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CLINICAL TRIAL REPORT

Safety and Effectiveness of Electroacupuncture During Colon Endoscopic Submucosal Dissection: A Randomized Controlled Trial

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Background: Endoscopic treatment of early colon neoplasms has evolved as a valid and less traumatic alternative to surgical resection. It can usually be performed with sedation on an outpatient basis. The present study was performed to determine the safety and effectiveness of electroacupuncture (EA) versus propofol sedation during endoscopic submucosal dissection (ESD) for early colon neoplasm.

Methods: A total of 150 adult outpatients undergoing ESD were selected and divided into the EA combined with propofol group (EP group), remifentanil combined with propofol group (RP group), and propofol group (SP group), with 50 patients in each group. All patients received standard sedation with propofol. Acupuncture was performed before intravenous propofol injection in the EP group. A density wave of 1–3 mA, 2/100 hz current was administered for 20 min before the induction of anesthesia. The effectiveness of sedation was measured by satisfaction levels, and pain and sedation scores were measured by questionnaires. Respiratory and hemodynamic complications were monitored and compared as indices of safety.

Results: Demographic data were comparable among the three groups. The total dose of propofol and the percentage of body movement in the EP group were lower than in the SP and RP groups ($P<0.01$). The incidence of hypotension and bradycardia in the SP and RP groups was higher than in the EP group. Patients who received the EA intervention showed a significant reduction in hypoxemia. The endoscopists felt that the procedure was more favorable in the EP group, but, there was no significant difference of patient satisfaction scores among three groups.

Conclusion: Sedation with EA is effective and safe for patients undergoing ESD, and could improve the satisfaction levels of patients and gastroendoscopists.

Keywords: electroacupuncture, endoscopic submucosal dissection, propofol, remifentanil

Introduction

Endoscopic submucosal dissection (ESD) is used in many hospitals as the acknowledged treatment for early intestinal cancer. Although enormous developments have been made in digestive endoscopy, ESD remains a time-consuming procedure, which demands good technique.[1,2] It is well known that it often causes the patient greater and longer discomfort and pain compared to other endoscopic procedures.[3] Therefore, it is extremely important to reduce the pain and discomfort deriving from ESD. Intravenous medication is used as standard practice to achieve a satisfactory level of quietness and cooperation during the ESD procedure. Although standard sedation methods for ESD are not established, most ESD procedures are performed under intravenous sedation with propofol. However, many studies have reported that the use of sedative and analgesic drugs can increase costs and cause adverse events in the process of ESD.[4,5]

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Propofol is a potent intravenous sedative that has been widely used in endoscopic procedures. It has eminent sedative and analgesic effects, and is associated with having a shorter recovery time and being fast acting.[6,7] It has been proved to be superior to benzodiazepines for gastroenteroscopy and operations. The main disadvantage of propofol is the risk of a rapid change from conscious to deep sedation with consecutive cardiorespiratory depression, especially in combination with an opioid or a benzodiazepine.[8] Previous research has also demonstrated that it has a dose-dependent inhibitory effect on the patient's circulatory and respiratory functions, which is always a concern for anesthesiologists.[9] However, it is difficult to control the depth of sedation and to inhibit unconscious body movements caused by the stress reaction to repeated drawing of the colonoscopy tube, which may affect the operation of ESD.[10] Therefore, it is important to reduce the necessary dosage of propofol and its associated risks, while retaining a satisfactory level of sedation for the endoscopist.

Acupuncture, a traditional Chinese medicine (TCM) therapeutic technique carried out with the aid of percutaneous thin needles, has been used to modulate homeostasis and treat many diseases by dredging the meridian or meridians.[11–13] In recent years, acupuncture has also been used more widely as a complementary medical treatment for various indications, such as pain, and postoperative nausea and vomiting (PONV).[14,15] Many studies have demonstrated that it can result in dorsal horn inhibition and stimulate the release of opioids. Acupuncture could decrease the need for sedative medication, which could reduce the use of narcotics, thus lowering the risk of respiratory and hemodynamic events during colonoscopies and facilitating the recovery of intestinal function.[16,17]

Electroacupuncture (EA) is an electrically driven acupuncture procedure using two needles, in which the stimulation frequency and intensity can be regulated, which facilitates the standardization of acupuncture and provides better analgesia compared with manual acupuncture. One of its advantages in clinical practice is that its stimulation frequency and intensity can be regulated according to the actual situation. Previous research has suggested that it can alleviate pain more effectively than pure acupuncture.[18] These results have been attributed to the ability of EA to block pain by activating a variety of bioactive chemicals. In addition, previous studies have demonstrated that EA can reduce discomfort, stress responses, and pain during barostat-induced rectal distension.[19,20] In particular, EA could reduce rectal distension-induced discomfort during colonoscopies. Therefore, EA could be used as an addition to routinely used sedation or anesthesia schemes, even in conventional clinical anesthesia. However, the sedative effect and safety of EA during ESD have not yet been verified. Accordingly, this study was carried out to investigate the safety and efficacy of EA as an analgesic and sedative approach for ESD. A discussion of recent randomized controlled studies is also incorporated in the report.

Methods

In the current study, a single-center randomized parallel trial was conducted. Enrollment started in July 2022 and follow-up was completed in August 2024. The study protocol conforms to the Consolidated Standards of Reporting Trials (CONSORT)[21] and Standards for Reporting Interventions in Clinical Trials of Acupuncture (STRICTA).[22] Written informed consent was obtained from all study participants before inclusion. This study was approved by the Second Affiliated Hospital of Nanjing University of Chinese Medicine's Institutional Review Board (IRB #201804001) and complied with the Declaration of Helsinki. The trial was registered, before patient enrollment, at the Chinese Clinical Trial Register: chictr.org.cn (ChiCTR2200061998).

Sample Size Calculation

Sample size was calculated by Pass software version 15.0 (NCSS, Kaysville, UT, USA), based on data from previous studies and preliminary experiments on sedation. Using a two-tailed test, a power of 0.90 and α=0.05, about 20%, were needed. Considering a dropout rate of 10%, the estimated sample size was at least 50 patients in each group; thus, a total of 150 patients were randomized.

Participant Eligibility

Participants were recruited through advertisements in local newspapers, social media, and hospital websites. In total, 150 participants of any gender were randomly allocated for elective general anesthesia in a 1:1:1 ratio, examined by the trial

investigators, and screened for eligibility at the Second Affiliated Hospital of Nanjing University of Chinese Medicine. All EA treatments and ESD procedures were performed at this hospital. Random numbers for allocation concealment were generated using SAS software (version 9.4; SAS Institute Inc., Cary, NC, USA), and sealed in corresponding envelopes. The practitioner, who was not associated with the study, allocated the participants according to the sealed opaque envelopes, after they had signed the informed consent form. Exclusion criteria were: 1) history of colectomy; 2) history of bowel stenosis; 3) history of neuropsychiatric disease; 4) refusal to participate; 5) history of severe heart, liver, kidney, or lung disease, 6) history of allergy to narcotic drugs; and 7) refusing sedation.

Allocation and Blinding

Patients were allocated randomly into three groups: electroacupuncture combined with propofol group (EP group), remifentanil combined with propofol group (RP group), and propofol group (SP group). All three groups would receive standard sedation with propofol/remifentanil. Patients and observers were blind to the patient's assigned group and drug treatments. The nurse and endoscopist were blind to the drug intervention program. Outcomes of the study were assessed by experimenters who were not involved in the intervention procedure. Inclusion criteria were: 1) aged 25–65 years; 2) American Society of Anesthesiologists (ASA) class I–II; and (3) body mass index (BMI) 19–27 kg/m^2.

Interventions

The patients underwent routine intestinal preparation, water prohibition, and fasting for 6 hours. After arrival at the examination room, non-invasive blood pressure (NIBP), heart rate (HR), and blood oxygen saturation (SpO_2) were monitored routinely, and routine oxygen was administered through a nasal catheter or face masks at a rate of 2–3 L/min. A venous channel was established in the wrist vein with a 20 G intravenous trocar. Each group received sedation with propofol using a target controlled infusion (TCI) system, which uses a weight- and age-adapted algorithm to obtain a preset plasma target level of propofol. Remifentanil was prepared as a 40 μg/mL solution and administered as 0.1 mg/kg/min continuous intravenous infusions to the patients in the RP group. The target sedation level was measured by the Observer's Assessment of Alertness/Sedation (OAA/S) Scale, with the aim of maintaining a score <3, which means lethargy, ie, patients responded if their name was called loudly and/or repeatedly. If the OAA/S score was ≥4, 0.5 mg/kg propofol was added to step up the TCI. Zusanli (Figure 1A), Sanyinjiao (Figure 1B), Neiguan (Figure 1C), and Hegu (Figure 1D) acupoints of patients in the EP group were confirmed as the positive poles. Then, 0.35 mm × 40 mm acupuncture needles were selected and connected to EA instruments (KWD-808I). The skin at each acupuncture point was disinfected with alcohol and dried. Then, the acupuncture needle was inserted and fixed. Manual manipulation, such as rotation or lifting, was used to induce the Deqi sensation (soreness, pain, swelling, heaviness, or numbness). The needles in each point were connected to EA instruments (KWD-808I), producing electrical stimulation with a sparse and dense pattern at a frequency of 2/100 hz.

The intensity of the continuous electrical current was regulated from 0.1 to 1 mA, according to the level that the patient could tolerate, 20 min before anesthesia induction. Similarly, patients were administered 1 μg/kg remifentanil before propofol TCI was started. The colonoscope was inserted after the eyelash reflex disappeared and following muscle relaxation. If the patient's HR was <60 beats/min, 0.5 mg atropine was administered intravenously. When mean arterial pressure was less than 70% of the base value or systolic blood pressure was <90 mmHg, ephedrine 10–15 mg was immediately injected intravenously. After the procedure, all patients were transported to the recovery room and monitored with vital signs. Discharge criteria were considered as the patient being awake with stable hemodynamics and able to walk without assistance.

Observational Indices

The vital signs of patients were constantly monitored during ESD, with HR, pulse oxygen saturation (SpO_2), electrocardiogram (ECG), and NIBP measured at 5-minute intervals. In addition, the total procedure time, drug amounts, time of administration, recovery time (from the end of the operation to OAA/S score ≥4), and respiratory and cardiovascular problems were all monitored and recorded.

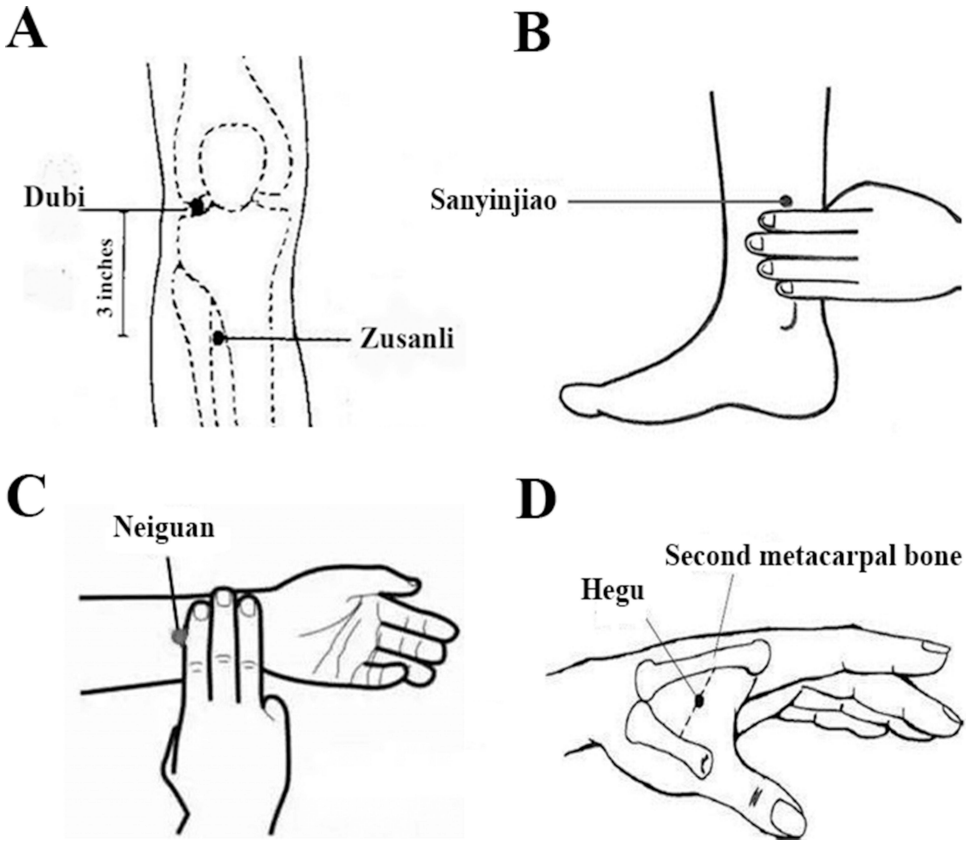

Figure 1 Location of electroacupuncture points: Zusanli (**A**), Sanyinjiao (**B**), Neiguan (**C**), and Hegu (**D**).

Furthermore, serious complications, including hypoxemia (SpO_2 declining to <90%), respiratory depression (frequency <6 breaths/min), hypotension (less or more than 20% of baseline or occurrence of any arrhythmia), abnormal heart rate (less or more than 20% of the first HR determined), were immediately treated according to the symptoms and recorded. Satisfaction levels of both the patient and endoscopist, as well as the pain score, were measured by questionnaires. Visual analogue scale (VAS) scores were used to assess the degree of colorectal discomfort 30 min after the operation (0–10 points: 0, No discomfort; 10, Discomfort cannot be tolerated), as well as the endoscopist's satisfaction and the patient's satisfaction (0–10 points: 0, Not at all satisfied; 10, Quite satisfied). All patients stayed in the recovery room with SO_2, ECG, and NIBP monitoring for at least 2 hours after the operation.

Statistical Analysis

SPSS version 19.0 (IBM Corp, Armonk, NY, USA) was used for data analysis. Data were expressed as mean ± standard deviation, and enumeration data were presented as percentages. Quantitative variables were analyzed using ANOVA. Categorical data were compared by the chi-squared test, and the rank-sum test was used for nominal categorical data comparison. Statistical significance was considered as $P<0.05$.

Results

A total of 165 patients were assessed for eligibility. Of these, 15 patients were excluded from the study: five reported a history of colectomy, two reported a history of allergy to narcotic drugs, four refused sedation, one had perforation of the colon, and three reported lung disease (Figure 2). Baseline characteristics of the patients in the three groups are shown in Table 1. The baseline characteristics of the patients, including sex ratio, age, BMI, ASA classification, and operation time of the examination, with all patients leaving the recovery room within 30 min, did not differ among the three groups.

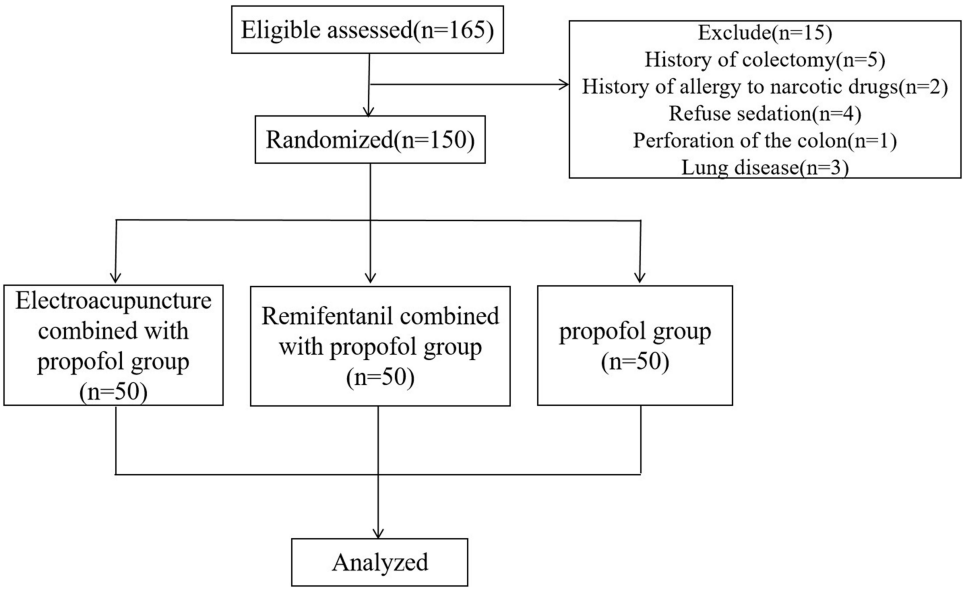

Figure 2 Flowchart of the study.

The dosages of propofol in the SP group (282.6±52.3 mg), EP group (186.4±57.6 mg), and RP group (221.5 ±53.9 mg) were increased significantly (Table 2). When a patient made a body movement that interrupted an operation, 20 mg of intravenous propofol was added to deepen the sedation level. As shown in Tables 2 and 3, the rate of occurrence of body movements in the EP group (2%) was significantly lower than that in the SP group (22%). Additional propofol boluses were required in one patient in the EP group (2%), three patients in the RP group (6%), and 11 in the SP group

Table 1 Demographic Data of Patients in the Three Groups

Characteristics	EP Group (n=50)	RP Group (n=50)	SP Group (n=50)	*P* Value
Gender (M/F)	32/18	34/16	31/19	0.43
Age (years)	53.7±12.7	49.7±12.6	50.7±12.1	0.46
BMI (kg/m^2)	23.8±3.0	23.1±2.5	23.4±2.4	0.13
Operation time (min)	29.8±5.2	30.2+4.9	28.6±4.8	0.26

Note: Values are expressed as numbers or mean ± standard deviation.

Table 2 Treatment Outcomes and Drugs Used in the Three Groups

Characteristics (n=50)	EP Group (n=50)	RP Group (n=50)	SP Group	*P* Value
Total dosage of propofol	186.4±57.6*	221.5±53.9*	282.6±52.3	<0.001
Additional propofol patients	1 (2)*	3 (6)	11 (22)	0.002
Dose (mg)	20*	26.7±3.5	52.3±8.8	<0.001
Colorectal discomfort	1.7±0.8*	3.2 ±1.3	3.9±2.4	<0.001
Patient's satisfaction	8.9±1.1	8.7±1.2	8.3±0.9	0.04
Operator's satisfaction	9.4 ± 0.8*	6.1±0.4	5.2±0.5	<0.001
Gastrointestinal motility				
No	3 (6)	5 (10)	1 (2)	0.307
Mild	43 (86)*	16 (32)	19 (38)	0.001
Uncontrolled	4 (8)*	29 (58)	30 (60)	0.001
Atropine treatment	1 (2)	3 (6)	1 (2)	1

Notes: Values are expressed as mean ± standard deviation or number (percentage). *P<0.05 versus SP group.

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Table 3 Adverse Events in the Three Groups

Characteristics	EP Group (n=50)	RP Group (n=50)	SP Group (n=50)	*P* Value
Hypoxemia	4 (8)*	17 (34)	16 (32)	0.003
Apnea	1 (2)*	7 (14)	8 (16)	0.01
Nausea and vomiting	2 (4)	3 (6)	2 (4)	1
Hypotension	5 (10)	8 (16)	7 (14)	0.538
Bradycardia	2 (4)*	5 (10)	5 (10)	0.239

Notes: Values are expressed as number (percentage). *$P<0.05$ versus SP group.

(22%). Moreover, the rate of uncontrolled gastrointestinal motility tended to be lower in the EP group (8%) than in the RP group (58%) and SP group (60%). Furthermore, 96% of endoscopists were satisfied with the procedural performance in the EP group, compared with only 74% in the SP group and 81% in the RP group. There were no significant differences in atropine consumption or patients' satisfaction levels among the three groups.

Although the rates of hypoxemia and apnea occurring in the EP group (8% and 2%, respectively) were significantly lower than in the RP (34% and 14%) and SP (32% and 16%) groups, there were no significant differences among the three groups in the incidence of bradycardia, hypotension, nausea, and vomiting (Table 3), and no patients required intubation or ventilation. No serious adverse events necessitating discontinuation of the procedure were encountered in any of the groups.

Discussion

In this study, EA significantly reduced the dose of propofol that was necessary to achieve an adequate level of sedation during ESD, and significantly reduced the occurrence of adverse effects. In addition, EA reduced the level of colorectal discomfort after ESD and increased the level of satisfaction of the endoscopist.

Acupuncture plays a very important role in TCM, as it can effectively relieve clinical acute and chronic pain. The modern theory of TCM holds that acupuncture analgesia derives from special connections in the central nervous system between pain impulses and acupoints. Acupuncture sedation and analgesia has been used in some surgical procedures as a partial substitute for pharmacological anesthesia. Compared with acupuncture, EA can provide ongoing stimulation with quantifiable intensity, frequency, and duration.[23] Previous studies concluded that EA can alleviate pain and other symptoms through a pair of needles placed on the area to be stimulated.[24–26] In addition, transcutaneous acupoint electrical stimulation could suppress the pain score during colonoscopy, and EA could significantly reduce patients' discomfort and pain during endoscopy. All of the acupuncture points selected in this study were based on the theory of TCM point selection. The Zusanli point was chosen because of its effects of alleviating abdominal pain and distension,[27] while the Hegu, Sanyinjiao, and Neiguan acupoints have been shown to have regulatory effects on the peristaltic action of the colon, as well as analgesic and sedative effects.[28,29] EA at different frequencies stimulates the release of central neurotransmitters and endorphins.[30] Finally, it can achieve a pain relief effect, regulating organ function. Several studies indicate that alternating stimulation with 2 hz/100 hz can induce the release of a variety of opiates to obtain better analgesic effects. In addition, the Hegu, Sanyinjiao, and Neiguan points were chosen to explore the efficacy of EA in achieving painless colonoscopy. In the current study, the use of EA in the EP group significantly reduced gastrointestinal motility and the total dosage of propofol compared with the SP and RP groups. These findings are consistent with the results on the effectiveness of acupuncture in previous studies.

There is often a need to pump air into the intestine to widen the visual field during ESD, which squeezes the intestinal wall and activates sympathetic nerves. Patients may feel abdominal pain and distension for several hours after the operation, which can cause anxiety and increase discomfort in patients. [31] It has been demonstrated that acupuncture can reduce sympathetic nerve excitability to realize a balance between the sympathetic nerve and the vagus nerve. [32] In this study, colorectal discomfort and the rate of additional propofol were significantly lower in the EP group than in the SP and RP groups. This suggests that EA inhibited intestinal sympathetic nerves and stimulated colonic peristalsis, which would rapidly expel the expanding gas to relieve abdominal distension and improve colorectal comfort. Moreover, the endoscopists' level of satisfaction was significantly higher in the EP group compared with the SP and RP groups. This may be related to frequent

body movements hindering the operation, which is the endoscopists' main focus. There was no significant difference in the satisfaction levels reported by patients among three groups. Therefore, it remains unclear whether EA can effectively reduce patient discomfort during colonoscopy. Higher levels of sedation are required for successful completion of ESD compared with routine colonoscopy and other therapeutic colonoscopy procedures. Propofol is widely used in anesthesia for ESD because it has a rapid onset and lasts for a short duration without any accumulation. However, it has a certain inhibitory effect on patients' respiration and circulation . [33,34] In addition, the propofol bolus and remifentanil infusion may result in significant respiratory depression during colonoscopy. In the current study, the high incidence of hypoxemia, apnea, and bradycardia in the RP and SP groups provides strong support that safety concerns over sedation performed by propofol or remifentanil are still valid. The study results indicate that EA anesthesia can reduce the need for intravenous and analgesic medication.

One limitation of this study is that although it provided a convenient method of anesthesia in colon ESD, it did not verify the exact mechanisms. EA seems to be a safe and effective substitution method. More research in this field is required, with more robust methodologies to ensure the efficacy of EA.

Conclusions

EA combined with propofol used for colon ESD can provide satisfactory operating conditions with effective analgesia and sedation. The results of this study suggest that EA can effectively reduce the dosage of propofol to achieve fewer adverse reactions and shorter recovery time.

Abbreviations

ASA, American Society of Anesthesiologists; BMI, body mass index; EA, electroacupuncture; ESD, endoscopic submucosal dissection; HR, heart rate; NIBP, non-invasive blood pressure; OAA/S, Assessment of Alertness/Sedation ;SpO_2, blood oxygen saturation; TCM, traditional Chinese medicine; VAS, visual analogue scale.

Data Sharing Statement

All data generated or analyzed during this study are included in this published article.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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