Randomized clinical trial of Entonox® versus midazolam–fentanyl sedation for colonoscopy

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Background: Intravenous sedation for colonoscopy is associated with cardiorespiratory complications and delayed recovery. The aim of this randomized clinical trial was to compare the efficacy of Entonox® (50 per cent nitrous oxide and 50 per cent oxygen) and intravenous sedation using midazolam–fentanyl for colonoscopy.

Methods: Some 131 patients undergoing elective colonoscopy were included. Patients completed a Hospital Anxiety and Depression questionnaire, letter cancellation tests and pain scores on a 100-mm visual analogue scale before, immediately after the procedure and at discharge. They also completed a satisfaction survey at discharge and 24 h after the procedure.

Results: Sixty-five patients were randomized to receive Entonox® and 66 to midazolam–fentanyl. Completion rates were similar (94 versus 92 per cent respectively; P = 0.513). Patients receiving Entonox® had a shorter time to discharge. They reported significantly less pain (mean score 16.7 versus 40.1; P < 0.001), and showed better recovery of psychomotor function immediately after the procedure and at discharge. Patient satisfaction was higher among patients who received Entonox® (median score 96 versus 89; P = 0.001).

Conclusion: Entonox® provides better pain relief and faster recovery than midazolam–fentanyl and so is more effective for colonoscopy. Registration number: ISRCTN81142957 (http://www.controlled-trials.com).


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Introduction

Colonoscopy is considered to be the ‘gold standard’ investigation for the assessment of colorectal disorders and is one of the most frequently performed procedures in modern medicine. With screening programmes shown to reduce mortality from colorectal cancer, and their subsequent introduction in the USA and the UK, referrals for colonoscopy have increased. At the same time, there is increasing awareness among the general population that colorectal symptoms require investigation.

A prerequisite for successful colonoscopy is good analgesia and sedation during the procedure. Pain and vasovagal reactions are common, necessitating the administration of analgesic and sedative agents. Colonoscopy is now performed on an outpatient basis and the analgesia and sedation used must ensure comfort and safety, as well as a rapid recovery of function so that the patient is fully alert at discharge.

Colonoscopy is generally performed with the patient sedated using a combination of benzodiazepines and an opioid, mostly midazolam and fentanyl or pethidine (meperidine). Although such intravenous sedation provides varying degrees of pain relief, it is associated with a small but definite risk of cardiopulmonary complications of 0.1–0.54 per cent, and a mortality rate of 0.03 per cent. Oxygen desaturation seems in part to be due to medication, even when an attempt is made to titrate the dose.
Patient-controlled nitrous oxide mixed with oxygen (50:50; Entonox®, BOC Gases, Guildford, UK) has been shown to be effective and safe13, even under adverse cardiac conditions. This weak inhalation anaesthetic agent has anaesthetic, sedative and anxiolytic properties. Entonox® has a low blood/gas solubility ratio, and therefore has a fast onset and clearance time. It is used to alleviate pain in dental treatment, in ambulatory care including ischaemic heart disease, and during prolonged labour.

The aim of this randomized clinical trial was to evaluate the role of Entonox® as an sedative–analgesic in colonoscopy compared with intravenous midazolam–fentanyl, in terms of analgesic efficacy, depth of sedation, rate of complications, recovery of psychomotor function and time to discharge.

Methods

This trial was performed in the endoscopy unit at Castle Hill Hospital, Cottingham, UK, between April 2005 and March 2006. The study was approved by the South Humber Research Ethics Committee and the Clinical Trials Unit, Medicines and Health Regulatory Authority, and was preregistered with the European Clinical Trials Database (EudraCT number 2004-004890-26) and the International Standard Randomised Controlled Trial Number Register (ISRCTN81142957). It was undertaken according to International Conference on Harmonization good clinical practice standards, including on-site monitoring and source data verification.

All patients undergoing elective colonoscopy were invited to participate in the trial. They received detailed information leaflets about the trial 2 weeks before the procedure, and also had an opportunity to discuss the trial with the coordinator. Informed written consent was obtained from all patients before randomization. Patients with a history of pneumothorax or severe bronchial asthma, previous colonic resection, intolerance to any of the drugs, those undergoing upper gastrointestinal endoscopy and colonoscopy simultaneously, and those taking opiates were excluded from the study.

Randomization and allocation concealment

Block randomization was used, with stratification based on the types of endoscopist: doctors, nurse colonoscopists and non-medical non-nurse colonoscopists (also known as non-medical colonoscopists). A block size of six was used to help concealment of allocation. The assignments were held in sequentially numbered, opaque sealed envelopes. The envelopes were opened sequentially and only after the participant’s name, address, date of birth and other details had been written on the appropriate envelope at a central location, by a person unrelated to the trial. Neither the patients nor the colonoscopists were blinded to the treatment modality.

Interventions

Patients were randomly assigned to receive either intravenous midazolam (2 mg/ml; Hypnovel®, Roche, Welwyn Garden City, UK) and fentanyl (0.05 mg/ml; Sublimaze®, Janssen-Cilag, High Wycombe, UK) or inhaled Entonox®. They were informed about the relevant procedure, the reasons for sedation and the technique.

Patients randomized to intravenous sedation received 0.075–0.1 mg fentanyl, followed by 1-mg incremental doses of midazolam (2 mg/ml) up to a maximum of 10 mg. All patients received supplemental oxygen at the rate of 2–3 l/min during the procedure. Colonoscopy was performed 5 min after the last dose of midazolam. The colonoscopist was allowed to give further doses of midazolam, if warranted, throughout the procedure.

Those randomized to Entonox® inhaled the gas through a mouthpiece for a full 120 s initially, for a further period until the caecum was reached, and as required thereafter. If the patient found the procedure too uncomfortable or the colonoscopist judged that the patient was in discomfort, intravenous sedation was given, but only after a washout of 4–5 min.

All patients were assessed continuously throughout the procedure, in accordance with the guidelines of the British Society of Gastroenterology14. The aim of conscious sedation was that the patient should be able to obey commands at all times. Patients were allowed to recover after procedure and discharged by recovery room nursing staff according to pre-existing discharge criteria.

Colonoscopy

All colonoscopies were performed according to a standard operating procedure with Pentax video colonoscopes (Pentax, Hamburg, Germany). Colonoscopy was carried out by three different types of colonoscopist: doctors (colorectal consultants), senior nurses with experience of more than 5000 colonoscopies and non-medical colonoscopists. Completion to the caecum was documented based on two of three landmarks: the ileocaecal valve, the appendicular orifice and/or the triradiate fold.
Data collection

Demographic and clinical features recorded for all patients included age, sex, weight, height, clinical indications, past and family history, results and procedural findings.

All participants completed a Hospital Anxiety and Depression questionnaire, baseline letter cancellation test and scored pain on a 100-mm visual analogue scale before randomization, but after giving consent to be included in the trial. Patients who refused to participate were asked their reasons for doing so, such as past experience with any of the drugs or frightened by the idea of deciding own sedation. These patients also completed questionnaires before and after the procedure.

The primary endpoint was the degree of pain experienced by the patient during the procedure assessed on a 100-mm visual analogue scale (VAS). Measurements were taken immediately and at 15-min intervals after the procedure until discharge. Patients also marked a VAS at 24 h after colonoscopy after allowing recovery from sedation.

Secondary endpoints included degree of sedation, patient, nurse and endoscopist satisfaction, complication rate, time to reach the caecum and total colonoscopy time, completion rate, degree of psychomotor recovery and time to discharge.

The degree of sedation was measured on the Modified Observer’s Assessment of Alertness/Sedation Scale (MOAAS)\(^ {15,16} \), at 1-min intervals throughout the procedure and at 5-min intervals during recovery.

Patient satisfaction was measured at discharge and 24 h after colonoscopy by means of a 100-mm VAS, which was incorporated into a previously validated patient satisfaction questionnaire for colonoscopy\(^ {17} \). Nurse and endoscopist satisfaction was measured using a similar 100-mm VAS, as part of a different questionnaire.

Psychometric tests were administered immediately upon arrival of the patient in the recovery area and then at 15-min intervals until discharge. Inability of the patient to perform the tests immediately on return to the recovery room was noted. Psychomotor recovery was assessed using the letter cancellation test\(^ {18} \), which measures concentration and perception. The patient was presented with a sheet of paper containing a printed paragraph of 20 rows of 40 randomly arranged letters, and then asked to read from left to right and top to bottom, simultaneously marking through all the occurrences of a predesignated letter. The number of lines completed in 120 s and the number of times the predesignated letter was correctly identified were recorded. Postprocedure scores were compared with baseline values and results presented as percentage recovery of psychomotor function. This test has been shown to be an accurate means of measuring psychomotor recovery in the postendoscopy setting\(^ {18,19} \).

The efficacy of sedation was evaluated by endoscopists in terms of the rate of caecal intubation, time taken to reach the caecum, total colonoscopy time and complication rate. The colonoscopists also completed a questionnaire concerning the degree of sedation, difficulty of colonoscopy and difficulty in manoeuvring the patient. After the procedure the attending nurses completed a questionnaire for each colonoscopy concerning the perceived adequacy of sedation, ability of the patient to assist with moving during the procedure, and maximum depth of sedation.

Statistical analysis

The required sample size was estimated from the results of a pilot study in which the degree of pain experienced by 20 patients undergoing colonoscopy under Entonox\(^ {®} \) or intravenous midazolam–fentanyl sedation (10 patients in each group) was measured on a VAS. Using a power of 80 per cent and a two-sided level of significance of 0.05 (based on a Wilcoxon–Mann–Whitney statistic appropriate for a two-group comparison), it was calculated that a total sample size of 120 would be required to determine a difference of 15 points on a 100-mm VAS between groups. The 20 patients in the pilot study were not included in the final analysis for the randomized trial.

All analyses followed the intention-to-treat principle. No interim analyses were performed before analysis of the primary endpoint. Demographic and baseline characteristics were compared by means of two-way ANOVA for continuous data and Fisher’s exact test for categorical data. Differences in proportions were tested using the \( \chi^2 \) test or Fisher’s exact test for smaller samples. VAS scores, sedation scores, postoperative time to discharge and results of the letter cancellation test were evaluated using the Mann–Whitney \( U \) test. All \( P \) values are two tailed.

Results

Of a total of 176 patients assessed for eligibility, 45 were excluded (Fig. 1) because 13 were ineligible (seven had undergone surgical resection, two had a combined upper and lower gastrointestinal endoscopy, and four had severe asthma) and 32 patients refused to participate (20 patients did not want to participate in any trial as they were too anxious, and the remainder had inhaled Entonox\(^ {®} \) in the past and were not happy to participate). The remaining 131 patients were included in the trial, of whom 65

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Allocated to Entonox® n = 65
Received Entonox® n = 65

Allocated to midazolam–fentanyl n = 66
Received midazolam–fentanyl n = 66

Assessed for eligibility
n = 176

Excluded n = 45
Did not meet inclusion criteria n = 13
Refused to participate n = 32

Randomized
n = 131

Analysed n = 65

Analysed n = 66

Fig. 1 Flow chart of patients in randomized clinical trial

Table 1 Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Entonox® (n = 65)</th>
<th>Midazolam–fentanyl (n = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex ratio (M:F)</td>
<td>29 : 36</td>
<td>34 : 32</td>
</tr>
<tr>
<td>Median (range) age (years)</td>
<td>56 (39–70)</td>
<td>60 (41–69)</td>
</tr>
<tr>
<td>ASA grade</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>53</td>
<td>55</td>
</tr>
<tr>
<td>2</td>
<td>12</td>
<td>11</td>
</tr>
<tr>
<td>Median (range) preprocedure anxiety score</td>
<td>7.5 (3–10)</td>
<td>6.0 (2–12)</td>
</tr>
</tbody>
</table>

ASA, American Society of Anesthesiologists.

were randomized to receive Entonox® and 66 intravenous sedation with midazolam–fentanyl.

The two groups had similar demographic characteristics and American Society of Anesthesiologists grades, and there was no difference in preprocedure anxiety scores (7.5 (range 3–10) versus 6.0 (range 2–12); P = 0.143) (Table 1).

Indications for colonoscopy included symptoms (79 patients), family history (28) and follow-up (24). Colonoscopy findings included colorectal cancer (five), polyps (26), normal (53) and other pathology (47).

Median doses of midazolam and fentanyl were 4 (range 3–5) mg and 0.1 (range 0.05–0.1) mg respectively. There were no complications in either group, although one patient in the intravenous group complained of nausea which settled spontaneously. None of patients in the Entonox® group required additional sedation or conversion to intravenous sedation.

Twenty-one patients had undergone colonoscopy previously and another 11 had had flexible sigmoidoscopy. Of the former 21 patients, 19 had received midazolam with fentanyl or pethidine, whereas two had received pethidine only. Nine of these patients were randomized to Entonox® in the present trial and found the current sedation better. The remaining 12 patients received intravenous sedation during this study, of whom six found the current regimen better, two described no difference and the remaining four thought the current regimen was worse.

Pain

Patients in the Entonox® group recalled significantly less pain during colonoscopy than those receiving midazolam–fentanyl (mean VAS score 16.7 versus 40.1; P = 0.001; 95 per cent confidence interval (c.i.) of the difference 21.5 to 29.1). These differences persisted at different points after the procedure and also after 24 h (Table 2).

Depth of sedation

The median depth of sedation measured using the MOAAS was 4 (range 4–5) and 3 (range 3–4) in patients
recovery in the intravenous sedation group could not be immediately upon return to the recovery area, whereas 89—the easiest, and 100—the most difficult ever seen—50 is very difficult. Values in parentheses are ranges, *Mann–Whitney U test.

Intubation rates and completion time

Caecal intubation rates were 94 and 92 per cent respectively (P = 0.513). Two patients in the Entonox® group had an impassable stricture/cancer, one had poor bowel preparation and in another patient it was not technically possible to complete the colonoscopy beyond the hepatic flexure. In the intravenous sedation group, three patients had poor bowel preparation, one patient had a technically difficult colon and one patient had a distally obstructing cancer. There was no difference between the groups in time to reach the caecum or total completion time (Table 3).

Psychomotor recovery and time to discharge

Patients in the Entonox® group had recovered 92–2 (range 89.5–96.0) per cent of their baseline psychomotor function immediately upon return to the recovery area, whereas recovery in the intravenous sedation group could not be calculated as most patients were unable to answer the letter cancellation test due to the effects of sedation. Values at 15 min after the procedure were 94 (range 92.5–100) and 68 (range 60.8–71.1) per cent respectively. At the time of discharge, significant differences remained and psychomotor function had fully recovered only in the Entonox® group (Table 4). Patients undergoing colonoscopy under intravenous sedation had a longer time to discharge.

Patients’ assessment

All patients completed the satisfaction questionnaire before being given their results so that the colonoscopy findings did not affect the satisfaction scores. The median satisfaction score was significantly higher in patients who received Entonox® (96 versus 89; P = 0.024; 95 per cent c.i. of the difference 4 to 12) (Table 3). These differences persisted when patient satisfaction was assessed 24 h after the procedure. More patients in the Entonox® group would agree to a repeat colonoscopy under the same sedation (89 versus 73 per cent; P = 0.011. Sixty per cent of patients

### Table 2 Pain scores on visual analogue scale

<table>
<thead>
<tr>
<th></th>
<th>Entonox® (n = 65)</th>
<th>Midazolam–fentanyl (n = 66)</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>16.5 (0–24)</td>
<td>39.6 (18–91)</td>
<td>0.001</td>
</tr>
<tr>
<td>30 min</td>
<td>16.6 (0–24)</td>
<td>40.0 (18–91)</td>
<td>0.001</td>
</tr>
<tr>
<td>At discharge</td>
<td>16.7 (0–25)</td>
<td>40.1 (18–92)</td>
<td>0.001</td>
</tr>
<tr>
<td>24 h after procedure</td>
<td>15.0 (0–25)</td>
<td>38.1 (15–94)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values in parentheses are ranges. *Mann–Whitney U test.

### Table 3 Patients’, endoscopists’ and nurses’ assessments

<table>
<thead>
<tr>
<th></th>
<th>Entonox® (n = 65)</th>
<th>Midazolam–fentanyl (n = 66)</th>
<th>P§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients’ assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median satisfaction score†</td>
<td>96 (90–100)</td>
<td>89 (20–95)</td>
<td>0.001</td>
</tr>
<tr>
<td>Agree to repeat use of same sedation*</td>
<td>58 (89)</td>
<td>48 (73)</td>
<td>0.011†</td>
</tr>
<tr>
<td>Endoscopists’ assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caecal intubation*</td>
<td>61 (94)</td>
<td>61 (92)</td>
<td>0.513‡</td>
</tr>
<tr>
<td>Median time to reach caecum (min)</td>
<td>18 (6–24)</td>
<td>20 (5–23)</td>
<td>0.812</td>
</tr>
<tr>
<td>Median completion time (min)</td>
<td>26.5 (18.0–47.5)</td>
<td>31.9 (20.4–51.8)</td>
<td>0.761</td>
</tr>
<tr>
<td>Median difficulty of colonoscopy‡</td>
<td>17 (10–31)</td>
<td>14 (12–30)</td>
<td>0.714</td>
</tr>
<tr>
<td>Median satisfaction score†</td>
<td>95 (90–100)</td>
<td>90 (70–100)</td>
<td>0.061</td>
</tr>
<tr>
<td>Nurses’ assessment</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median satisfaction score†</td>
<td>95 (30–100)</td>
<td>90 (20–100)</td>
<td>0.168</td>
</tr>
<tr>
<td>Adequate sedation–analgesia*</td>
<td>56 (86)</td>
<td>50 (76)</td>
<td>0.013</td>
</tr>
<tr>
<td>Difficulty in manoeuvring*</td>
<td>3 (5)</td>
<td>14 (21)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Values in parentheses are ranges, except *Values are percentages. †On a 100-mm visual analogue scale. ‡On a 100-mm visual analogue scale, where 0 is the easiest, and 100 the most difficult ever seen—50 is very difficult. §Mann–Whitney U test, except ‡‡ test.
who received Entonox® reported requiring additional sleep compared with 95 per cent of those who had intravenous sedation ($P = 0.032$). Median time to return to normal activities after the procedure was 1.5 (1–4) h and 9.5 (8–12) h respectively ($P = 0.011$).

**Endoscopists’ assessment**

The endoscopists assessed the technical difficulty of procedures carried out with the two types of sedative. Median scores for difficulty were similar, as were satisfaction scores for sedation (Table 3). Analysis of the endoscopists’ perception of difficulty in manoeuvring patients during colonoscopy showed that more patients sedated with midazolam–fentanyl were difficult to move.

**Nurses’ assessment**

There was no difference in nurses’ assessment of satisfaction with either type of sedation (Table 3). Only three patients in the Entonox® group were difficult to manoeuvre during the procedure compared with 14 patients in the intravenous sedation group.

**Effect of type of colonoscopist**

Subgroup analysis revealed no differences between the three types of colonoscopist in terms of time to reach the caecum, completion and complications rates, sedation or pain scores, patient or nurse satisfaction, and recovery times.

**Discussion**

This randomized clinical trial has shown that sedation with Entonox® is effective for colonoscopy. Both diagnostic and therapeutic procedures were performed efficiently, with a high completion rate and no complications. Patients experienced less pain and discomfort, recovered earlier from sedation and were discharged home faster than those given intravenous sedation. Use of Entonox® was also associated with higher patient, endoscopist and nurse satisfaction scores.

Colonoscopy can be uncomfortable, necessitating the administration of analgesics and sedatives. The commonly used benzodiazepine–opioid combination can cause cardiorespiratory depression and occasionally death, especially in elderly patients. An important reason for this is lack of a clear dosing regimen and difficulty in dose titration. As intravenous sedation causes cardiorespiratory depression, the alternative would be to use brief analgesia (with sedation) that offers fast recovery without risk of complications. Entonox® clearly seems to fit the bill. It is effective and easy to administer; the patient inhales through a special mouthpiece attached to a cylinder and this obviates the need to administer additional oxygen through a different nasal cannula. The onset of action is rapid and the effect is apparent within 1–2 min. Patients tend to become slightly drowsy, but remarkably more relaxed in the initial 2 min, which contributes to pain relief.

The primary outcome measured in this study was pain perceived by the patient, which was assessed at different times after the procedure. Measurement of pain after 24 h is important as the effects of sedation are minimized by then. Pain perception at 24 h also influences the patient’s decision to attend for repeat colonoscopy if necessary.

There were no complications in either group. There is virtually no risk of overdose with Entonox® as the patient’s level of consciousness governs his or her ability to maintain the flow of gas. There is no risk of inhalation of the gas by colonoscopy staff, as it flows through a one-way valve and does not leak into the environment.

The total procedure time was similar in both groups. However, psychomotor function recovered more rapidly in patients sedated with Entonox®, owing to rapid elimination of the gas from the body, usually within 30–45 s after stopping inhalation. These patients were discharged earlier and were able to return to routine activities more quickly than those receiving intravenous sedation. Potentially, with 100 per cent recovery of psychomotor function after the use of Entonox®, as also noted previously, there is no apparent reason why patients should not drive home immediately after discharge. However, the manufacturer’s recommendations require patients to stop driving for 12 h after a procedure.

Colonoscopy is considered to be one of the biggest constraints to achieving the current UK targets (National Health Service targets) for treatment of colorectal cancer, primarily owing to long waiting lists. Sedation is the major factor that keeps the patient in the recovery area after a colonoscopy. Vargo and colleagues have shown that the practice efficiency for colonoscopy can be improved, in terms of both number of procedures and cost effectiveness, if recovery is faster than achieved with conventional intravenous sedation. Although the present study demonstrated faster recovery with Entonox®, the issue of colonoscopy turnover was not addressed specifically.

Patient satisfaction is another area where current practice is suboptimal and use of Entonox® also addresses this issue. Higher patient satisfaction with Entonox® was related to the reduced pain and faster recovery.
Entonox® sedation is essentially patient controlled and this probably contributed to greater patient satisfaction as well. Inhalation of the gas as necessary, with longer and deeper breaths allowing greater volumes in the lungs, not only helps in relieving discomfort and pain, but alleviates anxiety as the patient is in control of their own pain relief. Currently, there is a low uptake of colorectal cancer screening by patients in the USA. It is therefore essential to optimize the experience of colonoscopy, by minimizing discomfort and allowing early resumption of normal activities. This will lead to an increase in the number of patients willing to undergo the procedure for screening.

The present results differed from previous studies on the use of Entonox® for colonoscopy in that Entonox® was shown to be superior to intravenous agents. The dose of midazolam used in this trial (median 4 mg) was comparable to that used in previous studies. Forbes and Collins used a median of 4.7 mg midazolam, but still concluded that intravenous sedation was better than Entonox®. Importantly, the doses of midazolam in the participant and non-participant groups in our study were similar, hence confirming the absence of any bias.

A limitation of this study is that the patients and endoscopists were not blinded to the type of sedation. Even though it has been shown previously that the noise made by Entonox® cylinders can be masked, the pilot study demonstrated that this is difficult to achieve. However, even without blinding, it was possible to address the issues of whether Entonox® is able to provide sufficient sedation—analgesia and whether it could be adopted in a busy endoscopic unit. None of the endoscopists had previously used Entonox® for sedation, and this should reduce any bias. Furthermore, the person collecting the data was blinded to the treatment offered. Another limitation of the trial is that the primary outcome was measured using a VAS, as no absolute pain scoring systems are available for colonoscopy. However, it was possible to compare VAS scores between the two groups, and to establish that Entonox® was associated with less pain. Baseline scores were also collected to determine whether patients were already in pain before the procedure.

An agent with shorter duration of action would be desirable for providing sedation in colonoscopy, one that permits more rapid recovery of function, while providing good patient comfort during the procedure and with a safety profile equivalent to that of medications currently in use. The authors believe that Entonox® offers all these benefits and can potentially replace intravenous sedation for all routine colonoscopies.

**Acknowledgements**

The authors declare no conflict of interest.

**References**

15. Chernik DA, Gillings D, Laine H, Hendler J, Silver JM, Davidson AB et al. Validity and reliability of the Observer’s Assessment of Alertness/Sedation Scale: study with...