



LUND UNIVERSITY

Clinical Evaluation of Closed-Loop Administration of Propofol Guided by the NeuroSENSE Monitor in Children

van Heusden, Klaske; Dumont, Guy A.; Soltesz, Kristian; Petersen, Christian; West, Nicholas; Umedaly, Aryannah; Ansermino, J. Mark

2012

Document Version:

Peer reviewed version (aka post-print)

[Link to publication](#)

Citation for published version (APA):

van Heusden, K., Dumont, G. A., Soltesz, K., Petersen, C., West, N., Umedaly, A., & Ansermino, J. M. (2012). *Clinical Evaluation of Closed-Loop Administration of Propofol Guided by the NeuroSENSE Monitor in Children*. Abstract from The American Society of Anesthesiologists (ASA) Annual Meeting, Washington, District of Columbia, United States.

Total number of authors:

7

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Clinical Evaluation of Closed-Loop Administration of Propofol Guided by the NeuroSENSE Monitor in Children

K. van Heusden, Ph.D., G.A. Dumont, Ph.D., K. Soltesz, C. Petersen, Ph.D., N. West, A. Umedaly, J.M. Ansermino M.D.

University of British Columbia, Vancouver, British Columbia, Canada

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 remifentanyl (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 (T_{ind}) are calculated according to the definitions from [4], see Table 1. Blood plasma concentrations (C_p) calculated using the Paedfusor model ([5], defined up to 16y) and the Schnider model (17y, [6]) at T_{ind} 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:

Clinical Evaluation of Closed-Loop Administration of Propofol Guided by the NeuroSENSE Monitor in Children

K. van Heusden, Ph.D., G.A. Dumont, Ph.D., K. Soltesz, C. Petersen, Ph.D., N. West, A. Umedaly, J.M. Ansermino M.D.

University of British Columbia, Vancouver, British Columbia, Canada

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.

