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Original Article

The hemodynamic effect of an intravenous antispasmodic on propofol requirements during colonoscopy: A randomized clinical trial

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ABSTRACT

Purpose: Hemodynamic status during induction of anesthesia may modify the amount of propofol needed to induce loss of consciousness (LOC). This study was aimed to evaluate the effect of antispasmodic-induced tachycardia on the concentration of propofol at the effect-site for inducing LOC when deep sedation was executed for colonoscopy.

Methods: One hundred and sixteen adult patients were randomly assigned to receive either 20 mg of the antispasmodic Buscopan intravenously (Buscopan group; $n = 58$) or normal saline (control group; $n = 58$) for colonoscopy. After administration of Buscopan, the antispasmodic or normal saline, propofol was given by means of target-controlled infusion to induce LOC. We recorded patient characteristics, hemodynamic profiles, effect-site propofol concentration upon LOC, total propofol dosage for colonoscopy, and colonoscopy outcomes.

Results: There were no significant differences in the characteristics between the two groups. Although the patients receiving Buscopan had a higher heart rate than those of the control group (101 ± 15 beats/minute vs. 77 ± 13 beats/minute; $p < 0.001$), we found no significant difference between two groups in the effect-site propofol concentration for inducing LOC (3.9 ± 0.6 μg/mL vs. 3.8 ± 0.6 μg/mL; $p = 0.261$) nor total propofol dosage required for colonoscopy (3.2 ± 1.4 mg/kg vs. 3.1 ± 1.1 mg/kg; $p = 0.698$). Both groups had comparable colonoscopy outcomes, including percentage of patients completing the procedure and total procedure time.

Conclusion: The hemodynamic responses to intravenous Buscopan neither affected the effect-site propofol concentration needed to induce LOC, nor the total propofol dosage required for colonoscopy in this study. There is no need to modify the dosage of propofol in patients subject to Buscopan premedication in colonoscopy.

1. Introduction

Colonoscopy is the best available method of detecting colonic polyps, the precursor lesions of colorectal carcinomas. However, misdiagnosis rates of polyps in colonoscopy are reported to range between 2.1% and 26%, depending on the size of polyps.[1] The use of an antispasmodic agent during colonoscopy may reduce colonic spasm and improve visualization of the mucosal surface, which may therefore decrease the rates of the polyp misjudgment, especially in patients with a moderate to marked degree of colonic spasm.[2] In fact, some endoscopists routinely administer antispasmodic medication to their patients receiving colonoscopies.[3]

Propofol is a hypnotic commonly used for sedation during colonoscopy in our institute. Previously, several studies had demonstrated that changes in cardiac output might modify the pharmacokinetics of propofol in animal studies.[4–6] Clinical studies, too, had suggested that cardiac output[7] and even heart rate[8–10] might influence the propofol requirement to induce anesthesia. Premedication with an antispasmodic drug, which can block the muscarinic receptor and exert a parasympatholytic action, has been

Conflicts of interest: All authors declare no conflicts of interest.

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associated with a significant increase in heart rate.[3,11,12] The use of antispasmodic premedication may affect the efficacy of sedation used, but how it affects the sedation requirements is unknown. In addition, some studies, examining the benefit of an antispasmodic agent for colonoscopy in patients receiving light-to-moderate sedation, have reported conflicting results.[11–14] The primary objective of our study was to evaluate the effect of antispasmodic-induced tachycardia on sedative requirements (propofol). As a secondary objective, we aimed to evaluate the benefit of an antispasmodic agent in patients receiving deep sedation for colonoscopy.

2. Materials and methods

This prospective study was carried out in a single institution from October 2009 to October 2010. We recruited patients aged between 18 years and 75 years who were to receive planned colonoscopies. We excluded patients with a history of colonic resection or any other intra-abdominal surgery, a history of hypertension or antihypertensive drug treatment (e.g., β-blockers), glaucoma, obstructive uropathy, autonomic dysfunction, use of anticholinergic medication, a predicted difficult airway, or an allergy to propofol. We also excluded patients with insufficient bowel preparation (large amounts of solid fecal material found or <90% of mucosa seen as graded by the endoscopists)[15] and those with cardiac diseases (e.g., cardiac arrhythmia). The protocol for this study was approved by the research ethics committee of Chang Gung Memorial Hospital (981554A3), and written informed consent was obtained from all patients.

All patients were instructed to take a standard colon preparation agent the day prior to the examination. Patients were attending on the day the elective colonoscopy was scheduled to be performed. Once a patient gave (his or her) consent, an anesthesia nurse, who was not involved in the sedation procedures, collected demographic data and took a history of the patient's prior experiences with colonoscopies. Immediately after this interview, the assigned nurse inserted a 22-gauge IV catheter into the patient's right forearm. Saline infusion (0.9%) was running to keep the intravenous line patent, after which, each patient opened a sealed envelope containing a computer-generated code indicating whether he or she would receive 20 mg of scopolamine butylbromide[3] (Buscopan; Boehringer Ingelheim, Yamagata, Japan) (Buscopan group) or an equivalent volume of normal saline (control group) intravenously. Five minutes before the patient was brought to the operating room, the Buscopan or normal saline was administered by a nurse managing the endoscopy. No other medication was administered prior to sedation. Patients, endoscopists, and anesthesiologists were blinded to which group the patients belonged.

All patients were monitored using electrocardiograms, continuous pulse oximetry, and noninvasive blood pressure measured at 5-minute intervals. After baseline hemodynamic profiles were obtained, the patient was placed in the left-lateral position. Supplemental oxygen (6 L/minute) was administered through a face mask. Patients received supplemental intravenous alfentanil 10 μg/kg as analgesic premedication. Lidocaine (40 mg) was administrated intravenously to reduce the pain that might be caused by the injection of propofol. Propofol was administered intravenously using the Base Primea system (Fresenius, Brezins, France). This delivery system displays effect-site concentrations (drug concentration at site of action) estimated by Schneider's pharmacokinetic model,[16] which is based on the patient's age, sex, weight, and height.

A previous study reported the half maximal effective concentration (EC50) for effect-site propofol concentration at loss of consciousness (LOC) to be 4.14 μg/mL.[17] In the current study, the propofol infusion was started with an initial effect-site concentration of 3 μg/mL and increased in increments of 0.5 μg/mL every 4 minutes until the patient had lost eyelash reflex and exhibited no response to a verbal command. This clinical endpoint was defined as LOC and was assessed every 15 seconds during the induction of anesthesia. The effect-site concentration of propofol required for LOC was recorded. After LOC was achieved, the colonoscopy procedure was started. The goal in the current study was to achieve deep sedation, defined as a level of sedation whereby patients lose consciousness and are unable to respond to the stimulus from colonoscopy.[18] If the desired sedation level was not achieved during colonoscopy (indicated by such signs a purposeful muscular movement or eye opening), the target effect-site concentration was increased by 0.5 μg/mL step by step. If no purposeful muscular movement or cardiopulmonary depression (e.g., SpO_2 (arterial O_2 saturation) < 90%; systolic blood pressure < 20% of the baseline or <90 mmHg) was found, the target effect-site concentration was decreased by 0.5 μg/mL stepwise.

To reduce interindividual variability in the assessment of the level of sedation, an anesthesiologist, blinded to the hemodynamic profiles of patients, was solely entrusted to shoulder the anesthetic procedures to provide deep sedation for all patients. Audible tones of monitors were silenced or turned away to avoid the possibility that the anesthesiologist or the endoscopist might be aware of whether the patient was receiving Buscopan or the normal saline. Another anesthesiologist, who was not involved in the anesthetic procedures, was responsible for monitoring the safety of the patient. If any signs of airway obstruction or respiratory depression arose, a simple jaw thrust or chin lift was performed. Positive pressure ventilation was performed as required in the event of hypoxemia (SpO_2 < 90%). Ephedrine (8 mg) was administered intravenously if the systolic blood pressure fell to <20% of the baseline level or <90 mmHg.

All colonoscopies were carried out by two responsible endoscopists, each of whom performed >300 colonoscopies using a standard adult colonoscope (CF–230I, Olympus Optical Co., Tokyo, Japan). Electronic images, polypectomies, and biopsies were performed as indicated during the procedures. Each individual endoscopist documented cecal intubation based on the visualization of the ileocecal valve and appendiceal orifice. After the procedure, the endoscopist rated the degree of colonic spasm (spasm score; 1 = no spasm encountered; 5 = marked, long waiting and very difficult to examine)[12] and difficulty of the procedure (difficulty score; 1 = easy; 5 = very difficult). We recorded the total procedure time, defined as the period between the time the colonoscope first touched the anus to the time it was withdrawn.

At the end of the procedure, we discontinued the infusion pump and recorded the total dosage of propofol required. We reckoned and recorded the time it took for the patient to regain consciousness, defined as the period between the time that the patient was first requested to open his eyes after discontinuing the infusion pump to the time the patient actually did. After the patient had fully recovered in the recovery room, an investigator who was blinded to group allocation recorded the willingness of the patient to attempt colonoscopy again (yes/no) and the patient's satisfaction score with the sedative technique using a five-point score of 1–5 (the higher the score, the greater the level of satisfaction). Patients were discharged from the post anesthesia care unit when they met with positive modified Aldrete score criteria.[19]

The primary outcome measurement was effect-site propofol concentration needed for LOC. Based upon our preliminary data, the effect-site propofol concentration at the LOC level without Buscopan premedication was 3.7 ± 0.6 μg/mL. One previous study reported that tachycardia from atropine premedication could lead to a difference of 10% in propofol dosage requirement (from 2.22 mg/kg to 2.45 mg/kg).[10] Assuming that there can be 10%