Remifentanil Closed-Loop Delivery Based on the Difference between Response Entropy and State Entropy

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Introduction- Excessive facial electromyographic (FEMG) activity during general anesthesia may indicate inadequate antinoception. The difference between response entropy (RE, GE Healthcare, Helsinki, Finland) and state entropy (SE), represents activity between 32-47 Hz, which is largely FEMG activity. Remifentanil can be titrated by an algorithm that maintains RE-SE between a lower and upper boundary condition and can be delivered in a closed-loop system. This study compared closed-loop remifentanil delivery to standard care. The principal outcome measure was time to verbal arousal following drug discontinuation.

Methods- 60 patients scheduled for anterior cruciate ligament (ACL) repair signed informed consent in this IRB approved study. Patients were randomized to closed-loop (CL) or standard TCI care (SC). General anesthesia was induced with RUGLOOP TCI (Demed, Temse, Belgium), targeted effect-site concentrations (Ce) were propofol 5 mcg ml⁻¹ (Schnider kinetics) and remifentanil 4 ng ml⁻¹ (Minto kinetics). In group CL remifentanil was delivered by the closed-loop system, propofol was delivered by algorithm to maintain a SE of 50. In group SC remifentanil Ce was adjusted by usual clinical practice and propofol Ce was adjusted to maintain a SE of 50. Drugs were discontinued at the end of surgery. Time to arousal to verbal stimulation and orientation were determined. Predicted propofol and remifentanil Ce at surgical milestones were determined. Groups were compared with t-testing or Kaplan-Meier survival analysis as appropriate (SigmaStat 3.0, SPSS, Chicago, IL).

Results- 29 patients in each group completed the study. Demographic data, surgical times, average SE values and hemodynamic variables were not significantly different. Time to verbal arousal (figure 1, mean ± S.D.) was significantly faster in the CL group, 5.3 ± 2.7 min compared to SC, 7.2 ± 3.7 min (p=0.031). Time to orientation was also faster: 7.4 ± 2.7 min and 9.8 ± 4.1 min, respectively (p=0.012). Predicted remifentanil Ce during surgery was significantly greater in the CL group compared with SC (4.9 ± 1.7 mcg ml⁻¹ vs. 3.9 ± 1.0, respectively, p=.006) and propofol was significantly lower (2.6 ± 0.9 ng ml⁻¹ vs 3.3 ± 1.0, p=.005, figure 2).

Discussion-Closed-loop delivery of remifentanil based on the difference between response and state entropy during ACL reconstruction resulted in faster times to arousal and orientation than in the standard care group. The differences in the remifentanil Ce and propofol Ce during surgery may account for the differences in emergence times. Other types of surgery and outcomes need to be evaluated with the closed-loop system.

References-
2. Anesthesiology 2007; 107: A735.[figure1][figure2]

From Proceedings of the 2009 Annual Meeting of the American Society Anesthesiologists.

Figure 1
Figure 2

AVERAGE SURGICAL EFFECT-SITE CONCENTRATIONS