PHARMACOKINETIC ACCURACY OF THE NSRI DURING PSEUDO-STEADY STATE

Norbert Sigmond[1]; Matthias Bächtold[1]; Volker Hartwich[1]; Martin Luginbuehl, MD, Ph.D[1]; Peter Schumacher, MSc, PhD[2]; Thomas Bouillon, MD, PhD.[3]

Bern University Hospital, Bern, Switzerland [1], Sentec AG, Therwil, Switzerland [2], Novartis, Basel, Switzerland[3]

Background: The noxious stimulation response index (NSRI) reflects the combined potency of a hypnotic and an opioid as a number between 100 (no drug) and near 0 (very deep anesthesia) and is calculated from predicted effect site concentrations [1]. We determined the prediction error (PE) of propofol, alfentanil and corresponding NSRI based on measured plasma concentrations.

Methods: In 40 patients (ASA 1 or 2) anesthetized with propofol TCI (Schnider[2]) and alfentanil boluses, five arterial blood samples were drawn and plasma propofol and alfentanil concentrations were measured with gas chromatography mass-spectrometry. Samples from pseudo-steady state episodes (predicted effect site within ± 10% of plasma concentration) were included in the analysis. The performance error (PE = (Cmeasured – Cpredicted)/Cmeasured)) for propofol (Schnider [2] and Marsh [3]), alfentanil Scott [4], related NSRI and the corresponding MDPE's and MDAPE's were calculated [5]. The delta NSRI (ΔNSRI=NSRImeas-NSRIpred) was also determined.

Results: 59 blood samples from 34 patients met the inclusion criterion. Spearman rank order correlation did not reveal a correlation of the MDPE and MDAPE of propofol (Schnider and Marsh respectively) and alfentanil (Scott). The median (IQR) delta NSRI was 9.4(-1.4/19.9) and 5.0(-2.9/20.5) when based on propofol Schnider and Marsh respectively. MDPE and MDAPE are presented in Tab. 1.

Table 1. PE, MDPE and MDAPE in pseudo-steady state.

	MDPE	MDAPE
Prop Schnider	1.8 (-14.5/25.8)	23.0 (9.1/35.9)
Prop Marsh	2.6 (-19.5/36.5)c	27.7 (15.4/41.2)
Alfentanil Scott	-34.3 (-42.5/-17.3)a	35.2 (20.9/43.3)b
NSRI (Prop S)	18.2 (-2/45.0)	23.9 (12.5/45.6)
NSRI (Prop M)	9.6 (-3.9/45.7)c	20.2 (7.1/46.1)

Legend to Tab 1: Numbers are median (inter-quartile range). ANOVA on ranks (Tukey test): a $p<0.05$ between MDPE alfentanil Scott and MDPE Prop Schnider, Prop Marsh, NSRI Prop S and NSRI Prop M, b $p<0.05$ for MDAPE propofol Schnider and alfentanil but not related NSRI.

Conclusion: The MDAPE (accuracy) of the NSRI and of the single drugs were similar, while the MDPE (bias) of propofol and alfentanil were divergent. The delta NSRI was independent of the selected Pk model for propofol. The estimated probability of responsiveness in propofol alfentanil anesthetised patients as expressed by NSRI may be lower than expected.

References:

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Summary: The absolute performance error of the NSRI in pseudo-steady state does not exceed the absolute performance error of the single drugs.