**Modern drug for the induction of general anesthesia with sedation in anesthesiology today - propofol**

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In modern anesthesiology promising neingalatsionnym anesthetic agent is Propofol (Propofolum), which is used for the induction and maintenance of general anesthesia for obespechengiya sedative effect in patients on mechanical ventilation (ventilation) in the conditions of intensive care, as well as during surgical and diagnostic procedures [1-5]. Propofol has been developed in the UK the company Imperial Chemical Industries, under the working title ICI 35868 as a new intravenous induction agent. Started in the early 1970s, phenol derivatives with hypnotic properties led to the development of 2,6-diisopropylphenol (2,6-bis (1-methylethyl) phenol, C12H18O). The first clinical trials were conducted in 1977 and showed the possibility of using propofol as an anesthetic agent for induction of anesthesia. In 1985 was developed as a form of propofol 1% (10 mg / ml) isotonic emulsion comprising 10% soybean oil, sodium hydroxide, purified egg phospholipids and water. Emulsified form entered the pharmaceutical market in 1986 under the trade name Diprivan (an abbreviation of the English. Diisopropyl intravenous anesthetic - diisopropyl intravenous anesthetic). Due to its unique properties, propofol is widely used in the world of anesthesiology, but in the Russian Federation its use is limited due to the higher cost compared to some other types of anesthetic agents. 2,6-diisopropylphenol - unreactive phenol derivative is of the phenol ring to which are attached two isopropyl groups. Propofol is virtually insoluble in water but soluble in fats, which explains the modern drug solvent composition: 10% soybean oil, 1.2% purified egg phospholipids (emulsifier), 2.25% glycerin and sodium hydroxide to control pH. Propofol - opaque slightly viscous liquid milky white. This is explained by the scattering of light color small (approximately 150 nm) droplets of oil which it contains. There are forms of propofol which contain sodium pyrosulfite or ethylenediaminetetraacetic acid as an antimicrobial agent to prevent bacterial growth in the formulation. An ampoule preparation contains 20 ml of a 1% solution of propofol (10 mg / ml); also available bottles 50 and 100 mL of 1% and 2% solution for infusion.

Developed a water-soluble prodrug - FOSPROPOFOL (trade name - Lusedra), approved by the FDA in 2008. Fospropofol rapidly metabolized by the action of alkaline phosphatase to propofol. Due to the high lipid solubility of propofol rapidly penetrates into the brain, which causes almost immediate onset of action (loss of consciousness occurs through the space required for the delivery of the drug in blood from the forearm to the brain). The peak effect is approximately 90 seconds. The maximum duration of use of propofol 1% (10 mg / ml) - 7 days. Propofol is a fast obscheanesteziruyuschim means, anesthetic and sedative effects is due to the positive modulation of the inhibitory neurotransmitter GABA function through ligand-controlled GABAA receptors. At the same relative stability of hemodynamic parameters of the cardiovascular system (heart rate, blood pressure) on the entire maintenance period prtyazhenii Propofol general anesthesia [1-5]. Propofol has a nonspecific effect on the level of lipid membranes of neurons of the CNS. Does not have the initial exciting action. Recovery from anesthesia is usually not accompanied by headache, postoperative nausea and vomiting. In most patients, general anesthesia occurs within 30-60 seconds. Duration of anesthesia, depending on the dose and concomitant medications, from 10 minutes to 1 hour. Patient awakens from anesthesia and quickly clear consciousness, able to open the eyes appear after 10 min.

Propofol 1% (10 mg / ml) was injected in / by injection or continuous infusion undiluted and diluted with 5% p-rum glucose or 0.9% sodium chloride-set, or 0.18% of sodium p-rum chloride and 4% p-rum glucose infusion bags made ​​of polyvinylchloride or glass bottles. Before using the contents of the package is shaken. After applying all started packing destroyed. Propofol contains no antimicrobial preservatives and therefore support the growth of microorganisms. Therefore, transfusion of Propofol in a sterile syringe or vice versa for infusion should be carried out under aseptic conditions, immediately after opening the ampoule or vial opening. Introduction emulsion should start immediately. Propofol infusion and equipment should be kept in aseptic conditions throughout the infusion period. Other drugs and fluids in addition to propofol must be administered as close as possible to the injection point. For propofol should not be used for infusion sets with microbiological filters. Contents of an ampoule or a vial of Propofol-Lipuro, as well as the contents of the syringe infusion / injection is intended for single use only and can only be used for one patient. Emulsion which remained after the introduction of the package is not intended for re-use. With continuous propofol infusion to control the rate of administration should be used dosing burette, drip, syringe pumps or volumetric infusion pumps. In accordance with its general recommendation for all types of fat emulsions for parenteral administration, the duration of continuous propofol infusion of one infusion system should not exceed 12 hours. Not later than 12 h infusion line and capacity for Propofol should be removed or replaced by a new system. Propofol that remained in the system after it is turned off or replacement, not intended for reuse.

Introduction diluted Propofol 1% (10 mg / ml) was also required with the use of burettes, droppers, syringe pumps or volumetric infusion pumps for controlling the infusion rate, as well as to prevent random uncontrolled infusion of large volumes of undiluted Propofol-Lipuro. Maximum dilution should not exceed one part to four parts Propofol 5% solution of glucose or 0.9% sodium chloride-ra, or 0.18% solution of sodium chloride and 4% solution of glucose (minimum concentration for propofol - 2 mg / ml). The mixture should be prepared immediately before use in aseptic conditions and used within 6 hours from the time of manufacture. Propofol is not recommended to mix with other p-rami for injection or infusion. Simultaneous administration of propofol and 5% solution of glucose or 0.9% sodium chloride-ra is possible with U-shaped compound near the injection site. To reduce the severity of the pain at the time of start of the injection is recommended to use a mixture of propofol 1% lidocaine for injection without preservatives (20 parts Propofol 1% (10 mg / ml) and one part of 1% lidocaine for injection). Before the introduction of muscle relaxants on the basis of atracurium and mivakuriya infusion system after administration of propofol must be pre-rinse.

Propofol should be used only in a hospital or a specially equipped offices day hospital by trained specialists, as well as in the ICU. During the infusion need to constantly monitor the function of blood circulation and respiration (eg ECG, pulse oximetry) and be available to special kits to ensure a patent airway, artificial ventilation and other resuscitation equipment. Propofol administered for diagnostic and surgical procedures should be two different specialist. Usually propofol infusion is accompanied by the introduction of additional analgesics. Propofol-Lipuro introduced in /. Dosing of p-ra is determined individually depending on the patient's response. In order to induce anesthesia Propofol recommended titrated (bolus or infusion 20-40 mg propofol every 10 seconds for an adult patient in a satisfactory state) depending upon the patient's response to the onset of clinical signs of the onset of anesthesia. For the majority of adult patients under the age of 55 years required dose of propofol - 1.5-2.5 mg / kg body weight. For patients under this age, as well as patients with class III and IV (ASA - American Association of Anesthesiologists), in particular with impaired cardiac function, a necessary dose for induction of anesthesia will be lower, and the total dose of propofol may be reduced to a minimum - 1 mg / kg body weight. It should also use smaller introduction rate (about 2 ml, which corresponds to 20 mg of propofol per 10 seconds).

For maintenance of anesthesia can use a constant propofol infusion or repeated bolus injection. The technique repeated bolus injections may be administered additional doses of 25-50 mg propofol (propofol 2.5-5 ml) in accordance with clinical requirements. While maintaining anesthesia by continued infusion dosing regimen is usually determined within 4-12 mg propofol per 1 kg of body weight per hour. While maintaining general anesthesia required level of analgesia is generally achieved by continuous infusion dosing regimen of 9 to 15 mg of propofol per 1 kg of body weight per hour. For children up to 3 years required dose may be increased within the recommended dosing regimen, as compared with the doses used for older pediatric patients. Dosing volume should be calculated individually, with particular attention should be paid to the need for adequate anesthesia. In clinical studies, maintenance of anesthesia in children under the age of 3 years duration of application is 20 minutes, the maximum duration of administration - 75 min. Thus, it is recommended not to exceed the maximum time of application of the drug 60 minutes, except where indicated in a longer reception, such as when the instantaneous hyperpyrexia excepting contact with volatile substances. Propofol should not be used for induction and maintenance of anesthesia in infants under the age of 1 month. In order to provide sedation patients who are ventilated intubation recommended propofol administered by continuous infusion. The infusion rate is determined in accordance with the required depth of sedation. Generally, to achieve the required level of sedation using propofol dosing of 0.3-4 mg per 1 kg of body weight per hour. It is not recommended to use propofol for sedation of ICU patients under the age of 16 years.

Propofol with the help of "diprifuzor TSI" is not recommended for sedation of patients in intensive care. For sedation during surgical or diagnostic procedures and dosing infusion rate depend on individual clinical response. In most cases it is necessary to start sedation 0.5-1 mg of propofol per 1 kg of body weight for 1-5 min. Maintaining sedation is achieved by titrating propofol infusion to achieve a desired level of sedation. For the majority of patients required dose - 1.5-4.5 mg / kg / h. If necessary, the rapid increase in the depth of anesthesia possible additional bolus of propofol 10-20 mg (1-2 ml Propofol). Patients Class III and IV on the scale ASA dose can be reduced. For elderly patients, patients with severe general condition, patients with category III and IV (ASA), and patients with hypovolemia, the dose may be reduced further, depending on the severity of the patient and the technique used anesthesia. For induction of anesthesia Propofol slowly titrated according to the patient's response to the onset of clinical signs of the beginning of anesthesia. The dose is determined in accordance with age and / or body weight of the patient. For most patients over the age of 8 years for the induction of anesthesia needs about 2.5 mg of propofol per 1 kg of body weight. For children under the age of 8 years may need to use higher doses (2.5-4 mg propofol per 1 kg of body weight). Due to lack of clinical experience in patients at risk (category III and IV (ASA)) is recommended to use a lower dose.

Propofol is absolutely contraindicated in case of hypersensitivity to the drug, children under 1 month of age and adolescents up to 16 years for the purpose of sedation effekta. Propofol is relatively contraindicated in epilepsy, hypovolemia, dyslipidemia, anemia, decompensated with severe diseases of the cardiovascular system, respiratory system, kidneys and liver, the elderly and immunocompromised patients, as well as during pregnancy and lactation. Propofol crosses the placental barrier and can have a dampening effect on the fetus (Category effects on the fetus by FDA- B). Data from studies conducted in nursing mothers indicate that a small amount of propofol passes into breast milk. It is believed that it is not harmful to the baby if the mother starts breastfeeding within a few hours after the administration of propofol. Among the side effects Propofol marked decrease in blood pressure, bradycardia (sometimes severe), short-term cessation of breathing, shortness of breath, seizures and rarely epistotonus, pulmonary edema; in a period of awakening - headache, nausea, vomiting, postoperative fever (rare), pain at the injection site, phlebitis and venous thrombosis (depending on the duration of application).

Propofol is compatible with preparations for spinal and epidural anesthesia, with the drugs used in sedation with muscle relaxants and analgesics. Propofol can be used simultaneously with other drugs for anesthesia (premedication, inhalation anesthetics, analgesics, muscle relaxants, local anesthetics). Information about serious interactions with these drugs have been reported to date. Some of these drugs acting on the central nervous system, can also lead to the inhibition of the function of the cardiovascular and respiratory systems, which ultimately enhances the action when used in conjunction with propofol. It is shown that the simultaneous use of benzodiazepine drugs parasympatholytics, means to lengthen the inhalation anesthetic effect and reduce the frequency of breathing. With the additional administration of opioids in the preparation of the patient for surgery increases the incidence of apnea and increased its продолжительность.Применение suxamethonium and neostigmine increase the risk of bradycardia and cardiac arrest. Note that simultaneously with the reception of agents for sedation with propofol, inhalation anesthetics and anesthetic effects can amplify and cause side reactions in the cardiovascular system. Combined use of depressants, acting on the central nervous system, such as alcohol, general anesthetics, narcotic analgesics, increases their sedative effect. A temporary increase in the level of propofol in the blood and a corresponding increase in the frequency of apnea may be caused by the intake of fentanyl. Simultaneous use of fat emulsions, such as propofol, cyclosporin and may cause leukoencephalopathy. For additional injection during regional anesthesia can use smaller amounts of Propofol dosing. Propofol should not be confused with other p-rami for injection or infusion, with the exception of 5% solution of glucose, 0.9% solution of sodium chloride, or 0.18% solution of sodium chloride and 4% solution of glucose and 1% solution of lidocaine for injection.

In case of overdose, marked depression of the cardiovascular and respiratory systems. For the treatment of this complication on a background of oxygen used ventilator, infusion of plasma substitutes and administration of vasopressor drugs. In cases where there is a risk of side effects associated with activation of the vagus nerve, it is advisable before the induction of anesthesia in / introduction anticholinergic. Should not be used in obstetric practice, because Propofol crosses the placental barrier and can cause neonatal depression (possibly use in the I trimester during operations to abortion). Storage Conditions Propofol at the temperature up to 25 ° C, do not freeze. It is not recommended to remove the packing from the carton. It is recommended to shake the container before use. Any number of emulsions, which remained in the pack after use, not intended for reuse. If, after shaking the package can be identified two layers of fluid, the drug should not be used [1-5].

Thus, the current low toxicity anesthetic drug with sedative action of propofol in the arsenal Anaesthetist extends the effective and safe general anesthesia for surgical and diagnostic procedures for patients of different ages. Currently available under the trade names: DIPROFOL (emulsion in'ektsy 20 ml and 50 ml ampoules and vials - PAT "Pharmak", Kiev, Ukraine), propofol-NEW (emulsion in'ektsy of 10 ml and 100 ml in bottles - TOV firm "Novofarm-Biosynthesis", Ukraine), AKVAFOL (emulsion for infusion in 12 ml, 20 ml and 50 ml vials - DAEVON Farmasyutіkal Co. Ltd, Korea), Diprivan (emulsion for infusion of 50 ml in vials and 20 ml ampoules - Corden Pharma SpA / AstraZeneca SK Lіmіted, Іtalіya-UK, England), propofol Fresenius (emulsion / in the 50 ml vials and 20 ml ampoules - Frezenіus Kabі Avstrіya GmbH, Austria)-Lipuro propofol 1% (emulsion for infusion of 20 ml ampoules at 50 ml and 100 ml vials - B. Braun Melsungen AG, Germany), PROFOL (emulsion for infusion of 10 ml, 20 ml, 50 ml and 100 ml vials - Klerіs Layfsaynsіz Lіmіted, India) [1].

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