Title: Monitoring the risk for a "valley of inadequate anesthesia" using bispectral index and the noxious stimulation response index during different inflow speeds of sevoflurane.

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Abstract

Introduction: The "valley of inadequate anesthesia" refers to an increased risk for awareness, movement or hemodynamic instability evoked by an insufficient inflow of volatile agents to compensate for the gradual elimination of intravenously administered boluses of induction agents. The combined drug effects of volatile and intravenous drugs should ensure a sufficient hypnotic drug effect and immobility (as respectively quantified by bispectral index (BIS, Medtronic) and the noxious stimulation response index (NSRI, Dräger)), while maintaining stability in arterial blood pressure (ABP) and heart rate (HR). NSRI is a derivative of the probability of tolerance of laryngoscopy, as estimated by Hannivoort et al. for most combinations of propofol, opioids and volatile agents.[1] NSRI of 20 equals an estimated probability of immobility in response to laryngoscopy of 90%. We compare the time course of BIS, NSRI, ABP and HR after a bolus of propofol and sufentanil, followed by three different inflow speeds of sevoflurane. We hypothesize that BIS and NSRI should stay below 60 and 20, respectively, at all times between the start of sevoflurane and reaching a target of 1.0 MAC. We also compare ABP and HR between groups.

Methods: 33 ASA score I-III patients (age range: 27-86 years; BMI range 22-34 kg/m^2) presenting for abdominal surgery received sufentanil (0.2 µg/kg) and propofol (1 or 2 mg/kg, depending on age) followed by intubation of the trachea, 2.5 min after loss of responsiveness and rocuronium (0.6 mg/kg). Sevoflurane was administered (after randomization) in a 'slow'(n = 9), 'medium'(n = 8), and 'fast'(n = 9) group; defined by a time constant of respectively 10.9, 5.7, and 2.6 min wash-in time towards 1.0 MAC. These inflow speeds are similar to those used in a commercialized automatic controller of the inflow of volatile agents (Flow-I, Maquet). BIS and NSRI were blinded to the anesthesiologist. For all measures, the 95% confidence interval (CI 95%) of the difference of means was calculated at one minute intervals between minutes 0 to 25 after propofol ($p < 0.05$ if zero is outside 95% CI). An escape bolus of sufentanil (0.1 µg/kg) was allowed per protocol (and included in the NSRI calculations) to counter movement, tachycardia or hypertension indicating insufficient anesthesia at any time.

Results and discussion: Extra sufentanil was needed in all groups, for movement (1 in slow, 1 in medium, 1 in fast), for tachycardia (1 in slow, 1 in medium and 1 in fast), and for hypertension (3 in medium, 2 in fast). Figure 1 shows the time course of BIS, NSRI, HR and MAP. All groups included cases with BIS > 60 and/or NSRI > 20 (n in slow > medium > fast). High BIS and NSRI were not always consistent.

Figure 2 shows similar BIS and NSRI during the first 8 minutes in all groups, confirming equipotency for these measures till the start of sevoflurane. Mean NSRI differs between slow and medium, slow and fast and medium and fast (respectively from minute 10 to 18, 10 to 20 and 10 to 14) evoked by the deliberate differences in inflow speed of sevoflurane. Mean BIS differs between slow and medium and slow and fast (respectively from minute 15 to 16 and 11 to 24). Heart rate and blood pressure did not differ between groups. A Brice questionnaire found no cases of explicit recall.

Conclusion: After a bolus dose of propofol, sufentanil, and rocuronium, both BIS>60 and NSRI>20 warn the anesthesiologist for an increased risk of a "valley of inadequate anesthesia". ABP and HR don't identify differences in drug potency between groups. A higher initial dose of sufentanil (e.g. 0,3 µg/kg) might reduce the need for escape treatment.

Reference

1. Hannivoort LN, et al., Br J Anaesth. 2016 May;116(5):624-31.

Figure 1: Raw data:
Time course of individually measured bispectral Index (BIS), noxious stimulation response index (NSRI), heart rate and mean arterial blood pressure in all groups. Each black line is data from a single patient. The dotted lines indicate the thresholds for BIS (40 and 60) and for NSRI (20).

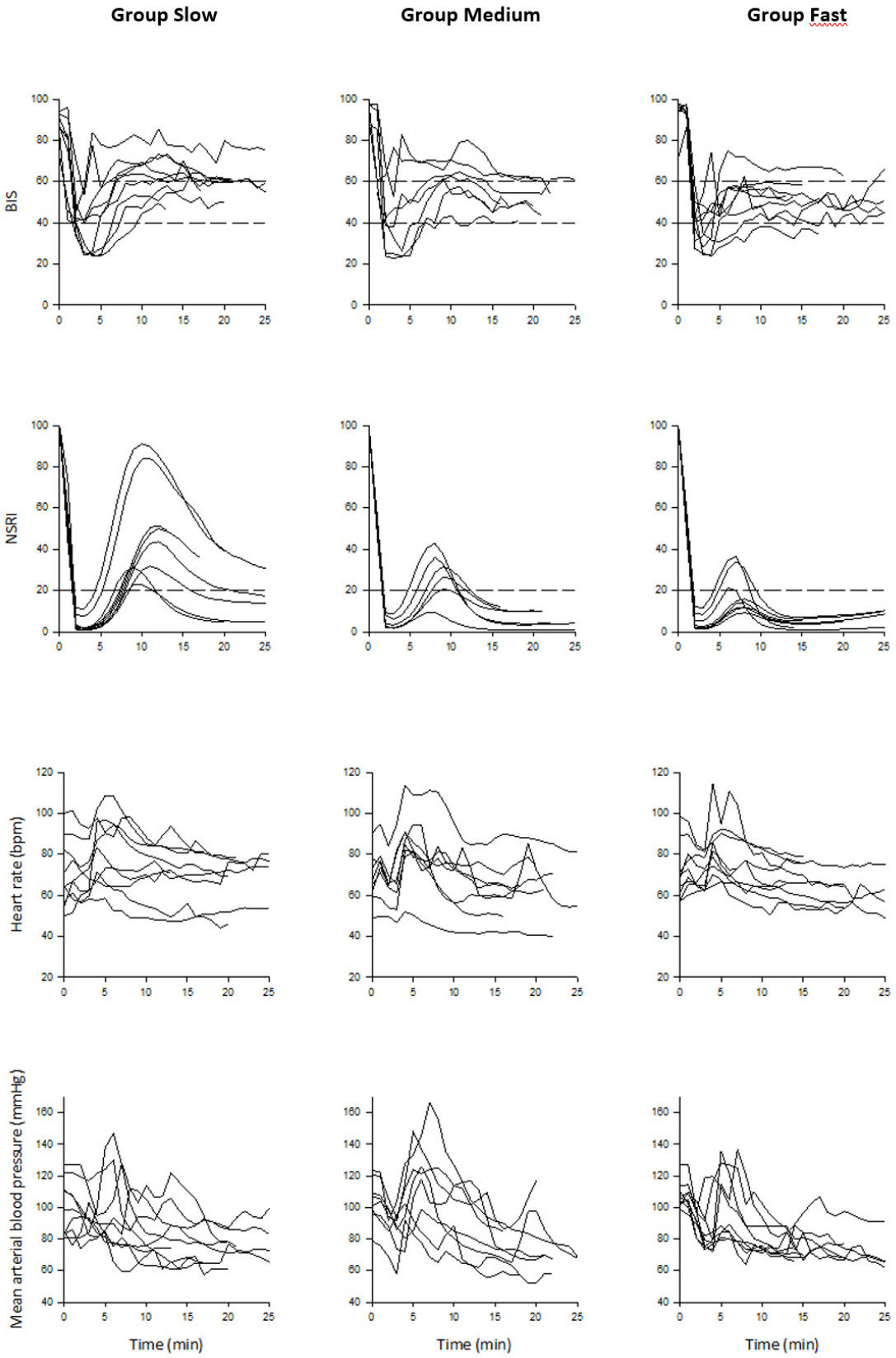

Figure 2: Difference of means between groups with 95% confidence intervals at one minute intervals. Bispectral index (BIS), noxious stimulation response index (NSRI). Black dots are the differences of the means between the groups. The light dots and the triangles are respectively the upper and lower margins of the 95% confidence interval. P < 0.05 when the zero line is outside of the 95% confidence interval.