Prediction of the Effect-Site Concentration of Remifentanil Based on the Pupillary Light Reflex

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Introduction: The pupillary effects of opioids have been previously studied and described [1,2], in particular its effects on the pupillary reflex dilation (PRD) response and the pupillary unrest under ambient light (PUAL). On the other hand, and although the miotic action of opioids on the pupil is widely known, the dose-response changes of the pupillary light reflex have not been described. The aim of this study was to assess the Pupillary Light Reflex (PLR) association with different concentrations of remifentanil, and the possibility of predicting remifentanil concentrations based on the different parameters of this reflex.

Methods: Preliminary data from an observational prospective study was used, and 6 patients were included. They were scheduled for ambulatory procedures under sedation. Remifentanil was administered using a TCI pump from Fresenius Base Primea docking station (Fresenius - Kabi, Germany) using Minto PK-PD Model. Before starting, and at each target concentration after equilibration between plasmatic and biophase, the PLR was measured using a portable infrared pupillometer (AlgiScan® - IDMed, France). The pupillometer applied a flash of visible light and measured the initial diameter, the minimum diameter obtained afterwards, the response latency and velocity of contraction. These variables were then analyzed in the IBM SPSS Modeler software.

Results: A total of 22 measurements of PLR were obtained with concentrations ranging from 0 to 4 ng/mL. The model presenting best accuracy was a Bayesian network (figure 1), with an accuracy of 81,8% (figure 2).

Conclusions: These preliminary results suggest that is possible to predict the effect site concentration of remifentanil based on the PLR. This also shows that the PLR changes in a dose-dependent manner with remifentanil. Based on these results, it might be possible to establish equipotency relationships among opioids using the PLR. However, further data is needed to enhance this model.

References:

1. Neice AE, Behrends M, Bokoch MP, Seligman KM, Conrad NM, Larson MD. Prediction of Opioid Analgesic Efficacy by Measurement of Pupillary Unrest. *Anesth Analg*. 2017;124(3):915-921. doi:10.1213/ANE.0000000000001728

2. Larson MD. Mechanism of opioid-induced pupillary effects. *Clin Neurophysiol*. 2008;119(6):1358-1364. doi:10.1016/j.clinph.2008.01.106

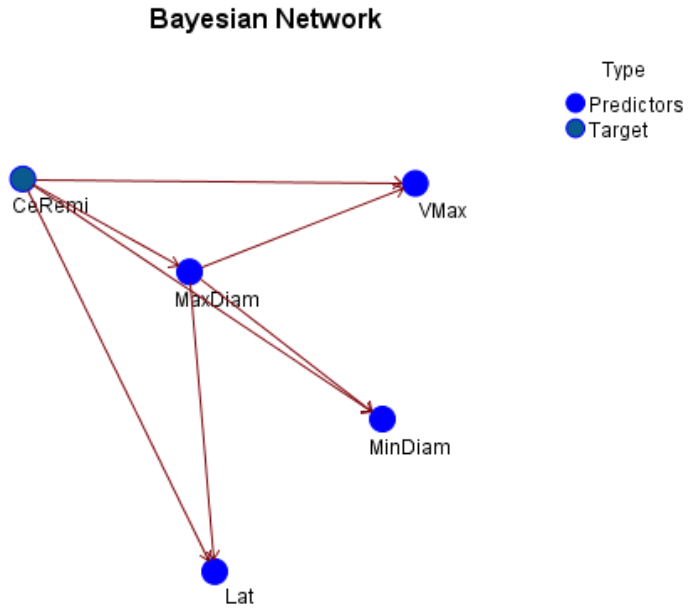

Figure 1 - Illustration of the Bayesian network used

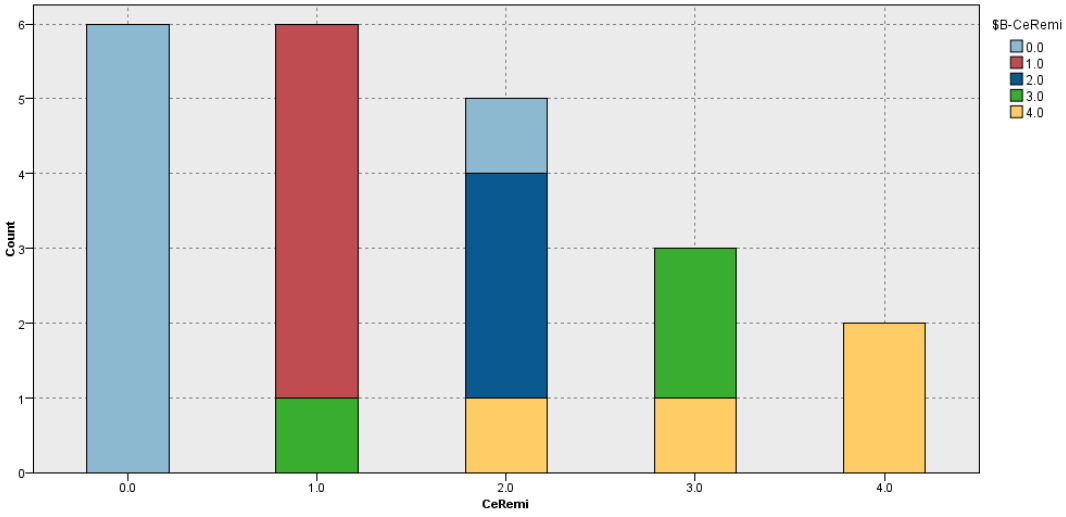

Figure 2 - Accuracy of the predictions for each Remifentanil effect site concentration