Closed-loop control of Propofol Anesthesia in Adults with a Robust Proportional-Integral-Derivative Design

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Introduction: Feasibility of closed-loop control of propofol anesthesia with a simple, robustly tuned Proportional-Integral-Derivative (PID) controller has been shown in adults[1] and children[2]. Interpatient variability was taken into account in the design of these robust controllers, resulting in a system expected to provide adequate control of anesthesia for a large range of patients[3]. The purpose of this study was to collect data for the design of a remifentanil control system, using robust PID control for propofol anesthesia in adults, at our research site in Vancouver, Canada. This controller is equivalent to the controller we evaluated in France[1]. It was hypothesized that the control performance would be consistent between the two sites and study populations.

Methods: With approval from Health Canada, the local research ethics board, and written informed consent, ASA I-III adults, requiring general anesthesia for elective surgical procedures, were enrolled. Target controlled infusion was used to administer remifentanil[4], at the discretion of the anesthesiologist. Propofol infusion was closed-loop controlled using feedback from the NeuroSENSE WAV_{CNS} measure (NeuroWave Systems, Cleveland Heights, OH). The clinician could overwrite the system at any time, administer additional drug boluses, and change the WAV_{CNS} setpoint as deemed appropriate. The closed-loop controller is functionally equivalent to the system we previously tested in France[1].

Results: 55 adults (Table 1) were enrolled in the study, 51 of the cases were completed entirely in closed-loop. Induction of anesthesia was completed in a median [IQR] of 3.8 [1.35] min. Table 1 shows a comparison of data from this study with the results obtained in France. Of note, a burst suppression ratio (BSR) >10% occurred in 582 min out of a total of 6031 min of closed-loop control. 5 subjects made up 47% of this time, 20 patients made up 89%. In the study in France, 54 min were reported with BSR >10% out of 2545 min total.

Conclusions: The achieved control performance is comparable to the performance obtained in France; WAV_{CNS} within 10 units of the setpoint was achieved in 85% of the time versus 87% in France. The time spent >10 units above the setpoint is lower, while the time spent > 10 units below the setpoint is higher than observed in France. Four patients made up 33% of the time spent >10 below the setpoint. In these cases the safety system was active and did not allow further reduction of propofol infusion (predicted effect site concentration[5] reaching 1 or 1.5 mcg/ml). Burst suppression occurred more often than in the study in France. This could be related to the slightly older population, or to lower remifentanil dosing at our institution. In many cases BSR occurred after induction of anesthesia, and coincided with an overshoot in the measured WAV_{CNS}. Higher remifentanil infusion may reduce propofol requirements for induction of anesthesia, reducing the expected overshoot and BSR.

[1] Proc Am Soc Anes Ann Mtg.2011, A1170 [2] Paediatr Anaesth. 2013;23(8):712-9. [3] Anesth Analg. 2013;117(5):1130-8. [4]Anesthesiology.1997;86(1):24-33.[5]Anesthesiology. 1998;88(5):1170-82.

Table 1 Comparison of results in France and Vancouver. Values are reported as median [interquartile range].

	Hôpital Foch, France, reported in [1]	**Vancouver, Canada**
n	20 (7 male)	51 (30 male)
Age (yrs)	55 [26]	64 [13]
Weight (kg)	76 [24]	83 [21]
Height (cm)	158 [13]	173 [15]
Case duration (min)	112 [58]	99 [109]
WAV_{CNS} within 10 of the setpoint	87%	85%
$WAV_{CNS} > WAV_{SP} + 10$	7%	2%
$WAV_{CNS} < WAV_{SP} - 10$	6%	13%
Mean CE_{Prop} [5]	2.4 [1] mcg/ml	3 [1.2] mcg/ml
Mean CE_{Remi} [4]	4.9 [1.1] ng/ml	3.8 [1.6] ng/ml
Median propofol consumption	103 [58] mcg/kg/min	93 [55] mcg/kg/min
Median remifentanil consumption	0.14 [0.06] µg/kg/min	0.10 [0.05] µg/kg/min