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QUALITY AND PATIENT SAFETY

Evaluation of a novel closed-loop total intravenous anaesthesia drug delivery system: a randomized controlled trial

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Editor's key points

- Automatic feedback control depends on having a reliable, measurable control variable.
- An automatic system for closed-loop administration of i.v. anaesthesia drugs was compared with manual control.
- Bispectral index and a compound analgesia score were used as the target controls.
- Time within excellent (≤10%) and good (11–20%) range of the two targets was better with the automatic system.

Background. We have developed an automatic anaesthesia system for closed-loop administration of anaesthesia drugs. The control variables used were bispectral index (BIS) and Analgoscore for hypnosis and antinociception, respectively.

Methods. One hundred and eighty-six patients were randomly enrolled in two groups. Propofol, remifentanil, and rocuronium were administered using closed-loop feedback control (closed-loop, $n = 93$) or manually (control group, $n = 93$). The clinical performance of hypnosis control was determined by calculating the offset from a BIS of 45: 'excellent', 'good', 'poor', and 'inadequate' control was defined as BIS values within 10%, from 11% to 20%, from 21% to 30%, or >30% offset from the target. The clinical performance of analgesia was defined as the offset from Analgoscore values. Data presented as mean (standard deviation) (95% confidence interval).

Results. Excellent or good control of hypnosis was achieved significantly longer in the closed-loop group [47.0 (9.8%) (45.0/49.0), 34.4 (4.7%) (33.5/35.4)] than in the control group [37.3 (14.3%) (34.4/40.2) and 32.3 (7.6%) (30.7/33.7)], respectively ($P<0.0001$ and 0.0085). Poor and inadequate control of hypnosis was significantly shorter in the closed-loop group [10.8 (5.0%) (9.8/11.8) and 7.7 (6.2%) (6.4/9.0)] than in the control group [14.7 (6.8%) (13.3/16.0) and 15.8 (14.7%) (12.8/18.8)], respectively ($P<0.0001$). Excellent control of analgesia was achieved significantly longer in the closed-loop group [78.7 (16.2%) (75.4/82.0)] than in the control group [73.7 (17.8%) (70.1/77.3)] ($P=0.0456$).

Conclusions. The closed-loop system was better at maintaining BIS and Analgoscore than manual administration.

Keywords: closed-loop systems; McSleepy

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The use of closed-loop systems in anaesthesia can improve the quality of drug delivery.[1] Closed-loop systems consist of a 'brain'—a central operating system with built-in algorithms—an 'effect'—a target control variable—and an 'actuator'—a drug delivery system, such as a syringe pump. These three elements are connected by a feedback system, which allows the automated control of drug delivery in order to maintain a pre-set target value of the control variable without any manual input.[2] By frequent sampling of the control variable and more frequent changes of drug delivery rates than with manually delivered anaesthesia, greater stability of the control variable may be achievable.[3] The performance of a closed-loop system for anaesthesia depends on the reliability of the control variable;[4] therefore, adequate target parameters must be used for each of the three components of general anaesthesia: hypnosis, analgesia, and neuromuscular block. The bispectral index (BIS) is a dimensionless number derived from processing the phase and frequency relations of the component frequencies of the EEG. It ranges from 0 (isoelectric brain activity) to 98 (consciousness). A value from 40 to 60 is considered as representing an adequate state of hypnosis.[5] Numerous studies have used the BIS value as a control variable for a closed-loop system to deliver anaesthetic drugs, outperforming manual administration.[3 6–8] The application of closed-loop control for opioids faces the problem of lack of

an optimal method to measure intraoperative pain when communication with the patient is impossible.[4] Haemodynamic measurements have mostly been used and found to be useful in administering opioids during surgery.[9 10] A novel score (Analgoscore) using heart rate (HR) and arterial pressure was recently presented and successfully used to titrate closed-loop remifentanil administration.[11] Monitoring neuromuscular block is easy to achieve using mechanomyography, acceleromyography, electromyography, or phonomyography; closed-loop systems for various neuromuscular blocking agents have shown good performance.[2 12 13] The present study was designed to introduce an automated expert-based closed-loop delivery system (McSleepy) that monitors all three components of general anaesthesia throughout surgery and i.v. administers appropriate doses of the respective drugs based on the acquired data achieving a completely automated anaesthesia control of induction and maintenance. The aim of our study was to compare the performance of McSleepy in maintaining given levels of anaesthesia—hypnosis monitored via BIS, antinociception monitored via Analgoscore—with manual administration of total i.v. anaesthesia (TIVA).

Methods

This study was designed as a randomized controlled trial. After approval from the local Institutional Ethics Committee (McGill University Health Centre, Montreal General Hospital, Montreal, Quebec, Canada) and written informed consent, 186 patients age ≥18 yr undergoing elective surgery requiring general anaesthesia with an expected duration of ≥60 min were enrolled in the study (Fig. 1). Patients who had previous cranial neurosurgical procedures, neurological disorders, or who were allergic to anaesthetic study drugs were excluded. Inclusion criteria were patients undergoing elective surgery, aged 18–85 yr. Excluded were patients unable to provide informed consent, comatose patients, patients with dementia, or allergy to propofol.

McSleepy is an automated, expert-based closed-loop anaesthesia drug delivery system that integrates the three components of general anaesthesia: hypnosis, analgesia, and muscle relaxation. The BIS was used as the control variable for hypnosis in order to calculate propofol infusion rates to maintain a pre-determined target set-point. The target of BIS was set as 45.[3] The Analgoscore, a pain score derived from HR and mean arterial pressure (MAP), was used as the control variable to titrate the effective dose of remifentanil. This score is calculated by measuring the offset percentage between the measured and target value of HR and MAP using expert-based rules. The Analgoscore scale ranges from −9 (very profound analgesia) to +9 (very superficial analgesia) in increments of 1.[11] Neuromuscular monitoring was performed every 15 min at the adductor pollicis muscle; train-of-four (TOF) ratios were automatically computed and sent to the anaesthesia delivery system. Rocuronium was given by the system, if the type of surgery demanded surgical relaxation. In this study, the anaesthesia delivery system gave a bolus of 0.2 mg kg^{-1} of rocuronium for every TOF ratio >25%. A lockout period of 20 min before the end of surgery was chosen, during which the system did not give any additional rocuronium but could be manually overridden; this was manually

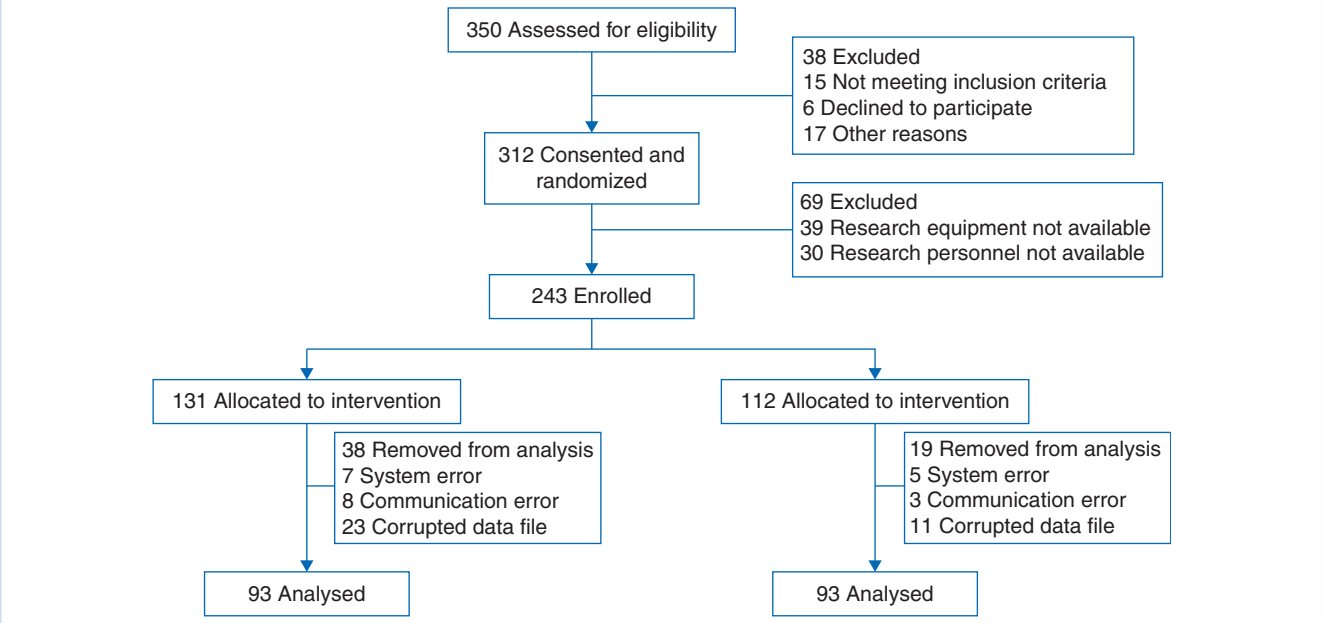

Fig 1 Flowchart of the trial.