Propofol infusion syndrome – between myth, reality and threat

In this issue of *Romanian Journal of Anesthesia and Intensive Care*, Gurman presents a review on the propofol infusion related syndrome (PRIS) [1]. The topic of PRIS is old and new in the same time, as it was approached in the literature. A number of studies focused mainly on description, clinical picture and incidence were published in the '90s, when the name and definition of this entity was launched by Bray in 1998 [2].

After a few years “break”, a coming back of this topic in the literature after 2000 was registered when more cases, mechanisms, physiopathology, prophylaxis and therapeutic options were discussed. The entity itself is questioned in the light of recent developments in the field [3].

The PRIS is, thus, according to some opinions but questioned by others [3], a clinical entity with a well defined clinical picture. Its incidence is reported between 1.1-31% in different studies [4-6]. It is accompanied by an increased mortality, reported in different studies between 18% and 30% [4, 6].

The difference range in mortality figures comes from the number of criteria used for diagnosis. If more criteria are used for diagnosis, the incidence is small, while by using only one criterion, for example lactic acidosis, or permissive criteria, the incidence is unusually high [6-8]. Cravens et al. used a negative excess base of –2 mEq/L or less as case definition in patients receiving propofol and undergoing radiofrequency ablation, which led to an incidence of 24% [7], while Iyer et al. reported a proportion of 35% of patients developing non-life-threatening features of PRIS on an 11-years statistics among patients receiving propofol for refractory status epilepticus [9]. It is still a matter of discussion which and how many criteria should be used to define this syndrome and also whether there are differences in incidence and mortality by the patient’s condition that were taken in consideration.

Mechanisms include an imbalance between energy demand and offer at cellular level produced by uncoupling oxidative phosphorylation and the energy production in the mithocondria as an effect of propofol, leading to muscle necrosis, lactic acidosis, rhabdomyolysis and cardiac contractility depression. Increased plasma level of free fatty acids (FFA), impaired FFA utilization, inflammatory response suppression with an increased risk of sepsis and the effects of increased sympathetic stimulation have all been involved in PRIS physiopathology [1, 10, 11]. Genetic predisposition should also be considered in future studies.

In the light of these facts, Gurman’s review [1] is welcome since it brings in attention a clinical entity that may escape to one’s mind, shadowed by the patients’ clinical picture and severe condition. Moreover, last developments in this area must be known and introduced in the clinical practice.

The clinical picture consists in lactic acidosis, rhabdomyolysis, cardiac arrhythmias, hypotension, hyperkalemia, hyperlipemia and renal failure, which are very well described in the review as well as in the literature [8, 9]. Risk factors for developing PRIS include age, sepsis, poor oxygen delivery, severe cerebral injury and high propofol dosage [1, 10].

Predisposing factors are cumulative dose of propofol, severe critical illness of central nervous system (CNS) or with respiratory origin, infusion of catecholamines, infusion of corticosteroids, inadequate delivery of carbohydrates, and subclinical mitochondrial disease [12].

Treatment options, although not specific, include immediate stop of infusion, vasopressors or glucagon and fluids to correct hypotension, carbohydrate administration to help lipid metabolism [1, 13, 14]. Hemodialysis, hemofiltration and extracorporeal membrane oxygenation have all been tried with some success [12, 15].

The review is focused on the prophylaxis of PRIS and this is easy understandable taking into consideration that treatment is neither specific nor highly efficient. Prophylaxis of PRIS will thus include minimizing propofol dose and duration of infusion in high risk patients, avoiding lipid overload by assessing other
sources of fat calories that are administered to the patient (e.g., parenteral or enteral nutrition), assuring adequate delivery of carbohydrates and by monitoring serum triglycerides in any patient receiving propofol in doses > 4 mg/kg/hour or for more than 48 hours [1, 10].

The use of propofol with an increased concentration of lipids (2%) will lead to a decreased lipid load [16]. Meanwhile one must not forget that propofol lipid load must be taken into consideration when assessing lipid balance of critical patient.

Other strategies not directly related to PRIS, such as sedative rotation, adding short acting opioids (e.g. remifentanil) or alpha-2 agonists (e.g. clonidine and dexmedetomidine) may lead to a decreased dose and/ or interval of propofol use thus avoiding risk factors for developing PRIS.

The review is accompanied by an interesting case presentation that gives the author the possibility to discuss the clinical picture and treatment of PRIS.

What is also interesting is the debate on the definition of PRIS as a well-defined entity or just as a condition associated with a clinical context that may mimic the clinical picture of PRIS. Nevertheless, one must keep in mind this syndrome and try to avoid the risk and predisposing factors when using propofol infusion for patients’ sedation in the ICU. Prophylaxis strategies for avoiding PRIS should also be included in patient management in order to reduce its morbidity and mortality.

In summary, Gurman’s review brings once more to our attention an important clinical condition related to long-term propofol infusion. Gurman extended the reviews published on the topic, by adding the most recent findings and a useful clinical debate on PRIS as a distinct clinical entity. The review also brings into the light the diagnosis and prophylaxis of PRIS, as a way to improve the outcome of the critical patient in ICU.

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