

Figure 1: Pupillary Pain Index (PPI) mean and 95% CI, for 4 different remifentanyl EC levels. (ANOVA,  $p < 0.001$ )

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**Background:** The importance of personalized medicine is becoming increasingly recognized in anesthesia. Titration of the different drugs used in anesthesiology has become possible due to monitors that allow us to measure the different effects. However, regarding the analgesic effect, there are not many available solutions yet. The Pupillary Reflex Dilation has been studied as a surrogate for measuring the nociception/antinociception balance of patients, both in the operating theater as well as in intensive care.<sup>1</sup> The aim of this study was to assess the Pupillary Pain Index (PPI) association with different concentrations of remifentanyl.

**Methods:** This was an observational prospective study, where 34 consecutive patients were enrolled. Patients scheduled for neurosurgical procedures, with general TIVA anesthesia with propofol and remifentanyl were considered when no premedication was used. Induction began with an infusion of remifentanyl targeted for a constant concentration using Minto PK Model and then an infusion of propofol at 200 mL/h was started until loss of consciousness was observed. Afterwards, an infrared portable pupillometer (AlgiScan—IDMed, France) was used to assess the Pupillary Dilation Reflex and its derived index PPI. Following this measurement, remifentanyl concentrations could be increased or decreased if deemed necessary by the anesthesiologist. The PPI consists in measuring the pupillary dilation in response to a continuously increasing electric stimulus discharge, that stops when  $> 13\%$  dilation from baseline is achieved, or when 60 mA is reached. PPI measurements were taken after loss of consciousness and before surgery, at moments when no other stimulus were present. For each measure of the predicted effect-site concentration (EC) of remifentanyl (Minto PK model) and of propofol (Schnider PK Model); and the BIS value were noted. Data are mean  $\pm$  SD or %.

**Results:** A total of 78 measures of PPI were done. Patients' data were:  $57 \pm 15$  years;  $73 \pm 21$  kg;  $162 \pm 8$  cm; 60% female; 11.5% ASA I; 80.8% ASA II; Remifentanyl EC  $2.4 \pm 1.5$  ng/mL; propofol EC  $3.7 \pm 1.3$   $\mu$ g/mL; BIS  $46.1 \pm 8.2$ ; PPI  $4.8 \pm 3$ . A correlation was observed between the remifentanyl EC and PPI ( $R = -0.46$ ,  $P < 0.001$ ), but not between PPI and propofol EC or BIS. A correlation was observed between BIS and propofol CE ( $R = -0.26$ ,  $P = 0.028$ ), but not with remifentanyl. Tukey HSD test showed that the different is mainly due to concentrations  $< 3$  versus  $\geq 3$  ng/mL.

**Conclusions:** We found a significant correlation between the remifentanyl concentration and PPI, showing that PPI discriminates different levels of analgesia. No correlation was found with propofol or BIS. However, there was no clear discrimination between all levels of remifentanyl concentrations analyzed. Further research should be done, with more data and more stratified levels of remifentanyl.

**ACK:** LAETA-INEGI.

**Reference:**

1. Barvais L, Engelman E, Eba JM, et al. *Br J Anaesth*. 2003;91:347–352.

#### [SNACC-50] Analgesic Interpatient Variability of Remifentanyl Assessed Through Pupillary Dilation Reflex

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**Background:** Although there has been significant focus on unconsciousness and amnesia, identifying the neural signatures of effective analgesia has received less attention.<sup>1</sup> Currently, appraisal of intraoperative nociception is mostly done through the assessment of the autonomic response to noxious stimuli, whether it is through heart rate variability, heartbeat intervals, plethysmographic pulse wave amplitude, skin conductance or pupillary response.<sup>2</sup> The known wide inter-patient variability of the hypnotic effect, namely in the amount of propofol needed to achieve loss of consciousness, led us to question if this variability also happened for the analgesic effect. In this

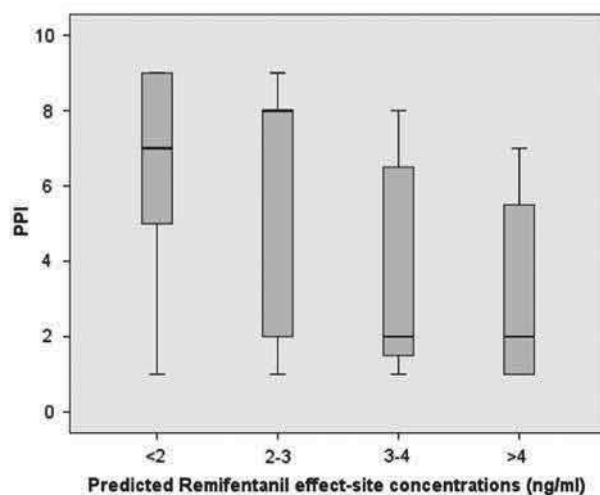


Figure 1: PPI data distribution in the four different remifentanyl concentration levels.

Table 1: PPI values for the different Remifentanyl concentration levels.

Remifentanyl EC	N	PPI (mean $\pm$ SD)	PPI (min – max)	PPI – IQ range and %
< 2 ng/ml	21	6.33 $\pm$ 2.6	(1 – 9)	[5–9] 80%
2– 3 ng/ml	18	6.11 $\pm$ 3	(1 – 9)	[2 – 8] 300%
3–4 ng/ml	20	3.7 $\pm$ 2.7	(1 – 8)	[1.25 – 1.75] 440%
> 4 ng/ml	19	3.16 $\pm$ 2.3	(1 – 7)	[1 – 6] 500%

study, we evaluated the interpatient variability of the Pupillary Dilation Reflex (PDR) response to different levels of remifentanyl, administered using target controlled infusion with the Minto PK Model.

**Methods:** This is an observational prospective study, where 34 consecutive patients were enrolled. Patients scheduled for neurosurgical procedures, with TIVA (using target controlled infusion systems) with propofol and remifentanyl were considered when no premedication was used. Induction began with a constant remifentanyl concentration using Minto PK Model and then an infusion of propofol at 200 mL/h was started until loss of consciousness was observed. Afterwards, an infrared portable pupillometer (AlgiScan—IDMed, France) was used to assess the Pupillary Dilation Reflex and its derived index Pupillary Pain Index (PPI). Remifentanyl concentrations could be increased if deemed necessary by the anesthesiologist. The PPI is calculated from the PDR to a continuously increasing electric stimulus discharge. PPI measurements were taken after loss of consciousness and before surgery, at moments when no other stimulus were present. For each measure of PPI the predicted effect-site concentration (EC) of remifentanyl and of propofol (Schnider PK Model); Data are mean  $\pm$  SD or %.

**Results:** Thirty-four consecutive patients were enrolled, and a total of 78 measures of PPI were done. Figure 1 shows the PPI variability for different levels of remifentanyl EC and Table 1 shows the PPI values for the four levels of remifentanyl. The variability found ranged from 80% to 500%, depending on the effect site concentration of remifentanyl. The higher the concentration, the larger the variability. The mean PPI is the difference between the different Remifentanyl EC levels (ANOVA  $P < 0.001$ ).

**Conclusions:** The variability of the analgesic effect was as high as 500%. This suggests that more attention should be paid to the individualization of intraoperative analgesia, as different patients have different analgesic needs, and these need cannot be predicted only through PK-PD models. Further research should be done, with more data and more stratified levels of remifentanyl.

**ACK:** LAETA-INEGI.

#### References:

1. Mashour GA. *Anesthesiology*. 2013;118:239–240.
2. Edry R, Recea V, Dikust Y, et al. *Anesthesiology*. 2016;125:193–203.

[SNACC-51] The Effect of Sevoflurane-Air Versus Sevoflurane-

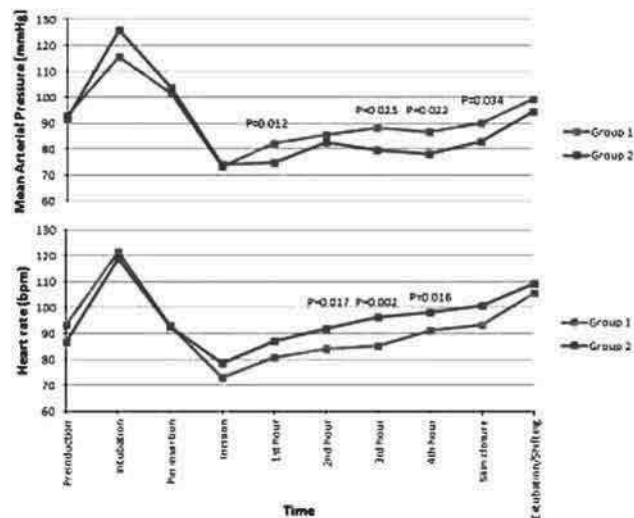


Figure 1: Intraoperative heart rate and mean arterial pressure trends

#### Nitrous Oxide Anesthesia on Length of ICU and Hospital Stay in Patients Undergoing Cerebellopontine Tumour Surgery: A Randomized Controlled Trial

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**Background:** Nitrous oxide ( $N_2O$ ), a unique anaesthetic agent, has both advantages and disadvantages, especially in neurosurgical patients. Various studies evaluating the use of  $N_2O$  in different surgical populations have been inconclusive so far.

**Objectives:** To compare duration of ICU and hospital stay in patients receiving sevoflurane based general anesthesia with/without  $N_2O$ , for elective cerebellopontine angle (CPA) tumor excision surgery. Secondly, we

Table 1: Primary and secondary outcomes

	Group 1 (n=24)	Group 2 (n=24)	p-value
ICU stay (hours)*	66 [15.8–332.1]	39.75 [15.8–308.2]	0.076
Hospital stay (days)*	7.77 [3.2–29.3]	6.34 [3.3–28.2]	0.322
Condition at discharge**			
Complete recovery	15 (62.5)	17 (70.8)	
Incomplete recovery	9 (37.5)	7 (29.2)	0.540
Intraoperative parameters			
Duration of anaesthesia (minutes)***	488.3 (168.1)	489.2 (119.6)	0.910
Brain bulge**			
Grade I	11 (45.8)	14 (58.3)	
Grade II	10 (41.7)	8 (33.3)	
Grade III	3 (12.5)	2 (8.3)	0.510
Significant hemodynamic variations**			
Maintenance			
Tachycardia	6 (25)	16 (66.7)	0.004 <sup>a</sup>
Bradycardia	12 (50)	5 (20.8)	0.035 <sup>a</sup>
Closure			
Tachycardia	6 (25)	13 (54.2)	0.039 <sup>a</sup>
Hypotension	0 (0)	9 (37.5)	0.003 <sup>a</sup>

\*Median [range]; \*\*n (%); \*\*\*Mean (SD)