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Introduction

In closed-loop administration of propofol, drug infusion is automatically adjusted based on feedback of a measure of the clinical effect. This is expected to improve stability of the depth of anesthesia, reduce drug overdosing and reduce the effect of interpatient variability. It is also expected to overcome the limitations of target controlled infusion in children related to the large interpatient variability in pharmacokinetics (PK) and pharmacodynamics (PD) and the debated validity of pediatric PK/PD models [1]. The objective of this study was 1) to evaluate the clinical feasibility of closed-loop delivery of propofol guided by the NeuroSENSE monitor during induction and maintenance of anesthesia in children and 2) to assess the performance of a simple robustly tuned proportional-integral-derivative (PID) controller during moderately stimulating procedures.

Methods

Following REB approval, and informed consent/assent, 45 children aged 7-17 (see Table 1), ASA I-II, requiring anesthesia for elective upper or lower gastrointestinal endoscopic investigations were enrolled for evaluation of the closed-loop system. The system uses feedback from the NeuroSENSE monitor that provides the WAVcns index as a measure of the depth of hypnosis [2]. Propofol is delivered by an Alaris TIVA infusion pump. In addition to the robust PID controller, the control system contains necessary safety layers and alarms. After initial testing of a robust PID controller for children [3], the PID controller was retuned to improve speed of induction of anesthesia and the rate of response to stimulation. Both induction and maintenance of anesthesia were closed-loop controlled. The infusion was initiated with a bolus of 25 mg of propofol over 15 s to reduce the pain on injection related to slow infusions of propofol. A bolus of remifentanil (0.5 mcg/kg) was administered before the start of induction of anesthesia, followed by a continuous infusion (0.03 mcg/kg/min).

Results

Two cases were excluded (insufficient signal quality (1), inclusion criteria not met (1)). Typical performance measures including induction time (Tind) are calculated according to the definitions from [4], see Table 1. Blood plasma concentrations (Cp) calculated using the Paedfusor model ([5], defined up to 16y) and the Schnider model (17y, [6]) at Tind varied from 2.3 to 7.7 mcg/ml. Figure 1 shows the observed interpatient PK/PD variability.

Conclusions

Robust PID control of propofol infusion guided by the NeuroSENSE monitor can automate induction of anesthesia with limited overshoot in children age 7-17y. It can provide adequate and stable depth of hypnosis during maintenance of anesthesia in moderately stimulating procedures, despite the large interpatient variability in PK/PD behavior in children. Further investigations to improve the performance of the automated system include the addition of control of analgesic agents and individualization of the control strategy.

[1] Coppens et al. Anesthesiology 2011; 115(1) [2] Zikov et al. IEEE Trans Biomed Eng 2006; 53 [3] Soltesz et al. Proc. of IFAC PID 2012 [4] Liu et al. Anesthesiology 2006, 104(4) [5] Absalom et al. Br. J. Anaesth. 2005; 95(1) [6] Absalom et al. Br J Anaesth 2009; 103(1)

Summary:

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This contribution describes the results of a clinical evaluation of closed-loop controlled propofol infusion in children. The system was evaluated in 43 cases requiring anesthesia for elective upper or lower gastrointestinal endoscopic investigations. Automated induction of anesthesia using a simple robustly tuned proportional-integral-derivative (PID) controller led to limited overshoot in children age 7-17. Depth of anesthesia was adequate during maintenance of anesthesia despite the large interpatient variability in PK/PD behavior in children.

Table 1.

Demographics	**22 M, 11 y (7, 17)** **38 kg (21, 69)** **149 cm (121, 182)**
Global Score	18.8 (5.8, 82.5)
Case length [min]	24 (5, 82)
% of time within +/-10 of the setpoint	88 (39, 100)
Induction time, Tind [s]	249 (77, 367)
MDAPE	11.6 (2.8, 23.2)
MDPE	-9.4 (-21.6, 6.0)
Minimum WAVcns index during the case	36.6 (30.4, 47.6)
Wobble	6.2 (2.8, 12.6)
Mean propofol infusion during maintenance of anesthesia [mcg/kg/min]	250 (110, 579)
Propofol consumption at Tind [mcg/kg]	2575 (970, 5328)

Tind, MDAPE, MDPE, Wobble and the Global Score are calculated as defined in [4]. Results are given as median (min, max).

Figure 1. Variability of propofol consumption and predicted Cp at Tind and during maintenance of anesthesia.