31. ESTIMATION OF CEREBRAL CONCENTRATIONS OF FENTANYL IN THE LIGHT OF THE SHAFER PHARMACOKINETIC MODEL, ACHIEVED DURING GENERAL INTRAVENOUS ANAESTHESIA PERFORMED BY INTERMITTENT BOLUS: PROSPECTIVE, CONSECUTIVE, EXPERIMENTAL STUDY

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Introduction. Total intravenous anaesthesia (TIVA) is induced by the pharmacodynamic interaction between opioid analgesics (eg. fentanyl) and hypnotics (eg. propofol) in the brain. The depth of the anaesthesia is calibrated according to the intensity of the surgical stimulus, which is variable during the operation. Respectively, it is necessary to frequently adjust the doses and the rate of administration of intravenous anaesthetics, in order to obtain those cerebral concentrations (Ces), which will counterbalance the effects of surgical stress. Target controlled infusion (TCI) techniques according to a pharmacokinetic algorithm (PK / PD) have significantly improved the performance of modern anaesthesia. To date, 3 PK / PD models for fentanyl have been developed: Shafer, Scott, and Hudson.

Aim of study. The study aimed to reflect, for the analgesic component of TIVA, the accuracy of the achievement and the possibility of maintaining over time a cerebral concentration (Ces) of fentanyl, adapted to the surgical procedure (exp.), compared to the values recommended in the literature (L). The brain concentrations (Ces, ng / mL) of fentanyl, achieved in TIVA, administered manually, were retrospectively simulated through the prism of the PK / PD Shafer model.

Methods and materials. Informed, written agreement. Ethical authorization of the study. Prospective, consecutive enrollment of 15 patients (ASA I-II), beneficiaries of gynecological celioscopic interventions. Retrospective simulation (Shafer) with TIVA Trainer software of exact doses and timing of fentanyl administration in real TIVA. Descriptive statistics (mean and standard deviation) were performed with GraphPad Prism 8 software.

Results. Age: 31.2 ± 4.9 years; body weight: 75.3 ± 15.0 kg; BMI 26.8 ± 4.7 kg / m2. Duration of the intervention: 36.0 ± 11.4 min; duration of anesthesia 59.0 ± 13.4 min. Total peranesthetic consumption of propofol 620.0 ± 193.9 mg, fentanyl - 400 ± 100 mcg. Ces results obtained (Shafer) at key moments: intubation (exp: 0.2 ± 0.1 ng / mL vs L: 6.0-8.0 ng / mL), incision (exp: 0.2 ± 0.1 ng / mL vs. L: 3.0-6.0 ng / mL), base operating time (exp: 0.8 ± 0.7 ng / mL vs. L: 3.0-5.0 ng / mL), end of intervention (exp: 1.0 ± 0.9 ng / mL vs. L: 3.0-5.0 ng / mL), extubation (0.7 ± 0.7 ng / mL vs. L <2 .0 ng / mL), transfer (0.5 ± 0.6 ng / mL vs. <2.0 ng / mL).

Conclusion. (1) The pharmacodynamic interaction between fentanyl and propofol is deeply synergistic; Lower doses of fentanyl are required to balance low- and moderate-intensity surgical stress. (2) Manual administration, with an intermittent bolus of fentanyl under general intravenous anaesthesia, appears to result in lower brain concentrations of fentanyl than recommended in the literature, but no clinical signs of underdose have been observed during the anaesthetic process. (3) To ensure the guaranteed optimal brain concentrations of fentanyl depending on the intensity of the surgical stress, it is necessary to specifically monitor nociceptive trafficking (ANI index) and administer anaesthetics using TCI technology.