Short Review

Regional Anesthesia in Surgery and Intensive Care: Are We Doing Enough?

The last decades saw a growing interest in Regional Anesthesia (RA) techniques in both surgical and Intensive Care Unit (ICU) settings, as testified by the increasing number of meta-analyses on the matter [1]. It is relatively easy to find and demonstrate the various advantages of these anesthetia and analgesia techniques for soft outcomes, such as reduced post-surgical consumption of analgesic drugs [2], respiratory complications [3], infections and duration of recovery in surgical department or ICU [3,4]. Developing interest in long-term outcomes (months to year) extended to influence of RA in morbidity and mortality, persistent pain and cancer prognosis. Various pooled analyses of controlled randomized studies, showed an unequivocal although weak signal toward a statistically significant improvement on post-operative survival [5-8]; moreover, a recent web-based consensus conference identified RA as a possible mortality-reducing intervention according to the results of four published meta-analyses, even if it still defines the effect on postoperative mortality as a controversial topic [9]. Such a statistically significant reduction of mortality was also found in randomized controlled trials published in the last 15 years, regarding both anesthesia [10] and intensive care [11]; unfortunately, statistical methodological issues that prevent generalization of their findings plague the last two papers. In 2017 Bugada and coworkers published a large review of perioperative outcome benefits of RA, underlining the importance of continuous RA techniques in controlling surgical stress or the inflammatory response to surgery, through direct anti-inflammatory effects and the effective block of neural afferents and sympathetic activation [12]. Inflammation is considered a major factor to develop pain, hyperalgesia and persistent post-surgical pain [13]. Local anesthetics as sodium channel blocking drugs, with the interruption of nociceptive transmission decrease neurogenic inflammation, also have intrinsic anti-inflammatory properties; one potential mechanism is the modulation of G-protein-coupled receptor signaling, another one is an epigenetic mechanism, namely interfering with DNA methylation [14]. The effects of continuous RA are the best known decrease in opioid doses and better pain control, other advantages include the maintenance of intraoperative normothermia, earlier awakening from general anesthesia thus reducing need of inhalation agent, maintenance of tissue perfusion and oxygenation, reduced cardiac stress, earlier and less painful mobilization, decreased insulin resistance, and lesser respiratory dysfunction after surgery. These benefits last for 24-48 hours after surgery [15]. Long term influences of RA are still controversial, and there are few available studies up to date. Most recently there is a growing interest on the impact of RA in cancer progression and recurrence. Potential mechanisms involved are attenuation of the surgical stress, reduced immune impairment and better host defense; better analgesia and associated less opioid administration improve immune function, as does a general anesthetic dose reduction, even if a direct effect of local anesthetics is not definitely proven in human trials [16].

Capdevilla and coworkers report pain and its treatment as a key issue for ICU patients. Ensuring optimal pain relief can improve rehabilitation, outcomes and decrease complication rate, and could be best achieved with RA. Unfortunately, clinicians probably afflicted by a generic fear of adverse effects from local anesthetics frequently neglect this option [17]. Regional anesthesia has proven useful at least in some peculiar ICU conditions such as acute necrotizing pancreatitis. Two studies have shown a statistically significant improvement in peripancreatic perfusion and pain control, and a non-significant reduction in ICU length of stay [4,18]. Another setting in which RA proved useful is reducing costs frequently neglect this option [17]. Regional anesthesia has proven useful at least in some peculiar ICU conditions such as acute necrotizing pancreatitis. Two studies have shown a statistically significant improvement in peripancreatic perfusion and pain control, and a non-significant reduction in ICU length of stay [4,18]. Another setting in which RA proved useful is reducing costs frequently neglect this option [17].

In recent literature, RA was shown to be extremely safe. The Italian Registry of Complications associated with Regional Anesthesia [21] is a prospective web-based multicenter population-based registry involving teaching and non-teaching Italian hospitals, with the aim to detect RA complications, register associated data about technique, equipment, medications and patient, as well as detect RA side effects outcomes in a long-term (six months) follow-up. The
study enrolled patients undergoing different types of procedures, such as adult major and minor surgery, pediatric surgery, obstetric anesthesia, and chronic pain management. Each center was asked to fill out a universal form including the total number of interventions and the number of Central Neuraxial Blocks (CNBs), Peripheral (PNBs) and Continuous Peripheral Nerve Blocks (CPNBs) performed during the study period. In the form following every complication, each center collected data about the patient (age, weight, ASA), the type of surgical techniques, the thromboprophylaxis, the performed anesthesia (type of needle, use of ultrasound or nerve stimulation, type and dose on drugs), the performer experience and the number of attempts. They registered a total of 117,182 procedures; 63,692 were RAs: only five cases of major complications (death, hemodynamic/respiratory failures, hemorrhagic or infectious complications, permanent neurologic deficits; incidence of 0.07/1000) and 24 cases of minor complications (post dural puncture headache, local anesthetic systemic toxicity, transient neurologic symptoms, minor hemodynamic involvement; incidence of 0.38/1000) were reported. With a total of 34,147 CNBs (4,954 epidurals/CSEs blocks and 29,193 subarachnoid blocks) and 29,545 PNBs/CPNBs, they registered two complications related to epidural/CSEs: one epidural abscess and one case of post dural puncture headache; 12 complications related to sub-arachnoid blocks: two patients with major side effects, three patients with lower limb dysesthesia/paresthesia without permanent neurological deficit and seven patients with local anesthetic systemic toxicity; 15 complications related to peripheral nerve blocks: 10 cases of local anesthetic systemic toxicity (10 patients presented minor symptoms, seven patients presented major signs of cardiovascular and neurologic toxicity), two cases of major hemodynamic and respiratory events and three cases were registered as or pro-longed sensory-motor block [21].

Demonstration of a statistically significant reduction (p<0.05, power=0.8) in mortality between RA and general anesthesia from 3% to 2% would require a RCT enrolling more than 8000 patients. That would deprive 4000 control patients of certain benefits of RA such as improved quality of analgesia and reduction of systemic opioid consumption [22], so we should consider investigating rare outcomes with methodologies based on large prospective registries (such as cited RICALOR), or large database studies. Despite not being “perfect” from a methodological perspective, they still provide reliable and acceptable results, as well as important insights on clinical practice which would certainly benefit the patients.

References