme age.

DISCUSSION

Sedation has become an essential element in improving patient satisfaction when a colonoscopy is performed and to facilitate the diagnostic or therapeutic work of the endoscopist. The level of sedation must be adapted to the procedure to be performed in such a way that the desired objectives are achieved (9). Conscious, moderate or superficial sedation with benzodiazepines and opiates has been the most widely used method for colonoscopy, although there are not many studies analyzing their results (5-7). Recently, in some countries, this has been increasingly replaced by deep sedation with propofol (8).

Sedation with midazolam and opioids achieved good tolerance in most patients who underwent an outpatient colonoscopy in our center. The figures were between 91 and 86.7% of cases according to the subjective assessment of the patient and the doctor respectively. These results are consistent with the few studies that assess tolerance to colonoscopy under conscious sedation with benzodiazepines and opiates. In a meta-analysis including eleven clinical trials in which colonoscopy was performed, the majority under conscious sedation with benzodiazepines

Table 2. *Patient characteristics in terms of tolerance to colonoscopy*

	Good tolerance n = 273 (91%)	Bad tolerance n = 27 (9%)	p value
Females (n, %)	142 (52%)	20 (74.1%)	*0.02*
Age (median age, p25-p75)	54 (45-63.7)	63 (41-70)	0.21
Weight (median kg, p25-p75)	79.5 (67-89)	70 (60-86.5)	0.07
Height (median m, p25-p75)	1.64 (1.58-1.71)	1.59 (1.55-1.62)	*0.05*
BMI (median, p25-p75)	28.4 (25.29-32.4)	28.2 (23.9-33)	0.68
History of abdominal surgery (n, %)	120 (44.1%)	14 (51.9%)	0.44
History of IBS	24 (9.2%)	4 (15.4%)	0.3
Previous colonoscopy	103 (38%)	12 (44%)	0.5
Pain during previous colonoscopy (VAS scale) (median, p25-p75)	17.5 (4-51.5)	43 (14.7-67.2)	0.08
Anxiety prior to colonoscopy (VAS scale) (median, p25-p75)	30 (9-53)	44 (17.5-68.7)	0.07
Indication for colonoscopy: screening or follow-up for polyps	154 (56.4%)	9 (33.3%)	*0.02*
Cecal intubation	246 (90.1%)	14 (51.9%)	*0.01*
Dose of midazolam (media mg, SD)	2-0.8	1.63-0.9	*0.01*
Dose of pethidine (media mg, SD)	43.1-13	36.9-13.8	*0.01*
Total time for procedure (median minutes, p25-p75)	22 (18-28)	30 (9-53)	*0.02*
Difficult procedure according to endoscopist	54 (19.8%)	16 (59.8%)	*0.01*
Deficient preparation of colon	66 (24.7%)	7 (26.9%)	0.8

IMC: body mass index; VAS: visual analog scale; IBS: irritable bowel syndrome.

Table 3. *Multivariate analysis of potential predictors of poor tolerance to ambulatory colonoscopy*

Model 1. Inclusion of variables obtained before procedure			
Variables	**OR**	**IC 95%**	**p value**
Gender	2.2	0.9-5.5	0.09
Previous anxiety	1.0	0.9-1.02	0.19
Indication for colonoscopy	2.78	1.1-6.6	*0.02*
Model 2. Inclusion of variables obtained before and after the procedure			
Variables	**OR**	**IC 95%**	**p value**
Gender	1.19	0.4 -3.4	0.75
Previous anxiety	1	0.99-1.02	0.35
Indication for colonoscopy	2.92	1.03-8.2	*0.04*
Difficulty of procedure	4.68	1.6-13.6	*0.01*
Duration of procedure	1.03	0.9-1.09	0.17
Dose of midazolam	0.5	0.2-1-09	0.08
Dose of pethidine	0.97	0.9-1.0	0.12

and opioids, satisfaction was observed in 89% of cases, with less than 10% reporting pain on examination (21). In a prospective study of a sample of 143 patients, jointly analyzing oral endoscopy and colonoscopy, a telephone survey was conducted 24 hours after the examination, and patients showed satisfaction in 87% of cases (15). In another prospective study of 368 patients analyzing colonoscopy under sedation with midazolam and fentanyl and using the Rex scale to assess pain, it was observed that in 71% of the cases the pain was mild, in 17% it was moderate and only 10% wanted more sedation for future explorations (13). In a retrospective study of 21,763 colonoscopies, with sedation with midazolam and fentanyl administered by an anesthetist, a good tolerance was found in 91.8% of the cases, and according to the endoscopist, in 97.9% of the cases (20). Finally, in a retrospective study with midazolam and fentanyl administered by an endoscopist, a good tolerance was observed in 86.9-88.3% of cases, as assessed by a categorical scale of the pain suffered (22).

There are also studies that analyze tolerance to colonoscopy using a VAS scale, as in our work. In a prospective sample of 510 colonoscopies, Hazeldine et al. observed a good tolerance (VAS < 30) in 87.2% of cases (11). This value is very similar to the study by Schroeber et al., with a satisfaction of 83.9% (23). However, Padmanabhamn et al., in a prospective study of 300 patients per arm comparing propofol *vs* midazolam and fentanyl, observed a better tolerance, amounting to 94%. In this case, it should be noted that sedation was carried out by anesthetists with high doses of midazolam and fentanyl (24). Hayee et al., in a clinical trial comparing fentanyl *vs* meperidine associated with midazolam, with 300 patients per arm, observed a mean value of VAS of 15-17, which was very similar to our findings (25). Finally, Aljebreen et al., in a prospective study involving 270 patients, obtained an average value of 34 (somewhat lower if assessed by the endoscopist, but higher than our findings). This was perhaps caused by initiating sedation with lower doses of midazolam and meperidine (26).

The cecum was successfully reached in 86.7% of the cases, which is comparable to other studies (23,26). When the cases in which the exploration could not be completed for reasons unrelated to sedation were excluded, this figure exceeded 90%, complying with the minimum standard recommended by the ESGE (27).

Side effects were scarce. They occurred in 5.3% of cases and were mild in nature. These results are comparable with others, placing their frequency at 4.4 to 26% (11,22,23). The reason percentages vary depends mainly on whether low blood pressure, either symptomatic or not, is included or not among the side effects. Our study, which was not focused on detecting all possible complications, did not include low blood pressure as a secondary effect, since the recording of arterial blood pressure is only systematically performed in patients with cardiovascular or respiratory disease.

As such, the findings of our study support the recommendations that conscious sedation is adequate for conventional colonoscopies, achieving a good tolerance in the majority of cases (9).

In our study, a worse tolerance to colonoscopy was observed in women, when the indication was different from a screening procedure, or the monitoring of polyps, and when the anxiety was greater prior to the exploration. In addition, the findings were associated with variables dependent on exploration and sedation, such as the difficulty and length of time of exploration and sedatives dosage. There are not many studies that analyze the factors associated with a worse tolerance to colonoscopy, especially in the context of sedation with benzodiazepines and opiates.

Being female was associated with a worse tolerance in our univariate study but not in the multivariate study. This factor has been found in three studies in which sedation with benzodiazepines and opiates was also performed, although only one of them was prospective and focused exclusively on colonoscopies (12,13,20). In other studies, colonoscopy was performed without sedation (26,28). The hypothesis that has been used to explain this worse tolerance in women is based on the anatomy of the pelvis. This could cause the formation of a loop in the colonoscope, resulting in tension in the meso and causing pain. It has also been associated with the colon being of greater length. Both factors may be related to the endoscopist perceiving the colonoscopy to be difficult (29).

Anxiety prior to the procedure correlated with the value of the VAS, but this was not the case in the qualitative or multivariate studies. These findings are consistent with previous research. Causes of pre-colonoscopy anxiety include the waiting time prior to the procedure, fear of pain, possible diagnosis, suffering a complication, embarrassment, or the need to repeat the procedure due to poor preparation (13-15,19,26,28).

The duration of the exploration was also related to levels of pain as shown in other studies (13,14). A longer exploration time could be associated with a greater insufflation of the colon and a loss of effectiveness of the drugs used due to their half-life, and therefore, with a greater sensation of pain. In our study, total doses were assessed but the number of sedative bolus repetitions during the examination was not analyzed. This circumstance should be analyzed in future studies to determine if the lack of repetition of intravenous sedative boluses makes longer explorations more painful.

Reduced tolerance was associated with lower doses of benzodiazepines and opiates, as in the study by Eckardt et al. (13). This is a logical finding since the drugs used have anxiolytic, amnesic and analgesic functions. It has been observed that there is a negative correlation in our study between drug doses and age. However, lower doses have not been related to comorbidities. The clinical guidelines advise a reduction in the dose of benzodiazepines and opiates in these two circumstances, and the findings probably reflect this. Nevertheless, there was no correlation between worse tolerance and older age. Reduced tolerance could also be related to not using repeated boluses of sedatives in longer procedures or by not using higher starting doses, as has been suggested in a recent study (22). Therefore, something which should be studied in greater detail in future research is the reason for using lower doses of sedatives or the need to use higher starting doses, either of which could lead to a change in recommended clinical guidelines (9).

The indication for colonoscopy not related to family screening for CRC or the monitoring of polyps was also associated with lower tolerance. This finding is consistent with those of another study in which the screening colonoscopy is taken as a reference (20). Individuals who undergo screenings or the follow-up of polyps are usually asymptomatic. In other cases there are certain pathologies that can cause pain, such as diarrhea or inflammatory bowel disease, which could also explain the differences.

Finally, another factor associated with worse tolerance in our study was the endoscopist's subjective assessment of a difficult exploration. This perception was also considered as being associated with worse tolerance in a retrospective study, in an indirect way, taking into account the need for increased sedation rather than the VAS assessment (18). There is no established definition of a difficult colonoscopy. From a subjective point of view, an endoscopist could assess an exploration as being difficult in a number of different circumstances. These could include the presence of rigid or acute angles, the formation of loops due to the existence of a lax meso column, a redundant colon, weakly muscled abdominal walls, the need to change the patient's posture or press on the abdominal wall, or the need to rectify the colonoscope repeatedly. All of these situations would usually result in cecal intubation taking longer. Takahasi et al. defined this as an intervention in which cecal intubation takes more than 16 minutes (30). Therefore, although this could be an important factor in the prediction of pain, it has the disadvantage of being a feature that is only discovered when the endoscopy is taking place and, therefore, it does not serve as a way of selecting patients for deeper sedation before the exploration itself.

In terms of the limitations of the study, it is worth mentioning its unicentric nature. This makes its extension to other environments with different demographic or socio-cultural characteristics difficult. Nevertheless, the findings are consistent with other studies conducted in other countries. It is also a study with a large sample which uses a multivariate method to avoid possible biases.

Another limitation is that pain assessment was made, based on the subjective assessment of the patient, as good and bad and by means of a VAS scale. No differences were found in the factors associated with a worse tolerance between using the subjective evaluation, good or bad, compared to a rating of VAS < 30 (mild) or higher. It must be borne in mind that the perception of pain is subjective and that the VAS scale is among the most widespread methods for assessing pain in multiple clinical contexts. In fact, this method has been used in other studies and we consider it to be more appropriate than indirect measures, such as total doses of drugs, since the use of these depends on the decision of the doctor performing the sedation. We also believe that the VAS assessment should be that of the patients themselves. As we observed in our study, although there is a significant correlation between the assessment of pain by the patient and that of the doctor and nurse, and it is closer than that reported in another paper, it remains only moderate (25). Another possible limitation is the moment in which pain assessment is carried out. The best time to make the evaluation has not been proven. In some studies it has taken place during the exploration; in others, at the end of the exploration; in others, at the time of discharge from hospital; and in others, a few days later (12-15,25,31). When satisfaction surveys have been carried in the place of exploration, they offer more positive results than when sent a few days later, suggesting that the presence of endoscopy personnel may well influence the answers provided by the patients (31). Given the variability in the method and timing of pain assessment, it would be interesting to develop recommendations from endoscopy societies. It would also be interesting to design studies to assess the validity of specific surveys of pain assessment and the degree of patient satisfaction with the colonoscopy procedure.

Despite the various limitations, we consider that this prospective study with a significant number of patients provides interesting findings concerning this form of sedation for outpatient colonoscopy, which is so widespread worldwide.

In conclusion, conscious sedation with benzodiazepines and opiates in our context when performing an ambulatory colonoscopy achieved good tolerance in the majority of patients, with few side effects and an adequate rate of cecal intubation. Therefore, our findings support the recommendations made by scientific societies that superficial sedation is adequate for routine colonoscopies.

Pre-procedure anxiety, being female and indication for colonoscopy are prior factors that may be associated with worse tolerance. The doses of sedatives used, the length of time of the process and the difficulty of any given colonoscopy are intraprocedural factors that are also associated with worse tolerance. These circumstances are important in adapting sedation to the needs of patients, although it has not been possible to develop a prediction model that allows patients to be selected for deep sedation. For this reason, more studies concerning this issue would be advisable. They should be multicentric in nature and use standardized methods of pain assessment, especially in those countries in which deep sedation with propofol has economic or legal limitations.

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