Background: The importance of personalized medicine is becoming increasingly recognized. Titration of the different drugs used in anaesthesiology 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 theatre as well as in intensive care (1). The aim of this study, was to assess the Pupillary Pain Index (PPI) association with different concentrations of remifentanil.

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 remifentanil were considered when no premedication was used. Induction began with an infusion of remifentanil 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: Pupillary Pain Index (PPI). Following this measurement, remifentanil 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 PPI the predicted effect-site concentration (EC) of remifentanil (Minto PK model) and of propofol (Schnider PK Model); and the BIS value were noted. Data are mean±SD or %.

Results: A total of 78 measures of PPI were done. Patients’ data were: 57±15years; 73±21Kg; 162±8cm; 60% female; 11.5% ASA I; 80.8% ASA II; Remifentanil EC 2.4±1.5ng/ml; propofol EC 3.7±1.3 ug/ml; BIS 46.1±8.2; PPI 4.8±3. A correlation was observed between the remifentanil 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 remifentanil. Tukey HSD test showed that the different is mainly due to concentrations <3 ng/ml versus ≥3 ng/ml.

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


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