

# PROPOFOL AND REMIFENTANIL SPARING EFFECT OF NITROUS OXIDE USING CLOSED-LOOP ANESTHESIA CONTROLLER

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**Background:** We have developed a proportional-integral-derivative controller allowing closed-loop propofol and remifentanyl administration guided by the Bispectral (BIS) monitor<sup>1</sup>. Nitrous oxide (N<sub>2</sub>O) has a hypnotic and analgesic effect. We investigated whether the coadministration of N<sub>2</sub>O would reduce the amount of propofol and remifentanyl required during closed-loop anesthesia maintenance. Drug consumption in all patients, in both men and women was analyzed.

**Methods:** Patients (ASA I-IV) who were scheduled for minor or major surgery lasting more than 1 hour were randomized in this multicenter trial (11 centers and 34 investigators, NCT00547209). After induction patients were allocated to receive 60 % nitrous oxide-40 % oxygen (N<sub>2</sub>O group) or 60 % air – 40 % oxygen (Air Group). In both groups the Dual-loop controller was used to provide induction and maintenance. Anesthesia depth was evaluated by the percentage of time in which the BIS was in the range 40-60 (BIS<sub>40-60</sub>). Data is presented as mean±SD. Statistical analysis was performed using student-t or Chi-squared tests; p<0.05 was considered significant.

**Results:** 302 patients were included in the N<sub>2</sub>O Group, 299 in the Air group. The Dual-loop controller was able to provide anesthesia induction and maintenance for all patients. N<sub>2</sub>O and Air groups were similar regarding age (56 ± 16 vs 57 ± 17 yr), weight (74 ± 15 vs 74 ± 16 kg), height (169 ± 9 vs 168 ± 8 cm), maintenance duration (154 ± 106 vs 156 ± 105 min), sex ratio Male/Female (157/145 vs 154/145), use of neuromuscular blocking agent (43 vs 49 % of patients). At similar BIS<sub>40-60</sub> (76 ± 15 vs 74 ± 13 %), N<sub>2</sub>O decreases propofol (4.8 ± 1.7 vs 5.1 ± 1.6 mg.kg<sup>-1</sup>.h<sup>-1</sup>, p=0.032) and not remifentanyl (0.19 ± 0.09 vs 0.20 ± 0.10 μg.kg<sup>-1</sup>.min<sup>-1</sup>, NS) consumption, in the N<sub>2</sub>O vs Air group respectively. The subgroups of men, N<sub>2</sub>O<sub>men</sub> (n=157) and Air<sub>men</sub> (n=154) were well balanced with respect to demography, morphometry and surgical procedure. At similar BIS<sub>40-60</sub> (79 ± 14 vs 78 ± 13%), propofol (4.5 ± 1.8 vs 4.5 ± 1.2 mg.kg<sup>-1</sup>.h<sup>-1</sup>) and remifentanyl (0.19 ± 0.09 vs 0.18 ± 0.07 μg.kg<sup>-1</sup>.min<sup>-1</sup>) consumptions were similar (N<sub>2</sub>O<sub>men</sub> vs Air<sub>men</sub> group respectively). The subgroups of women, N<sub>2</sub>O<sub>women</sub> (n=145) and Air<sub>women</sub> (n=145) were well balanced with respect to demography, morphometry or surgical procedure. At similar BIS<sub>40-60</sub> (73 ± 14 vs 71 ± 13), propofol (5.0 ± 1.7 vs 5.6 ± 1.8 mg.kg<sup>-1</sup>.h<sup>-1</sup>, p=0.004) and remifentanyl (0.18 ± 0.09 vs 0.21 ± 0.10 μg.kg<sup>-1</sup>.min<sup>-1</sup>, p=0.029) consumptions decreased with the coadministration of N<sub>2</sub>O (N<sub>2</sub>O<sub>women</sub> vs Air<sub>women</sub> group respectively). No cases of awareness with recall were recorded.

**Conclusions:** The Dual-loop controller allowed an unbiased administration of propofol and remifentanyl. These results demonstrated that the sparing effect of N<sub>2</sub>O on propofol and remifentanyl consumption is related to gender. N<sub>2</sub>O coadministration allowed significant decrease of propofol and remifentanyl consumption in women but the impact is not clinically relevant.

## References:

1. Liu et Al. Anesth&Analg in Press.