**Abstract** *(in English – Times New Roman 12 - max. one page)* Deadline for receipt: March 31, 2023

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| Title: Study of the Hypnotic Effect of Magnesium Using the Spectral Entropy of the Electroencephalogram during Total Intravenous General Anesthesia: a Randomized Double-blind Placebo-controlled Clinical Trial  Author(s): G Van Munster, MD 1, F Beck, MD 1,3, PY Hardy, MD 1,2, M Carella, MD1,2, V Bonhomme, MD, PhD 1, 3.  Affiliation of author and co-authors:   1. Department of Anesthesia and Intensive Care Medicine, Liege University Hospital, Liege, Belgium 2. Inflammation and Enhanced Rehabilitation Laboratory (Regional Anesthesia and Analgesia), GIGA-I3 Thematic Unit, GIGA-Research, Liege University, Liege, Belgium 3. Anesthesia and Perioperative Neuroscience Laboratory, GIGA-Consciousness Thematic Unit, GIGA-Research, Liege University, Liege, Belgium   Hospital/Institute: Department of Anesthesia and Intensive Care Medicine, Liege University Hospital, Liege, Belgium |
| **Objective:**  To assess whether magnesium sulfate (MS) is effective at reducing the necessary concentrations of propofol to induce pharmacological hypnosis during general anesthesia.  **Background:**  MS acts as a calcium channels blocker and a inotropic N-methyl-D-aspartate receptor blocker, and is mainly used to reduce the systemic response to surgical stress as part of a multimodal anti-nociceptive regimen.1 More controversial is its contribution to the alteration of consciousness and level of hypnosis.2 We aimed at investigating whether MS is capable of reducing the concentrations of propofol needed to induce pharmacological hypnosis during total thyroidectomy (TT).  **Methods:**  Between October 21th, 2021, and April 8th, 2022, 33 patients scheduled for TT were enrolled for this prospective, double-blind, randomized, controlled trial. The Trial was approved by the Comité d’Ethique Hospitalo-Facultaire Universitaire de Liège (study number 2021/190) and was registered in the European Clinical Trial Register (EudraCT: 2021-002824-19). Patients were randomly divided into two groups. Prior to induction of anesthesia, patients received 50 mg.Kg-1 ideal body weight of MS 10% intravenously over 10 minutes (Group MG) or the same volume of normal saline (Group CO). General anesthesia was induced and maintained using a target-controlled infusion (TCI) of propofol (Schnider model), adjusted according to the State Entropy (SE) of the electroencephalogram. Propofol effect-site concentration (Ce) was initially set at 1.5 μg.mL-1, then increased by steps of 0.5 μg.mL-1 every 2.5 minutes until a SE value between 50 and 60. The patient, surgeon and anesthesiologist were blinded to group affiliation. A blinded observer noted the highest propofol Ce and total propofol consumption during the study period. The primary endpoint of the study was the between-group comparison of propofol Ce required to achieve a 50-60 SE value. Secondary outcomes were the absolute propofol dose (mg.Kg-1.min-1) and the time required to achieve a 50-60 SE value. Data were analyzed using Fisher’s exact, Student-t, or Mann-Whitney *U* tests, as appropriate. A two-tailed P-value <0.05 was considered statistically significant.  **Results:**  Demographic characteristics were comparable between groups. No significant between-group differences were observed regarding the highest propofol Ce during induction [µg.mL-1, mean (SD); group MG 3.79 (0.62) and group CO 4.03 (0.77) , *P*=0.32] (Figure), time to achieve targeted SE [minute, mean (SD); group MG 8.31 (3.2) and group CO 8.7 (4.13), *P*=0.76] and total dose of propofol [mg.Kg-1.min-1, median (IQR); group MG 0.25 (0.21 – 0.30) and group CO 0.26 (0.25 – 0.30), *P*=0.37].  **Conclusions:**  In patients scheduled for TT, our data suggest that MS is not effective as an hypnotic adjuvant during induction of general anesthesia.  **Figure:**  Box plot propofol effect-site concentration obtained in each group. Bold line = median; lower error bar = minimal data value; lower box limit = lower quartile; upper box limit = upper quartile; upper error bar = maximum data value; dot = outlier.  **Declaration of interests:** V. Bonhomme has received funds and research support from Orion Pharma as well as honoraria from Medtronic. He is the Editor-in-Chief of the Acta Anaesthesiologica Belgica. Other authors declare no conflicts of interest.  **Funding:**Department of Anesthesia and Intensive Care Medicine, Liege University Hospital, Liege, Belgium.  **References:**   1. Woolf CJ et al., *Pain* 1991; 44 (**3**):293-299. 2. Khafagy HF et al., *Korean J Anesthesiol* 2012;63 (**2**):113-9. |